

Home Mechanical Ventilation

A CANADIAN THORACIC SOCIETY CLINICAL PRACTICE GUIDELINE

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INTRODUCTION

More than 50 years ago individuals with polio courageously led the challenge of maintaining mechanical ventilation outside of institutions and quietly initiated a more independent, patient-centered and collaborative approach to respiratory health care. Today, the drivers for home mechanical ventilation (HMV) are different. The rising costs of hospital care, the advent of commercially available noninvasive masks and positive pressure ventilators, have fuelled greater demand for HMV. However, the desire of individuals to maintain a quality of life (QoL) in their homes remains the prevailing impetus. The present HMV clinical practice guideline is intended to be a resource for physicians, healthcare providers, policymakers and individuals at risk for or currently using ventilatory support in the home. The objective is to identify and support ventilated patients who are presently at home, as well as those transitioning to home-based care, where QoL is the greatest and costs are minimized. Developed by The Canadian Thoracic Society (CTS), these guidelines intend to provide the most up-to-date information and evidence-based recommendations to enable practitioners to manage the provision of preventive airway management and home ventilation.

These guidelines are composed of disease-specific sections in addition to overriding subjects such as ethical considerations, transition to home and airway clearance. In the discipline of respiratory medicine there are extremely few prospective or randomized trials. As a result, most recommendations are based on retrospective or descriptive studies and, to a great extent, on consensus of the CTS HMV committee.

Recommendations strive to achieve a balance between an exceptional standard of care illustrated in the literature and the reality of healthcare in Canada where geographical health care and economic barriers may require compromise to ensure the availability of the best care possible. This approach may also allow greater applicability to jurisdictions where, for example, polysomnography may be unavailable or so difficult to obtain as to present unacceptable barriers to appropriate, timely introduction of noninvasive ventilation (NIV). Nevertheless, some subjects considered to be important by the committee are not addressed in the literature. Some jurisdictions have access to provincial ventilator pools, in which equipment and knowledgeable health care professionals are available at relatively minimal cost, to ensure the success of HMV. The literature does not address questions regarding government-funded equipment pools. On important issues for which literature is lacking, but strong expert opinion was available, recommendations were made by the HMV Guideline Committee.

No article in the literature, to our knowledge, addressed the appropriate addition of a back-up ventilation system aside from patients fully ventilated through a tracheostomy; accordingly, it remains uncertain as to precisely when an individual on NIV should have an additional ventilator or when alarms should be required. The general recognition that NIV is not designed for full 24h life support has resulted in this uncertainty. However, patients are, in fact, using 24h NIV, without which they are at risk for acute respiratory failure. This area of risk management will need attention in future investigation. Throughout the recommendations; it is assumed (aside from that clearly stated in the section on Transition to Home) that appropriate training will be provided to patients and caregivers.

These guidelines do not address negative-pressure body ventilators or abdominal ventilators because positive-pressure ventilators have, with few exceptions, completely replaced negative-pressure ventilators in the home. Although potentially of significant clinical value in the follow-up of patients on NIV, no recommendations are made on the use of digital information and down-

loads from bilevel devices. Additional research is desperately needed to address many of these critical questions.

The present guideline focused on HMV in the adult population. There are some important differences in HMV in the pediatric population and also in the transition phase into adult programs. The committee recognized these areas and hope that future guidelines will address them.

Preventive airway management and HMV is a complex, interdisciplinary component of respiratory care and clinical practice. This component requires a continuum of chronic disease management involving many layers of expertise from government and professional education to home care services, acute and chronic health facilities and independent living facilities. The goal of HMV – and, thereby the goal of these guidelines – is to ensure the continued health of patients at risk for and currently using ventilatory support in their homes where QoL is greater and cost to the healthcare system is the lowest.

The present document is the source document of the guideline. The link for the executive summary published in the July/August 2011 edition of the Canadian Respiratory Journal is available on line at <http://www.respiratoryguidelines.ca/guideline/home-ventilation>.

SOURCE DOCUMENT

Questions

What evidence best informs the practice of HMV among patients who are at risk for or require ventilatory assistance? For all patients, there are special issues in the approaches to airway clearance or in making the transition to home that determine the suitability of HMV. Outcomes of interest include survival, pulmonary function, sleep parameters, cognition, patient and caregiver QoL and ethical considerations.

Objective

The objective of the present clinical practice guideline is to provide guidance to patients, caregivers, and health care teams on the role of HMV for a variety of patient populations.

Target Population

The current clinical practice guideline applies to all adult individuals who are at risk for or are using HMV. Individuals with amyotrophic lateral sclerosis (ALS), central hypoventilation syndrome (CHS), chronic obstructive pulmonary disease (COPD), kyphoscoliosis, obesity hypoventilation syndrome (OHS), spinal cord injury (SCI), Duchenne muscular dystrophy (DMD), muscular dystrophies (MDs) other than DMD, myopathies and myotonic dystrophy (Steinert's Muscular Dystrophy [SMD]) are of special interest and are considered individually in the present clinical practice guideline.

Target Users

The present clinical practice guideline is intended for use by the health care teams that care for individuals who are at risk for or require ventilatory assistance. Respiriologists, physiatrists, neurologists, family practitioners, nurses, respiratory therapists, physiotherapists and other health care professionals can use these guidelines to help inform their clinical practice with regard to HMV. This guideline is also intended for use by ventilator-assisted individuals (VAIs) and their caregivers to help them make informed decisions on HMV.

Methodology

Guideline Development

This clinical practice guideline was developed according to the convention of the 23-item AGREE II instrument - the current gold standard in the appraisal of practice guidelines (1). The HMV Expert Committee, comprising respirologists, a physiatrist and a respiratory therapist with content expertise in each of the topic areas, a research coordinator, and a methodologist, conducted a systematic review of the literature that was current to June 2010. Before completion, the guideline was distributed to content experts in Canada and other countries with similar programs for the opportunity to provide feedback concerning the collection and interpretation of the evidence, as well as the development and content of the recommendations. Key stakeholders, from the Ministry of Health, VAls, interested groups including respiratory therapists, ALS, MD, and spinal cord networks were invited to review and provide input on the document. Final consensus on the recommendations from the CTS HMV Committee was reached through a formal voting process that was anonymized. The literature will be periodically reviewed (biannually) and the guideline will be updated as new or compelling evidence is identified.

Literature Search Strategy

The literature search strategy was designed to address questions related to broad issues with HMV, such as approaches to airway clearance, making the transition to home, and also to inform each sub-section of the home ventilation guideline with specific patient populations.

The literature was searched using MEDLINE (OVID: 1980 through June 2010), Embase OVID: (1980 through June 2010), HealthStar (1980 through June 2010) the Cochrane Library (OVID; Issue 1, 2009), the Canadian Medical Association InfoBase, and the National Guideline Clearinghouse. Reference lists of related papers and recent review articles were also scanned for additional citations.

The literature search of the electronic databases combined the following MeSH heading terms and text search terms to identify the body of published evidence on HMV related to the following: Disease Related Conditions: Lung diseases/ or Lung Diseases, Obstructive/ or Chronic Obstructive Pulmonary Disease/ or COPD.mp. or Neuromuscular Diseases/ or Respiratory Insufficiency/ or respiratory insufficiency.mp. or respiratory failure/ or respiratory failure.mp. or breathing failure.mp. or breathing difficult*.mp. or respiratory muscle weakness.mp. or ("pulmonary function" and failure).mp. or Respiration Disorders/ or Respiration/ or Hypercapnia/ or pulmonary disease.mp. or amyotrophic lateral sclerosis.mp. or Amyotrophic Lateral Sclerosis/ or ALS.mp. or Obesity Hypoventilation Syndrome/ or OHS.mp. or Hypoventilation/ or hypoventilation.mp. or spinal cord injury.mp. or spinal cord injury/ or Spinal Cord Injuries/ or SCI.mp. or muscular dystrophy.mp. or Muscular Dystrophies/ or Kyphoscoliosis/ or Kyphoscoliosis.mp. or Postpoliomyelitis Syndrome.mp. or post-polio syndrome.mp. or post polio syndrome.mp. or polio syndrome.mp. or post-polio syndrome.mp. or post poliomyelitis.mp. or postpolio syndrome.mp. or (postpolio and syndrome).mp. or PPS.mp. or neuromuscular disease/ AND Treatment Related Terms:artificial ventilation/ or ventilator/ or ventilated patient/ or Oxygen therapy/ or assisted ventilation/ or Ventilators, Mechanical/ or Ventilation/ or Ventilators, Negative Pressure/ or ventilators negative pressure.mp. or ventil\$.ti. or mechanical ventilation.mp. or Positive-Pressure Respiration, Intrinsic/ or Intermittent Positive Pressure Ventilation/ or Pulmonary Ventilation/ or positive-pressure respiration.mp. or Positive-Pressure Respiration/ or NIV.mp. or NIPPV.mp. or VAl.mp. or Respiration, Artificial/ AND Health Care Setting Terms:Family centered care/ or home care/ or Home Care Services/ or home.ti. or home ventilat\$.mp. or (home.mp. and Long-Term Care/) or Home care.mp. or homecare.mp.

orH MV.mp. or home ventil*.mp. or (assisted living and ventilator).mp. or ventilator assisted living.mp. or (home ventil* and Mechanical).mp. or (home ventil* and machine*).mp. or (oxygen equipment and home).mp. or home ventilation program*.mp. or home mechanical ventilation.ti.
ANDLimits: Humans, English, All Adult: 19+ years.

Study Selection Criteria

Articles were selected for inclusion in the systematic review of the evidence if they reported data on the role of HMV among adult individuals who require ventilatory assistance. More specifically, articles which met this criterion must have addressed the question: Does HMV lead to better patient, caregiver, or system outcomes more so than other currently available ventilation and management options (E.g. ventilation in a chronic care facility (hospital etc.), or no mechanical ventilation)? Studies were required to report data on at least one of the following outcomes of interest: survival, pulmonary function, sleep parameters, airway clearance techniques, cognition, VAs and caregiver QoL, making the transition to home or ethical considerations.

Given the nature of the topic, it was accepted amongst the CTS HMV Committee members that the strength of the evidence from the published literature varied considerably, and in many cases would not be sufficient to inform recommendations on the topic. In the event of modest data, it was agreed that expert consensus would be used to form the recommendations. As such, only the highest levels of evidence considered sufficient to inform recommendations were chosen for each subsection of the guideline. In descending order of preference, minimum levels of evidence were gathered to inform the clinical questions. Sources included were clinical practice guidelines, systematic reviews, meta-analyses, randomized controlled trials, non-randomized comparative studies, prospective single-cohort studies, retrospective single-cohort studies, and case studies.

Articles were excluded from the systematic review of the evidence if they were reported in a language other than English.

Critical Appraisal

The strengths and weaknesses of the evidence were carefully considered in the generation of the recommendations. Although the majority of the evidence on this topic area is modest, the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology was used to inform the generation of recommendations and critically appraise the strength of the evidence (2). **Where no evidence was available the committee made a recommendation when a consensus was reached and then the recommendation was identified as such (Table 1).**

Organization of results

This guideline is divided into separate sub-sections by patient population. Each section describes the literature findings. Key recommendations and the supporting level of evidence were developed for each section and where possible, barriers to implementation of recommendations were identified.

Table 1 - Grading Recommendations

Grade of Recommendation/ Description	Benefit vs Risk and Burdens	Methodological Quality of Supporting Evidence	Implications
1A/strong recommendation, high-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	RCTs without important limitations or overwhelming evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1B/strong recommendation, moderate quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1C/strong recommendation, low-quality or very low-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Observational studies or case series	Strong recommendation but may change when higher quality evidence becomes available
2A/weak recommendation, high-quality evidence	Benefits closely balanced with risks and burden	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation best action may differ depending on circumstances or patients' or social values
2B/weak recommendation, moderate-quality evidence	Benefits closely balanced with risks and burden	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or social values
2C/weak recommendation, low-quality or very low-quality Evidence	Uncertainty in the estimates of benefits, risks, and burden; benefits, risk, and burden may be closely balanced	Observational studies or case series	Very weak recommendations; other alternatives may be

From reference 2. RCTs Randomized controlled trials

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2. Guyatt G, Gutterman D, Baumann M, Addrizzo-Harris D, Hylek E, Phillips B, Raskob G, Lewis S, Schunemann H. Grading Strength of recommendations and quality of evidence in clinical guidelines: report from an American College of Chest Physicians task force. *Chest* 2006;129:178-81.

SECTION I.

Airway Clearance in at-risk and Ventilator Assisted Individuals

Introduction

Ventilatory support is capable of reliably providing volume and pressure for adequate ventilation, but this can only be assured if the airways remain clear of mucus and debris. Airways encumbered by secretions will result in reduced ventilation and contribute to low ventilation/perfusion states which can in turn lead to resorption atelectasis and shunt. Retained secretions increase the risk for pneumonia and respiratory failure. During long-term invasive tracheostomy ventilation, airway clearance, usually by suctioning, is routine. However, during NIV, there is a tendency to neglect the need for airway clearance techniques and focus on ventilation alone. In neuromuscular disease (NMD) patients, recognizing this principle is equally important – even before the need for ventilatory support - and is critical in addressing the issues of worsening respiratory mechanics and the inability to cough effectively.

The approach to airway clearance can be divided into three patient phases; 1) at-risk individuals who do not yet require mechanical ventilation, 2) those currently using NIV and 3) those requiring invasive tracheostomy ventilation (TV).

Clinical monitoring and interventions for airway clearance in patients who are at risk for respiratory failure must precede the actual onset of ventilatory failure. Primary care physicians, physical medicine physicians, neurologists, and pediatricians must also be cognizant of this need for preventative strategies as respirologists and critical care physicians may only become involved once an acute crisis has developed. In contrast to the at risk individuals, long-term ventilation of some patients is unpredictable; e.g. ARDS, polytrauma, and acute neurologic events. Even COPD, although a significant risk, is unpredictable and relatively unresponsive to preventive strategies. However, in more predictable conditions, including NMD such as ALS, DMD, myopathies and restrictive thoracic diseases (kyphoscoliosis, post-polio syndrome), individuals benefit from preventive strategies to ensure regular airway clearance. Unfortunately, each of these techniques suffers from the lack of well-designed prospective trials. As such, recommendations were informed by observational studies and professional consensus.

Normal Airway Clearance Mechanisms

Cough is not normally required in order to clear the airway of the usual daily mucus production (1). If secretion volumes overwhelm the normal mechanisms, as seen in acute bronchitis, or if the mucociliary blanket is dysfunctional, as in emphysema or ciliary dyskinesia, then cough is necessary to maintain airway clearance. In obstructive airways disease, expiratory muscle function is not usually the limiting factor but instead, intrinsic airway compression and airflow limitation limit peak expiratory airflow velocities. These factors limit the effectiveness of cough and predispose to secretion retention and lower respiratory tract infection. Patients with NMDs are predominantly considered at risk for inspiratory muscle weakness and failure. However, they are also characterized by “expiratory muscle failure” and are generally free of intrinsic airways disease. Although at risk, therapies directed at obstructive airways diseases may have minimal effect on the overall effectiveness of cough or the incidence of exacerbations. In contrast, therapies directed at airway clearance in NMD may be highly effective in increasing expired airflows and volumes.

In order to cough effectively, a volume of 60 to 90% TLC is inspired, the glottis is closed tightly and a period of ‘iso-volumetric’ contraction of the expiratory muscles ensues, followed by the rapid release of the glottis at high intra-thoracic pressures (2). This produces a high velocity

expiratory flow which clears mucus from the central airways through shear forces (3). These mechanisms are impaired in patients with NMD. Inspiratory muscle weakness prevents achievement of adequate lung volumes, glottic impairment prevents adequate upper airway closure with expulsive opening, and expiratory muscle weakness prevents the necessary generation of high intra-thoracic pressures. Noninvasive airway clearance strategies are directed at improving cough effectiveness through transient increases in lung volumes (LVR or “breath-stacking”), addition of manual abdominal pressure to increase expiratory forces (manually assisted cough) and when necessary, mechanical generation of positive and negative airway pressures (mechanical insufflation-exsufflation) to accelerate expiratory flows.

Airway Clearance in Patients At-Risk or Using Noninvasive Ventilation

The approach to both patients at risk and to those already using NIV is essentially the same, although those using NIV with lesser respiratory reserve may require brief removal of NIV to attend to airway clearance. As respiratory muscle weakness progresses and/or bulbar dysfunction develops, cough effectiveness declines (1,2,4). Furthermore, already weakened muscles become more impaired during upper respiratory tract infections (5). In 10 patients with NMD during 13 episodes of upper respiratory tract infection, DiMarco and colleagues observed that Vital Capacity (VC), maximum inspiratory pressure, and peak expiratory pressure fell an average of 13%, 25%, and 29%, respectively, within the first 24–36 hours of illness (6). In patients with ALS, Servera and colleagues determined that a combination of bulbar function (Norris Score) (7), and PCF values during clinical stability predicted an inability to adequately clear secretions during chest infection (8). Techniques directed at maintaining airway clearance, precisely when spontaneous abilities are reduced, are critical to the prevention of morbidity and mortality in this population.

Although a minimal PCF of 160 L/min has been demonstrated to be required to prevent re-intubation (9), American Thoracic Society consensus guidelines indicate that PCFs of less than 270 L/min in DMD patients identify those who are likely to be at risk and benefit from preventive airway clearance techniques (10,11). Such an approach may be applicable to other NMD patients, with the caveat that these values are not corrected for age, sex or height. Failure to provide adequate airway clearance may be the sole cause for a stable patient, with or without NIV, to develop acute respiratory failure, require emergency admission, and to then be at high risk for invasive airway support.

Lung Volume Recruitment

Under normal conditions, awake individuals sigh, yawn or otherwise achieve lung volumes close to total lung capacity several times hourly. Failure to fully inflate the lungs causes an increase in lung tissue and chest wall elastance, decreasing compliance and increasing work of breathing (12). Similarly, inspiratory and expiratory muscle weakness, results in reduced lung volumes in part due to reductions in lung and chest wall compliance (13-15). The inability to take periodic deep breaths can alter alveolar surface forces and result in alveolar collapse. Lung Volume Recruitment (LVR) (16) refers to the technique of stacking sequential breaths on top of each other using a hand-held resuscitation bag and holding each volume with the closed glottis (17). This technique allows the individual to achieve a maximal lung volume, closer to normal predicted volume. This volume has been referred to as the maximum insufflation capacity [MIC](18). The degree to which an individual is capable of volume recruitment is proportional to the lung and chest wall compliance as well as the bulbar function (19,20). A similar technique to LVR, manual hyperinflation (MHI), has been evaluated in intubated patients in the ICU (21,22). Hodgson et al. (21) evaluated lung compliance and secretion volume in 18 patients who served as their own controls. They compared side positioning and suctioning alone to this plus the addition of MHI using a resuscitation bag at pressures up to 40 cmH₂O. They found a significant

increase in lung compliance and volume of secretions in the patients when they received the addition of MHI. Choi and Jones (22), with a similar design, confirmed these findings with a 22% increase in static lung compliance following MHI. Although no specific evaluation has been performed, it is reasonable to expect that LVR, often provided at pressures exceeding 40 cm H₂O, would result in similar increases in respiratory system compliance.

There is some information which supports the potential benefits of this strategy in improving outcomes in patients with NMD. Bach found the use of LVR in combination with an airway clearance protocol was associated with a reduced number of hospitalizations in 24 prospective patients with DMD when compared to 22 retrospective controls (11). In an observational study, Kang determined that 30 of 43 ALS patients were able to achieve a higher MIC establishing an important MIC-VC difference (18). In an observational study where again patients behaved as their own 'pre-protocol' controls, Tzeng showed that once LVR and other noninvasive airway clearance techniques were established there was a significant reduction in subsequent hospital days per year (20). The population included DMD, ALS and Kyphoscoliosis. The individual effect of LVR was not established as it was a component of a therapeutic protocol. More recently Bach has shown in a case series that 94.9% of 78 DMD patients are capable of significantly increasing their PCFs with LVR (23).

LVR also provides for improved voice volume and may relieve dyspnea. It has been recommended three to four times daily, but no data are available to determine the optimum frequency of sessions or number of full lung inflations. Furthermore, the frequency required may be different for maintenance of effect than for initial therapy. Since LVR volume response is proportional to respiratory system compliance and bulbar function one would expect the greatest response in a clinical context where bulbar function and respiratory system compliance are optimum. As such, a patient with tetraplegia with normal lung and chest wall compliance may demonstrate a 300 or 400% increase in VC with LVR. A patient with post-polio kyphoscoliosis with a rigid chest wall may have a relatively small increase in MIC but demonstrate greater increases in PCF due to the intrathoracic pressures obtained. (see Figure 1-1). In addition, the ability to perform LVR is a useful skill to develop in preparation for mouthpiece ventilation (MPV) if and when required (19).

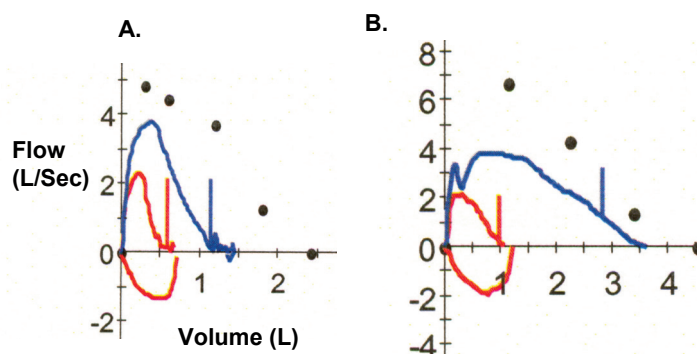


Figure 1-1) Flow volume loops of individuals with kyphoscoliosis (post-polio) (A) and tetraplegia (B). Spontaneous vital capacity (red) and maximum insufflation capacity with lung volume recruitment (blue)

Patients with sufficient upper extremity strength are able to perform their own LVR whereas those with weakness or paralysis require a caregiver to administer it, or if possible use glossopharyngeal breathing [GPB] (24), or MPV with a volume ventilator. Increases in PCFs can be measured using a hand-held peak flow meter or with pulmonary function equipment. No serious consequences of LVR have been documented. During breath-holding, patients with tetraplegia and diminished sympathetic tone may develop symptomatic hypotension particularly if upright in a chair. An abdominal binder may be helpful in preventing this and patients may need to be treated in a more recumbent position. Some patients also experience musculoskeletal discomforts with LVR due to over-stretching of soft tissues. Contraindications for LVR, as for the CoughAssist®, include active hemoptysis, recent or current barotrauma, bullous emphysema and significant hypotension.

Review of literature

Table 1-1 Literature Search Results for Lung Volume Recruitment

Author Year (Ref)	Study Type	# of Pts.	Outcomes				
			Outcome 1 Lung vol/flow	Outcome 2 Respiratory compliance	Outcome 3 Sputum weight	Outcome 4 Freq LRTI	Outcome 5 Freq of Hosp Adm
Bach, 1997 (11)	Observational Retrospective Controls	22 conventional, 24 protocol	NR	NR	NR	NR	Signif. Diff with protocol
Kang, 2000 (18)	Observational	43 ALS	30/43 increase MIC	NR	NR	NR	NR
Tzeng, 2000 (20)	Observational	47 NMD (DMD, KS, ALS, others pre/post protocol)	Trained but no results stated	NR	NR	NR	1.06 ± 0.84 vs. 0.03 ± 0.11 days per yr p<.003
Hodgson, 2000** (21)	Own Controls	18 (ICU-ETT)	NR	8.5 vs. 0.2 ml/cmH ₂ O <.001	5.5 vs. 3.5 gm, p<0.039	NR	NR
Choi, 2005** (22)	Own Controls	15 (VAP-ICU)	NR	Δ35 to 43 ml/cmH ₂ O p<.001	NR	NA	NA
Bach, 2007 (23)	Case Series	78 DMD	94.9% pts able PCFmic>PC Fsp 289 vs. 164 L/min p<.001				

**** Note:** Manual hyperinflation with resuscitation bag used; the same effect as LVR

Manually Assisted Coughing

Manually Assisted Coughing (MAC) or “quad cough” is a therapeutic technique commonly used to compensate for weakened expiratory muscles (25). The patient, either seated or recumbent at approximately 30 degrees, inspires fully. A rapid, one- or two-hand abdominal thrust is then provided by the therapist or caregiver just below the xyphisternum, timed just prior to glottic opening. A number of variations can be applied including; single-handed, a forearm across the chest to stabilize the thorax as well as lateral costal compression during pregnancy or just following PEG tube placement. PCFs can be substantially increased if LVR is performed prior to MAC which is then performed from the MIC. In 21 neuromuscular patients Bach observed a spontaneous, unassisted PCF of 1.81 +/- 1.03 L/sec and an increase in PCF to 3.37 +/- 1.07 L/sec with LVR alone and to 4.27 +/- 1.29 L/sec by applying LVR with addition of a MAC (26,27). A PCF of 270 L/min (4.5 L/sec) or greater is desired in order to prevent morbidity secondary to upper respiratory tract infections in patients with NMD (10). A recent observational study has also shown that while MAC significantly increases PCF in patients with DMD, LVR alone was more effective than MAC alone but the combination achieved the greatest improvements (28).

Mechanical In-Exsufflation

The CoughAssist® (Phillips Respironics) device is the only mechanical in-exsufflator (MI-E) available in Canada. It is a portable apparatus which generates inspiratory pressure, followed by expiratory (negative) pressure in the airway which simulates the effect of a cough. Historically,

similar devices were developed for the treatment of polio patients in iron lungs. The device generates a positive inspiratory pressure to provide lung inflation followed rapidly by a negative pressure to create high expiratory flows which shear mucus away from the airway. It can be applied through an artificial airway but is most often used noninvasively through a full face mask. No randomized controlled trials of in-exsufflation have been published. Studies are limited to case reports, observational and cohort designs (29,30,31,32) and have demonstrated utility in respiratory infection, reversal of atelectasis and assistance in weaning from mechanical ventilation. Optimum pressures have also been determined in a lung model (33,34). In 10 patients with SCI, tracheostomies and airway secretions, significant increases in % FVC, FEV₁ and PEF were demonstrated after treatment (35). With MI-E in stable ALS patients, those with and without bulbar weakness were able to achieve peak expiratory flows of 3.35 and 4.34 L/sec respectively without voluntary expiratory force (32). Those with such bulbar weakness that their baseline PCFs were below 2.7 L/sec were unable to benefit from MI-E. Although limited by the lack of randomized trials, published reports do consistently demonstrate positive outcomes and the absence of significant adverse effects. Suri has recently reported a patient with tetraplegia and one with DMD, each of whom developed a pneumothorax associated with use of mechanical insufflation-exsufflation (36). Investigators studying NIV today commonly indicate the use of airway clearance techniques (37) and insist that such treatments must be considered when evaluating outcomes of NIV (38). Chatwin showed in a prospective controlled trial in NMD patients that PCF could be significantly increased with MI-E from a baseline of 169 to 235 L/min ($p<.001$) (39). In a retrospective survey of 18 patients with SCI and experience with both MI-E and tracheostomy suctioning, MI-E was preferred to suctioning because it was less painful, less irritating and less tiring (40). Sancho demonstrated a significant improvement in SaO₂, peak and mean airway pressures compared to suctioning in tracheostomy ventilated ALS patients (32).

Table 1-2 Literature Search Results for Mechanical In-Exsufflation

Author Year (Ref)	Study Type	# of Pts.	Outcomes				
			Outcome Preference	Outcome PCF	Outcome Dyspnea	Outcome O ₂ Sat	Outcome Resp Parameter
Sancho, 2004 (30)	Observational Cohort	11-non-bulbar 15-bulbar ALS	NR	Bulbar; 3.35, Non-bulbar; 4.34 L/s All >2.7 L/sec	NR	NR	
Pillastrini, 2006 (34)	Observational	non-random control SCI, N not reported	NR	NR	NR	↑2.4% no diff from control	24%↑ FVC, 33%↑ FEV ₁ 29% ↑ PEF All $p<.01$
Sancho, 2003 (31)	Prospective Crossover	6 ALS, trach	NR	NR	NR	↑SaO ₂ , $p<.05$	mean Paw, Peak Paw, $p<.05$
Garstang, 2000 (39)	Retrospective Survey	18 SCI	Pain, Irritation, Tiring, $p<.01$	NR	NR	NR	NR
Chatwin 2003 (38)	Prospective Controlled	22 NMD 19 Control	NR	Increase PCF; In-Ex, $p<.001$	NR	NR	NR

The CoughAssist® is recommended to be used only in cooperative patients and may be of little assistance in patients with insufficient upper airway stability to maintain patency during the negative pressure or exsufflation phase (32). The device is most applicable for those with neuromuscular or chest wall diseases and is unlikely to be of significant benefit in obstructive airways disease (41). The device may be a significant added expense for many patients but can also be incorporated in program of cost-effective, interdisciplinary care.

Additional Mechanical Devices

Devices which are not commonly used in Canada for ventilator assisted individuals (VAIs) include high frequency chest wall oscillation (HFCWO) and intrapulmonary percussive ventilation (IPV). HFCWO involves the use of a chest shell or a vest which produces small, rapid, positive and negative pressure swings transmitted through the chest wall to the airways. Inspiratory/expiratory ratios of pressure and timing can be adjusted in order to favour higher exhalation velocities. These devices have been applied most often in patients with normal cough capacity, such as CF, in an effort to improve the rheology of tenacious sputum. HFCWO has been demonstrated to be as effective as chest physical therapy in CF but few studies have been performed in NMD patients. Lechtzin and colleagues conducted a randomized trial of HFCWO in ALS patients with an average FVC of 66% predicted, half of whom used NIV (42). While the majority wished to continue therapy and there was a reduction in breathlessness on a visual analogue scale, no difference in decline of FVC was noted, no measures of sputum clearance were obtained, and there was an increase in nocturnal cough associated with HFCWO. The inclusion criteria likely meant that patients had sufficient FVC to achieve an adequate cough and airway clearance if secretions were mobilized. Chaisson randomized a small number of ALS patients to HFCWO vs. standard care (43). There was an insignificantly greater loss of FVC and shorter survival in treated patients compared to standard care. Compliance with HFCWO was highly variable; from 10 to 90%. Concern has been raised about the use of HFCWO in patients who are unable to cough and in whom; mobilized secretions may be retained in other lung segments resulting in worsened gas exchange. Whether or not the combination of HFCWO with effective assisted coughing or the CoughAssist® would achieve superior and safe airway clearance is unproven. The combined cost of both devices would be prohibitive for most societies.

Noninvasive IPV is another mechanical airway clearance device (44). It can be administered through an endotracheal tube or noninvasively via a mouthpiece or a full face mask and superimposes high frequency alterations in airway pressure at frequencies 100 to 300 breaths per minute on top of a spontaneous breathing pattern. Some models can provide full ventilatory support during therapeutic sessions. Recent reports of a number of cases have demonstrated the effectiveness of IPV in reversing pulmonary consolidation and atelectasis which had not responded to usual therapies (45,46,47). This device has not yet been widely adopted and its role in overall airway management remains to be clarified.

General Clinical Approach to Airway Clearance

The overall approach to noninvasive airway clearance is illustrated in the following diagram. Effective airway clearance depends upon adequate peak expiratory flows, and it is this variable which dictates the management strategy. Such an approach is based on the consensus that patients who are able to produce PCFs above 270 L/min are at much less risk of acute respiratory failure due to secretion retention (10,11). The required PCFs can be achieved spontaneously with MAC, with LVR, with LVR accompanied by MAC or, if these techniques remain inadequate, with the use of the MI-E with or without the addition of a MAC.

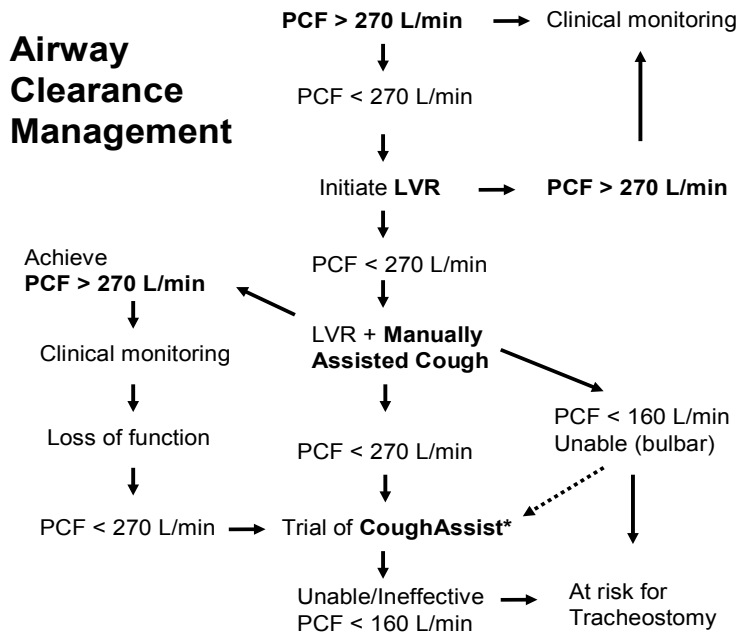


Figure 1-2) Flow diagram for preventive airway clearance techniques. LVR: Lung volume recruitment; PCF: Peak cough flow. *Note: Manually Assisted Cough can be added to increase effectiveness of CoughAssist® (Philips Healthcare, USA)

Airway Clearance in Patients Using Tracheostomy Ventilation

Regular use of a suction catheter is the standard technique of airway clearance in a patient with an artificial airway (48). Humidification is also critical in ensuring secretions are thin enough to be mobilized effectively (49). Heat/moisture exchangers (HME) have been associated with increased dead space, minute ventilation, neuromechanical drive, $p\text{CO}_2$ and respiratory rate, as compared with heated humidity (50,51,52). These differences may be critical in a spontaneously breathing individual but are less likely to be important if ventilation is fully controlled. The presence of a cuffed endotracheal tube or cuffed tracheostomy tube impairs the normal mucociliary clearance mechanisms and may increase the risk for infection (53,54). As such, any effort that can be made to provide cuffless ventilation may reduce such risks as well as other risks associated with an inflated cuff (55). Adequate sustained ventilation must be ensured as some patients with more rapidly progressive conditions such as ALS may not have clinical aspiration but inadequate ventilation (56). Where possible, cuffless tracheostomy ventilation will also enable the patient to utilize alternative, noninvasive methods of airway clearance such as LVR with MAC, as well as use of a one-way speaking valve. During MI-E administration the tracheostomy cuff, if present, should be inflated, as the complete seal enhances the effectiveness of MI-E. One must rely on glottic control or closure of the upper airway during MI-E if a cuffless tube is used.

Secretions from the respiratory tree are normally carried up the mucociliary blanket and the daily volume is estimated between 10 and 100 ml/day (57,58). Particularly in the presence of an inflated cuff and inadequate cough these secretions must be cleared. Adequate mobility of the patient may augment airway clearance (59,60). Suctioning with a catheter, although routine, is not a benign intervention, and deep suctioning has been associated with airway trauma, alveolar collapse and hypoxemia (61,62). Shallow, minimally invasive suctioning has been demonstrated in intubated ICU patients to have fewer adverse effects with equivalent outcomes

in duration of intubation, ICU stay and mortality, although deeper suctioning is recommended when necessary (63). The level of sterility required in the home has been debated. Sterile conditions are required in hospital where multiple caregivers are involved and the environmental bacteria are more frequent, but only clean conditions are felt to be necessary in the home environment (64,65). Catheters which employ off-set holes have been demonstrated to be more effective (66). A number of clinicians have used the CoughAssist® in critical care patients with anecdotal benefit. Investigators have found that tracheostomized patients with ALS and those with spinal cord injury who used both traditional suctioning and MI-E preferred the MI-E (32,40). No randomized controlled studies of MI-E in the ICU are available but a number of case reports and series indicate its value in clearing atelectasis and assisting in the weaning process (67). One controlled trial of MI-E in spinal cord injury reported significant increases in FVC and FEV1 in patients treated with MI-E compared to an untreated control group (35).

Conclusion

Adequate airway clearance may be the single most critical therapeutic intervention that prevents acute respiratory failure, undesired intubation and tracheostomy in patients at risk for or using NIV. Airway clearance strategies may help to maintain lung and chest wall compliance through its positive effects on MIC (67) and peak expiratory flows. Individuals who are at greatest risk are those with impairment of inspiratory and expiratory muscles and glottic dysfunction. Many noninvasive techniques are well established including LVR, MAC and MI-E. Several of these noninvasive strategies can also be applied to tracheostomy-ventilated patients in whom cuff-inflation and invasive suctioning have traditionally been the sole method of ventilation and airway clearance. More research is needed to identify the ideal methods of noninvasive and invasive airway clearance in the home to optimize the effectiveness of mechanical ventilation and enhance QoL for VAIs.

Research Questions

1. LVR; Do repeated maximum inflation capacity (MIC) maneuvers benefit this patient population? Are lung mechanics i.e. FRC and compliance, improved? How long lasting are these effects? What inflation pressures provide maximal benefit? Does this improve other outcomes such as declining lung function or independent breathing time? What frequency or pattern of MIC maneuvers yields the optimum results, and in which populations?
2. Weaning with noninvasive techniques; Do patients who have prior experience with oral inflation, i.e. through MIC or cough assist, have greater success at switching (from invasive ventilation) to NIV oral mouthpieces compared to those without this experience?
3. In patients capable of both therapies which is more effective in prevention of respiratory complications and improved QoL; LVR with MAC or MI-E?
4. Does provision of a home oximeter improve outcomes (Emergency visits, admissions, intubations) in patients using NIV and airway clearance strategies?
5. What is the degree of adherence with or effect on QoL as a result of recommended LVR therapies in patients at risk or using NIV?

Section I. Recommendations

The following recommendations are based on limited evidence from the literature search and consensus of the HMT expert panel.

For at-risk individuals and patients using NIV:

1. Education and preventive strategies in airway clearance must precede the need for mechanical ventilation whenever possible. (Consensus)
2. In the absence of contraindications, LVR techniques should be introduced with measurement of PCFs and MIC in those with PCFs < 270 L/min. (GRADE 1C)
3. MAC is recommended alone or in addition to LVR to increase PCFs to > 270 L/min. (GRADE 1C)
4. In the absence of contraindications, MI-E should be recommended for patients unable to achieve PCFs > 270 L/min with LVR and/or MAC particularly during respiratory infection. (GRADE 1C)

For invasive ventilation:

1. As long as adequate, sustained ventilation is ensured, long-term tracheostomies should be cuffless or cuff deflated if possible. (GRADE 2C)
2. Heated humidity is recommended over heat-humidity exchangers. (GRADE 1A)
3. Minimally invasive rather than deep suctioning is recommended when possible. (GRADE 2B)
4. MI-E and MAC for tracheostomy airway clearance should be strongly considered through tracheostomy to complement or replace deep suctioning. (GRADE 1C)
5. Clean, as opposed to sterile, conditions are adequate for home secretion clearance and suctioning. (Consensus)

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SECTION II.

Transition to Home (Patients Admitted to Hospital)

Introduction

As modern health care continues to evolve, more sophisticated, technology-based medical care is being provided outside the traditional hospital environment. The transition to community based care has been influenced by such factors as patient and family preference, user-friendly technology, limited acute care bed space and economic pressure on hospital budgets (1,2).

HMV is increasingly considered as a therapeutic option for VAIs who would otherwise be restricted to the hospital environment. Intuitively, the preferred location for VAIs is in the home because QoL is enhanced, integration to the community is maximized and costs are reduced (3,4,5). An additional, very important potential benefit of HMV may be the low frequency of hospital re-admissions and reduced duration of hospital stay. (6)

Review of Literature

When offering guidelines for the transition to home of VAIs, expert opinion is frequently the highest level of evidence, as randomized controlled studies do not exist, and in fact, may be difficult to pursue.

Thirty articles were deemed eligible for inclusion in the systematic review of the literature relevant to the transition of the VAI to the community. Most of them are descriptive and reflect the approach and point of view of the authors in regards to the transition to home of VAIs.

Table 2-1. Literature Search Results for Transition to Home of VAIs

Author Year (Ref)	Study Type	# of Pts.	Outcomes				
			Outcome 1	Outcome 2	Outcome 3	Outcome 4	Outcome 5
Lindahl, 2006 (2)	Descriptive	13	Experiences of being dependent on a ventilator and living at home	Persons with a negative approach, experience suffering from poor care, and usually are those with more comprehensive care needs	Usually patients with more comprehensive care needs, indicate ignorance and uncaring attitudes create unnecessary suffering provoked by uncaring personnel	Others spoke of caregivers who were competent and deeply committed to their work	Further research needed to gain more complete knowledge about the thoughts, values and conditions that constitute daily work for the various professionals responsible for providing care in patients' homes
Markstrom 2002 (4)	QoL Questionnaire results	91	Patients on HMV reported good perceived health despite severe physical limitations				
Lindahl, 2003 (7)	Patient Interview	9	Caring for persons with HMV is not a well- developed field of expertise	Further research focusing on individuals' experiences of how HMV affects their home and daily lives is needed.			
Warren, 2004 (8)	Descriptive	-	Interdisciplinary approach to the training	Critical pathway outlining necessary steps to coordinate discharge planning process of a patient with a tracheostomy who requires mechanical ventilation			
Avendano, 2000 (10)	Book chapter	-	A rehabilitative approach to VAIs				
Van Kesteren, 2001 (12)	Semi-structured interviews	38 patients & family members	Families and caregivers of tracheostomized patients on continuous ventilation reported increased emotional stress over time				

Author Year (Ref)	Study Type	# of Pts.	Outcomes				
			Outcome 1	Outcome 2	Outcome 3	Outcome 4	Outcome 5
Wagner, 2000 (13)	Descriptive Role of the patient care teams in chronic disease management	Effective chronic illness management generally rely on multidisciplinary teams	Successful teams include skilled pharmacists and nurses	Teams address issues that are not usually the domain of the physician	Consulting with medical specialists and their participation in education contribute to better outcomes		
Lujan, 2006 (16)	Prospective observational study	16	Outpatient initiation of HMV is an effective and efficient alternative to the traditional in-hospital method for Noninvasive HMV				
Brooks, 2008 (17)	Descriptive	10 pts & 10 caregivers	Participants identified the need for initial and ongoing training to address specific needs of ventilator users				
Neistadt, 1996 (21)	Descriptive	-	Approach to functional activity evaluation and training that helps therapists increase the effectiveness of their functional skills training for older adults				
Bertrand, 2006 (25)	Descriptive	35	Structured follow up with professional support at home has a positive effect on the outcome				
Vitacal, 2007 (28)	Retrospective survey to identify level of burden in real life	792	COPD had greater number of hospitalizations than patients with neuromuscular disorders(NMD) and chest wall deformities	Underlying disease, level of dependency, hours on mechanical ventilation, presence of a tracheostomy, home distance from hospital and hospital access are the causes of major care burden	More than 50% of patients selected as care burden having NMD and COPD, necessitating family and health care services care respectively		

Author Year (Ref)	Study Type	# of Pts.	Outcomes				
			Outcome 1	Outcome 2	Outcome 3	Outcome 4	Outcome 5
Marchese, 2008 (30)	Descriptive	77	Tracheostomy-intermittent positive-pressure ventilation (TIPPV) for respiratory failure is well received by patients, is safe and provides longer survival	COPD and ALS patients had a three-fold higher risk of death than patients with other causes of chronic respiratory failure	83 % of patients were pleased they had chosen TIPPV	55% of caregivers were pleased that patients had chosen HMV	
Jankey, 2008 (10, 11)	Book chapter	Treating persons with Long -Term Mechanical ventilation is a challenging but rewarding experience	It is important to be aware of the psychological difficulties and stressors of VAls	VAls require attention to both their medical and psychological needs			
Tearl, 2007 (18)	Evaluation of the training of caregivers looking after tracheostomized children on HMV		Program met the adults' learning needs	Recommend ongoing evaluation and refinement of training programs			
Rossi, 2001 (26)	Evaluation of psychological & psychosocial impact on caregivers of tracheostomized patients	40 caregivers answered a questionnaire at beginning of study and 1 yr later	Tracheostomy causes significant strain in the caregivers	Caregivers as well as patients led very restricted personal lives			
Vitacca, 2006 (24)	Pilot Study	35	Telemedicine for home monitoring of patients in HMV may be possible				

Discussion

Transition to HMV occurs in stages including:

1. Identifying the patient as suitable for HMV
2. Feasibility assessment
3. Preparation to leave
4. Discharge

Caring for persons with HMV is not a well-developed field of expertise (7) and when the HMV is initiated in a hospital setting, the successful transition to home is a complex process (8). The value of careful planning cannot be underestimated and communication among interdisciplinary team members is essential. Patient, family, caregivers and an interdisciplinary team of health care professionals must work together to create a comprehensive care plan for discharge to a safe, effective, and sustainable home environment. Once a VAI is discharged to the community, it is important that they maintain an open line of communication with the health care providers. This should include the primary care physician (family doctor) and the respiratory medicine specialist caring for the patient in the community, to promote and facilitate safety and medical stability. To this end, a well-structured follow-up program must also be established from the beginning (9).

Although chronic respiratory failure and the consequent need for long term/chronic ventilatory support can result from a variety of diagnoses, in all cases there are constants to be addressed when transitioning to home, taking into consideration the relevance of the underlying disease in contributing to morbidity and mortality. There are both medical and non-medical factors that determine the suitability of a VAI to go home on ventilatory support. A comprehensive assessment of the patient must be carried out by an interdisciplinary health care team who will ultimately provide the necessary training - ideally with a rehabilitative approach (10). Often overlooked, individuals discharged to the community on a ventilator have a particular set of psychosocial issues that must be addressed. In some cases, these issues will determine the success of the program. The patients considered for HMV can present with anxiety related to their loss of control, dependency on others, changes in their social role and changes in family dynamics. In addition VAIs experience the effects of the disruption of plans for the future, uncertainty about the future, permanent changes in physical appearance and bodily functions, inability to communicate effectively and diminished roles and responsibilities within the family and the society (11,12).

Of universal importance to every transition is a comprehensive plan for education and training of patient and caregivers. Depending upon the setting in which the patient is being prepared for HMV, the composition of the interdisciplinary team will vary and accommodations must be considered. For instance, if no occupational therapist is available, a physiotherapist or a nurse must address the activities of daily living. Although it is a limiting factor, the absence of a respiratory therapist on the team might be filled by a physician experienced in HMV and a respiratory nurse. The ability of team members to cross professional boundaries to fully prepare the patient is essential (13).

Patient Selection and Feasibility Assessment

The VAIs considering transition from the hospital to the community should fulfill the following conditions:

1. Medical stability (other than those on palliative care)

2. No need for constant monitoring
3. No need for frequent laboratory tests and treatment changes
4. Available community placement: suitable accommodation, not always defined in physical terms
5. Available caregiver support appropriate to the level of needs and requirements of the patient
6. Patient caregivers are motivated to live outside the hospital setting
7. Available financial resources, personal or funded to cover costs not met by government programs
8. Patient caregivers are able to learn care routines
9. The support of family and friends is also helpful

The VAls and their families must be informed about the advantages and disadvantages of leaving the hospital. Although at home the VAls could be close to family members in a familiar environment, on leaving the hospital, they may feel isolated from professional help and might feel insecure and overwhelmed by the tasks involved in the care.

With the development of a greater range of comfortable, effective noninvasive interfaces, the majority of VAls will be managed with NIV. The indications for invasive positive-pressure ventilation (IPPV) are diminishing. Electively, IPPV is generally reserved for patients with uncontrollable airway secretions (despite aggressive airway clearance techniques), impaired swallowing leading to chronic aspiration and repeated pneumonias and severe facial dysmorphisms. Non-electively, IPPV may be continued in those patients who were initially intubated in an emergency and later are unable to fully wean from the ventilator or be comfortably and safely managed on NIV.

Two types of patients can be considered for HMV:

1. Elective initiation of long-term ventilation: These are patients in whom the disease process has/will invariably lead to respiratory failure. These individuals will be offered NIV according to the guidelines provided in other sections in this document, often as outpatients without the need for admission. They may choose to start ventilatory support after discussion and consideration of the ramifications of their decision. In this group, ventilatory support is usually noninvasive and nocturnal but up to 24 h NIV can be provided successfully.
2. Non-elective initiation of long-term ventilation: These are patients whose disease process or circumstances resulted in acute respiratory failure requiring prolonged ventilation. In time, they become medically stable but remain ventilator-assisted for all or part of the day. In this group of individuals, ventilatory support is often invasive via tracheostomy and may include patients in need of total care or relatively close supervision. For this group, it is recommended to consider a full swallowing assessment, including video-fluoroscopy, prior to the transition to the home. If aspiration risk is small, patients might reassume oral intake which will facilitate their care. This assessment will also assist in determining feasibility of cuff deflation or changing to an uncuffed tracheostomy tube with the potential for speech, taste, smell. Decannulation and progression to NIV must be considered wherever possible.

Transitioning to Home

The need for a smooth transition to the home is similar for all patients, from the fully independent individual who is electively initiated in NIV, to the fully dependent individual requiring non-elective invasive ventilation. The type of home setting suitable and available for

the VAls will vary from person to person and region to region. Frequently the Occupational Therapist and Social Worker will be the best team members to assess the suitability of the private home situation. Supportive Living Centres, such as attendant care facilities, are a scarce resource but may be considered amongst other options such as direct provincial or government funding for home care for those individuals willing to live in the community.

Once a ventilated patient has been identified as suitable for HMV, the in-hospital care routines should be reviewed and changes implemented as quickly as possible. This review is to be considered from the perspective of limited professional caregiver supervision and intervention in the community. Additionally, the majority of community caregivers have limited formal training for looking after individuals with complex medical needs. Simplification of care is particularly important when VAls are to be transferred out of the Intensive Care Unit (ICU) to a less intense level of care where the HMV will be organized. Transferring to a 'stepdown' unit can be considered "weaning the patient from the ICU" (14) and the beginning of rehabilitation. According to Thomas, the aim of rehabilitation is to achieve the greatest return of physical, psychological, social, vocational, recreational and economic functions within the limits imposed by the illness and physical impairment (15). It is important that the ICU team, include the family in the daily routine, once the patient has been identified as requiring long-term ventilation. This approach will improve competency and confidence.

Establishing the Mechanical Ventilation Parameters for the Transition to Home

Home ventilators are not generally equipped to provide the highly specialized modes of ventilation available in the critical care setting. The ventilator model, mode of ventilation, the interface and the parameters need to be established early in the transition process. The benefit of doing this work at the beginning of the program will be to maximize the patient's compliance, confidence and comfort. The success of the long-term ventilation depends on adapting the mechanical ventilation to the patient's needs.

To establish the best parameters for discharging the patient home, day-time ABGs are drawn and trends monitored noninvasively both during unassisted ventilation (where possible) and during mechanical support. Nocturnal assessment of the ventilatory support can be followed with pulse oximetry and transcutaneous/end-tidal carbon dioxide monitoring or with a full polysomnographic study if necessary. The most appropriate approach to ventilation will be driven by a combination of available technology and patient comfort. Although the patient is no longer 'weaning', every effort to maintain even minimal ventilator-free time should be encouraged. Establishment of a maximal ventilator-free time may increase the patient's feeling of security and independence as well as improve the safety of the home setting.

Interface

1. NIV: There are many choices of masks/pillows and it will be the patients' comfort as well as overall effectiveness of the interface that will dictate the best choice. Special attention is to be paid to preventing skin breakdown at the bridge of the nose as well as to the patient's sense of claustrophobia, especially with full-face masks. The addition of either heated or cold pass-over humidification may alleviate nasal congestion and increase compliance. Many patients also benefit from the addition of a chin strap to improve mask leak when present, even with an oro-nasal interface.
2. Invasive ventilation: Although the interface is invariably a tracheostomy tube, the specific features of each available tube warrants considerable investigation. As an example, unless there is an absolute need for a cuffed tracheostomy tube, consideration must be given to the possibility of either an uncuffed tube or cuff deflation. The opportunity for vocalizing is of paramount importance to the patient, in addition to regaining the sense of smell and to some

extent, taste. Speaking valves should also be investigated if appropriate. In addition to improving swallowing the provision of an in-line speaking valve will allow the patient to independently perform regular LVR [see Section I - Airway Clearance].

Equipment and Services

The interdisciplinary team will evaluate the range of equipment and services required to transfer hospital care routines into the home: hospital bed, ventilator, back-up ventilator and associated supplies, lifts for safe transfers, feeding tubes and feeding pumps, commode chair, power wheelchair, call bell systems and environmental control systems. For those patients unable to communicate, the speech language pathologist and the occupational therapist will advise with regard to alternative tools and techniques. Equipment and supplies must be ordered as early as possible in the transition process to avoid delays in the discharge to the community.

Many VAI's do not have the level of personal or insurance support to be able to cover the initial costs of the ventilator and associated respiratory equipment. In addition, if the equipment malfunctions or fail, they may not have the resources to repair or obtain replacement in a timely fashion, thus possibly necessitating return to hospital. Therefore, it is strongly suggested that a publicly funded system to support VAI's in the community includes timely access to equipment and a structured, ongoing educational program. A number of excellent examples exist in some provinces in Canada.

Home Preparation

In certain cases, an assessment of the home setting is recommended for safety and accessibility (7). This is particularly useful when renovations are to be made. The home environment needs to be able to support the technological needs of the patient. The renovations necessary to accommodate the VAI's and the additional caregivers must start as soon as the decision of home ventilation has been made.

Caregivers

Few formal reports address the impact of the burden of care on family's life and QoL of the caregivers of HMV patients as family members (usual caregivers) need to assume the care of technically challenging dependent individuals.

Sufficient caregiver support is a crucial element in assessing the suitability of a VAI to go home although not everyone will require the same level of support. For a fully dependent patient, a routine care plan with coverage for 168 hours of care a week (24 h/day) must be produced. Sufficient caregiver support must be arranged to allow for sick time, vacations and unscheduled personal commitments. Government funded caregiver support may vary by region, but is generally limited. Without strong family and/or friends' commitment, transition to the community might not be possible. Training caregivers under 18 years of age or full time students should be avoided or considered carefully. Parents of young children may also be unsuitable care caregivers because of the time commitments to the children, especially if the VAI is not part of the household.

Ideally, the VAI should be treated as the primary caregiver and taught to direct and/or perform his or her own care. Occasionally, the patient may find himself in situations where they have to guide an untrained bystander to perform care. In addition, when the VAI's are trained as primary caregivers, they have a sense of confidence, independence and dignity.

As part of the training of families and caregivers, it is important that they be prepared to provide an increasing level of care related to the progression of disease/disability.

Financial Considerations

In Canada, although provincial health care systems provide financial support toward the cost of supplies and equipment, there are always additional expenses to be managed by the patient and family. All possible avenues of funding must be explored and maximized. When paid caregiver support is required, financial issues are frequently the barrier to moving into the community. The role of the provincial funding resources and the role of the home care services need to be fully explained, together with the 'hidden costs', for example, lost wages for a family caregiver who must stay at home or for un-reimbursed medical items and supplies.

Education and Training

The education of patients and caregivers should be holistic and individualized as the degree of dependency differs among the VAI's. The location and the duration of the education and training will vary depending on the training centre. Experienced home ventilation training centers have successfully implemented HMV on an out-patient basis. This particularly would apply to the training of those individuals in whom NIV is electively initiated (16)

Regardless of the location and duration of the training, at least one study has recommended the development of standardized training modules adaptable for use in formal as well as on-site training programs (17). An evaluation of a respiratory therapist driven family education program for caregivers of children on HMV, a comprehensive program demonstrated a positive impact in the performance and satisfaction of the caregivers (18). Although the duration and location may affect outcomes, the size of the training centre or regional treatment prevalence may not (19). The education and training sessions must include the following key issues: respiratory care, nursing care including feedings, dressing and toileting, activities of daily living, safe transfers and mobility aids, leisure activities, psychosocial issues, medications management and management of emergency situations.

The respiratory care training and education for all VAI's and caregivers need to include:

1. Basic respiratory anatomy and physiology
2. Airway management
 - Ventilator management and trouble shooting
 - Breath stacking, volume recruitment maneuvers and MAC
 - Use of the MI-E when available

For invasively ventilated individuals, additional respiratory education must include:

1. Tracheostomy and tracheostomy tube care
2. Suctioning (and MI-E, when available)
3. Manual Ventilation (bagging)
4. Tracheostomy changes

Training sessions should accommodate the different learning capabilities and needs of patients and caregivers. The use of oral, written and audiovisual material is recommended (20,21,22).

Table 2-2 Knowledge and skills

Knowledge and Skills that VAls and caregivers need to know prior to discharge to the community

- 1) Ventilator functioning and trouble shooting
- 2) Maintenance of ventilatory support with manual ventilation (bagging)
- 3) Maintenance and care of circuits and accessories (connections and cleaning)
- 4) Airway maintenance for tracheostomized patients (suctioning)
- 5) Care needs for totally or partially dependent VAls
 - a. Full range of motion to avoid contractures
 - b. Positional changes to avoid tissue trauma
 - c. Bladder and bowel routines
 - d. Management of medications
 - e. Feedings (oral or enteral)
 - f. Communication techniques
- 6) Management of emergency situations (what to do, who to call, where to go)

Links to Community Services and Resources

Links to community services and resources should be established well in advance of the discharge date. Home care, government nursing agencies and equipment supply companies must be contacted early in the transition process. Community services might be organized with the local discharge planner. Home care, including home visits from nurses, and other professional services such as physiotherapy, respiratory therapy, occupational therapy, social work or psychology, take time to arrange. Links to local transportation services should be investigated, to allow patients to leave the home either for leisure activities or for medical appointments. When available, link the VAl to community organizations such as March of Dimes, ALS Society, etc.

Where it is available, links to Respite Care facilities/organizations should be provided to that patient and family as part of the transition process.

At the time of discharge it is recommended that a checklist is used in order to cover all aspects of the necessary care that will be provided at the home (Appendix I page 37-41 of the present guideline)(23). The communication and coordination among numerous agencies involved in the care of the VAls at home, needs to be organized prior to the discharge to avoid gaps and misunderstandings that could jeopardize a safe and sustainable HMV.

When the patient is discharged, it is important to establish a plan for regular medical follow-ups. The primary care physician should be informed of the medical condition and needs of the patient. Ideally a schedule of reassessments should be given to the patient. If the transition occurs from the acute care hospital, a link to a community physician experienced in ventilatory care needs to be made, so the ventilatory parameters can be assessed and adjusted as necessary.

Trial Discharge

Progressive discharge with patients going home for one or two nights will allow the patient, caregivers and health providers to get information about gaps in the preparation for discharge to the community.

The patient and the caregivers are then able to apply and test their knowledge of managing at home. Once they return to the training centre, patients and families should be encouraged to share concerns and difficulties encountered in the home trial. Solutions are discussed with the transdisciplinary team to make the transition as smooth as possible.

Follow-Up

At follow-up, the tolerance and the effectiveness of the ventilatory support, the day-time ABGs and the gas exchange overnight need to be assessed. The choice of the frequency of follow-ups will depend on the natural course or the seriousness of the disease process and the availability of follow-up facilities. Assessment of the VAls during sleep is important to provide maximal nocturnal management. An assessment one to three months into HMV is recommended after elective initiation of nocturnal ventilatory support or, after discharging invasively ventilated patients. This can be done with noninvasive monitoring of oxygen saturation +/- carbon dioxide level during the night while the patient is on ventilatory support for those on nocturnal ventilation only. Where expertise exists, it is suggested that the patient bring the ventilator or the memory card to the clinic for download in order to assess compliance and effectiveness of ventilatory therapy at each visit. Many bilevel ventilators provide detailed information on parameters such as hours of use, airway pressure, mask leak, minute ventilation and proportion of patient-triggered breaths. Although there is no definitive evidence to date, this information may provide important long-term data on which to optimize therapy.

For VAls that require continuous ventilation, the assessment should be both during the day time and at night. Subsequently, annual reassessments are recommended. This can be done in a hospital setting, in a respiratory sleep laboratory or at home. A pilot study showed that home monitoring of patients on HMV is also possible through telemedicine (24). When the assessment is done at home, the advantage is that it is closer to the patient's real life because they are in their usual environment. It is important however, that overnight assessment include both monitoring of the oxygen saturation as well as the level of carbon dioxide, as normal oxygen saturation is not necessarily an indication of effective ventilation.

The home management of VAls is a dynamic process. In certain cases, patients require increasing assistance from the ventilator, and in those VAls that require more than 14 hours/day of ventilatory support, a second ventilator needs to be provided in case of mechanical failure. An emergency plan must be in place for such inevitable events as a power failure. In patients in whom NIV is no longer effective, switching to a tracheostomy and invasive ventilation needs to be discussed and implemented if the patient so wishes. This change however, must be addressed with the patient and family to avoid dramatic situations, especially when HMV is no longer possible and in light of the increasing demands for the care of a tracheostomized and fully VAI.

In all cases, supportive follow-up is important. In a study of follow-up of 35 children on home ventilation, the authors found that professional support had a positive effect on outcome, and the program was found to provide safe and necessary HMV for children with severe chronic respiratory failure (25).

Family Considerations

Families play an important role as informed caregivers providing much needed support at home to improve the VAls QoL. Families also extend the VAls personal independence. However, home ventilation poses a great strain on family members (26,27,28,29).

In a report of the attitudes toward home ventilation from the caregivers of 77 consecutive patients on invasive home ventilation, half of them (55%) were happy with the patients' choice and would encourage them to choose long-term ventilation again; 38% considered it a major burden to have the patient at home because it affected their entire life style, and almost half (43%) reported the nighttime was especially burdensome and stressful because of the patient's anxiety and chronic insomnia, possibly related to the fear of unexpected sudden death (30).

Safety Considerations

The requirements to provide a safe environment for the VAls in the community have not been researched, but will undoubtedly vary from individual to individual and to home setting to home setting. It is difficult to make recommendation which could apply to the different degrees of dependence of the VAls as well as the resources available to care for them. Considerations should be given to remote ventilator alarms, response time to alarm bells, qualifications of caregivers and communications among the caregivers and the interdisciplinary health care team.

Conclusion

The transition to home is a complex and demanding process for VAls, and requires highly sophisticated technology. Effective initiation and optimal monitoring of treatment are essential elements of successful HMV. The HMV committee recommends that an interdisciplinary team of health care professionals is of utmost importance for successful transition to home – provided that decisions are made under the leadership of a physician who is experienced in long-term ventilation. Commitment, motivation and preparation from patients' families and caregivers are also crucial for a successful transition to HMV. Family preparation is especially important in the establishment of care at home for VAls who are not fully independent.

Medically complex VAls often depend on several medical devices and services whose need must be determined and that must be in place prior to discharge. The training, the acquisition of all the equipment and the preparation of the home environment take time. Moreover, the needs of the patient, the family and caregivers and the home health care team, must also be taken into consideration. Currently, the number of qualified and skilled health care professionals and places where home ventilation training is provided are limited and in contrast the number of VAls who might benefit from HMV is growing.

Research Questions

1. HMV poses many logistical and economic barriers. Does providing a more centralized agency offer theoretical advantages over other currently available options? Can a centralized agency improve outcomes? What is the current state of provision of HMV nationally and are there significant interprovincial or regional differences? Are there care gaps that need addressing? Is there an ideal size for a central agency?
2. How is home care equipment such as ventilators, in-exsufflators and a home care plan accepted in the hospital setting? What can be done to facilitate continuity of experienced care from the home setting to the hospital?

Recommendations

In the long-term, successful transition to the community of VAls is dependent upon the selection of suitable candidates and a comprehensive training approach. The training program may occur in the hospital setting, a private home or a clinic setting. While every VAl is entitled to be considered without prejudice of such factors as age, disease process or financial status, not all will be successful transitioning or living in the community. The investment by the patient, family, caregivers and health care team in time, education, training, equipment, financial resources and home set up can be substantial. In addition, the emotional burden for the patient and family may be overwhelming. In most cases, VAls returning to the community will receive part or all of their immediate care from caregivers with little or no formal medical training and as such maintaining success in the home remains a challenge.

The following recommendations are based on limited evidence from the literature search and consensus of the HVM expert panel.

1. The candidate should be medically stable without constant or frequent monitoring, tests or treatment changes. (Consensus)
2. The candidate and family must be motivated (Consensus):
 - a) VAls must express interest in transitioning/living in the community.
 - b) The family should express commitment to having the VAl live in the community.
 - c) The family is willing to provide support (physical, emotional, financial).
3. The candidate must have an adequate home setting (Consensus):
 - a) Identifiable home to live in, suitable to the needs of the VAl.
 - b) Home is adaptable as necessary.
4. The candidate must have sufficient caregiver support (Consensus):
 - a) Caregivers identified and committed to provide sufficient hours of care to meet the needs of the VAl.
 - b) Available government-funded care hours identified.
5. The candidate must have access to adequate financial resources (Consensus):
 - a) Sources of financial assistance identified and accessed.
 - b) Sufficient financial resources available to meet projected costs.
6. The candidate must have access to equipment appropriate for the needs (Consensus):
 - a) Appropriate equipment selected and ordered.
 - b) Sources for ongoing supplies identified.
7. There must be comprehensive initial training, plus ongoing education and training for patient and caregivers once they are in the home setting (Consensus):
 - a) Initial education organized to accommodate learning, practice and inclusion of caregivers in the care routine as early as possible.
8. The candidate must have access to health care support in the community (Consensus):
 - a) Follow-up care available as appropriate (tracheotomy tube changes, ventilator reassessments, and assessment of the ongoing effectiveness of the ventilatory support).
 - b) Medical follow-up to allow for appropriate changes to the mode of ventilation (ie, from invasive to noninvasive and vice versa, from continuous to nocturnal and vice versa).
 - c) Professional services available postdischarge.
 - d) A government-funded ventilatory service is necessary to provide appropriate access to equipment and respiratory care.

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SECTION II. APPENDIX I - Tools - Education Check Lists

1. NONINVASIVE VENTILATION

Learning Objectives: At completion of training, the participant will be able to:

A. Patient Care	Date	Caregiver Initials
1. Describe the parts of the respiratory system and how they function (in very general terms only).		
2. Describe how changing body position or eating a meal can affect breathing.		
3. Explain the importance of drinking water and/or using a humidifier to manage secretions.		
4. Describe why heart rate (pulse) or breathing rate may change with activity or illness.		
5. Describe possible signs and symptoms of a chest infection.		
6. Explain the importance of proper hand hygiene in preventing the spread of infection.		
7. Explain what is meant by the term 'aspiration' and will know one symptom to watch for.		
B. Ventilator/ Bilevel Pressure Device Care	Date	Caregiver Initials
1. Describe the purpose of a ventilator/ bilevel device and when a patient might need one.		
2. Demonstrate what needs to be turned on <u>and checked</u> when starting the ventilator/ bilevel device at the bedside.		
3. Demonstrate how to change the water in the humidifier. What kind of water is used in the humidifier?		
4. Demonstrate how and when to make ventilator/ bilevel device setting changes.		
5. Demonstrate how to check the ventilator high and low pressure alarms.(Volume Ventilator only)		
6. Describe the kind of situations that make the low-pressure alarm ring and what to do. (Volume Ventilator only)		
7. Describe the kind of situations that make the high-pressure alarm ring and what to do. (Volume Ventilator only)		
8. Describe any other alarms on the ventilator. (Volume Ventilator only)		
9. Demonstrate how to assemble and disassemble the ventilator/ bilevel device circuit.		
10. Demonstrate changing circuit and checking the device after changing the circuit.		
11. Describe how and when to clean the circuit, interface and change the filters.		
12. Explain how to put on the interface properly		
C. Funding, Equipment Supply and Emergency Management	Date	Caregiver Initials

1. Explain the role of the Provincial Government in funding the equipment.		
2. Explain where the ventilator comes from and how to contact them.		
3. List the respiratory equipment provided by the Provincial Government.		
4. Explain when to call an emergency number (e.g. 911).		
5. Explain the name, phone number and role of the home care company.		
6. List the supplies that come from the home care company, how to place an order and funding.		
7. Describe the role of the home care company in an emergency.		
8. List the supplies not covered by government funding that the patient is responsible for.		
9. Describe the role of the Health care Centre that prepared and trained the patient for the future care.		
10. Explain the role of the family physician in the care of the patient.		
11. Describe the role of the Health care Centre that prepared and trained the patient in an emergency.		
12. Describe the role of the acute care hospital in an emergency or power failure situation.		
D. Suctioning/ Manual Ventilation	Date	Caregiver Initials
1. Explain why a patient might need oral suctioning.		
2. Demonstrate how to correctly set up the suction equipment.		
3. Demonstrate clean suctioning technique <u>including</u> asking the patient for direction before and during suctioning.		
4. Explain why suctioning should be done only when needed, trying to avoid over suctioning or frequent suctioning.		
5. Explain how to troubleshoot the suction unit.		
6. Describe correct disposal of dirty suction equipment including suction catheters and gloves.		
7. Demonstrate how to stock the portable suction bag for use outside the home.		
8. Explain where supplies such as suction catheters come from.		
9. Explain the importance of the manual resuscitation bag.		
10. Demonstrate how to test and use the manual resuscitation bag.		
11. Demonstrate proper use of the mechanical in/exsufflator if available (Interface, pressure settings, frequency of use).		

Caregiver Signature: _____
Facility Name: _____
Address: _____
Instructor Signature: _____
Facility Name: _____
Address: _____

Date: _____

Date: _____

Health care Centre
 Respiratory Therapy Services, 123 Main Street

2. INVASIVE VENTILATION

Learning Objectives: At completion of training, the participant will be able to:

A. Patient Care	Date	Caregiver Initials
1. Describe the parts of the respiratory system and how they function (in very general terms only).		
2. Describe how changing body position or eating a meal can affect breathing.		
3. Explain why a patient with a tracheostomy tube might not be able to speak.		
4. Explain the importance of drinking water and/or using a humidifier to manage secretions.		
5. Describe why heart rate (pulse) or breathing rate may change with activity or illness.		
6. Describe possible signs and symptoms of a chest infection and the <u>caregiver's</u> responsibilities in the care of the patient.		
7. Explain the importance of proper hand hygiene and gloves in preventing the spread of infection.		
8. Explain when to call 911.		
B. Funding, Equipment Supply and Emergency Management	Date	Caregiver Initials
1. Explain the role of the Provincial Government in funding the equipment.		
2. List the supplies not covered by government funding that the client is responsible for.		
3. Explain where the ventilator came from and how to contact them.		
4. List the equipment provided by government funding.		
5. Explain the name, phone number and role of the home care company.		
6. List the supplies that come from the home care company, how to place an order and funding.		
7. Describe the role of the home care company in an emergency.		
8. Describe the role of the Health care Centre that prepared and trained the patient in the future care		
9. Describe the role of the Health care Centre that prepared and trained the patient in an emergency.		
10. Explain the role of the family physician in the care of the client.		
11. Describe the role of the acute care hospital in an emergency or power failure situation.		

C. Tracheostomy Care/ Speaking Valves	Date	Caregiver Initials
1. Explain why a patient might need a tracheostomy.		
2. Name the parts of the tube.		
3. Explain how to properly clean around the tracheostomy stoma and describe what equipment is needed.		
4. Demonstrate correct inflation and deflation of a cuffed tracheostomy tube.		
5. Explain the purpose of an inner cannula.		
6. Demonstrate the proper technique for inserting or removing an inner cannula.		
7. Describe how to clean and take care of a speaking valve.		
8. Demonstrate how to properly connect and disconnect the patient from a ventilator.		
D. Suctioning/ Manual Ventilation	Date	Caregiver Initials
1. Explain why a patient might need suctioning.		
2. Demonstrate how to correctly set up the suction equipment.		
3. Explain why it is important to use two gloves when suctioning.		
4. Demonstrate clean suctioning technique <u>including</u> asking the patient for direction before and during suctioning.		
5. Explain why suctioning should be done only when needed, trying to avoid over suctioning or frequent suctioning.		
6. Explain what to do if blood is suctioned from the trachea.		
7. Explain what difference it might make if the patient takes blood thinners.		
8. Explain how to troubleshoot the suction unit.		
9. Describe correct disposal of dirty suction equipment including suction catheters and gloves.		
10. Demonstrate how to stock the portable suction bag for use outside the home.		
11. Explain where supplies such as suction catheters come from.		
12. Explain the importance of the manual resuscitation bag.		
13. Demonstrate how to test and use the manual resuscitation bag.		
14. Demonstrate proper use of the mechanical in/exsufflator if available (Tracheostomy adapter, pressure settings, tubing changes for secretions, cuff inflated/deflated).		
E. Ventilator Care	Date	Caregiver Initials
1. Describe the purpose of a ventilator and when a patient might need one.		
2. Demonstrate what needs to be turned on <u>and checked</u> when starting the ventilator at the bedside.		
3. Demonstrate what needs to be turned on <u>and checked</u> when starting the ventilator on the wheelchair.		
4. Demonstrate how to change the water in the humidifier.		

5. Explain what kind of water is used in the humidifier.		
6. Explain what needs to be plugged in when the wheelchair is not in use.		
7. Demonstrate how and when to make ventilator setting changes.		
8. Demonstrate how to check the ventilator high and low pressure alarms.		
9. Describe the kind of situations that make the low-pressure alarm ring and what to do for the patient.		
10. Describe the kind of situations that make the high-pressure alarm ring and what to do for the patient.		
11. Describe any other alarms on the ventilator.		
12. Explain how to give an MDI/ puffer with the ventilator.		
13. Demonstrate how to assemble and disassemble the ventilator circuit.		
14. Demonstrate changing the ventilator circuit and checking the ventilator after changing the circuit.		
15. Describe how and when to clean the ventilator circuit and change the filters.		

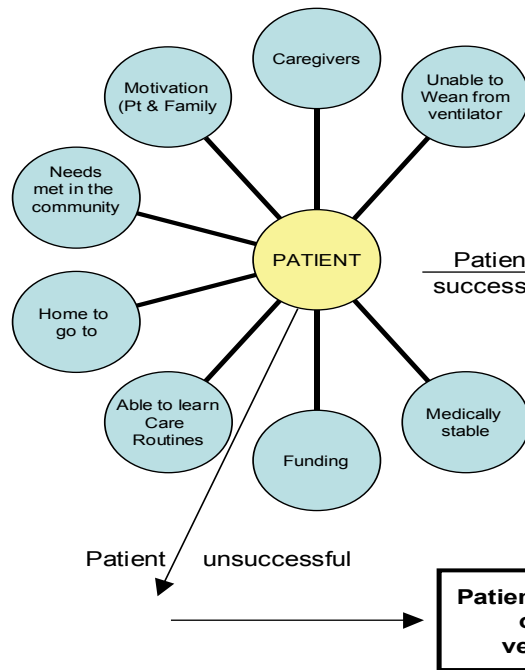
Caregiver Signature: _____ **Date:** _____
Facility Name: _____
Address: _____
Instructor Signature: _____ **Date:** _____
Facility Name: _____
Address: _____

Health care Centre
 Respiratory Therapy Services, 123 Main Street

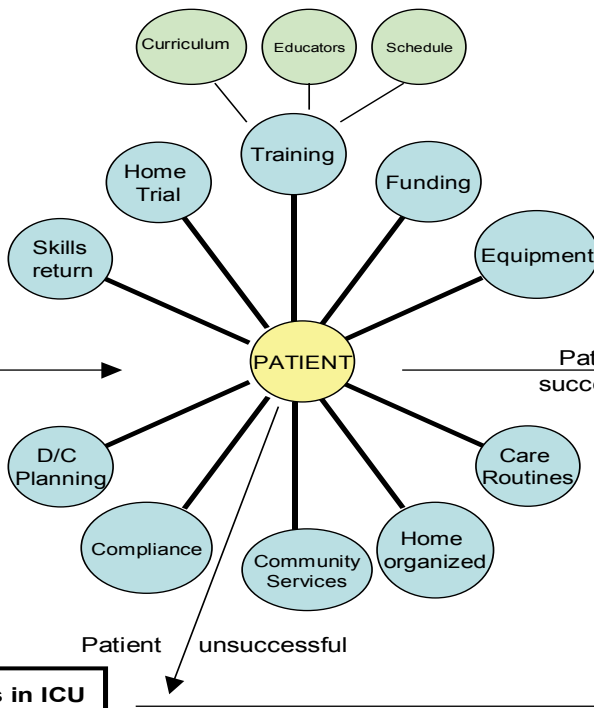
SECTION II. APPENDIX II - Overview: Transitioning to Home

Transition to Home (Invasive Ventilation)

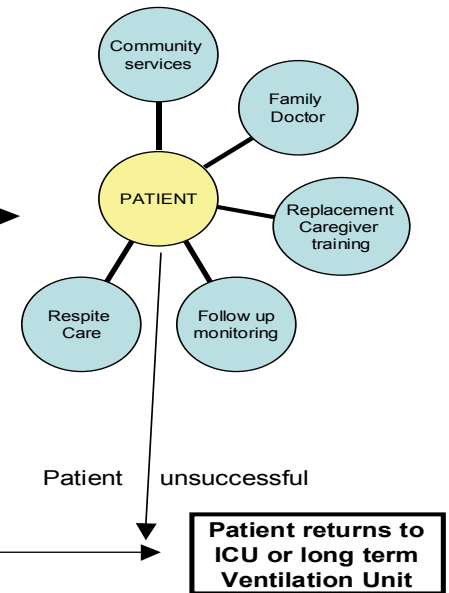
Stage 1 – Patient Selection & Feasibility



Stage 2 – Training



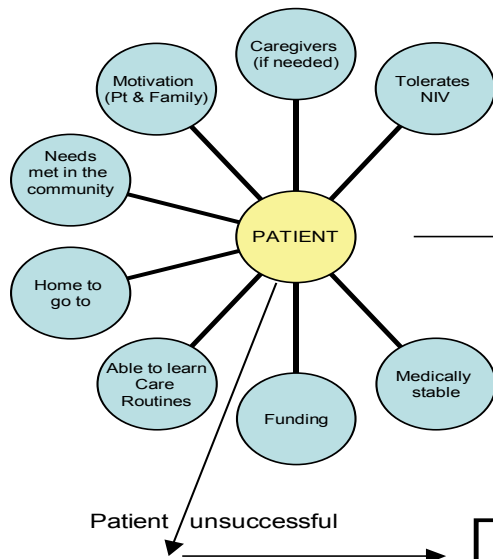
Stage 3 – Discharge/ Home



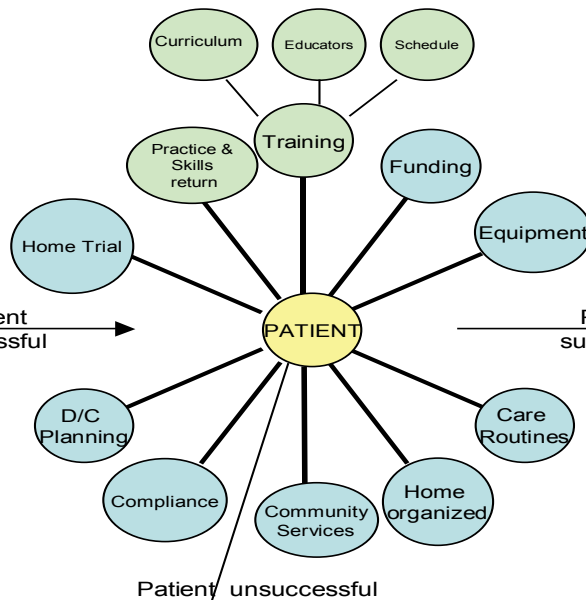
APPENDIX II (cont'd)

Transition to Home (Noninvasive Ventilation)

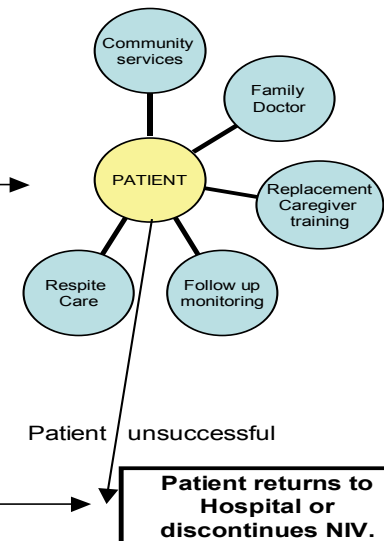
Stage 1 – Patient Selection & Feasibility



Stage 2 – Training



Stage 3 – Discharge/ Home



SECTION III.

HMV for Patients with Amyotrophic Lateral Sclerosis (ALS)

Introduction

ALS is a neurodegenerative disorder involving both upper and lower motor neurons that results in the progressive weakness of skeletal muscles. Generally, onset of weakness is characterized as either limb or bulbar. Rarely, first presentation may be with respiratory failure secondary to early respiratory muscle involvement (1). Regardless of site of first onset, death usually occurs as a result of progressive respiratory muscle involvement; with 50% of patients dying within three years of symptom onset (2). Bulbar onset generally has a shorter survival time than limb onset ALS (3). The rapid progression to death separates ALS from most other NMDs for which NIV and tracheostomy ventilation is considered. ALS is also distinct from other ventilated medical conditions, including other NMDs, by virtue of having the poorest survival on ventilation. In one series, only 5% of ALS patients using mechanical ventilation were alive after five years as compared to more than 60% of patients with other neuromuscular diagnoses(4). Ninety-five percent of the ALS patients using home ventilation in the Swedish Home Mechanical Ventilation register (4) were using NIV, a number similar to data from the North American ALS CARE database, which has remained largely unchanged since 1996 when it was created (5).

There continues to be debate regarding the ethics of prolonging survival in such a rapidly progressive disorder. Despite the potential for benefit of NIV in ALS, the majority of patients die without using this therapy. In 1999 Mello published a survey of multidisciplinary ALS clinics and found that only 15% of eligible patients were on NIV (6). Two years later Bradley et al. looked at the ALS CARE database, and found less than 10% of patients were on NIV (7). The ALS CARE database was reviewed again in 2006, following many reports of positive outcomes with the use of NIV, and found that 36.2% of patients considered to be candidates by current guidelines were actually using NIV (8). A recent Canadian survey of ALS centres across the country found that NIV was used by only 18.3% of patients, while only 1.5% was reported as tracheostomy ventilated (9). Part of the reluctance may be on the part of the patient, not wanting to extend survival; however, there is also a marked variation in practice from center to center as was highlighted by the Eurovent study (10) which surveyed 483 European centers.

Review of Literature

Monitoring of Respiratory Function

Measuring lung function in ALS serves two purposes. Firstly, it has been shown that some measures of lung function are better predictors of survival than functional rating scales (2,3,11,12). The second reason for monitoring lung function assumes that we have an intervention whose timing relies on knowledge of this data such as NIV and gastrostomy feeding tubes.

Earlier literature focused on measures of lung function that predict daytime hypercapnea as this has been a frequently used criterion to initiate mechanical ventilation. More recently, there has been a focus on predicting nocturnal sleep disordered breathing for the purpose of earlier initiation of ventilation before onset of daytime hypercapnea. Lyall looked extensively at predictors of daytime hypercapnea (13). He assessed VC, FEV1, Peak inspiratory pressure ($P_{I_{max}}$), Peak expiratory pressure ($P_{E_{max}}$), sniff transdiaphragmatic pressure (P_{di}), sniff oesophageal pressure (P_{oes}), sniff nasal pressure (SNP), cough gastric pressure (P_{gas}), bilateral cervical magnetic stimulation (CMS) P_{di} and ABGs. Sniff P_{di} and CMS P_{di} had the greatest

predictive power for the presence of hypercapnea. Of the less invasive tests, SNP had the best predictive power. This predictive power was limited to those patients without significant bulbar dysfunction. No test reliably predicted hypercapnea in the patients with bulbar dysfunction. Morgan also found the SNF useful (14). He found a SNF less than 40 cm of H₂O significantly correlated with nocturnal hypoxemia and quoted a median survival of only 6 months with a SNF < 40 cmH₂O. Others have found SNP as a useful measure in ALS as it can be performed by most patients even those with advanced disease and bulbar dysfunction (15). It is also more sensitive than the FVC for muscle dysfunction in early disease. P_{imax} is also a sensitive measure of early muscle dysfunction and can be used late in the disease to predict survival, but requires the patient to tolerate and be able to seal at the mouthpiece in order to perform the test.

Sitting VC may remain normal even when respiratory muscle weakness is present making it an insensitive measure of muscle weakness. However, when FVC falls to less than 50% predicted, survival was limited to nine months with most patients dying by six months in one older study (11). Other authors have also noted the poor prognosis of patients with a FVC < 50% predicted (12,16) and, therefore, it is recognized that FVC, when very low, is specific for impending respiratory failure and death. More sensitive to respiratory muscle weakness and diaphragmatic dysfunction in particular, is the supine VC. Bye et al showed a correlation between percentage fall in VC from the erect to the supine position and the lowest saturation during REM sleep (17) suggesting that a drop in VC from the erect to the supine position may be used to predict abnormalities in breathing during sleep that are associated with diaphragm dysfunction. Others have found that this change in VC from the erect to supine posture correlates well with symptoms (18). One author found a Borg dyspnea scale ≥ 3 upon assuming the supine position a useful predictor of a SNP ≤ 40 and impending respiratory failure (19).

Lung function is essential in the follow up of ALS patients, but equally important is a history that focuses on symptoms of daytime dyspnea, orthopnea, poor sleep, excessive daytime sleepiness, morning headache and fatigue. In a paper by Vender (20), the onset of dyspnea and rate of decline of VC predicted survival. Excessive daytime sleepiness and poor sleep were very sensitive in predicting sleep disordered breathing, though not specific enough to use alone. Finally, orthopnea was found by David (21) to be a good predictor of sleep disordered breathing.

Sleep Disordered Breathing

There are many reasons that poor sleep occurs in patients with ALS. Limited ability to change body position, pain, and anxiety may all be factors. As with other neuromuscular disorders that involve respiratory muscles, sleep fragmentation by breathing related arousals has been reported. Table 3-1 outlines 7 studies that characterize breathing related sleep abnormalities specifically in patients with ALS (21-27). Among these studies patient selection varied widely. In the studies of David (21) and Berlowitz (26) patients selected had more advanced disease. The mean FVC in David's study was 52% of predicted and all patients in Berlowitz's study complained of symptoms suggesting sleep disordered breathing. On the other hand, patients in Kimura's study (24) were asymptomatic and in Atalaia's (27) patients were selected with normal pulmonary function and diaphragm function.

Given bulbar involvement by ALS, the possibility of upper airway obstruction during sleep giving a picture of obstructive sleep apnea has been raised; however, in a study of ALS patients with bulbar dysfunction, Ferguson (23) found obstructive apneas did not occur. This group of seven studies reported a decrease in total sleep time and sleep efficiency, increased stage 1 sleep and reduced REM sleep. The predominant pattern of sleep disordered breathing was not obstructive apneas, but rather, mixed apneas, central apneas and hypoventilation. In four of these studies (21-23,26), at least one subject was treated with NIV. Observations included

improvement in sleep architecture, decreased breathing related arousals, improved oxygenation during sleep and improved symptoms related to sleep disordered breathing. In another study by Newsome-Davis (28) cognitive impairment before and after NIV was studied and improvement in cognitive function was found that was assumed to be related to correction of sleep disordered breathing by NIV.

Table 3-1. Sleep Disorders in ALS

Author year (Ref)	Study Type	# of Pts # of Pts with SDB	Type of testing	OUTCOMES						
				Mean O ₂	Lowest O ₂ sat	Type of Apnea	Δ tCO ₂	RDI/ AHI	REM Sleep	Comment
Gay 1991 (22)	Prospective Observation	21 18	Polysomnography	91.8± 4.7	81.9± 10.3	9 OSA 7 mixed 2 central	NR	11.3± 12	NR	-Difficulty sleeping and EDS sensitive for desat.≤80%. Not specific. -Mixed population -One patient studied with nocturnal CPAP/bilevel-no comment on sleep architecture
Ferguson 1996 (23)	Prospective Controlled	18 (10 Controls) 8	Polysomnography	89.4± 4.7 in REM	NR	Hypovent	NR	10.5± 22.4	↓	-All Bulbar. 1/18 Wheelchair bound -14/18 orthopneic -1st night effect -No OSA in ALS pts
David 1997 (21)	Retrospective	17 16	Polysomnography	NR	55-95%	6 central 7 mixed 2 myoclonus 1 ↑ WOB	0-25 torr	NR	NR	-Mean FVC 52% -EDS and orthopnea related to ↑BRA -Am headache non-specific -Decreased BRA , improved oxygenation and decreased pCO ₂ with Bilevel
Kimura 1998 (24)	Prospective	18 (11 bulbar) 3 (+bulbar)	Eden trace	97%	Mean 86%	Mixed	NR	7.7±11.6 1.8±1.2	NR	-Asymptomatic for SDB/resp symp -RDI greater in bulbar vs non -No treatment in study
Berlowitz 2006 (26)	Retrospective	74 - unclear	Polysomnography	NR	NR	NR	NR	25.5 mean all grps	↓	-3 groups: No ventilation, NIV, tracheostomy ventilaton -Improvements in desaturations and BRA with ventilation -Looked at survival in the groups -Referred for polysomnography late -Looked at treatment effect on sleep-improved sleep architecture with increased REM and decreased Stage 1, decreased arousals, less time spent hypoxemic
Atalaia 2007 (27)	Prospective	11 8	Polysomnography	94%	83%	Mixed apnea Hypovent	NR	15	↓	-Study of 11 ALS patients with normal PFTs and diaphragm function and abnormal nocturnal oximetry -No treatment applied

Tracheostomy Ventilation

Historically, ventilation, if it occurred in ALS, was done through a tracheostomy. Since the introduction of NIV, tracheostomy ventilation is uncommon and thought to be a less desirable option (29). Not all patients are tolerant of, or able to successfully use noninvasive supports. The only option may be tracheostomy, if prolonged survival is desirable. The estimated incidence of tracheostomy ventilation is now only 3-5% of ALS patients in the ALS CARE database (5), and even lower in a recent Canadian survey with only 1.5% of patients ventilated in this way (9). Concern has been raised regarding the patient and caregiver satisfaction with this choice. In a retrospective review of patients using tracheostomy ventilation, Oppenheimer found that 90% of patients were happy with their decision of tracheostomy and 94% of caregivers felt this way as well (30). He found the 3-year survival to be 58% and five-year survival 33% in his series of patients. In another study comparing health-related quality of life (HRQoL) in both patients and caregivers supported with either tracheostomy ventilation or NIV, they found a good overall QoL in patients, but a very high burden of care for tracheostomy ventilated caregivers, 30% of whom rated their own QoL lower than the patient's QoL (31).

Though chosen by some, tracheostomy may result from an acute deterioration and intubation when a personal directive is unavailable. Following tracheostomy for acute respiratory failure, a recent Italian study (32) reported that none of the patients died in hospital; however 70% were discharged completely ventilator dependent, and 28% partially ventilator dependent. Only one patient was liberated from mechanical ventilation. None of the patients had their tracheostomy removed. Bach has described decannulation after tracheostomy in a select group of ALS patients with preserved bulbar function and the ability to generate an assisted PCF of >160 L/min (33,34). Despite these occasional reports and the possibility of an extended period of NIV after decannulation, tracheostomy will be required in the future as bulbar function deteriorates if patients choose invasive ventilation in the hope of prolonged survival. This was reported in Bach's study (33).

In section I - airway clearance in this guideline, uncuffed tracheostomy tubes are recommended when possible. However, a recent study by Sancho et al. (35) looked at the type of tracheostomy tube required for effective ventilation in ALS and found that for 35.7% of the patients, a cuffed tube was required with advancing bulbar dysfunction as a result of excessive air leak and hypoventilation.

A study looking at predictors of the choice for long-term tracheostomy ventilation found that patients tended to be younger, have young families and be of a higher socio-economic status than patients who did not choose this option (36). It remains an option in carefully selected patients after lengthy discussion of the pros and cons.

Assessment of Benefit of NIV in ALS

Most of the ventilation that occurs in patients with ALS currently is NIV (5). Subsequent review of the literature therefore focuses on NIV in ALS. As seen in Table 3-2, 16 studies were identified that address the question of benefit of home NIV or timing of initiation of NIV by patients with ALS. In these studies, outcomes of interest included survival, HRQOL, pulmonary function, gas exchange, sleep parameters, cognition, and timing of initiation of NIV.

Table 3-2. Benefits/Timing of NIV in ALS

Author year (Ref)	Study Type	Controls	# of Pts	Indication for Ventilation	Place of Initiation Ventilator Used Titration Method	Outcomes						
						Survival	HRQOL	Pulmonary Function	Sleep Parameters	Blood Gases	Cognition	Timing of Initiation
Bourke 2006 (37)	RCT	Yes, RCT	41 Pts 19 control 22 NIV	Orthopnea+ MIP<60 or Symptomatic daytime ↑pCO ₂	Inpatient VPAP/ST Noct sats, Day ABG Pt comfort	↑	SFF36 - I SAQLI - I CRQ - I	NR	NR	NR	NR	NR
Pinto 1996 (38)	Prospective	Yes, 1st 10 pts	20 Pts 10 control 10 NIV	Abnormal daytime ABG	NR Bilevel NR	↑	Analog scale life satisfaction - I (modest)	NR	NR	NR	NR	NR
Aboussouan 1997 (39)	Prospective	Yes, pts intolerant of NIV	39 Pts 21 control 18 NIV	Orthopnea or symptomatic daytime ↑pCO ₂	Clinic PLV100 or Bilevel/ST Comfort pCO ₂ , symptoms	↑	NR	NR	NR	NR	NR	NR
Newsom- Davis 2001 (28)	Prospective	Yes, no respiratory difficulty or sleep issues	19 Pts 10 control 9 NIV	↑pCO ₂ and sleep disturbance	Inpatient NR NR	NR	ESS – I HAD anxiety score→ HAD depression score→	NR	I	I	I	NR

Author year (Ref)	Study Type	Controls	# of Pts	Indication for Ventilation	Place of Initiation Ventilator Used Titration Method	Outcomes						
						Survival	HRQOL	Pulmonary Function	Sleep Parameters	Blood Gases	Cognition	Timing of Initiation
Jackson 2001 (40)	Prospective randomized	Yes, standard care with NIV if FVC<50%	13 Pts 6 control 7 early NIV	Early- nocturnal desats Standard- FVC<50%	NR NR NR	NR	SF36 – vitality I SAQLI – no change	NR	NR	NR	NR	FVC correlates poorly with symptoms. Recommend earlier start.
Aboussouan 2001 (41)	Prospective	Yes, intolerant pts	47 Pts 24 control 23 NIV	New orthopnea ± ↑pCO ₂	Clinic PLV100 or bilevel/ST Chest rise and comfort	↑	CRQ - I	No Δ in rate of decline ↓ FVC and ↓FEV1 on NIV start.	NR	NR	NR	NR
Lyll 2001 (42)	Prospective	Yes, ALS with similar disability & no SDB.	27 Pts 11 control 16 NIV	Symptomatic ↑pCO ₂ and documented SDB	NR NIPPY Comfort, ERBG	NR	SF-36 – vitality I ESS – ↓ with NIV	NR	NR	I	NR	NR
Bourke 2003 (43)	Prospective	No	22 pts 10 compliant	Orthopnea or Symptoms or ↑pCO ₂ , or AHI>10	Inpatient VPAP/ST Noct sats, ABG, comfort	*	SF-36 – I CRQ - ↓ SAQLI -I ESS - I	↓rate of decline in FVC.	NR	NR	NR	Ranked benefit dependent on start criteria
Pinto 2003 (44)	Prospective	Yes, historical	42 Pts 24 standard 18 early	AHI > 15 and normal daytime ABG	NR NR NR	NR	NR	NR	NR	NR	NR	Survival improved with earlier initiation using AHI>15

Author year (Ref)	Study Type	Controls	# of Pts	Indication for Ventilation	Place of Initiation Ventilator Used Titration Method	Outcomes						
						Survival	HRQOL	Pulmonary Function	Sleep	Blood Gases	Cognition	Timing off Initiation
Farrero 2004 (45)	Retrospective	Yes, Before protocol	64 49 "early" 15 "late" or pre- protocol	Symptoms, VC<50%, ≥500ml ↓, pCO ₂ > 45, Noct desat	Inpatient PLV100 or VPAP/ST Comfort, ABG, Noct sats	↑ in non-bulb early grp	NR	NR	NR	NR		Survival on NIV & total survival time improved in non-bulbar group if done early
Lo Coco 2006 (46)	Prospective	Yes Intolerant pts	71 Pts 44 control 27 NIV	Symptoms or FVC< 50% or MIP<-60 or pCO ₂ ≥45 or Nocturnal desaturation	Inpatient Bilevel/ST Comfort, ABG, leaks, sympt	↑	NR	↓ rate of decline in FVC	NR	NR	NR	NR
David 1997 (21)	Retrospective	No	17 Pts	Abnormal PSG	NR bilevel NR	NR	NR	NR	I	I	NR	NR
Kleopas 1999 (47)	Retrospective	Yes, NIV<4hr/d or Refused NIV	122 Pts - 32 < 4 hrs/d - 52 refused - 38 NIV	Symptoms or FVC<50% or FVC 15% 3 mo decrease	NR Bilevel NR	↑	NR	↓ rate of decline in FVC (trend)	NR	NR	NR	NR
Bach 2002 (33)	Retrospective	No	86 Pts	NR	NR PLV100 NR	↑	NR	NR	NR	NR	NR	NR
Berkowitz 2006 (26)	Retrospective	Yes No NIV or Trach	118 Pts No NIV 52 Trach 23 NIV 43	Respiratory failure or imminent failure	NR Bilevel PSG	↑	NR	NR	I	NR	NR	NR
Lechtizin 2007 (48)	Retrospective	FVC<65% FVC≥65%	92 Pts 67<65% 25≥65%	No clear criteria	NR NR NR	↑ ≥ 65%	NR	NR	NR	NR	NR	Survival improved with NIV for FVC ≥ 65%

NR= not reported, SDB = Sleep Disordered Breathing

I = improved

* = survival correlated with compliance

↑ = increased

→ = unchanged

↓ = decreased

Study Characteristics

Of the 16 studies identified addressing the question of benefit or timing of NIV in ALS patients, only one was an RCT (37). An additional 15 prospective or retrospective studies were identified that contributed to the question of benefit or timing of NIV in this population. In many of prospective studies there is a control group; however, the validity of the comparator group is often questionable.

Difficulty arises in comparing these studies or performing a meta-analysis as the methodology varied from study to study. For example, the indication to initiate ventilation varied widely, and the place of initiation was not consistent or not reported at all. These studies constitute the sum of our current knowledge and, though significant methodological flaws are apparent, the finding of benefit is relatively consistent.

Outcomes

Survival

The only RCT with survival as a primary outcome was recently performed by Bourke (37). They screened 121 patients and ultimately recruited 92 patients to be followed every two months until randomization which was performed if they met one or both of the pre-defined criteria: orthopnoea with $P_{I_{max}}$ less than 60% predicted or symptomatic daytime hypercapnea. Ultimately, 41 were randomized and the data analyzed for all patients and then subdivided into “better” or “poor” bulbar function. Looking at all patients, those using NIV showed a modest survival advantage from randomization to death over those patients randomized to standard care excluding NIV: (219 (range 75-1382) days vs 171 (1-878) days). In the subgroup with “better” bulbar function, they showed a much longer survival time (216 (range 94-681) days vs. 11 (1-283) days) post randomization. There were six deaths of nine patients in the control group with better bulbar function within two weeks of enrollment. Five of the six had severe respiratory muscle weakness at enrollment. The “poor” bulbar function group showed improvement in HRQoL if receiving NIV, but no survival benefit was seen in NIV users, 222 (range 75-1382) days vs 261 (6-878) days). The mean duration of daily use in this group, however, was less than four hours. In addition, the numbers were small and not powered to show survival benefit in the subgroup with poor bulbar function.

Four prospective studies (38,39,41,46) and three retrospective studies (26,47,33) reported prolonged survival in those using NIV. In the largest of these studies, a retrospective chart review, the authors reported survival data on 122 patients with ALS (47). In that study, patients were divided into three groups: Those using bilevel more than 4 hours per day(hr/d), those using it less than 4 hr/d and those refusing bilevel. Bilevel was offered when the patients presented with symptoms of respiratory insufficiency, when their FVC dropped below 50% of predicted, or if their FVC dropped more than 15% within a three-month period. The mean FVC at the time of bilevel initiation or offer was less than 40% of predicted suggesting advanced disease. The group using bilevel more than 4 hr/d had a significantly longer survival from time of diagnosis than those refusing bilevel (35.5 ± 23.6 vs 29.5 ± 12.7 months), but the difference between those using bilevel more than 4 hr/d and those using it less than 4 hr/d was not statistically significant.

The survival benefit was modest in most of the reported studies; however, in one retrospective descriptive study reported by Bach (33) the survival benefit in selected patients with preserved bulbar function could be measured in years even when requiring continuous NIV.

Pulmonary Function and Gas Exchange

Four studies have reported the rate of decline of VC before and after initiation of NIV (41,43,46,33). Three of these studies (43,46,33) suggested a slowing of decline of lung function after successful initiation of NIV. One study (41) reported a decrease in VC after initiation of NIV which was not reported by others looking at pulmonary function (43,46,33).

Of those studies reporting gas exchange after initiation of NIV (21,28,42), all show an improvement with reduction of daytime pCO₂ after initiation of nocturnal ventilation.

Quality of Life

In the single RCT (37), improved HRQoL was reported for patients randomized to NIV compared with patients randomized to standard care with no NIV. In a subgroup analysis, those with “better” bulbar function experienced a large improvement across several measures of HRQoL for the group randomized to NIV. The sub-group of patients classified with “poor” bulbar function also showed improvement in HRQoL if receiving NIV, though the improvement was less marked.

In the remaining prospective studies reporting HRQoL (38,28,40-43), the authors consistently reported improvements in QoL in certain domains in those using NIV. Many different QoL tools have been used. They have included the short form health survey (SF-36), the chronic respiratory index questionnaire (CRQ), and the modified Calgary sleep apnea QoL index (SAQLI). In an early study an analog scale of life satisfaction was used. The Epworth sleepiness scale (ESS) has also been used to assess sleepiness thought secondary to sleep disordered breathing. Improvement in all domains of these HRQoL questionnaires was not seen. As physical function declines related to increasing disability, the domains addressing physical function worsened; however, domains pertaining to mental health, energy/vitality, social isolation, fatigue and mastery show sustained improvements.

Cognition

Improvement in two of seven cognitive tests with a trend toward improvement in two others was reported following treatment of documented sleep disordered breathing in one prospective study (28) looking specifically at this endpoint. In that study the authors concluded that nocturnal hypoventilation and sleep disturbance may cause cognitive dysfunction in ALS and that these deficits may be partially improved after NIV over a period of six weeks. They felt that this cognitive improvement was important and may have implications for improved HRQoL.

Place of Initiation of NIV

In many of the studies looking at NIV in ALS, the site of initiation of ventilation is not reported. The majority of studies in which the site of initiation is reported, initiate ventilation during an inpatient admission. A recent study from Italy (49) initiated NIV in hospital and found the time to tolerance of NIV in this setting to be 5 ± 2 days although the average admission was 12 ± 2 days. All 37 patients were tolerant of NIV at discharge and 35/37 patients, including those with severe bulbar dysfunction, remained on NIV after 1 year. Two studies report outpatient clinic initiation, both by the same author (39,41). None of the studies have compared initiation in different settings in an attempt to establish the most appropriate site of initiation of NIV.

Timing of Initiation of NIV

Five studies reported in Table 3-2 (40,43,44,45,48) try to address the issue of timing and many other studies speak indirectly to this question as the indications for initiation of ventilation may include symptoms alone without the requirement for an abnormal measure of lung function or hypoventilation (39,41,43,46,47). Orthopnea is often the symptom for which ventilation is started (38,39,41,45,47). Bourke’s study (43) strongly supports initiation of ventilation for symptoms.

The author reports that four patients were initiated on NIV for the sole indication of nocturnal desaturation without symptoms. Of the four patients, only one was compliant with NIV and continued to use it. Conversely, in the same study, the author reported the greatest benefit and compliance in patients that complained of orthopnea.

Fallat (11) made the observation in an early study looking at spirometry in ALS that most patients died within six to nine months of falling below a FVC of 50% of predicted. This led to the widespread use of this value to trigger initiation of ventilation and still appears in most review and guideline statements. One study exploring earlier initiation of NIV looked retrospectively at the survival of patients in whom NIV was started at a FVC % predicted of greater than or less than 65%. There were 67 patients in the standard therapy group and 25 in the early initiation group. There was a survival benefit from time of diagnosis to death in those starting NIV with a FVC > 65% of predicted. Of note, however, the authors comment that patients in the “early” group frequently, though not always, had pulmonary function or ABG abnormalities that would have qualified them for NIV by other conventional measures.

In the study of Ferraro (45), a protocol of systematic respiratory assessment was implemented to enable earlier identification of patients meeting criteria for ventilation and compared patients enrolled in the protocol to patients who were ventilated before the initiation of the protocol. Of note is that the survival on NIV was no different for the two groups as a whole. Only if the non-bulbar patients were analyzed did the survival on NIV and total survival time improve with the protocol. They also noted that the survival of hypercapnic patients with bulbar dysfunction who were tolerant of NIV improved over those that were not.

In a study by Pinto et al. (44), the authors compared a group of historical controls who received NIV for diurnal respiratory insufficiency with a group of ALS patients screened every three months with nocturnal oximetry and initiated on NIV when they demonstrated more than 15 periods of nocturnal desaturation per hour. The authors reported that survival was improved if NIV was started with evidence of nocturnal sleep disordered breathing, but prior to daytime blood gas abnormalities. However, when looking at the subgroup with bulbar dysfunction, the survival benefit was not detected suggesting that this conclusion may only apply to ALS patients with better bulbar function.

Type of Ventilator and Settings

A study comparing volume and pressure targeted ventilators has not been done in patients with ALS. In three studies examining the benefit of NIV in ALS, both types of ventilators were used in the same study (39,41,45) implying that the authors considered the two modes equivalent for the purpose of assessing benefit. Studies comparing the two modes have been reported on mixed populations (50-53). Schonhofer's study (52) included both restrictive and obstructive diseases, two processes with very different mechanics. The conclusion of these studies reporting on mixed groups was that either mode is appropriate for use in most patients. It is interesting to note, however, that in Schonhofer's study he reported about one-third of the patients to be bilevel “non-responders” with elevated PCO₂ and reduced nocturnal saturation when treated with BiPAP. In this study, “non-responders” were returned to volume ventilation. He concluded that the majority of patients successfully treated with volume-cycled ventilation could also be adequately maintained on pressure controlled ventilation; however, his data shows that some cannot be well ventilated on BiPAP and require a volume targeted mode. In other studies comparing the two modes of ventilation, authors report a patient preference in some. Bach proposed volume cycled ventilators in one study looking at noninvasive support in the ALS population given that the ventilator could then be used to breath stack to MIC as an aid to airway clearance (33).

Another question that remains unanswered is the optimal way to determine appropriate ventilator settings in this population. Looking at the protocols described in the studies reported in Table 3-2 there is no consistency in the method used. In fact, only eight of the 16 studies described how the ventilator settings were determined. Only one of the 16 studies used a polysomnography to establish ventilator settings (26). Three of the 16 studies (37,43,45), two by the same author, used nocturnal oximetry after initial empirically setting the ventilator. Six studies report using daytime ABGs or ear lobe gases to adjust ventilator settings (37,39,42,43,45,46). Seven studies report adjusting ventilation to patient comfort and symptoms (37,39,41-43,45,46). Most of the studies report using more than one criterion. There are advantages to the use of polysomnography in arriving at ventilator settings. Fanfulla (54) highlights patient ventilator asynchrony that may be missed without information available from a PSG. This study, however, did not include patients with ALS.

Another important question is whether a backup rate is required when applying ventilation with Bilevel pressure ventilators. Not all of the studies in Table 3-2 that recorded using bilevel stated whether the S or the ST mode was applied. Of those that did, all used the ST mode. Volume-cycled ventilators require a rate to be set.

Diaphragm Pacing/Inspiratory Muscle Training

Since 2007, diaphragm pacing has also been reported in 38 patients with ALS (55) and there is an ongoing trial targeting this therapy in 100 patients with ALS. The initial goal with this therapy was to reduce the rate of decline in lung function. The laparoscopic insertion of the electrodes into the diaphragm in patients with a forced vital capacity (FVC) of greater than 50% predicted has been shown to be safe with no mortality and low morbidity (56). Applied positive airway pressure (PAP) may still be required during pacing to avoid upper airway collapse. In the small number of ALS patients reported to date, there may be a slower rate of decline of lung function, which was extrapolated to a longer ventilator-free survival rate. Report of the larger series of ALS patients is pending; however, this technology is not yet approved for ALS patients in Canada.

As in other NMDs, inspiratory muscle training has been investigated in ALS patients. A recent study (57) looked at the effect on lung volumes and inspiratory pressures using threshold loads titrated to 60% of the SNP over weeks. The study was 12 weeks in duration and followed patients after inspiratory training ended. This study had a sham device and the patients appeared to be effectively blinded to the treatment. They suggested an overall trend for improvement in the inspiratory muscle training group. The Sham group, however also demonstrated some improvement in pressures during the study. Changes were not sustained after termination of the training period as has been noted in other patient populations. The authors cautiously interpreted their results as showing the potential for strengthening of respiratory muscles and delaying the restrictive defect, but warned of over-interpretation due to small sample size, short training period and the sham training effect. Given potential benefits they are proceeding with further clinical trials in this area.

Airway Clearance

The importance of airway clearance is highlighted in Section I - Airway Clearance. There have been studies conducted specifically in the ALS population, however, that warrant mention. One study (58) investigated predictors of ineffective cough during chest infections in patients with stable ALS. They found that a Norris bulbar scale of <29 (normal function is 39), PCF <4.25 L/sec and PCF/PVT (peak cough flow/peak velocity time) in stable ALS patients predicted ineffective cough with a chest infection and, therefore, suggested that assisted clearance

techniques be introduced when patients reach one or more of these thresholds. Another study in ALS patients (59) showed that PCF could be dramatically increased with various assisted-cough techniques, even in patients with bulbar dysfunction, a group in whom it has been challenging to achieve good clearance of airway mucous. Finally, a study assessing the efficacy of MI-E in stable ALS patients (60) also found that this technique could generate clinically effective PCF in all patients but those with very severe bulbar dysfunction (MIC=FVC).

Discussion

The bulk of the studies investigating outcomes of NIV use have been observational cohort studies. In some studies, attempts have been made to control for NIV and the control groups have included historical controls, consecutive patients recruited prior to use of NIV, ALS patients with similar disability but without respiratory failure, and patients that have either refused or been unable to tolerate NIV. Using these types of controls may be misleading as different phenotypic subtypes of ALS may have different survival rates. This is typically the case with bulbar onset or severe bulbar involved patients whose survival is generally significantly shorter than limb onset (3) and whose tolerance of bilevel may be poor (39,45,61). The single RCT was small and had the unfortunate random occurrence of a large number of patients with very severe respiratory muscle weakness being randomized to the control group. Their early deaths skewed the results in favour of the treatment group bringing into question the conclusion that NIV conferred a strong survival benefit in this subgroup of patients. Bulbar patients in Bourke's study (37) did not seem to show a survival benefit with NIV. It is of note, however, that the average duration of use of bilevel was less than four hours in these patients. The minimal duration of use to confer benefit with NIV has not been determined, though Kleopa (47) suggested that less than four hours may be inadequate though the results in this group did not reach significance.

Though the evidence is weak in these studies, it is relatively consistent in favor of benefit to patients able to tolerate NIV. In ALS patients, the survival benefit is modest in comparison to other diagnoses for which home ventilation is commonly recommended. The improvement in QoL, including improvements in measures of daytime fatigue and sleepiness, seems a more relevant endpoint in this patient population. Sustained improvements in HRQoL were seen in most studies. Most importantly, there was no deterioration in HRQoL with NIV use apart from expected changes in domains related to physical functioning secondary to increasing disability, which were also found in the control groups. Cognitive improvement felt to be related to treatment of documented sleep disordered breathing was also found in one study and may also have important implications to HRQoL (28).

When considering NIV in ALS patients it is important to acknowledge the difference in patients with preserved bulbar function and those with severe bulbar dysfunction as their tolerance of NIV and outcomes with NIV may be vastly different (39,45,61). Though bulbar dysfunction has frequently been an identified factor for poor tolerance of NIV, it does not preclude successful NIV in all affected patients and therefore a trial of NIV in bulbar predominant patients is reasonable. If tolerated, it has been shown to improve HRQoL, though its effect on survival is generally absent. Hypercapnic patients with bulbar dysfunction who tolerate bilevel seem to be the exception and did demonstrate a survival benefit in one study (45). As a result of the limited survival advantage in the bulbar sub-group it is reasonable to suggest a trial, however, if tolerance is poor and repeated trials are distressful to the patient there seems little point in persisting.

Even with ALS patients with preserved bulbar function, the improvement in survival with NIV is modest and measured in months, not years with isolated exceptions in the patient group with

well-preserved bulbar function, when compared to other patient populations to whom NIV is recommended. It is therefore important in this population to be ever cognizant of QoL as an important outcome measure.

Accepting that benefit does occur with NIV in this population, timing then becomes an important question. There seems little doubt that $FVC < 50\%$ predicted portends a poor prognosis with death occurring in less than nine months in an older study (11). The observation has been made that many patients are symptomatic before they reach this hallmark for ventilation. Some symptoms, such as orthopnea and excessive daytime sleepiness, correlate well with nocturnal respiratory disturbances (21) and also have been found to be associated with compliance and benefit (improved HRQoL) with NIV (43). It is important to note that orthopnea often begins when daytime PCO_2 is normal and when FVC is greater than 50% of predicted(21). It seems logical to incorporate such symptoms in the assessment that will lead to ventilation. Symptomatic daytime hypercapnea was the indication to ventilate in some studies that showed benefit and therefore, should an elevated PCO_2 and symptoms exist, the decision to ventilate is reasonably straight forward. In addition, the initiation of ventilation with symptoms of dyspnea or sleep disordered breathing plus any objective measure of muscle weakness would be supported by current literature. Initiation for asymptomatic physiologic changes such as nocturnal desaturation would be difficult to support with currently available data. In the study of Pinto (2003), it was not stated whether the patients with nocturnal desaturation were symptomatic (44). Though survival time on NIV in the early treatment group was prolonged, total survival was not clearly impacted by early ventilation. Without this information, screening of asymptomatic patients with the intent of initiating ventilation cannot be recommended. Poor compliance with ventilation in Bourke's study (43) of patients with nocturnal desaturation, but without symptoms would argue against this practice. However, following VC (upright and supine) or mouth or nasal pressures for the purpose of following disease progression and prognostication in asymptomatic patients is still a useful process.

Over recent years the trend has been to initiate NIV earlier before diurnal hypercapnea develops. One argument used is that NIV may slow the decline in VC as was suggested in several studies in which rate of progression of decline in VC before and after NIV was followed (43,46,33). This was interpreted as possible slowing of disease progression. The survival data reported above would argue against this however. The single study using higher FVC as a reason for earlier initiation did not, in fact, suggest that ventilation was started earlier, given that most of the "early" group already demonstrated other standard guideline criteria for initiation of ventilation. This study suggests that the upright FVC in itself may not be a good criterion to use for initiation unless it is very low.

Volume-cycled ventilators were used when NIV first came into practice for chronic respiratory failure. The introduction of bilevel pressure flow generators for sleep apnea and obesity hypoventilation provided a less costly option which also offered the advantage of leak compensation. These devices were rapidly introduced for ventilation of restrictive disorders and have become the initial preferred option. One caution with bilevel pressure devices is that most require a minimum expiratory pressure to avoid re-breathing and can be set with an end expiratory pressure of no less than four cm H_2O . In patients whose respiratory muscles have become very weak, this can cause increased work of breathing and patient-ventilator asynchrony with activation of expiratory muscles (54). One clear advantage of the volume-cycled ventilators is their ability to allow breath stacking for LVR and airway clearance.

The question of the need for polysomnography for initiation of ventilation and follow up of ALS is an interesting one. As stated above, patient ventilator asynchrony can occur and a

polysomnography would detect this. Unfortunately, sleep is poor in the ALS population for reasons other than sleep-related arousals and the sleep lab setting may accentuate these non-sleep related problems leading to limited data obtained. There are authors that argue both for (62,63) and against (64,65) a polysomnography in determining settings in neuromuscular patients, however, in all the studies assessing NIV in ALS, only one employed polysomnography, which suggests that benefit can be seen without the need for polysomnography. ALS is unique among the diseases for which assisted ventilation is prescribed in its rapid progression. There may be a long delay to obtain a polysomnography in many centers, a delay which these patients cannot afford. If there is difficulty in arriving at settings empirically, however, a polysomnography may be of value. As the survival benefit is modest as reported in most studies, one could argue that symptoms, which have a bearing on HRQoL, should be the primary outcome in these patients in which case use of polysomnography and also ABGs may be unnecessary. Of the 16 studies reported here, only six used ABGs to adjust settings. As many ALS patients, especially those with bulbar dysfunction may struggle adjusting to assisted ventilation, ABGs may be useful in trying to decide if the ventilator is having a physiologic benefit and in reassuring patients, but should not necessarily be considered a requirement.

In looking at the predominant type of sleep disordered breathing found in ALS (Table 3-2), mixed or central apneas or hypoventilation seemed most prevalent with obstructive events being much less common. This would argue for the requirement of a backup rate or ST mode when on BiPAP. Of those studies reporting the type of bilevel pressure ventilation used, all reported using ST mode. Other studies reported using a volume-cycled mode of ventilation which required setting a respiratory rate.

Though the majority of the studies reporting on NIV in ALS report starting ventilation in an inpatient setting, there were studies reporting outpatient initiation and there are no studies comparing the two specifically in ALS patients. Cost and occupancy constraints in hospitals are increasing and there were two recent reports comparing site of initiation in mixed populations and more such studies are currently being conducted. In Canada the current practice varies widely and is largely dependent on personal experience and resources.

At present there is inadequate evidence to support the use of diaphragm pacing in this population as a means of delaying onset of ventilation and potentially prolonging survival. In addition, there is no convincing evidence for inspiratory muscle training in this population though this is an area of active research.

Planning for end-of-life care is critical in this population and discussions surrounding the course of ALS and treatment options should begin early and lead to a clear statement of goals of care and a personal directive. Patients die without ventilatory support, by withdrawal of this support and on support. In all of these circumstances, palliation of symptoms of dyspnea and anxiety is critical and involves adequate doses of both narcotics and benzodiazepines. (66)

Conclusion

The majority of the studies investigating outcomes of NIV use have been observational cohort studies, with only a single RCT to date. Although the evidence base is modest, it is relatively consistent in favour of benefit to patients able to tolerate NIV. In ALS patients, the survival benefit is modest compared with other diagnoses for which HMV is commonly recommended. The improvement in QoL, including improvements in measures of daytime fatigue and sleepiness, seems to be a more relevant end point in this patient population. Sustained improvements in QoL were seen in most studies. Most importantly, there was no deterioration

in QoL with NIV use apart from the expected changes in domains related to physical functioning secondary to increasing disability. Initiation of ventilation for symptomatic daytime hypercapnia or orthopnea secondary to muscle weakness seems clear. Earlier initiation for nocturnal hypoventilation with normal daytime PCO₂ or based on higher FVC may be of benefit, but the evidence to date is limited.

Research Questions

1. Does early initiation of NIV improve outcomes in ALS? In particular, should patients with bulbar impairment be provided earlier trials of NIV to enhance tolerance of NIV and successful ventilation?
2. Does diaphragm pacing have a role in ALS?
3. What is the optimum manner in which to follow patients with ALS using NIV?
4. Is inspiratory muscle training effective in delaying time to ventilation?

Recommendations

The following recommendations are based on limited evidence from the literature search and consensus of the HNV expert panel.

1. Regular monitoring of ALS patients is advised from time of diagnosis every two to six months and varies with anticipated rapidity of disease progression and should include the following:
 - a) Symptom review to include orthopnea, dyspnea, poor sleep, excessive daytime sleepiness, poor concentration, morning headache.(GRADE 1C)
 - b) Measurement of sitting FVC.(GRADE 1C)
 - c) Measurement of one or more of the following: supine VC, SNP, P_{Imax} (MIP). (GRADE 1C)
 - d) Measurement of ABG, or end-tidal CO₂ (ETCO₂) when hypercapnia is suspected.(GRADE 1C)
 - e) Nocturnal oximetry ± transcutaneous CO₂ (tCO₂) when symptomatic sleep disordered breathing is suspected. (GRADE 2C)
 - f) Measurement of PCF. (GRADE 1C)
2. NIV should be offered to patients with any one of the following:
 - a) Orthopnea (GRADE 1B)
 - b) Daytime hypercapnia (GRADE 1B)
 - c) Symptomatic sleep disordered breathing (GRADE 1C)
 - d) FVC < 50% predicted (GRADE 1C)
 - e) SNP < 40 cmH₂O or P_{Imax} < 40 cmH₂O (GRADE 1C)
3. Ventilator settings should be adjusted for optimal patient comfort and improvement of symptoms. ABGs and/or nocturnal oximetry and/or polysomnography are not required, but may be helpful in some circumstances.(GRADE 1C)
4. When bilevel pressure ventilators are used for NIV, a backup rate is recommended. (GRADE 1C)
5. Indicators of the effectiveness of ventilatory support should include symptom resolution, overnight oximetry and/or ETCO₂. (Grade 1C)
6. NIV should be considered the preferred option for ventilation even when ventilation is required 24 h per day. Elective tracheostomy ventilation may be considered and is

dependent on regional resources and careful discussion with the patient and caregivers. (GRADE 1C)

7. Long-term invasive ventilation can be offered after acute respiratory failure requiring invasive ventilation, if the patient and caregivers fully understand the consequences and appropriate support is available. (GRADE 2C) (See Section II - Transition to Home)
8. Lung volume recruitment maneuvers should be introduced with declining VC. (GRADE 1C) (See Section I - Airway Clearance)
9. Methods to assist secretion clearance should be initiated when PCF is less than 4.25 L/sec or the Norris bulbar score is <29. (GRADE 1C)

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SECTION IV.

HMV for Patients with Central Hypoventilation Syndrome (CHS)

Introduction

Hypoventilation can develop as the result of two mechanisms. One mechanism results when loads placed on the ventilatory muscles are excessive. Excessive loads can occur when the muscles are weak and unable to cope with normal mechanical lung function, i.e. muscular dystrophy, or when the muscles are not weakened but there is an excessive load presented by abnormal lung mechanics, e.g. obstructive lung disease. The second mechanism occurs when there are no excessive loads, lung function is normal and there is no evidence of ventilatory muscle weakness. In this situation there is diminished ventilatory drive from the respiratory centers in the brainstem. These centers have their own rhythm but are normally stimulated by hypercapnia or hypoxia, thus maintaining normal ABGs. Ventilatory drive is believed to arise from the medulla (pre-Botzinger complex) and pons. Inspiratory and expiratory neurons in the medulla then send descending neurons to spinal motoneurons that innervate the ventilatory muscles. Accordingly, damage to the brainstem centres can lead to reduced ventilatory drive and result in CHS.

Review of Literature

In many cases a clear-cut pathology is identified as a cause of the CHS (See Table 4-1). In other cases no neurological abnormality is identified and this is idiopathic central hypoventilation syndrome also known in the past as Ondine's curse. Recent evidence has emerged which probably explains the cause of many cases of idiopathic CHS: as a mutation in a paired-like homeobox gene (PHOX2B) (1). In children this is the main cause of congenital CHS (C-CHS) (2). The finding that adults with late-onset central hypoventilation syndrome (LO-CHS) in many cases have a similar gene mutation indicates the need for these mutations to be examined in any adult with idiopathic or unexplained CHS (3). There is autosomal dominant inheritance of this mutation. Parents and siblings of C-CHS patients should be tested for the mutation as they may be potential hypoventilators (3). Parents may be asymptomatic but carriers of the mutation, as there may be incomplete penetrance. Many parents may be negative which suggests a high spontaneous mutation rate. The PHOX2B gene encodes a key transcription factor in the development of the autonomic nervous system and many cases of C-CHS are associated with Hirschsprung's disease where dysfunction results from abnormalities in cells arising from the neural crest. The degree of hypoventilation is more severe in patients with longer alanine expansions as part of the gene mutation. Some present at birth with profound hypoventilation whereas others with short alanine expansions may have LO-CHS and present in childhood or as adults. There are other genetic mutations leading to CHS in association with Parkinson's disease i.e. Perry Syndrome (4,5) or in association with Nemaline myopathy (6) (Table 4-1). In the pediatric population a very rare condition termed rapid-onset obesity with hypothalamic dysfunction, hypoventilation, and autonomic dysregulation (ROHHAD) has been identified but is not explored further in this section.

Sleep is associated with worsening hypoventilation in most patients with CHS and daytime ventilatory responses to hypercapnia or hypoxia are absent (18). This worsening in sleep is related to some well-established effects of sleep on ventilatory drive. During sleep in normal subjects there is reduced wakefulness drive to breathe as originally described by Orem (7). This wakefulness drive is thought to arise from cortical influences, whereas at night ventilation is largely a brainstem function (autonomic). Ventilatory responses to loaded breathing are reduced during sleep (8). During REM sleep ventilatory responses to chemical stimulation (CO_2 , O_2) are reduced (9). Similarly, ventilatory drive in response to loaded breathing during non-REM sleep is

reduced compared to wakefulness (10). Accordingly patients with CHS tend to have a reduced tidal volume during sleep and frequently exhibit central apneas. Polysomnography reveals no increase in ventilation in spite of increasing CO₂ levels during the night. Central sleep apnea occurs probably due to the shape of the ventilation/PCO₂ curve. The shape of this curve dictates that, when CO₂ is elevated, small increases in ventilation lead to relatively large reductions in PCO₂. Decreases in PCO₂ below the apnea threshold then result in apnea (11). Typically these patients have normal conscious control of breathing, i.e. can ventilate normally when asked to (12,13).

The diagnosis of CHS is best done by standard polysomnography with the addition of a measure of CO₂ such as transcutaneous CO₂. A progressive elevation of CO₂ during sleep supports nocturnal hypoventilation and confirms the severity. An early morning ABG can also confirm the degree of hypoventilation. In the absence of abnormal lung or ventilatory muscle function the diagnosis of CHS is established. Imaging of the brainstem should be performed to exclude unsuspected acquired causes of CHS (see Table 4-1). Where no cause of CHS is determined, genetic analysis to identify the PHOX2B gene is advised.

Patients with CHS present with varying degrees of severity. Severe C-CHS presents at birth with profound hypoventilation which requires continuous invasive ventilatory support. Alternatively, adults presenting in later life, for example with LO-CHS or an acquired form of CHS, may initially only have nocturnal hypercapnia. Eventually these patients usually progress to diurnal hypercapnia with daytime symptoms. These daytime symptoms commonly include morning headaches, sleepiness and confusion, and dictate the need for nocturnal ventilatory support, if not already initiated.

Table 4-1. Etiology of Central Hypoventilation Syndrome

Acquired Brainstem Disease	Cerebrovascular accident Tumor or space occupying lesion Syringomyelia Post poliomyelitis Trauma Arnold Chiari malformation CNS infection Neurodegenerative processes Multiple system atrophy
Congenital CHS	PHOX2B mutations Perry Syndrome Nemaline myopathy
Idiopathic	

The literature search revealed 10 articles reporting on the management of CHS patients. Due to the rarity of CHS there is little evidence to support an optimal approach to management. The largest reported follow-up in CHS is in C-CHS (14-19). Mechanical assisted ventilation in the home is the main form of nocturnal ventilatory assistance. These reports are all retrospective case series. Vanderlaan(17) reported long term outcomes in 196 affected children. Weese-Mayer(18) reported long-term outcome on 32 children. Trang et al (2) reported 43 long-term survivors of CCHS. Oren et al. (15) reported on six children with C-CHS. If ventilation is severely affected at birth and continuous ventilatory support is required, invasive ventilation via a tracheostomy is needed. In this situation and as time progresses phrenic pacing has been used in the daytime resulting in improved mobility and freedom from the ventilator (14,17). In many cases, however, nocturnal ventilatory support alone is required and then NIV is sufficient

(17,19). Trang et al. found that only three of the 50 subjects required 24 h support after long term follow-up(2). Also in Vanderlaan's series (mean age 10 yrs) 82% required ventilatory support only during sleep. Thirty-four percent could do this at birth and 66% by one year. The majority were decannulated between ages 6-11 when they could adjust to NIV. 40 of the 196 patients had phrenic pacers, 40% of whom used their pacers just at night, whereas 17(43%) required continuous ventilation and used their ventilators at night. These patients used their pacemakers only in the daytime often to improve mobility. In two subjects the pacer was used in the daytime with NIV at night thus allowing removal of the tracheostomy. A recent ATS statement on the management of C-CHS has made recommendations which recognize that these patients need invasive ventilation when presenting at birth and a variety of ventilatory supports depending on their situation later in life (20). Adults with acquired CHS or one of the other forms of congenital CHS usually manage with NIV alone but may also require invasive ventilation or phrenic pacers depending on the circumstance. Management of the C-CHS in children is complicated and best done under the supervision of specialized clinics. The transition to adulthood in these patients warrants close attention and carefully designed care plans may be best established via "Transition Clinics".

Diaphragmatic Pacing

In 1972, Glenn et al (21) reported diaphragmatic pacing by phrenic nerve stimulation in high level quadriplegic patients. Initial attempts utilized high frequency stimulation (25-30 Hz) and were only partially successful due to lack of adequate muscle conditioning. The result was that the diaphragm would fatigue or become injured. Subsequently with an appropriately low frequency stimulus (7-10 Hz) diaphragm conditioning was shown to be possible (22). Long-term follow-up (average 13.7 years) revealed about half of these patients (6/12) maintain fulltime pacing. Although there is the potential for phrenic nerve damage, none has been reported and threshold currents have remained stable (22). Reasons for returning to mechanical ventilation in these patients on chronic pacing were mainly due to lack of social support, finances or knowledgeable caregivers. The advantages of diaphragmatic pacing in spinal cord injury are independence from mechanical ventilation allowing more mobility as well as other features such as improved speech and smell. Phrenic pacing has also been shown to be effective in CHS (14,23). Chen et al (14) report long-term follow up on 16 patients with C-CHS treated with pacing. The pacemaker provided effective ventilation in the daytime for C-CHS patients requiring 24 h support with a great improvement in patient mobility. Mechanical ventilation was still used at night but in those able to switch to nocturnal support pacing alone sufficed. In many patients with phrenic pacers, a tracheostomy is required to prevent upper airway obstruction. This obstruction occurs when the diaphragm contracts and the subsequent negative intra-airway pressure leads to passive collapse of the upper airway. In addition, a thoracotomy is required to place the electrodes and there is the potential risk of damage to the phrenic nerves (24). Thoracoscopic placement of the electrodes has been done in the pediatric population which could potentially limit the problem of a thoracotomy in adults (25). To assess patients for diaphragmatic pacing the phrenic nerves have to be intact. Thus, in spinal cord injury the level usually needs to be above C-3 without extension into lower cervical levels.

Diaphragmatic pacing by phrenic stimulation is quite expensive and this has in part limited the widespread use of this technique. More recently pacing by intramuscular electrodes placed via laparoscopy (Diaphragm Pacing Stimulation [DPS]) has been shown to be a feasible and more economical approach to diaphragm pacing (26,27). The phrenic nerves again need to be intact and the optimal placement of the electrodes requires mapping of the undersurface of the diaphragm to determine points of maximal nerve activation (27). Long-term experience with this procedure is developing in adults and in the pediatric population (28). In high-level quadriplegia or in CHS when continuous ventilatory support is required, DPS offers the multiple advantages

of freedom from the mechanical ventilator (28). Currently the hardware remains externalized with wires undermined to the subclavicular region.

Discussion

The literature review found most information regarding CHS in the pediatric literature where large case series were identified. In the adult population there is little data on long-term follow up reported and most reports focus on causes of acquired CHS. The results in children suggest that C-CHS can be quite profound at birth and ventilatory support more intense. As the child matures, however, breathing usually requires support at night alone. The options for nocturnal support include invasive ventilation via tracheostomy, NIV or diaphragm pacing. There is a preference for NIV or pacing as the child matures with the aim of decannulation (17). In the less common situation where 24 h ventilation is required diaphragm pacing allows for increased mobility in the day, and in some cases NIV can suffice at night with the potential for decannulation. Alternatively, NIV may be adequate for 24 h ventilator support when the patient is at the age to be capable of adopting it

Conclusion

In the adult population, there are little data regarding long-term follow-up, with most reports focusing on describing the causes of acquired CHS. In this setting, nocturnal NIV is often all that is required. In the pediatric population, C-CHS can be quite profound at birth, requiring continuous invasive ventilator support; however, as the child matures, breathing may require support at night only (17,19,22). The options for ventilator support include positive pressure ventilation (PPV) via tracheostomy, NIV or diaphragm pacing (22,23,27). . Transition clinics for children are important in providing a care plan, particularly for the more complicated patients with C-CHS as they move into adulthood.

Research Questions

1. What is the phenotypic expression of the different mutations in the PHOX2B gene? More descriptive data is needed to aid with identification and long term management of these patients
2. Should patients using diaphragm pacing rest their diaphragms at night using positive pressure ventilation?

Recommendations

The following recommendations are based on limited evidence from the literature search and consensus of the HMT expert panel.

1. The diagnosis of CHS in adults with less severe hypoventilation is best made by standard polysomnography with the addition of transcutaneous CO₂ or early morning arterial PCO₂ (GRADE 1C)
2. Once the diagnosis of CHS is established, it is strongly recommended that acquired causes should be excluded by magnetic resonance imaging (MRI) of the brainstem. (GRADE 1C)
3. Patients with CHS and no known cause should undergo genetic screening for the PHOX2B gene mutation. (GRADE 1C)
4. For patients confirmed to harbour the PHOX2B mutation, first-degree relatives should be offered genetic testing and screening for hypoventilation. (GRADE 1C)

5. CHS patients who require only nocturnal ventilatory support may be managed by NIV with a backup rate or diaphragmatic pacing. (GRADE 1C)
6. Severe CHS, mainly seen in C-CHS requires continuous invasive ventilatory support at birth, but as the child matures daytime diaphragmatic pacing can markedly improve mobility and in some cases NIV alone may suffice at night. (GRADE 1C)

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SECTION V

Long-Term Noninvasive Positive Pressure Ventilation in Patients with Stable COPD

In this section, noninvasive positive pressure ventilation (NIPPV) will replace 'NIV' because the term is commonly used in the COPD population.

Introduction

The goal of COPD treatment is to slow disease progression, reduce the frequency of exacerbations, alleviate dyspnea, improve exercise tolerance, improve health status and reduce mortality (1). This section discusses the relevance of long-term NIPPV in the context of stable COPD, considering the impact of this treatment strategy on these outcomes. Although several physiological outcomes such as ABGs, work of breathing and respiratory muscle strength can be improved by long-term mechanical ventilation, the clinical relevance of these outcomes from the perspective of the patient and/or health care system is uncertain.

Review of Literature

The 1996-2010 literature search strategy identified 17 studies evaluating the effects of NIPPV in patients with COPD. Two studies were retrospective (2,3) and three had a non-randomized prospective design (4-6). During the 1996-2010 period, we retrieved seven short-term (six weeks or less) (7-13) and five long-term (three months or longer) RCTs on this topic (14-18). We also found one randomized study comparing high versus low intensity NIPPV in 17 patients with COPD (19). This study will not be considered to inform treatment recommendations because of its short duration and because it was primarily a physiological study. For the purpose of providing guidance on the use of long-term NIPPV for patients with COPD, only RCTs of at least three-months duration will be considered (n = 5). This decision was made by the HMT guidelines committee because longer-term studies provide the highest level of evidence.

We are aware of a European multicentre trial that has been presented only in an abstract form. Because of limited information available from this study, it will not be discussed further (20). A UK study (21) evaluating NIPPV in hypercapnic patients with COPD after an episode of acute hypercapnic exacerbation is currently ongoing. Two long-term randomized cross-over trials published before 1996 (22,23) will also be considered for the present document. Thus, the recommendation about the use of NIPPV in COPD will be informed from a total of seven long-term (> 3 months) RCTs. Results of these trials and their inclusion criteria are summarized in Table 5-1 and table 5-2.

Two systematic reviews are available on this topic (24,25). A recent review of the literature was also consulted (26). The following COPD treatment guidelines were reviewed: The Canadian COPD guidelines (1), the GOLD guidelines (27), the National clinical guideline on management of chronic obstructive pulmonary disease in adults in primary and secondary care (28), and the ATS/ERS position paper on the treatment of COPD guidelines (29).

Table 5-1. Literature Search Results of HMV for Long-term NIV in Patients with Stable COPD

Author Year (Ref)	Study Type	# of Pts.	Outcomes					
			Dyspnea	Quality of life	Exercise capacity	Sleep	Mortality	Hospitalization
Strumpf, 1991 (22)	Randomized, cross-over NIV vs. usual care	23	No change	Not assessed	No change	No change	Not assessed	Not assessed
Meecham Jones, 1995 (23)	Randomized, cross-over NIV + LTOT vs. LTOT alone	18	Not assessed	Improved SGRQ symptom scores	No change	Improved sleep time and efficiency	Not assessed	Not assessed
Gay, 1996 (14)	Randomized, parallel group NIV vs. sham NIV	13	Not assessed	Not assessed	No change	No improvement	Not assessed	Not assessed
Casanova, 2000 (15)	Randomized, parallel group NIV + LTOT vs. LTOT alone	52	Reduced dyspnea	Not assessed	Not assessed	Not assessed	No change	No change at 1 year
Clini, 2002 (16)	Randomized, parallel group NIV + LTOT vs. LTOT alone	90	Reduced MRC scores	No change in SGRQ, improved MRF-28	No change	No change	No change	No change
Duiverman, 2008 (17)	Randomized, parallel group NIV + rehabilitation vs. rehabilitation alone	66	No further improvement in CRQ dyspnea subscale with NIV	No further improvement in total CRQ score with NIV Larger improvement in the MRF-28 cognition domain and total score with NIV	No further improvement in exercise capacity with NIV	Not assessed	Not assessed	Not assessed
McEvoy, 2009 (18)	Randomized, parallel group NIV + LTOT vs. LTOT alone	144	Not assessed	No change in SGRQ Deterioration in several subscales of the SF-36.	Not assessed	Increased % REM sleep	Improved survival	No change

Abbreviations: NIPPV: noninvasive positive pressure ventilation; LTOT: long-term oxygen therapy; SGRQ: St. George's Respiratory Questionnaire; MRC: Medical Research Council; CRQ: Chronic Respiratory Questionnaire; MRF-28: Maurgeri Foundation Respiratory Failure Questionnaire; SF-36: Short Form Health Survey.

Table 5-2. Inclusion criteria in studies of long-term NIPPV in Patients with Stable COPD

Author (Year)	Diagnosis	Blood Gas	NIV
Strumpf, 1991 (22)	FEV ₁ < 1L	No pre-established criteria. Mean PaCO ₂ = 49 (range 35-67)	IPAP = 15 EPAP = 2
Meecham Jones, 1995 (23)	FEV ₁ < 50% predicted	PaO ₂ < 60 mmHG PaCO ₂ > 45 mmHG	IPAP = 18 EPAP = 2
Gay, 1996 (14)	FEV ₁ < 40% predicted	PaCO ₂ > 45 mmHG	IPAP = 10 EPAP = 2
Casanova, 2000 (15)	FEV ₁ < 45% predicted	No pre-established criteria Mean PaCO ₂ = 51 mmHG	IPAP = 12 EPAP = 4
Clini, 2002 (16)	FEV ₁ < 1.5L	PaCO ₂ > 50 mmHG	IPAP = 14 EPAP = 2
Duiverman, 2008 (17)	FEV ₁ < 50% predicted	PaCO ₂ > 45 mmHG	IPAP = 20 EPAP = 6
McEvoy, 2009 (18)	FEV ₁ < 1.5L or < 50% predicted	PaCO ₂ > 46 mmHG	IPAP = 13 EPAP = 5

Abbreviations: FEV₁: Forced expiratory volume in 1 s; IPAP: inspiratory positive airway pressure (PAP); EPAP: expiratory PAP.

Outcomes

Dyspnea

Casanova et al used the MRC dyspnea scale and the Borg dyspnea scale to show that at three months there was a significant improvement in both scales in the NIPPV + O₂ group compared with the standard medical care group (15). However, by the sixth month, only the reduction in Borg dyspnea score was still statistically significant between the two groups (reduction of one unit). Clini et al. used the MRC dyspnea score and reported a reduction in dyspnea at 12 and 24 months in the NIV + O₂ group compared to the O₂ group (16). At 24 months, the difference in MRC dyspnea score amounted to 0.6 [95% CI: 0.15 to 1.05]. Stumpft et al., using the Mahler scales of dyspnea, did not report a reduction in dyspnea with NIPPV (22). The data of Gay and colleagues are difficult to interpret since only subjective data were presented about dyspnea (14). In one study, the use of NIPPV in association with pulmonary rehabilitation did not lead to a further reduction in dyspnea compared to pulmonary rehabilitation alone (17).

Quality of Life

HRQoL was assessed in two studies. Meecham Jones et al, in a cross over trial, reported a clinically (larger than -4) and statistically significant improvement in the St. George's Respiratory Questionnaire (SGRQ) symptom score after three months of treatment with NIPPV + O₂ compared to a period of similar duration with O₂ alone (23). In this study, the changes in SGRQ impact and total scores were improved compared to O₂ alone but not in comparison to baseline. The changes in SGRQ scores at 24 months between the NIPPV + O₂ group and the O₂ group in the study of Clini et al. were neither clinically or statistically significant (16). However, there was an improvement in the Maugeri Foundation Respiratory Failure Questionnaire (MRF-28) total score in the NIPPV + O₂ group compared to the O₂ group. The MRF-28 questionnaire was specifically designed to assess HRQoL in respiratory failure. NIPPV led to larger improvement

in MRF-28 cognition domain and total score when associated with pulmonary rehabilitation in comparison with pulmonary rehabilitation alone (17). In contrast to several studies reporting some improvement in HRQoL with NIPPV, McEvoy and colleagues found deterioration of several subscales of the SF-36 with NIPPV, suggesting that in some patients this treatment may be associated with negative impact on general health status (18).

Exercise Capacity

In one study, there was no improvement in treadmill walking time with NIPPV versus standard care (22). The six-minute walking distance has been an outcome in three studies (14,16,23). Meecham Jones reported a 53 m improvement in 6MWD [95% CI -37 to 143 m] (23). Gay et al reported a 13 m improvement in 6MWD [95% CI -55 to 81 m] (14). Clini et al reported no improvement in the 6MWD with long-term NIPPV (16). NIPPV in association with pulmonary rehabilitation did not further improved exercise tolerance compared to pulmonary rehabilitation alone (17).

Sleep

The impact of long-term NIPPV on sleep efficiency was evaluated in 4 studies (14,16,22,23). Only Meecham-Jones and colleagues reported improved sleep efficiency while the two remaining studies did not report a positive impact of long-term NIPPV on sleep quality. In the study of Clini et al., sleep was not improved with NIPPV. A modest improvement in sleep architecture has been reported by McEvoy and colleagues (18).

Mortality

Mortality could be assessed in the three trials with longer follow-up (15,16,18). In two trials, mortality was unaffected by NIPPV + O₂ when compared to O₂ alone (15,16). In contrast, McEvoy and colleagues reported a survival benefit of NIV + O₂ when compared to O₂ alone, when mortality curves were adjusted for baseline characteristics (hazard ratio: 0.63 [95% CI: 0.40-0.99, p = 0.045]) (18).

Hospitalization

The reduction of hospitalization has been an outcome in two trials (15,16). Casanova did not report a reduction in acute exacerbation, hospitalization and intubation with long-term NIPPV at one year, although the number of hospitalizations and intubations were lower at three months in the NIPPV + O₂ group in comparison with O₂ alone (15). Clini et al reported that, in comparison with the 3-year period preceding the study, there was a reduction in the risk of hospitalization with NIPPV + O₂ group but not in the O₂ group where the risk of hospitalization tended to increase (16). However, during the trial, there differences in the hospitalization rate and ICU admission rate between the two treatment groups were not statistically significant.

Review of the Current COPD Treatment Guidelines

The current COPD treatment guidelines are not explicit about the use of long-term NIPPV in patients with COPD. The CTS Canadian COPD treatment guidelines state that “there was insufficient evidence to recommend the use of NIPPV in hypercapnic patients with stable COPD” (1). The GOLD executive summary on COPD treatment recommendations mentions that “although long-term NIPPV cannot be recommended in patients with chronic respiratory failure due to COPD, the combination of NIPPV with LTOT may be of some use in a selected subset of patients, particularly in those with pronounced daytime hypercapnia” (27). Likewise the NICE concludes that “adequately treated patients with chronic hypercapnic ventilatory failure who have required assisted ventilation (whether invasive or noninvasive) during an exacerbation or who are hypercapnic or acidotic on LTOT should be referred to a specialist centre for consideration of long-term NIPPV” (28).

Discussion

Conducting a clinical trial investigating the efficacy of long-term NIPPV in patients with COPD is challenging. By definition, patients involved in these trials suffer from advanced chronic respiratory failure and, in some instances, from preterminal disease. A high dropout rate and a multitude of adverse events are, therefore, expected during such a trial. One problem in trying to interpret the current literature is the heterogeneity of the study population and the difference in the degree of ventilatory support among studies. Studies were either very small (14,22,23) or the investigators were unable to meet the predefined sample size to ensure sufficient statistical power to address the outcomes of interest (15,17,18).

Our interpretation is that the current literature does not support the use of NIPPV in stable patients with COPD with chronic hypercapnic respiratory failure. The dyspnea data are difficult to interpret considering the different dyspnea scales that were used in the different trials. In one study, the reduction in Borg dyspnea score was statistically significant and probably clinically significant, with a reduction in one unit occurring in the NIPPV group compared with no change in the control group (15). In another study (16), a 0.6 point difference in the MRC dyspnea score in favor of NIPPV was reported. The dyspnea data can probably be viewed as positive, although of modest magnitude and of uncertain clinical importance. The impact of NIPPV on HRQoL data was assessed in four studies that reached different conclusions on this issue (16-18,23). Although NIPPV may improve HRQoL as assessed by the SGRQ or by the CRQ when associated with LTOT (23) or rehabilitation (17), the largest studies reported no improvement in SGRQ scores (16,18). Using a questionnaire specifically designed to assess HRQoL in respiratory failure, evidence supporting improved HRQoL has been reported (16,17). In contrast, one study suggested that HRQoL may deteriorate with NIPPV (18). However, the clinical interpretation of this questionnaire is uncertain. Overall, it is difficult to draw a clear conclusion on the impact of NIPPV on HRQoL from the published evidence.

The impact of NIPPV on exercise tolerance, as assessed by the 6MWD, and on sleep quality is inconclusive (14-16,23). The initiation of long-term NIPPV in addition with O₂ was not associated with a reduced risk of hospitalization during long-term follow-up (12-24 months) when compared with O₂ alone (15,16). Finally, NIPPV did not prolong survival in two studies involving patients with stable COPD (15,16). A survival advantage of NIPPV when used in conjunction with LTOT compared with LTOT alone has been reported (18). The biological plausibility of this study is questionable because the level of positive pressure applied was low and failed to improved daytime PaCO₂.

Despite the limitations and the lack of clear supportive evidence, long-term NIPPV is widely used in patients with COPD. In some countries, COPD is one of the most rapidly rising indications for long-term ventilatory support (30). This is not trivial considering the large COPD population and the potential economic impact associated with long-term NIPPV in this population. Some experts would consider long-term NIPPV in patients with COPD and chronic hypercapnia experiencing repeated bouts of acute respiratory failure requiring ventilatory support in the hospital. The hope here is that this will reduce health care use (2,28). Given the lack of certainty about the efficacy of NIPPV in this patient population, isolated PaCO₂ elevation is unlikely to represent a useful clinical indication (26).

Technical Aspects of NIV in COPD

Some generalizations can be made about the technical aspects of long-term NIPPV in patients with COPD. First, pressure ventilators (bilevel positive pressure ventilation) are, by far, the most frequently used devices (30). These ventilators are usually interfaced with a nasal or full-face mask and the necessity of tracheostomy in these patients is rare. Clinical experience with long-

term NIPPV in COPD reveals that the benefits, if any, are more likely to occur in patients with stable PaCO₂ level greater than 55 mmHG (21) and when the level of inspiratory positive pressure is relatively high (greater than 15-18 cm H₂O). The recommended level of expiratory pressure is usually low, between 2-5 cm H₂O ensuring comfort while helping to reduce the work of breathing by counterbalancing the effect of intrinsic PEEP that may be present in this patient population (30). Problems with observance and/or tolerance to PPV are also common. Fifteen to 40% of patients enrolled in clinical trials were not adherent or did not tolerate the proposed ventilatory support (14,15,17,18,22).

Special Consideration of the Tracheostomized Patients with COPD

Patients with COPD may survive an episode of acute ventilatory failure treated with invasive mechanical ventilation in the intensive care unit and be discharged to the medical ward or to a long-term care facility with a tracheostomy in place. Specialized weaning units involving multidisciplinary care may be useful to achieve tracheostomy removal in these individuals (32-34). The experience reported by specialized weaning units indicates that in the majority of patients, the tracheostomy can be removed, usually within 3 months, and that the majority survive to hospital discharge, some requiring NIPPV (32-34). In some patients NIPPV can be used to assist weaning from the tracheostomy (34). A referral bias is likely to influence the outcome reported in studies from specialized weaning units as patients that they receive are selected as having survived an acute illness before being transferred. At this stage of the disease, patients with COPD usually have a poor outcome with a mean survival rate of 26 months in one study and a high likelihood of hospital readmission (34,35). Little is known about HRQoL and functional status in these patients.

Special Consideration of the Overlap Syndrome

Obesity, obstructive sleep apnea and COPD are common medical conditions; their concomitant presence in the same individual is therefore not unusual. The coexistence of obstructive sleep apnea and COPD is often coined the *overlap syndrome* (36). Obesity and sleep apnea may lead to hypercapnic respiratory failure when associated with airflow obstruction. This situation should be suspected when the degree of airflow obstruction is milder (FEV₁> 40% predicted) than usually seen in a *typical* case of hypercapnic respiratory failure that is solely due to advanced COPD. The overlap syndrome should be differentiated from chronic hypercapnic respiratory failure due to advanced COPD because these two conditions may require a different treatment (recommendation #3). If obstructive sleep apnea is suspected in a patient with COPD, a full sleep study may be warranted to obtain a definitive diagnosis. The overlap syndrome may be treated successfully with nasal continuous positive airway pressure (CPAP) and nocturnal oxygen.

Conclusion

The current literature of RCTs does not provide convincing evidence that NIPPV is effective in improving patient-oriented clinical outcomes such as dyspnea, exercise tolerance, HRQoL, hospitalization and survival in COPD.

Research Questions

1. The utility of chronic NIPPV in stable COPD patients is unclear. Do patients with repeated exacerbations and elevated pCO₂ benefit in terms of health related outcomes on NIPPV?
2. Are alternative approaches to NIPPV such as careful individual titration and high inspiratory pressures more effective in long term NIPPV in COPD?
3. Is a controlled backup rate or patient-initiated rate superior in terms of sleep quality, gas exchange or measures of pulmonary function?

Recommendations

The following recommendations are based on evidence from seven RCTs, review of systematic reviews and practice guidelines and consensus of the HMV expert panel.

1. The use of long-term NIPPV cannot be widely recommended in patients with stable COPD. (GRADE 1B)
2. Long-term NIPPV in COPD should only be considered on an individual basis. One subgroup of patients with COPD in which long-term NIPPV could be considered are those with severe hypercapnia ($\text{PaCO}_2 > 55$ mmHg) experiencing repeated episodes of acute hypercapnic respiratory failure that require in-hospital ventilator support. However, definitive proof of efficacy of long-term NIPPV in these patients will need to await future studies. (GRADE 2C)
3. The overlap syndrome, and concomitant COPD and obstructive sleep apnea (OSA) syndrome, should be differentiated from chronic respiratory failure that is solely due to advanced COPD. (GRADE 1C)

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SECTION VI.

HMV in Patients with Kyphoscoliosis

Introduction

Kyphoscoliosis is a well-recognized cause of respiratory failure (1). The most common cause is idiopathic scoliosis which begins in childhood. Kyphoscoliosis may also occur secondary to other disorders including NMD, vertebral disease, connective tissue abnormalities and thoracoplasty.

The degree of thoracic spinal deformity is the most important risk factor for the eventual development of respiratory failure. Surgically untreated patients with a VC below 45% of predicted values and a scoliotic angle greater than 110° are at particular risk of respiratory failure (2). Clearly patients with additional NMD or co-existent lung disease will be at greater risk, particularly as they age. Once respiratory failure or cor pulmonale develops, life expectancy with conservative therapy is poor. Up to 50% of untreated patients can be expected to die within one to two years without the initiation of oxygen or ventilatory support (3).

Due to such poor life expectancy, once respiratory failure develops, ventilatory support has been used in different forms in the treatment of patients with kyphoscoliosis and acute and chronic respiratory failure for the past 50 years (1, 4-7). Tracheostomy may be difficult because of deformity. Deformity also makes negative pressure devices difficult to fit, however, individually moulded cuirass ventilators have been used (4). Negative pressure devices are unable to prevent and may even cause upper airway occlusion during sleep (8-9). Patients with kyphoscoliosis often have OSA in addition to nocturnal hypoventilation (10). If there is evidence of upper airway obstruction on a negative pressure device then the addition of continuous PAP or a switch to positive pressure ventilation is required.

The development of noninvasive nocturnal ventilation in the 1980s has made NIV an accepted standard modality of care at the present time for patients with chronic respiratory failure caused by kyphoscoliosis (11-13). Encouraging initial reports of the efficacy of nocturnal NIV delivered by nasal mask resulted in widespread application of this therapy (10,14-16). Ellis and colleagues (10) studied seven patients with severe kyphoscoliosis and found that nasal mask ventilation was particularly suited to these patients. They demonstrated that over three months, nocturnal noninvasive mask ventilation significantly improved clinical measurements of respiratory function (daytime ABGs, lung volumes and respiratory muscle strength) and sleep architecture.

These initial reports demonstrating that nocturnal NIV was an effective therapy for respiratory failure in kyphoscoliosis resulted in a widespread adoption of this therapy without the support of randomized studies comparing NIV to the best standard therapy.

Review of Literature

As seen in table 6-1, a total of 12 studies were identified informing the primary outcomes of interest on the role of HMV in patients with kyphoscoliosis (17-28). An additional study reporting on outcomes of NIV in post-tuberculosis patients with the combination of respiratory failure and chest wall deformity is relevant (29). In addition to the identified studies, two reports on the timing of initiation of NIV (30,31), two reports on the mechanism of action of noninvasive nocturnal ventilatory support (32,33), and two reports on the mode of delivery of noninvasive ventilatory support (34,35) were also included in the review of the literature.

Table 6-1. Literature Search Results Informing HMV in Individuals with Kyphoscoliosis

Author Year (ref)	Study Type	No patients	Primary Outcomes of Ventilation in Kyphoscoliosis				
			Survival	ABGs	PFTs	Hospital days	QoL
Leger 1994 (17)	Retrospective	105 NIV		Improved	No change	Reduced	-
Simonds 1995 (18)	Retrospective	47 NIV	5yr = 80%	Improved	No change	-	-
Duiverman 2005 (19)	Retrospective	64 46/64 NIV	5yr = 80% 10 yr>60%	-	-	-	-
Brooks 2002 (20)	Retrospective	40 HMV 35/40 NIV	-	Improved	Improved exercise capacity	-	-
Baydur 2000 (21)	Retrospective	6 NIV	-	-	-	-	-
Strom 1992 (22)	Retrospective		-	-	-	-	-
Chailleux 1996 (23)	Retrospective	912 HMV 662 LTOT	NIV > LTOT	-	-	-	-
Gustafson 2006 (24)	Prospective	100 HMV 144 LTOT	HMV>LTOT	-	-	-	-
Buyse 2003 (25)	Retrospective	18 NIV 15 LTOT	NIV > LTOT	Improved	FVC, MIP Improved	-	-
Gonzalez 2003 (26)	Prospective	16	-	Improved	FVC, MIP, MEP improved	-	Improved
Schonhofer 2001 (27)	Prospective	20	-	Improved	Endurance time improved	-	-
Nauffal 2002 (28)	Prospective	35	-	Improved	-	Reduced	Improved

Abbreviations: NIV: noninvasive; HMV: home mechanical ventilation; LTOT: long-term oxygen therapy; ABGs: arterial blood gases; PFTs: pulmonary function tests; QoL: quality of life.

Outcomes

Survival

Survival was reported as an outcome in nine of the identified studies (17-25). Leger and colleagues (17) reported on a retrospective study of 276 patients with different respiratory disorders managed by nasal nocturnal NIV over a five-year period. 105 had kyphoscoliosis and 80 had post-tuberculosis sequelae. They found that with over two years or more of follow-up, the most favourable results were seen in the patients with kyphoscoliosis and post-tuberculosis sequelae. 80% of the patients with kyphoscoliosis and 76% of patients with post-tuberculosis sequelae continued noninvasive therapy through year two or longer. These patients demonstrated improvements in PCO₂ and PO₂ compared with baseline (p<0.0001). There was also a reduction in hospital days between the year before NIV and the year after (p<0.0001). Patients with NMD, COPD and bronchiectasis did less well.

There were 180 patients treated by nocturnal nasal NIV in the series of Simonds and colleagues (18) of whom 47 had early onset scoliosis. Patients were commenced on therapy between 1987 and 1992 for symptomatic chronic hypercapnic respiratory failure unresponsive to standard

measures including oxygen. The author found that patients with scoliosis, post-tuberculosis sequelae and post-polio patients had the best outcomes. The five-year actuarial probability of remaining on NIV for early onset scoliosis was 79% (95% confidence interval, 66% to 92%), for post-polio 100% and post-tuberculosis sequelae 94%. ABGs tensions were maintained over four years in these patients. The five-year survival appeared to be 80% for the patients with scoliosis. Deaths were due to concurrent disease, or progression of pulmonary hypertension in patients who presented late in the course of their disease.

Duiverman and colleagues (19) reviewed their experience of 64 patients with idiopathic kyphoscoliosis managed with ventilation (NIV= 46, Tracheostomy = 9, Negative pressure = 9) between 1956 and 2005, and demonstrated sustained benefit. The five-year survival was 84% and 10-year survival over 60%. Their pooled results of all patients managed (kyphoscoliosis = 64, post-polio = 30, miscellaneous = 20) with NIV demonstrated improved ABGs over five years ($p<0.001$). There was also slight improvement in FVC and FEV1 ($p<0.01$) at nine months in this group, with improvement maintained after five years of NIV.

Brooks and colleagues (20) reported data on 74 individuals with neuromusculoskeletal respiratory failure. She included all patients who completed a home ventilation training program and continued with home ventilation during all or part of the day for at least one year. There were 40 who had thoracic restrictive disease and 35/40 were ventilated noninvasively. Of those with thoracic restrictive disease, patients were followed for up to 10 years and only two patients died (5%). She found that home ventilation was associated with sustained long-term improvements in daytime ($p<0.004$) and nighttime ($p<0.003$) PCO_2 after five years in patients with thoracic restrictive disease. In addition, daytime PO_2 improved ($P<0.001$), and remained above baseline at 10 years. Exercise capacity increased in patients with restrictive thoracic disorders (six-min walk improved after ventilation established ($p<0.005$) and at two years ($p<0.01$)). Improvements were maintained for up to 10 years in the group with restrictive thoracic disorders.

A small number of patients with kyphoscoliosis were included in a series reported by Baydur and colleagues (21). They described 46 years of experience of long-term NIV in the community. They found that all six patients with kyphoscoliosis in their series tolerated NIV well and described decreased exertional dyspnea, more energy and increased ability to conduct daily activities, despite no overall change in VC or PCO_2 . Patients remained stable over a mean follow up of 2.5 years.

An analysis of the Swedish Oxygen Register was carried out to determine the efficacy of LTOT without ventilation in patients with hypoxic respiratory failure due to kyphoscoliosis. The survival rate was best for patients under the age of 65 and without complicating disease. The authors concluded that provided oxygen could be administered initially in a hospital setting without symptomatic hypercapnia, the risk of developing life threatening hypercapnia during LTOT was small, but over time patients might require a switch to ventilatory support (22).

The French ANTIDIR Observatory analysis of survival in patients receiving domiciliary oxygen therapy or mechanical ventilation included 1,574 patients with respiratory failure from kyphoscoliosis receiving either LTOT or ventilation, followed between 1984 and 1993 (23). The national non-profits network for home treatment of patients with chronic respiratory insufficiency (Association Nationale pour le Traitement à Domicile de l'Insuffisance Respiratoire Chronique Grave) was founded in France in the 1980's and in 1996 served 35,000 ventilator and/or oxygen dependent adults and children with respiratory failure from all causes. At that time ANTIDIR was responsible for nearly all ventilator-treated and 70% of all oxygen-treated

individuals in France. Medical information was collected annually. Oxygen therapy required that $\text{PaO}_2 < 55$ mmHg in a steady state on at least two occasions at least two weeks apart and treatment was required for at least 15 hrs/day. Mechanical ventilation required information on interface, presence of tracheostomy, and daily ventilator prescription. Follow up information documented; treatment modification, hospitalization, withdrawal and death. This directory remains the largest published database of patients with chronic respiratory failure treated with oxygen or mechanical ventilation.

In the ANTIDIR database, 56% of patients with uncomplicated kyphoscoliosis (n=912) and 87% of patients with complicated (usually obstructive lung disease) kyphoscoliosis (n=662) received oxygen alone. The remainder received ventilation. Overall, 60% of patients with uncomplicated kyphoscoliosis were alive at five years. Whereas, only 38% of patients with complicated kyphoscoliosis survived. The risk of death in patients with similar lung function, ABGs, age, sex and BMI receiving NIV was significantly less than those that received oxygen alone. The relative risk of death for those receiving NIV was 0.40 (confidence interval [0.26-0.8] $p < 0.001$) and for those receiving ventilation via tracheostomy was 0.45 (confidence interval [0.25-0.80] $p < 0.01$). Although selection bias is inevitable, the database supports a survival advantage for home ventilation rather than LTOT.

A prospective series using data from the Swedexox register of respiratory failure due to nonparalytic kyphoscoliosis in Sweden compared 100 patients receiving home mechanical ventilation with 144 patients receiving oxygen alone between 1996 and 2004 (24). The Swedexox register was set up in 1996 to follow all patients in Sweden with respiratory failure in whom oxygen therapy or HMV was initiated and patients were followed with survival as the primary outcome. Survival of patients with kyphoscoliosis receiving NIV was threefold better than that of patients treated with long-term oxygen alone and this was true regardless of gender, age, or the occurrence of concomitant respiratory disease (hazard ratio of 0.30 [confidence interval 0.18-0.51] $p < 0.001$). Overall survival at five years on HMV in uncomplicated kyphoscoliosis was 85%, and 65% in those with concomitant disease. The five-year survival on long-term oxygen treatment was 35% for uncomplicated kyphoscoliosis and 15% for those with concomitant disease. The decision to use mechanical ventilation was related to the preferences of the patient and the physician and selection bias and regional differences in care will have occurred in that study.

Utilizing the same database, Jager and colleagues (29) found improved survival in patients with chest wall deformity from post-tuberculosis sequelae who had developed respiratory failure. Out of 188 patients, 85 were treated with home ventilation and 103 with oxygen alone. Mechanical ventilation was associated with significantly better survival even after adjustments for age, gender, concomitant respiratory disease, blood gases and VC with an adjusted hazard risk of death of 0.35(95% confidence interval, 0.17-0.70).

Buyse and colleagues (25) carried out a retrospective analysis on all patients in their centre with kyphoscoliosis and respiratory insufficiency who started long-term oxygen and/or noninvasive nocturnal nasal positive pressure ventilation. The first study group consisted of all patients who started long-term oxygen between September 1990 and March 2001 (n =15). They were compared with all patients treated with NIV (n=18) from 1995-2001. Prior to initiation of treatment, PO_2 was lower, PCO_2 tended to be higher and VC tended to be lower in the patients treated with nocturnal NIV than in those who received long-term oxygen alone. The one year survival in the ventilated patients was higher (100% versus 66%) than in the patients receiving oxygen alone. Patients receiving ventilation demonstrated improvement in PO_2 (+54%), PaCO_2

(-21%), and maximal inspiratory mouth pressure (+33%), all absent from the patients on long-term oxygen without ventilation.

Arterial Blood Gases

As seen in Table 6-1, data on ABGs were reported in seven series (17,18,20,25-28). In four retrospective studies (17,18,20,25) improvements in ABGs compared to baseline were reported. Results are reported separately for the three remaining prospective studies (26-28).

Gonzalez (26) prospectively studied 16 patients with uncomplicated kyphoscoliosis who were treated with NIV. Inclusion criteria included stability and at least one of: - $\text{PCO}_2 > 45 \text{ mmHg}$, $\text{SpO}_2 < 88\%$ for 5 consecutive minutes during nocturnal oximetry, $\text{MIP} < 60 \text{ cm H}_2\text{O}$ pressure or $\text{FVC} < 50\%$. Patients were followed for three years. Mean PaO_2 increased at 36 months compared to baseline ($62.6 \pm 7.1 \text{ mmHg}$ vs. $67.8 \pm 8.8 \text{ mmHg}$ [$p < 0.05$]). There was improvement in nocturnal hypoxemia at six months ($p < 0.01$).

Schonhofer (27) studied 10 patients with thoracic restriction treated with NIV over six months. He compared this group with 10 matched controls who were not treated. Patients were stable and had either scoliosis or post-tuberculosis sequelae. For inclusion they were required to have $\text{PCO}_2 > 45$ and $< 55 \text{ mmHg}$. Patients were matched and alternately allocated to either group. Each group had eight patients with kyphoscoliosis and two with post-tuberculosis sequelae. No patient received oxygen. Significant improvements were noted in both PO_2 and PCO_2 in the treated group but not in the control group ($p < 0.01$) at the end of 3 months.

Nauffal (28) studied a total of 62 patients with restrictive disorders of whom 37 had kyphoscoliosis. Patients were studied prospectively and included if they had symptoms of dyspnea or morning headache and at least one of: - $\text{FVC} < 50\%$, $\text{MIP} < 60 \text{ cm H}_2\text{O}$, $\text{PCO}_2 > 45 \text{ mmHg}$, or $\text{SpO}_2 < 88\%$ for at least five consecutive minutes during nocturnal monitoring. The patients with kyphoscoliosis had a significant fall in PCO_2 maintained to 36 months (56.8 mmHg [SD 12.6] falling to 46 mmHg [SD 6.1] [$p < 0.05$]). In addition time spent with $\text{SpO}_2 < 90\%$ at night was significantly reduced through 36 months ($p < 0.05$).

Pulmonary Function

Measures of FVC and FEV1 were reported in six series (17,18,20,25-27). Of the four retrospective studies, two reported that measures of FVC and FEV1 show major stability with kyphoscoliosis on NIV (17-18), while one study reported improvements in six-minute walking distance after establishing home ventilation ($p < 0.005$) with improvement persisting at two years ($p < 0.01$) and still detectable up to 10 years, and one study reported demonstrated improvements in FVC (+ 47%) and MIP (+33%) at one year (25).

Of the two prospective studies, Gonzalez et al (26) reported improvements in FVC at 36 months compared to baseline ($37.9\% \pm 7.2\%$ vs. $47.5\% \pm 11.9\%$), and MIP improved from $55.8 \pm 17.4 \text{ cm H}_2\text{O}$ to $78.5 \pm 17.5 \text{ cm H}_2\text{O}$ and MEP from $53.8 \pm 17.7 \text{ cm H}_2\text{O}$ to $72.3 \pm 11.0 \text{ cm H}_2\text{O}$. In the study by Schonhofer et al (27), the authors reported an improvement in endurance time ($p < 0.0001$) in 10 patients treated with NIV compared with 10 matched controls with improvements noted in cycle ergometer, shuttle walk and inspiratory threshold loading tests.

Hospitalization

Two studies reported hospitalizations as an outcome of interest (17,28). In the retrospective series reported by Leger et al (17), there was a reduction in hospital days in the year following institution of ventilation compared with the previous year (34 ± 31 days reduced to 6 ± 6 [$p < 0.0001$]). Nauffal (28) reported a decreased hospitalization rate in the prospective series of 35 patients with kyphoscoliosis from 1.2 to 0.8 admissions per year ($p < 0.01$).

Quality of life

Two prospective series reported data on QoL as an outcome (26,27). Gonzalez et al (26) reported that patients self-reported reduced morning headache, reduced dyspnea, reduced diurnal drowsiness and improved sleep quality. Using a Spanish version of the SF36, Nauffal et al (28) reported that NIV was associated with improvement in health status with improvement in “physical role” and “emotional role” at three months, and the categories “social functioning”, “vitality” and “mental health” at six months.

Timing of Initiation of NIV

There is little data on the value of early initiation of NIV in kyphoscoliosis. A small number (n=7) of patients with kyphoscoliosis were included in a crossover study of NIV or oxygen in patients with nocturnal hypoxemia and daytime normocapnia in neuromuscular and chest wall disease. Dyspnea, morning headache and nocturnal hypoventilation all improved with NIV but not oxygen. From the total of 21 patients studied, 19 elected to continue ventilation rather than oxygen (30). The study by Ward (31) does demonstrate data supporting initiation of nocturnal ventilation in patients with neuromuscular and chest wall disease who have nocturnal hypercapnia with daytime normocapnia, but there were no patients with kyphoscoliosis in the control group.

Mechanism of Action of Noninvasive Nocturnal Ventilatory Support

The mechanisms by which noninvasive nocturnal ventilation is effective in improving daytime ABGs in kyphoscoliosis are not fully understood. It does appear that improvement in daytime hypoventilation may represent an adaptation of the central chemoreceptors through reduction of the profound hypercapnia that occurs during sleep (32). The ventilatory response to hypercapnia is improved and there may be an increase of the ability of patients to activate inspiratory muscles in addition (33). There is little evidence to support rest of fatigued respiratory muscles as a major contributing factor.

Mode of Delivery of Noninvasive Ventilatory Support

There were no compelling studies identified in the search of the literature of the different modes of noninvasive ventilatory support in kyphoscoliosis. In most series, nasal mask ventilation is used in the vast majority of patients.

Laserna and colleagues (34) compared the clinical course, blood gases, and lung function after one month of domiciliary noninvasive positive pressure ventilation with a volumetric ventilator and a bilevel pressure support device. Sleep pattern changes were assessed in a prospective randomized cross-over study in ten patients with chronic respiratory insufficiency due to kyphoscoliosis. After one month of use, the patients underwent clinical and functional examinations and polysomnography while using a ventilator. The same protocol was applied with a second device after a 10-day washout period. Baseline polysomnograms showed fragmented sleep with low percentages of deep non-REM sleep and of REM sleep as well as respiratory patterns characterized by desaturations. In all cases, symptoms and ABG improvements were significant with no difference between the two treatment periods. All but one patient had better tolerance of a bilevel PAP support mode than of a volumetric ventilator. This small study demonstrated that NIV was equally effective for patients with kyphoscoliosis whether administered with a volumetric ventilator or a bilevel device but subjective response and tolerance seemed to be slightly better than with bilevel.

Comparison of the assist/control mode and the control mode of delivery of noninvasive volumetric ventilation was done in a heterogeneous group of 110 patients with chronic hypercapnic respiratory failure. Patients with restriction secondary to NMD, kyphoscoliosis and

post-tuberculosis sequelae were studied. The assist control mode was used in 45 patients and the control mode in 65 patients. There were significant improvements in PaO₂ and PaCO₂ at 6 and 12 months with both modes of mechanical ventilation. There were no significant differences between the two modes on pulmonary function or blood gas parameters. The different types of ventilatory mode appeared to be comparable in patients with chronic respiratory disease. The study was not randomized and the choice of ventilation mode was dependent on the criteria of the attending physician. The patients were also a mixed group, 33 of the 110 patients had kyphoscoliosis, 29 NMD, and 38 post-tuberculosis sequelae (35).

Discussion

Support for the use of NIV in kyphoscoliosis has been established since the publication of a number of retrospective single cohort studies demonstrating improved survival compared to historical mortality (17-21). In addition, two observational registries have also directly compared survival between patients managed by LTOT or home ventilation and both have demonstrated that home ventilation has a significant survival advantage (23,24).

A number of smaller studies have confirmed earlier reports of improved gas exchange and indicate that NIV may improve some parameters of lung function, exercise endurance and QoL (26-28). These series strongly suggest that noninvasive nocturnal nasal ventilation offers a survival advantage to oxygen therapy alone as treatment for chronic respiratory failure in kyphoscoliosis. Evidence from these different case series demonstrate that once ventilation has been initiated in patients with kyphoscoliosis with respiratory failure, stability over a long period of time is possible. Improvement in ABGs over a long period may occur. A reduction in hospital days and improved exercise tolerance with stability of lung function can be anticipated.

Evidence is lacking to support the initiation of NIV on the basis of pulmonary function alone and patients with kyphoscoliosis who present with a VC which is less than 50% predicted can survive for many years before respiratory failure develops (2). In addition, follow up of patients presenting with acute hypoxic, hypercarbic respiratory failure caused by kyphoscoliosis has demonstrated that some patients can survive for years on oxygen therapy without ventilation (5).

Two comparative cohort studies have been published demonstrating that while many patients with chronic hypoxic hypercapnic respiratory failure can survive for a substantial amount of time with oxygen therapy alone, survival is best if NIV is instituted (23,24). While many case series of patients with kyphoscoliosis treated by NIV describe reduced symptoms of morning headache, dyspnea and improved energy, rigorous measurements of QoL are limited.

The 1999 consensus conference report by the American College of Chest Physicians has recommended that NIPPV be initiated for restrictive thoracic disorders including patients with both neuromuscular disorders and chest wall disorders in the presence of symptoms of respiratory failure such as fatigue, dyspnea, morning headache and either hypercapnia (PCO₂ greater than 45 mmHg) or nocturnal oxygen saturation less than 88% for five consecutive minutes. If there was evidence of progressive NMD, maximal inspiratory pressures less than 60 cm water or FVC less than 50% predicted were considered parameters for possible initiation of support (11). These guidelines remain applicable currently for patients with kyphoscoliosis. In addition there is some evidence that patients with daytime normocapnia and evidence of nocturnal ventilatory failure should be considered for nocturnal ventilatory support (30, 31)

There are no data to make definitive recommendations on mode of ventilatory support or ventilator settings, other than to relieve nocturnal hypoventilation, hypoxia and sleep apnea.

Interface should be individualized. There are no data to make definite recommendation on site of initiation other than to ensure close instruction, monitoring, support and follow up. Initiation of NIV in stable patients without hospitalization is possible (36).

Conclusion

Evidence is lacking to support the initiation of NIV on the basis of pulmonary function alone – indeed, there are many factors that must be considered. Patients with kyphoscoliosis who present with a VC of <50% predicted value can survive for many years before respiratory failure develops (2). Follow-up of patients presenting with acute hypoxic, hypercapnic respiratory failure caused by kyphoscoliosis has demonstrated that some patients can survive for years on oxygen therapy without ventilation (5). If oxygen therapy can relieve hypoxemia in patients with respiratory failure secondary to kyphoscoliosis without the development of hypercapnia, oxygen therapy alone can be considered; however, over time, monitoring for the development of CO₂ retention is critical, and the addition of ventilatory support may be required (22). Most patients with established chronic hypercapnic respiratory failure caused by kyphoscoliosis should be offered nocturnal NIV (17-29).

Research Questions

1. Patients with kyphoscoliosis can be managed with oxygen alone. The potential confounding factor is that administration of low-flow oxygen particularly at night may promote hypercapnia. Do patients with stable kyphoscoliosis and daytime eucapnia develop nocturnal hypercapnia with the institution of nocturnal oxygen?
2. Does the addition of regular LVR techniques with achievement of a MIC and increased PCFs affect the outcome of patients with kyphoscoliosis?
3. How can we best assess HRQoL in these patients and then does earlier initiation (nocturnal hypercapnia alone) of NIV improve this or other outcomes?

Recommendations

The following recommendations are based on limited evidence from the literature search and consensus of the HMT expert panel.

1. Patients with kyphoscoliosis should undergo periodic spirometry testing, and if FVC is <50%, ongoing review, assessing for evidence of hypercapnic respiratory failure should be instituted. (GRADE 1C)
2. Long-term nocturnal NIV should be offered to all patients with kyphoscoliosis who have developed chronic hypercapnic respiratory failure. (GRADE 1B)
3. Patients with hypoxemia but without hypercapnia may be managed cautiously with oxygen therapy alone while monitoring for development of hypercapnia. (GRADE 1C)
4. Oxygen therapy could be added to NIV, if considered necessary, for unresponsive oxygen desaturation (GRADE 1C)
5. Methods to assist secretion clearance should be initiated when peak cough flow is <270 L/min. (see Section I. Airway Clearance) (GRADE 1C)

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SECTION VII.

HMV for patients with Obesity Hypoventilation Syndrome

Introduction

Obesity Hypoventilation Syndrome (OHS) is best characterized as daytime hypercapnia not due to respiratory or NMD and accompanied by obesity and sleep disordered breathing (1). For the purpose of this review the definition of OHS is defined as follows:

1. Obesity ($\text{BMI} > 30 \text{ kg/m}^2$)
2. Daytime hypercapnia ($\text{PaCO}_2 > 45 \text{ mmHg}$)
3. Absence of other causes of hypoventilation

Sleep disordered breathing is very common among OHS patients although not necessarily a part of the definition. Most OHS patients (80-90%) also suffer from OSA, while hypoventilation without OSA and central apnea are less common (2).

The exact prevalence of OHS in the general population is not known. The prevalence of OHS in patients with OSA has been estimated to be between 20% to 30% (3). In a large French study of 1141 adults with OSA daytime hypercapnia was present in 9.8% of patients with $\text{BMI} > 30 \text{ kg/m}^2$ and $< 40 \text{ kg/m}^2$, and in 23.6% with a $\text{BMI} > 40 \text{ kg/m}^2$ (4). Despite this information, OHS still remains under-recognized. In one study of obese patients ($\text{BMI} > 35 \text{ kg/m}^2$) admitted to the hospital, 23% of OHS patients were correctly diagnosed and only 13% received treatment for OHS on discharge (5).

Because the rates of obesity are rising rapidly, the prevalence of OHS is likely to increase. It is estimated that the prevalence of morbid obesity ($\text{BMI} > 40 \text{ kg/m}^2$) in the United States has quadrupled between 1986 and 2000 (6). Similar trends are evident in Canada: between 1979 and 2004 the obesity rate in Canadian adults has increased from 13.8% to 23.1% while the percentage of Canadian adults with class III obesity has tripled (0.9% to 2.7%) (7). It is, therefore, not surprising that OHS is one of the most common reasons to initiate NIV. In a recent study of 1526 adults who started HMV in Sweden between 1996 and 2005, OHS constituted the largest group of ($n=422$ [28%]) (8). In another study (9), 59 of 111 patients who received nocturnal HMV in New Zealand had OHS. A review of all HMV prescriptions in a Swedish registry between 1996 and 2002 (10), revealed that the OHS group had the highest increase (8% to 17%) of all ventilated patients.

OHS subjects typically present with somnolence, headaches, dyspnea and limb edema. The majority of these subjects present with symptoms of OSA. OHS subjects have been shown to have increased mortality, hospitalization rates, high prevalence of pulmonary hypertension and increased use of health care resources. Decreased HRQoL, vigilance and CO_2 sensitivity have also been demonstrated. When compared to BMI-matched population these patients have high rates of CHF, angina and pulmonary hypertension (11). Compared to eucapnic patients with OSA, patients with OHS have a lower QoL, more somnolence, higher health care expenses and greater risk of pulmonary hypertension (12). OHS patients have higher rates of ICU admissions and a greater need for invasive mechanical ventilation (4).

This review describes the role of HMV in therapy of OHS. Therapies aimed at weight loss such as exercise and dietary modification, pharmacological therapy or bariatric surgery are beyond the scope of this chapter and are not discussed here.

Table 7-1: Definitions of OHS

SOURCE	DEFINITION(S)
Kryger <i>et al</i>	BMI > 35 kg/m ² and elevated awake PaCO ₂ . Overnight sleep study showing an increase in PaCO ₂ of over 10 mmHg.
CTS (Canadian Thoracic Society)	Sleep Hypoventilation syndrome (2006) A. One or more of the following: Right Heart failure Pulmonary Hypertension EDS not explained by other factors Erythrocytosis Hypercapnia when awake (PaCO ₂ > 45 mmHG) B. Sleep monitoring (one or both): An increase in PaCO ₂ during sleep greater than 10 mmHg from awake supine values. Sustained hypoxemia (<90%) not related to apnea or hypopnea.
AASM (American Academy of Sleep Medicine)	An increase in PaCO ₂ > 10 mmHg during sleep in comparison to wake supine value – option consensus.
ICSD2 (International Classification of Sleep Disorders)	Classified as sleep-related hypoventilation/hypoxemia due to neuromuscular or chest wall disorders. A neuromuscular or chest wall disorder is present and is believed to be the primary cause of hypoxemia. Polysomnography or sleeping ABG determination shows at least one of the following: A. Oxygen saturation during sleep <90% for more than 5 minutes with a nadir of 85% or less. B. >30% of TST with SaO ₂ <90%. C. Abnormally high or increased PaCO ₂ (relative to levels during wakefulness) during sleep.

Review of Literature

The literature search identified 11 studies (11,13-18,20,21,23,24) of HMV involving 378 OHS patients treated with bilevel or volume-cycled ventilation (n=274) or CPAP (n=104). The majority of studies were prospective cohort or retrospective in design, had different enrollment criteria, used different modes of ventilation and had different place of initiation of therapy, variable follow-up and dropout rates (Table 7-2). It must be emphasized that CPAP is not a ventilatory device and is not routinely used to treat hypoventilation; however, it is included in the present review because there are studies demonstrating its efficacy in a subset of OHS patients (see Table 7-1).

Table 7-2. Literature Search Results on Obesity Hypoventilation Syndrome

Author Year (Ref)	Study Type Duration	# of Pts	Mortality	HRQoL	Outcomes			
					Sleep	Gas Exchange	Vigilance	Other
Piper, 2008 (16)	RCT, CPAP vs.bilevel 3 months	36 (18 CPAP; 18 bilevel)	n/a	SF-36 improved in both	Subjective improvement in Bilevel (PSQI)	Improved In both groups bilevel =CPAP	Subjective sleepiness improved in both. Performance tests improved in both	
Heinemann, 2007 (15)	Prospective 24 months	35 bilevel	n/a	n/a	n/a	Improved	n/a	VC, ERV improved Hct,Hgb decreased
Banerjee, 2007 (20)	Prospective 1 night	23 CPAP	n/a	n/a	Improved: AHI, AI, TST, SpO ₂ <90%	n/a	n/a	
Perez de Llano, 2007 (13)	Retrospective 50 months	54 bilevel or Volume-cycled	n/a	n/a		Improved	Subjective sleepiness improved	Dyspnea improved
Storre, 2006 (18)	RCT X-OVER bilevel vs AVAPS 6 weeks	10	n/a		Improved in both equally SRI improved equally	TCO ₂ improved in AVAPS		Health care costs (physician fees and hosp. rates reduced after therapy).
Berg, 2001 (11)	Retrospective cohort CPAP or bilevel	20	n/a	n/a	n/a	n/a		Improved lung function, Hgb.
Budweiser, 2007 (14)	Prospective 41 months	126 PSV		n/a	n/a	Daytime and nighttime improved	n/a	
Hida, 2003 (17)	Prospective 3-6 months	26 CPAP	n/a	n/a	SF-36 improved	Hypercapnia improved in 51%	Subjective sleepiness improved	Headache, edema, dyspnea: improved
Kawata, 2007 (21)	Prospective 3 months	37 CPAP	n/a	n/a	Improved	PCO ₂ improved	n/a	
Chouri- Pontarollo, 2007 (23)	Prospective 5-7 nights	15 bilevel	n/a	n/a	n/a	No change in CO ₂	ESS, OSLE improved in low CO ₂ responders	
Masa, 2001 (24)	Prospective 4 months	22 OHS 14 KS 17 VCV 5 bilevel	n/a	n/a	n/a	responsiveness improved	Subjective improvement	

Outcomes

Mortality

There are no RCTs of NIV in OHS with mortality as an outcome and such trials are unlikely to be performed in the future on ethical grounds. Non-randomized prospective and retrospective studies suggest that treatment of OHS results in decreased long-term morbidity and mortality. The existing studies suffer from weaknesses such as the lack of appropriate controls, presence of confounders such the use of oxygen, small subject numbers and short follow-up.

In the largest cohort of 1526 adults receiving HMV in Sweden OHS mortality was 50% at 10 years (8). In one retrospective study, OHS patients who refused NIV had a mortality rate of 46% during an average 50-month follow-up (13). In a prospective study of 47 untreated patients followed for 18 months after discharge, mortality was 23% compared to 9% in patients with a similar degree of obesity but without hypoventilation (4). A retrospective study of 126 patients adherent to NIV reported two and five-year mortality of eight and 29.8% respectively (14). In multivariate analysis PaO_2 , pH and leucocytes were independent predictors of mortality; reduction in nocturnal PaCO_2 and hemoglobin at follow up was associated with improved survival.

Data from other retrospective trials of NIV in OHS indicate that the two to four-year mortality rate is less than 10% (11,13,15). In 54 patients treated with bilevel therapy and followed for 50 months there were three deaths (5.5% mortality). NIV was discontinued in five patients who achieved weight loss and in 16 who were switched from bilevel to CPAP (13).

Quality of Life

In a recent RCT, patients with mild OHS (defined as absence of significant nocturnal desaturation: $\text{SpO}_2 < 80\%$ for at least 10 minutes or a rise in transcutaneous CO_2 in REM sleep) were allocated to either CPAP or bilevel therapy (16). In the three-month follow-up there were significant improvements in SF-36 dimensions of physical functioning, role physical, vitality, social functioning in the bi-level group while only Vitality subscale score improved in the CPAP treated group (16). In a prospective study of 26 patients with mild OHS, findings indicated that three to six months of CPAP therapy improved HRQoL as measured by SF-36 (17). Another recent randomized control trial of bilevel S/T with and without AVAPS in 10 patients who failed CPAP therapy revealed no significant difference in QoL as measured by SRI or sleep quality between the two modes of ventilation after six weeks (18). There was a significant improvement in SRI summary scales in both groups. The existing literature therefore suggests that both CPAP and bilevel therapy improve HRQoL measures in OHS patients.

Sleep Parameters and Gas Exchange

Improvement in daytime hypercapnia has been demonstrated with NIV therapy and is related to duration and compliance with therapy. In one retrospective study of 75 patients those who used CPAP therapy for an average of 4.5 hours/night experienced larger improvement in PaCO_2 and PO_2 than those who did not adhere to therapy. Baseline PaCO_2 , FEV_1 and treatment adherence were predictors of an improvement in PaCO_2 . The need for daytime O_2 therapy decreased from 30% to 6% in CPAP-adherent patients (19).

Another retrospective study of 126 OHS patients reported a significant improvement in daytime gas exchange and lung function after an average of 41.3 months of NIV (12). A prospective study compared one night of CPAP titration in 23 patients with OHS (extreme obesity, $\text{BMI} > 50 \text{ kg/m}^2$) and 23 patients with eucapnic OSA who were matched for BMI, apnea/hypopnea index

and lung function (20). In 57% of OHS patients CPAP therapy resolved sleep disordered breathing and nocturnal hypoxemia at a mean CPAP pressure of 13.9 cm. H₂O. In the remaining 43% of OHS patients, however, nocturnal hypoxemia (18% of TST with SpO₂ <90%) was seen despite CPAP therapy. There was no assessment of daytime gas exchange and no follow up. In another study Kawata et al. (2007) demonstrated that CPAP therapy does not adequately treat hypercapnia in approximately half of OHS patients (21).

Similarly Piper et al (2008) reported that the initial response to CPAP therapy is inadequate in 18 out of 36 patients (16). Failure of CPAP therapy (either persistent hypoxemia or hypercapnia) usually prompts implementation of bilevel therapy. An RCT of AVAPS and bilevel in patients with OHS -who failed CPAP therapy and were persistently hypercapnic- revealed that modalities with tidal volume assurance, (such as AVAPS) were more successful in improving nocturnal and daytime ventilation at six weeks. However, there was no significant change in HRQoL or sleep quality between the two modes of ventilation (18).

In a previously quoted study by Piper et al there were significant improvements in daytime hypercapnia and daytime sleepiness scores, sleep quality and awake O₂ saturation in both CPAP and bilevel groups. At three months there were no significant differences between the groups in these outcome parameters and in mean compliance. Some patients with mild OHS who initially require bilevel therapy can be switched to CPAP after resolution of hypercapnia (22). This practice however has not been tested in RCTs and caution is advised as in many OHS patients CPAP therapy is inadequate.

Vigilance and Cognitive Function

Numerous studies of NIV in OSA have demonstrated improvement of subjective and objective somnolence. The evidence in OHS is more limited; there are five studies which investigate the effect of NIV on sleepiness and/or cognitive function. Most studies in OHS population use subjective scales such as ESS to assess response to therapy; only two studies attempted to evaluate vigilance more objectively and none used MSLT (16,23). In an RCT of CPAP and bilevel therapy, ESS improved significantly in both groups with no difference between the groups at three months; however there was a difference in subjective sleep quality as measured by PSQI favoring bilevel (16). In the same study there were no differences in treatment effect between CPAP and bilevel in the four performance tasks (Trails B, digit span forward, digit span backwards and digit symbol substitution). In a prospective study of 15 OHS patients treated with bilevel therapy there was no improvement in ESS or OSLEP tests after 5-7 nights of treatment although a subgroup of patients with impaired CO₂ responsiveness showed improvement (23). In the other three studies improvements in subjective somnolence have been demonstrated (13,17,24).

Health care Costs

There is only one study which evaluates the effect of NIV on health care costs in OHS. In a retrospective analysis of 20 OHS subjects in Manitoba matched to the general population and to obese controls Berg et al showed that untreated OHS subjects are more likely to be hospitalized in the five years prior to the diagnosis and generate higher physician fees (11). Seventy percent were admitted to the hospital at least once in the year prior to diagnosis; these patients spent a total of 76 days in ICU in the five years before treatment and eight ICU days in the two years after. Initiation of HMV was associated with 68% reduction in days hospitalized and significant reduction in physician costs in the two years after therapy.

Follow-Up

Frequent follow up of OHS patients started on CPAP or bilevel therapy is recommended to assess response to therapy, adherence, presence of side effects, and to implement pressure changes whenever necessary. Patients should be enrolled in a weight loss program and should have their weight measured at each visit. Those who are successful in losing weight may require change in NIV pressures or mode of therapy or may even discontinue NIV altogether. Those patients who undergo bariatric surgery should have the need for HMV re-evaluated. ABGs, serum bicarbonate levels, overnight oximetry and polysomnography have been used in clinical trials and are often used in clinical practice to assess response to therapy.

Discussion

There is sufficient evidence that majority of OHS patients can be managed effectively using nocturnal NIV. In one of the largest reviews of HMV only 1% of OHS patients were treated with invasive mechanical ventilation (8). NIV in these patients improves daytime ABGs, sleep hypoventilation, sleep fragmentation, dyspnea, edema, subjective sleepiness, HRQoL, and pulmonary hemodynamics. The evidence from one retrospective study suggests that NIV leads to a significant decrease in hospital admissions and length of hospital stay. NIV is initiated either in hospital setting when respiratory failure is first diagnosed or in the ambulatory environment typically in the sleep laboratory. The majority of patients are managed with nocturnal bilevel therapy; CPAP may be effective in cases of mild OHS and is typically started during an overnight polysomnography.

Conclusion

OHS is a common cause of respiratory failure and one of the most common reasons to initiate HMV. The existing evidence indicates that HMV using NIV is effective in majority of OHS patients and results in significant improvement in symptoms of somnolence, dyspnea, edema, and sleep quality, as well as improvements in gas exchange, sleep architecture and HRQoL. While there is still uncertainty about the optimal ventilatory mode in OHS, and because only one RCT compared CPAP and bilevel PAP, the existing evidence shows that bilevel therapy is effective in the majority of OHS cases, while CPAP is effective in a subgroup of OHS subjects with mild OHS and OSA. Newer ventilatory support modalities with tidal volume assurance have shown promise; however, additional long-term studies are required.

Research Questions

1. Treatment of OSA with nasal CPAP can normalize CO₂ in many patients. Are there features of hypercapnic obesity/hypoventilation patients which predict successful initial treatment with CPAP?
2. Are volume assured pressure support devices superior to conventional bilevel support in terms of effectiveness or sleep quality for patients with OHS e.g; REM-associated oxygen desaturation in morbidly obese?
3. What factors differentiate those with OHS from BMI-matched individuals; CO₂ responsiveness? Inspiratory load detection? Upper airway collapsibility?

Recommendations

The following recommendations are based on evidence from the literature search and consensus of the HMV expert panel.

1. NIV is the treatment of choice for OHS. (GRADE 1A)

2. In patients with OHS who have a minor degree of nocturnal desaturation and no nocturnal rise in PaCO₂, CPAP is a reasonable initial therapy provided that follow-up is arranged within one to three months to evaluate response to therapy. (GRADE 1B)
3. Under circumstances when access to more than one device (bilevel PAP or CPAP) is limited, bilevel therapy is recommended. (GRADE 1C)
4. In patients with OHS who experience significant nocturnal desaturation or a nocturnal increase in PaCO₂, bilevel PAP remains the therapy of choice. (GRADE 1B)
5. Polysomnography is useful for titrating and confirming efficacy of bilevel pressures. (GRADE 1C)

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SECTION VIII.

HMV in persons with Spinal Cord Injury

Introduction

Respiratory complications continue to be one of the leading causes of morbidity and mortality in individuals with spinal cord injury (SCI), despite advances in SCI care, for which acute and long-term mortality rates have declined (1). Although research has suggested dramatic improvement in survival for individuals with SCI over the past few decades, this is only in the critical first few years post-injury (2), and the life expectancies of ventilator-dependent patients with SCI have not improved (1). Ventilator dependence remains as a negative prognostic factor for survival among all patients with SCI (1). Since invasive ventilation is so commonly required in the early management of SCI, a greater focus on initial management, weaning and optimizing opportunity for NIV is provided in this section.

The degree of respiratory impairment in individuals with SCI depends on the level and grade of injury. Complete high cervical cord lesions (C1-C4) are associated with the greatest respiratory muscle dysfunction. Diaphragm involvement can be evaluated by diaphragm fluoroscopy, nerve conduction studies and EMG. Individuals with complete lesions at C1 and C2 cannot maintain effective spontaneous ventilation, and require immediate ventilatory support to survive. Lesions at C5-C8 result in weakness/paralysis of key respiratory muscles including the intercostal, parasternal, scalene, abdominal, but spare the diaphragm, trapezii, sternocleidomastoid, and the clavicular portion of the pectoralis major. Thoracic spinal cord lesions affect the intercostal and abdominal muscles, compromising the expansion of the upper chest wall as the diaphragm descends during inspiration and eliminating expiratory muscle function. Lumbar and sacral level lesions result in little respiratory impairment (3).

Individuals with SCI are intubated and ventilated following acute injury when there is intractable respiratory failure (deterioration in VC, peak expiratory flow rate, FEV1, or negative inspiratory force or blood gas derangements), particularly when NIV has failed, and/or when there is impairment of consciousness or aspiration with respiratory compromise. In the days following an injury, an individual with initial respiratory stability, may experience decline as the neurologic level of injury can ascend, patients fatigue, compromise occurs due to inability to cough secretions, atelectasis, and pneumonia.

Most patients acutely supported by a ventilator will recover spontaneous breathing (3); however, approximately 5% of individuals require ongoing ventilatory support (4). Respiratory function remains impaired with severity related to level and completeness of injury. Noted impairments include reduced FVC, FEV1, inspiratory capacity, lung and chest wall compliance, and expiratory reserve volume (5,6,7). With injuries affecting innervation of the abdominal muscles (cord lesions above L2), the ability to cough and clear secretions is compromised. There is a reduction in the peak expiratory flow rate necessary for secretion clearance in patients with SCI. Therefore measures for management of airway secretions and prevention/treatment of atelectasis and pneumonia must be employed, which can include: assisted coughing, use of a MI-E, glossopharyngeal breathing (GPB), breath-stacking/LVR and MAC. The Consortium for Spinal Cord Medicine has published a Clinical Practice Guideline for Respiratory Management following Spinal Cord Injury, which provides recommendations for care in acute SCI through to discharge to community, including protocols for ventilation, cuff deflation, weaning from ventilation, and transition to home (5).

Unfortunately, many specialized rehabilitation centres for patients with SCI, do not accept ventilated patients. Rehabilitation of patients on dedicated spinal units, even those ventilated, improves outcomes, including discharge to the community (8). In Canada, patients are either transported to one of a few centres nationally that accept ventilator-dependent patients, or remain in acute care or intensive care beds, without access to specialized spinal cord rehabilitation services that non-ventilator dependent patients receive. Weaning from the ventilator as soon as possible, when possible, or to NIV is recommended, both to facilitate further rehabilitation and community reintegration, and to reduce the morbidity associated with long-term invasive ventilation (1,2,5,8).

In addition to the muscle weakness, there are other contributors to respiratory impairment in patients with SCI. There is a high prevalence of OSA in patients with SCI, and appropriate therapy may improve QoL and other outcomes (9). Diminished lung compliance occurs over time due to impaired lung inflation. Children with SCI develop restrictive lung disease due to kyphoscoliosis, and are therefore at increased risk of respiratory compromise into adulthood.

Although alteration of pulmonary function and respiratory complications are a major cause of both morbidity and mortality in patients with SCI, there are no current guidelines for the long-term management of respiratory function in persons with SCI. An evidence-based review for spinal cord injury rehabilitation (SCIRE) addresses current best evidence for respiratory management following spinal cord injury, and summarizes key recommendations in areas including respiratory muscle training, assistive devices, secretion management, pharmacologic interventions and phrenic nerve stimulation (10).

Review of Literature

In addition to the described search strategy, a search was performed of Medline, with key words: spinal cord injury, ventilation, ventilator, (1996-2008 and 1950-2008), references of identified articles reviewed. In addition, two recently published practice guidelines were reviewed: Spinal Cord Injury Rehabilitation Evidence (www.icord.org/scire) Respiratory Management Following Spinal Cord Injury (2008) and the Respiratory Management Following Spinal Cord Injury: A Clinical Practice Guideline for Health care Professionals, by the Consortium for Spinal Cord Medicine (2005) www.pva.org. There were no RCTs or controlled trials of home mechanical ventilation in SCI. Studies identified were predominantly descriptive studies, retrospective cohorts, or case series.

ResultsTable VIII-1. Literature Search Results of HMV for individuals with SCI

Author Year (Ref)	Study Type	# of Pts.	Outcomes				
			Survival	Quality of Life	Morbidity	Transition to home/ NIV	Summary/ Notes
Hirschfeld 2008 (16)	Prospective comparison	32 MV and 32PNS	No difference	Improved speech/ employment in PNS; younger pt bias	Reduced resp infection in PNS		No validated outcomes used; observation only
Toki 2008 (21)	Case reports	2				dc home post wean IPPV to NIV	C1 tetraplegia; followed 1 yr post dc
Chiodo 2008 (20)	Retrospective review	26 VA				Predictors of weaning	Negative inspiratory force bedside and EMG, bedside FVC best predictors
Onders 2007 (17)	Case series	10 chronic VA		Improved post DPS; 8/10 day or full time DPS		Home based ventilator weaning post-op.	VA adults with SCI in childhood; ave 13 yrs post SCI
Shavelle 2006 (14)	Survival analysis	319	Factors related to survival age, level, grade, time since injury		Resp conditions leading cause of death		Inclusion VA, dc from hosp and 1 year post injury
Consortium for Spinal Cord Medicine 2005 (5)	Clinical Practice Guidelines				Respiratory care protocols	Recommendations for transition to home, protocols for weaning, ventilation, decannulation	Comprehensive; recommendations based on grading of evidence and expert consensus
Nelson 2004 (12)	Prospective cohort and descriptive	49	51% alive; average survival 8.7 yrs	N=17 with mean 11.1 yrs ventilation; SF- 36; BSI; Satisfaction with life			49 pts discharged from rehab vent dependent; 2- 23 years post injury among survivors
Peterson 1999 (18)	Note: non- randomized				Higher volumes improve weaning		What difference was seen?
Hall 1999 (13)	Descriptive	82 16 VA		Self-esteem, Reported high	Mean hospital days 6/year in ventilated	94% VA living in private residence	14-24 year follow up; all vent assisted "glad to be alive"; comparisons of VI and VA pts

Author Year (Ref)	Study Type	# of Pts.	Outcomes				
			Survival	Quality of Life	Morbidity	Transition to home/ NIV	Summary/ Notes
Peterson 1997 (19)	Review of experience ?Retrospective non- randomized				Reduced atelectasis with high volume/flow protocol		Protocol for vent dependent tetraplegia
DeVivo 1995 (11)	Nonconcurrent prospective	435 VA	15 yr survival 16.8%; 1 st year critical		Pneumonia leading cause of death		Vent status predicts survival
Bach 1994 (15)	Descriptive	87 complete tetraplegia (42 VA)		Life satisfaction and well-being; higher in VA than non-VA			Min 2 years post injury
Bach 1993 (21)	Retrospective	257 (50 SCI) VA pts				number weaned, how?	Description of noninvasive options of IPPV
Bach 1991 (22)	Uncontrolled, descriptive – retrospective	34 VA				of 30 trached; 12 weaned to NIV	Description of approaches to weaning to NIV
Bach 1990 (23)	Retrospective (?Case series)	25				23 converted to NIV; 17 trachs closed;	Mouth NIV most common
Bach 1990	Experimental	104 cuff trach (38 SCI) VA				91 converted to deflate or cuffless, 10 to NIV	Efficacy of deflated and cuffless TIPPV

Outcomes

Survival / Morbidity

DeVivo and Ivie (11) identified significantly reduced life expectancy for ventilator-dependent individuals following SCI, even when controlled for age, sex, and race. Additional prognostic factors did include age at injury, time since injury, level and completeness of injury. In adults, ventilator dependency is the strongest negative predictor of survival during the first year after hospital discharge (11). Nelson et al (12) have followed 49 survivors of childhood-onset SCI requiring long-term mechanical ventilation, identifying survival of 2-23 years. In Hall's (13) longitudinal study of high tetraplegic patients, there were no significant differences between hospitalization rates for ventilator assisted and ventilator independent persons who were 14-24 years post injury. In a survival analysis study, Shavelle et al (14) identified that trends in improved survival otherwise observed in SCI were not seen among ventilator-dependent SCI patients surviving the first critical years, and that ventilator dependency remained an independent risk factor for mortality. Respiratory complications were the leading cause of mortality, accounting for 31% of deaths (14). The authors stated that the excess mortality of individuals with ventilator dependency compared with similarly disabled non-ventilator dependent patients is due to respiratory disease.

Quality of Life

Physicians and health care workers often underestimate the QoL and life satisfaction of VAs (12,13). Hall (13) surveyed 82 high tetraplegic patients, members of a cohort who have been followed since 1984, with survey and interview data reported at 1-10 years post injury, and again at 10-21 years post injury. This study reports on this cohort of patients with complete C1-C4 tetraplegia, between 14-24 years post injury. Twenty percent of the group were ventilator assisted, defined as requiring ventilator support over 8 hours daily; the mean was 23.3 hours daily. The study found all individuals „ventilator assisted (VA) and ventilator independent (VI), expressed high HRQoL with 95% acknowledging they were “glad to be alive” (62/66 VI, 14/14 VA). There were few differences between HRQoL reported by VI and VA individuals, with 77% and 79% rating HRQoL as “good or excellent”. There were no differences between the groups in self-esteem (Rosenberg Self Esteem Scale). Individuals reported days out of house of mean 3.8 and 3.3 weekly for VI and VA groups.

Nelson's survey of 17 adolescents and young adults with a mean of 11.1 years of mechanical ventilation identified that social and environmental/family factors were the primary determinants of HRQoL (12). Bach reported that among a surveyed group of complete tetraplegic individuals, those with ventilator assistance were significantly more satisfied with their housing, family life, and employment than those who could breathe spontaneously (15).

Recently, authors have reported improved QoL indicators for individuals who have been successfully implanted with phrenic nerve or DPS (currently in clinical use in the US but not yet approved in Canada), enabling ventilator-free breathing after long-term ventilator dependency (16,17). Patients were reported in one case series of DPS to have improved community access, ability to travel, fewer secretions and need for suctioning (17).

Ventilator Weaning

Weaning from ventilation when possible is important due to recognized benefits including reducing tracheostomy-related complications, facilitating rehabilitation treatment and discharge to community, improving speech and communication. In Hall's survey (13), VA individuals used

higher skilled attendants, and required more hours of paid attendant services than VI individuals with high tetraplegia.

Although not the subject of an RCT, large volume ventilator tidal volumes have been demonstrated to decrease the time to wean, with fewer complications (5,18,19). Diaphragm needle electromyography can aid in predicting ability to wean, and bedside spirometry can measure an individual's readiness to wean (20). Unexpected failure of weaning should precipitate investigation for complications such as lung adhesions, entrapment, or deformation at former chest tube sites (5,10).

The Consortium for Spinal Cord Medicine has published Clinical Practice Guidelines which include protocols for weaning, discontinuation of weaning, and recommendations for progressive ventilator free breathing (5).

Transition to Home/Noninvasive Ventilation

There is evidence that indicates that there are fewer complications with NIV than invasive ventilation. However, the unavailability of the expertise required to wean invasive to NIV often limits the ability to offer this to the patient.

For individuals requiring long-term ventilation, noninvasive means can help avoid some of the complications associated with tracheostomy, such as granulation formation, stoma infection, tracheal perforation, stenosis, fistula formation, impaired voice volume, as well as improve likelihood of discharge home (21-23).

Noninvasive support can be delivered by intermittent PPV by a variety of interfaces (nasal, mask, oral, oro-nasal), and can aid in weaning from a ventilator. Noninvasive approaches require reasonably intact bulbar musculature and alert mental status. Bach and Alba (23) described a monitored sequence of manual and mechanical coughing techniques, progressive tracheostomy cuff deflation, and adjustment of ventilator volumes in successfully converting 23 of 25 high tetraplegia patients from invasive to noninvasive support. Toki reported on two C1 level tracheostomy ventilated patients successfully weaned and discharged to the community (24).

Follow-Up After Weaning/Long-Term Follow up

Once the patient with SCI has been successfully weaned, they may remain at significant risk for respiratory complications of atelectasis, retained secretions, pneumonia and respiratory failure particularly if their acute course was complicated or if residual atelectasis remains. Lifelong, noninvasive measures to maintain airway clearance are recommended.

Pulmonary function is compromised by most lesions of the spinal cord, and decline can occur over time. In order to minimize respiratory complications, individuals should be monitored annually to identify any further impairment of pulmonary function, gas exchange and for the gradual development of sleep-disordered breathing or respiratory failure. HMV with NIV should be initiated when indicated. There are no studies to help inform the initiation and follow up of latent respiratory failure in SCI.

Signs and symptoms of respiratory failure include paradoxical breathing, dyspnea, tachypnea, hypersomnolence, irritability, impaired concentration and cognitive function, corpulmonale and polycythemia.

Expert consensus recommendations among SCI experts in Canada include annual monitoring of PCF, overnight oximetry, and lung function including MIP, and VC. An annual blood gas for those at risk to evaluate for chronic hypoventilation is also suggested. Patients at risk are encouraged to employ LVR and airway clearance preventative strategies. Physiologic criteria that indicate potential need for assisted ventilation include: FVC <10ml/kg or under 25% predicted, PImax < 50cm H₂O, Daytime PaCO₂ > 50mmHg and nocturnal oxygen desaturation.

Discussion

Most patients with SCI are relatively young at time of injury. Patients with tetraplegia following SCI are often ventilated acutely following injury. Traditionally, tracheostomy is used for almost all tetraplegic patients in the acute hospitalization. Invasive ventilation is reported to place a heavy burden on a patient's family, thus making discharge to the home more difficult. In fact, many rehabilitation facilities are not equipped to admit ventilated patients, further reducing opportunities for already higher risk individuals to receive needed specialized rehabilitation therapies. Few patients with SCI have bulbar involvement, and ideally noninvasive means of respiratory support should be implemented wherever possible. Bach et al have reported on the use of noninvasive support of patients in the acute setting (25). The benefits aside from the avoidance of cost and tracheostomy complications include decreased risk of infection, lower risks of hospital-acquired pneumonia, improved speech/communication, and greater likelihood of discharge home. Protocols have been developed for ventilator weaning (5,19,22), and conversion to NIV where appropriate.

While this guideline is intended for adults, many persons with SCI are surviving childhood injuries into adulthood on long-term mechanical ventilation. It is thus important to consider their experiences and outcomes in the context of individuals living with ventilator-dependency. There have been reviews and reports published of prospective data collection/retrospective chart reviews of children and adults with SCI who were discharged with long-term ventilation, and are reported to do well with overall good QoL (12,13,15), with some studies even reporting QoL as better than non-ventilator dependent SCI survivors. Clinicians need to be aware of such positive outcomes when counseling their patients, and when engaged in decision making about long-term ventilation.

However, ventilator dependency remains the strongest negative predictor of long-term survival with SCI, with reports of 2.6 times greater mortality after the first year survival than other SCI patients (14). Respiratory diseases and complications remain the leading cause of death among patients with high level tetraplegia.

No studies were identified that evaluated potential differences in survival, morbidity, QoL between invasive or noninvasive home ventilated patients. There is limited evidence indicating that discharge to home is facilitated by having an individual weaned from invasive mechanical ventilation to noninvasive support.

Phrenic nerve pacing has been reported in descriptive studies as early as 1972 (27). Case controlled studies compared with mechanical tracheostomy ventilation have suggested evidence for increased survival, improved phonation and fewer airway secretions for the patients with phrenic pacing (28,29,30). The procedure does have complications and although possibly less costly than full tracheostomy ventilation is associated with greater expense than NIV.

DPS is an emerging option for patients who would otherwise require ventilation (17). Data recently presented has provided some evidence that with even 12 hours of ventilator use

(muscle rest), in multi-trauma patients, there is significant conversion of Type I to Type II muscle fibres (fast-twitch fatigable) in the diaphragm. Diaphragmatic pacing in trials with SCI and ALS patients is correlated with some degree of motor recovery of the diaphragm, as evidenced by electromyography (17). In a retrospective analysis, the outcomes of DPS in 10 adults on chronic HMV as a result of childhood SCI, were reviewed. All patients reported to prefer breathing with the DPS, and 4/10 were full time DPS users, four daytime users, and two who had scoliosis surgery pre-implantation were still undergoing diaphragm conditioning. All patients were reported to recognize improvements in QoL (17) (see Section IV for additional discussion of DPS). At the time of release of this source document however DPS was not yet approved for clinical use in Canada.

Conclusion

Ventilator dependency remains a negative predictor for survival following SCI, and invasive ventilation is associated with increased complications. Attempts to wean from ventilation should be considered whenever possible. Limited evidence suggests progressive ventilator-free breathing is more successful than intermittent mandatory ventilation. When ventilation is required, NIV has been demonstrated to be associated with fewer complications. Patients requiring home ventilation report good QoL and well-being, with recent case series (10,11) finding improved QoL with diaphragmatic and phrenic nerve pacing

Research Questions

1. SCI patients who do not require ventilation from the time of their injury may be at risk for development of hypoventilation and are not currently on mechanical ventilation. What are the ideal parameters to follow that might predict development of hypoventilation, can it be prevented and how is it best managed?
2. Does the presence of OSA in high-level spinal injury patients predispose them to the development of nocturnal and/or diurnal hypercapnia?
3. Can inspiratory muscle training or lung inflation techniques - which may improve chest wall and lung compliance, prevent the development of hypoventilation in high spinal cord injury patients?

Recommendations

The following recommendations are based on limited evidence from several studies and one Clinical Practice Guideline and the consensus of the HMV expert panel.

1. Protocols for weaning with progressive ventilator-free breathing (PVFB) should be considered for appropriate patients with tetraplegia who are dependent on ventilation. (GRADE 1C)
2. Each patient must be individually evaluated for the need for long-term ventilation either acutely or in follow up. Noninvasive support is preferable to invasive ventilation. (GRADE 1C)
3. Phrenic nerve pacing is recommended in selected individuals as an alternative to PPV alone. (GRADE 2C)
4. Regular airway clearance techniques (LVR, MAC and MI-E), clinical assessment and ongoing monitoring of pulmonary function is recommended to ensure adequate airway clearance. (GRADE 1C)

5. In the long-term, individuals with SCI who are ventilator independent, require regular monitoring to identify the development of sleep disordered breathing or respiratory failure and evaluate the need for NIV. (Consensus)

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SECTION IX.

HMV for patients with Duchenne Muscular Dystrophy

Introduction

Duchenne muscular dystrophy (DMD) occurs in approximately one in 3500 live male births. The disease is caused by mutations in the dystrophin gene, and leads to widespread muscle fibre necrosis along with fibrosis and fatty cell infiltration of muscle including the respiratory muscles. Becker muscular dystrophy is a less prevalent and more slowly progressive form of the disease, in which aberrant but partially functional forms of dystrophin are expressed in muscle. In DMD patients, nocturnal or full-time home ventilation has been used for 25 to 30 years, but has only come into frequent use since the 1990s.

Review of Literature

In addition to the initial search strategy described for the guidelines as a whole, a search was performed of Medline from 1980-2008 with cross-referencing of the following key words: Duchenne, pulmonary, respiratory, ventilation, NIV. The major clinical outcome measures sought in relation to long-term ventilation in DMD were survival, gas exchange (including during sleep) and pulmonary function, QoL and hospitalizations, and mode as well as timing of initiation for home ventilation. Table 9-1 shows studies that were deemed to have addressed one or more of the above clinical outcomes. In the majority of the studies selected for inclusion and analysis, the subject population consisted solely of DMD patients, although some studies containing a mixed population of NMDs were also included when there was a subgroup analysis of DMD patients, or when the data were deemed to be especially relevant and investigations specific to the DMD population were lacking. In addition to the information contained in Table 9-1, the detailed findings of several studies which are particularly informative due to their scope or design, and that have played an important role in forming the basis for our conclusions and recommendations, are outlined below. Note that although the early experience with mechanical ventilation in DMD mostly involved the use of negative pressure devices, these have been largely abandoned in routine clinical practice due to problems of upper airway obstruction during sleep (1) as well as cumbersome application. Therefore, the studies included in this analysis are mostly limited to those examining the effects of PPV.

Table 9-1- Summary of Major Literature Search Results for NIV in DMD

Author year (Ref #)	Study Type	# of DMD Ppts	Criteria for NIV Initiation	OUTCOMES				
				Survival	QOL and/ or Hospitalizations	Pulmonary Function	Sleep Gas Exchange and/ or Symptoms	Diurnal Gas Exchange
Bach 1987 (45)	Observational	31	Nocturnal MIPPV introduced when sleep end-tidal pCO ₂ > 55 mmHg	Increased versus historical controls	NA	NA	NA	NA
Bach 1993 (46)	Observational	43	Daytime and/or nocturnal MIPPV in “unweanable” ventilator-dependent patients	NA	NA	NA	Oxygensaturation > 92%	NA
Leger 1994 (36)	Retrospective chart review	16	Not defined (mean FVC = 14% pred; mean diurnal pCO ₂ = 55 mmHg)	NA	↓ Hospital	No Δ	NA	Trend toward ↓ pCO ₂
Vianello 1994 (23)	Case-control	5 NIV versus 5 Control	Symptomatic daytime hypercapnia (mean FVC 670 ml; mean diurnal pCO ₂ = 49 mmHg)	Increased	NA	↓ VC decline	NA	Improved
Rafael 1994 (22)	RCT	35 NIV 35 Control	FVC 20-50% pred with diurnal pO ₂ > 60 and pCO ₂ <45 (mean FVC = 1334 ml; mean diurnal pCO ₂ = 39 mmHg)	Decreased with “preventive” NIV	NA	No Δ	NA	No Δ
Rideau 1995 (32)	Observational	14	Onset of VC decline (mean FVC = 1756 ml)	NA	NA	↓ VC decline versus historical controls	NA	NA
Bach 1998 (41)	Mailand telephone survey	76	NA	NA	↓ Hospital	NA	NA	NA
Fanfulla 1998 (33)	Observational	10	Nocturnal ↓ pO ₂ , symptoms of sleep-disordered breathing (mean FVC = 753 ml; mean diurnal pCO ₂ = 44 mmHg)	NA	NA	↓ VC decline versus historical controls	Improved	No Δ

Author year (Ref #)	Study Type	# of DMD Ppts	Criteria for NIV Initiation	OUTCOMES				
				Survival	QOL and/ or Hospitalizations	Pulmonary Function	Sleep Gas Exchange and/ or Symptoms	Diurnal Gas Exchange
Simonds 1998 (34)	Observational	23 (5 acutely, 18 electively)	Acute respiratory failure; or symptomatic diurnal and/ or nocturnal hypoventilation (mean FVC = 306 ml; mean diurnal pCO ₂ about 60 mmHg in elective group)	Increased versus historical controls	SF-36 scores similar to other chronic diseases	NA	NA	Improved
Baydur 2000 (35)	Retrospective chart review	15	Symptoms of dyspnea or sleep-disordered breathing; or Diurnal pCO ₂ > 45 mmHg (mean FVC = 600 ml; mean diurnal pCO ₂ = 50 mmHg)	NA	No Δ Hospital	No Δ VC decline versus historical controls	NA	Trend toward ↓ pCO ₂
Hukins & Hillman 2000 (11)	Observational	8	Nocturnal ↓ pO ₂ (mean FVC = 910 ml; mean diurnal pCO ₂ = 54 mmHg)	NA	NA	No Δ VC decline versus historical controls	NA	Improved
Gomez- Merino 2002 (48)	Retrospective chart review	91	Not defined (mean FVC = 411 ml)	Increased versus historical controls	NA	NA	NA	NA
Eagle 2002 (25)	Retrospective chart review	183	Abnormal home oximetry and/or symptoms of hypercapnia	Increased versus historical controls	NA	NA	NA	NA
Jeppesen 2003 (24)	Retrospective chart review	243	Not defined	Increased versus historical controls	NA	NA	NA	NA
Mellies 2003 (37)	Observational	5 (1 Becker)	Diurnal hypoventilation or symptomatic sleep-disordered breathing (mean VC = 1200 ml; mean diurnal pCO ₂ = 46 mmHg)	NA	NA	No Δ VC decline versus historical controls	Improved	Trend toward ↓ pCO ₂

Author year (Ref #)	Study Type	# of DMD Pts	Criteria for NIV Initiation	OUTCOMES				
				Survival	QOL and/ or Hospitalizations	Pulmonary Function	Sleep Gas Exchange and/ or Symptoms	Diurnal Gas Exchange
Windisch 2003 (44)	Observational	17	Not defined	NA	SF-36 mental health scores higher than general population	NA	NA	NA
Yasuma 2004 (28) Konagaya 2005 (27)	Retrospective chart review	157	Not defined	Increased versus historical controls	NA	NA	NA	NA
Kohler 2005 (43)	Observational	14	Diurnal $pCO_2 > 49$ mmHg, nocturnal $\downarrow pO_2$, or symptoms of sleep-disordered breathing (mean FVC = 470 ml; mean diurnal $pCO_2 = 48$ mmHg)	NA	SF-36 mental health scores nearly normal	NA	NA	NA
Ward 2005 (49)	RCT	Out of 26 pts, 5 DMD (2 NIV versus 3 controls)	Isolated nocturnal hypoventilation with peak nocturnal $TcCO_2 > 49$ mmHg (mean FVC for all 26 pts = 0.81 ml)	NA	Improved in group of 26 pts	NA	NA	Improved in group of 26 pts
Toussaint 2006 (42)	Observational	42 (major bulbar dysfunction excluded)	Diurnal MIPPV introduced when $TcCO_2 > 45$ mmHg at end of daytime spontaneous breathing (mean VC = 534 ml; mean diurnal $TcCO_2 = 62$ mmHg)	Increased versus historical controls	Improved symptom scores	$\downarrow$ VC decline versus historical controls	NA	Improved
Eagle 2007 (26)	Retrospective chart review	40 NIV (+ spinal surgery in 27) versus 35 Control	Symptomatic nocturnal hypercapnia or FVC < 0.6 L	Increased with NIV	NA	NA	NA	NA
Soudon 2008 (50)	Observational	26 MIPPV versus 16 Trach	Ventilation for minimum of 15 hours/day (mean VC in 2 groups = 485 and 542 ml)	NA	MIPPV: $\uparrow$ Weight loss, $\downarrow$ Hospital and trach injuries	NA	NA	NA

NA = Effects of NIV not formally assessed or reported

Monitoring of Respiratory Function in DMD

The changes occurring in VC over time have been divided into three stages: 1) an initial stage during the first 10 years of life, in which VC increases as predicted with growth of the child, 2) a second stage, during which VC begins to plateau and 3) a final phase during which VC falls, at a rate up to 8-12% per year (2-5). In several studies, VC has been found to be the most important prognostic factor in DMD. Hence a peak VC value < 1200 ml was associated with a mean age of death of 15.3 years, as compared to survival in excess of 21 years in patients with a value > 1700 ml (6,7). Philipps et al (8) reported a median survival of 3.1 years and a five-year survival of only 8% once the FVC fell below 1 L.

Most studies suggest that VC < 40% of predicted and a maximum inspiratory pressure (MIP) of < 30 cm H₂O are predictive of nocturnal hypercapnia (9). This is consistent with a recent investigation in which it was found that nocturnal hypercapnia is likely to develop once VC falls to a mean value < 1,820 ml (= 37% predicted) (10). Values of FEV1 or FVC below approximately 20% predicted and MIP values less than approximately 25 cm H₂O have been reported as being predictive of awake hypercapnia (11,12). A significant correlation between reductions in VC and the fall in MIP over time was also reported (10,13), although other investigators have found a poor correlation between MIP values and mortality (8,11). Maximal sniff nasal pressure (sniff $P_{i_{max}}$) is a relatively new test of inspiratory muscle strength, which involves measurement of the pressure generated within an occluded nostril during a maximal sniff maneuver (14). It has been reported that sniff $P_{i_{max}}$ is easier to perform and has a better correlation to VC values than MIP in some neuromuscular patients (14,15), but a recent study suggested that MIP is more reliable than sniff $P_{i_{max}}$ in DMD patients (16).

Sleep-disordered breathing, consisting initially of obstructive events without hypercapnia, and followed later by central or pseudocentral (due to inspiratory efforts being too weak to be identified) and associated with hypercapnia, also occurs (17,18). A FEV1 value < 40% of predicted was found to be a sensitive (91%) but not specific (50%) indicator of hypoventilation during sleep, whereas a base excess $\geq$ 4 ml/L was highly specific (100%) but less sensitive (11). Nocturnal hypoventilation also correlated with an awake arterial pCO₂ value $\geq$ 45 mmHG (11). Sleep disordered breathing and hypercapnia are initially most manifest during REM sleep, when the neurally-mediated inhibition of non-diaphragmatic respiratory muscle function associated with the REM sleep state can no longer be effectively compensated by the weakened diaphragm.

There is also a deterioration of expiratory muscle function and particularly the effectiveness of cough in DMD patients. In one study, the lowest value of MEP found to be consistent with production of a satisfactory cough was on the order of 50-60 cm H₂O (19). In addition, it has been reported that a PCFs (PCF) value < 270 L/min (4.5 L/sec) identifies patients at increased risk for complications related to impaired airway clearance of secretions (20,21). A detailed discussion of the issues related to monitoring of cough effectiveness and the institution of airway clearance measures can be found within Section I of this document.

Impact of Home Ventilation on Major Clinical Outcomes

Effects of Long-Term Ventilation on Survival

In the only large randomized trial, Rafael et al (22) reported the results of a multi-centre study of 70 DMD patients (mean age 15.5 years) with FVC 20-50% of predicted and acceptable daytime ABG values on room air (pO₂ > 60 mmHG and pCO₂ < 45 mmHG), in order to determine whether “preventive” NIV (i.e., before the onset of diurnal respiratory failure) is able to improve survival. Patients (n=35 per group) were assigned to NIV for a minimum of 6 hours per night versus

conventional treatment (physiotherapy and antibiotics as needed) in the controls, with no corticosteroid therapy in either group. The mean FVC values at entry into the study were 1,334 ml and 1,135 ml in the NIV and control groups, respectively. Although not documented in the original report, in a subsequent Cochrane Review the primary author also stated that 19 of the patients (10 in NIV, 9 in control) had symptoms consistent with nocturnal hypoventilation. After adjusting ventilator settings, follow-up was every six months, and compliance was assessed by interviews and home visits. The study had to be terminated prematurely due to an increased number of deaths in the NIV group (n=8) versus the controls (n=2) at a mean follow-up of 52 months. Most deaths were caused by respiratory failure associated with infection and retention of secretions. Secondary endpoints (time to occurrence of daytime hypercapnia, time to decrease of FVC to < 20% of predicted, time to institute NIV due to respiratory failure) did not differ between the two groups. The authors suggested that a false sense of security may have led to delays in medical consultation during pulmonary infections in the NIV group. This study has generated controversy on several points which may have confounded the results, such as: 1) the presence of symptoms suggesting hypoventilation was not initially taken into account; 2) nocturnal values of pCO₂ were not measured either before or during the use of NIV; 3) there was a higher prevalence of cardiac dysfunction in the NIV group; 4) the intervals for follow-up were relatively infrequent; and 5) the degree of attention to cough assist techniques, as well as the ventilator settings during sleep, may have been suboptimal.

Vianello et al (23) performed a case-control study in which 10 unselected patients with advanced DMD were referred for possible NIV therapy due to symptoms consistent with chronic hypercapnia. The mean age was 20.1 years, severe cardiomyopathy had been excluded by echocardiography in the majority of patients, and all were free from respiratory infections at the time of evaluation. Half of the patients accepted NIV, whereas the other half rejected this option. There were no significant differences between the two groups at the outset in FVC (0.67 in the NIV group versus 0.74 L in the controls), although the NIV group tended to have lower daytime arterial pCO₂ values (48.8 mmHG versus 53.6 mmHG in the controls). Patients in the NIV group used their ventilator for at least seven hours/night. The patients in both groups were reevaluated at six-month intervals over two years. At the end of the evaluation period, all patients in the NIV group were alive, whereas four out of five in the control group had died. From the onset of the study, the mean survival of these four non-ventilated patients was 9.7 months; three died in association with a documented progression of hypercapnia, and one experienced sudden death at home. The two groups of patients in this study appeared to have similar features from a clinical and respiratory functional point of view. Although not randomly selected, the data strongly support the conclusion that NIV has a positive impact on survival in DMD patients with daytime hypercapnia and FVC below 1 L.

Jeppesen et al. (24) performed a retrospective chart review of the male Danish population from 1977-2002, during which time there were 243 verified cases of DMD. Medical records from two centralized centers for the respiratory support of patients with NMDs were examined for patterns of home ventilator use and survival. The overall prevalence proportion of mechanical ventilator use per 100 DMD patients increased from 0.9 in 1988 to 43.4 in 2002. For the 15-19 year old age group (1988-2001), the mortality rate per 100 years among DMD mechanical ventilator users was 3.8 versus 9.8 in non-ventilated patients. For the 20-24 year old age group, it was 2.6 versus 10.5 in the non-ventilated group. In the age group > 29 years of age, the mortality rate did not differ between DMD patients who used or did not use mechanical ventilation. The 2-, 4- and 6- year survival after initiation of mechanical ventilation were 93%, 91%, and 81%, respectively (initiation of mechanical ventilation between 1987 and 1995). While estimates of greater survival rose progressively from the beginning of the study (beginning a decade before

mechanical ventilation was introduced on a broad scale), the data support an additional positive impact of mechanical ventilation on survival.

Eagle et al (25) came to similar conclusions in a retrospective chart review of 183 patients diagnosed with DMD managed from 1967 to 2002. Survival was compared on decade by decade basis, and for the 1990s (the period during which home ventilation came into frequent use for the patients treated at this center), survival was also compared between the ventilated and non-ventilated populations. No patients received steroid therapy. Although the specific criteria for instituting home ventilation are not stated, it appears this was related primarily to the presence of symptoms, and no patients were ventilated prophylactically. Kaplan Meier curves show that the chance of surviving to 25 years of age was 53% in the ventilated group compared with 12% for those who died in 1980s and 4% in the 1970s. When survival since 1990 was compared between the ventilated and the non-ventilated populations mean survival was 19.3 years in the group not receiving ventilation and who died of respiratory failure, as compared to a mean survival of 25.3 years for those who were ventilated. The mean duration of ventilation was 60 months, and 15 of 24 ventilated patients were still alive at the time of publication of the study. Once again, there was improved survival from the 1960s to 1980s which could not be attributed to the use of home ventilation, but the data are consistent with a survival benefit related to the increased use of NIV from the 1990s onward.

More recently, Eagle et al (26) performed another retrospective chart review of 100 patients with DMD born between 1970 and 1990. Kaplan Meier survival analysis was performed to compare 3 groups of patients: 1) patients who had spinal surgery and subsequent nocturnal ventilation (n=27); 2) patients who received ventilation only (n=13); and 3) patients who received neither intervention (n=35). The indication for ventilation was development of symptomatic nocturnal hypoventilation or FVC < 0.6 L. Surgery was offered if the spinal curvature was progressive over a period of six months or Cobbs angle was more than 20°. Patients with severe cardiomyopathy were excluded from the survival analysis. Other than cardiomyopathy, the main reason for not receiving spinal surgery was patient or family preference. The mean age for introduction of home ventilation was 17.4 years in the group who had spinal surgery and 18.2 years in the group who did not. The percent survival at 24 years of age was 84% in patients who had both ventilation and spinal surgery, 35% in those who had ventilation only, and 11% in those with neither intervention. The median age of survival was 30 years, 22.2 years, and 17.1 years in the three groups, respectively. Interestingly, spinal surgery did not improve VC. Therefore, although the authors suggested an added survival benefit of spinal surgery in DMD patients undergoing NIV, the mechanism was unclear.

Finally, the conclusion that increased use of NIV has had a positive influence on survival in DMD is further supported by recently published results from the Japanese literature, involving a retrospective review of 157 DMD patients. Kaplan Meier survival analysis showed that the mean age of death was 31 years in the 73 patients who were treated with PPV after 1990, as compared to only 20.4 years in patients not receiving this treatment prior to 1990 (27,28).

Effects of Long-Term Ventilation on Gas Exchange and Pulmonary Function

The early studies of DMD patients treated with negative pressure devices indicated that in some patients, improvements in diurnal blood gas values could be achieved after the institution of nocturnal ventilatory support, despite a continued fall in VC over time (29,30). In general, these observations of improved ABG values during spontaneous breathing have been confirmed in subsequent studies of NIV use in DMD. In studies that have specifically examined the DMD population, there is conflicting evidence as to whether NIV significantly mitigates the usual annual decline of VC. Therefore, although in most neuromuscular disorders the improvements

in daytime gas exchange observed with nocturnal NIV appear to be due to reversal of impaired ventilatory drive rather than changes in respiratory muscle properties or pulmonary function (31), this has not been conclusively demonstrated to be the case in DMD.

In the study by Vianello et al (23) in which five patients were treated with NIV over two years, there was a reported improvement in pO_2 and pCO_2 compared with initial values (mean pO_2 81.6 versus 74.8 mmHg; mean pCO_2 46 versus 48.8 mmHg), with an apparent stabilization in VC after the first 6 months of treatment. Rideau et al (32) initiated NIV (approximately eight hours per day) in 14 DMD patients having a mean VC of 1,756 ml, and reported that the annual decline in VC (averaging 70 ml) over the next four years was reduced in comparison to historical controls. Similar results for VC decline were reported by Fanfulla et al (33) in 7 DMD patients treated for two years and having a mean VC of 753 ml at the time of initiating NIV, although awake ABG values were not significantly improved over the same period.

Simonds et al (34) provided data on 23 consecutive DMD patients referred for NIV (five after an acute episode of uncontrolled hypercapnia; 18 ventilated electively for symptomatic hypercapnia and confirmed nocturnal hypoventilation). The median duration of NIV use was 9.5 hours/day, and the patients were evaluated every three to six months. In the 18 electively ventilated patients, mean arterial pO_2 and pCO_2 values were approximately 60 mmHG at the initiation of NIV. After 6 months of treatment with NIV, there were major improvements in mean arterial pCO_2 values (to approximately 45 mmHG) as well as pO_2 (to approximately 80 mmHG) during spontaneous breathing on room air. Data for VC over the same period were not reported. The improvements in gas exchange were sustained for up to 6 years in a subset of patients.

Hukins and Hillman (11) prospectively compared diurnal respiratory function with outcomes of polysomnography in 19 patients with DMD. Of these patients, 8 were treated with NIV because of significant sleep hypoxemia (defined as spending at least 2% of total sleep time with an oxygen saturation below 90%). Over a mean follow-up of 0.9 years, there was a decrease in daytime arterial pCO_2 values (from 54 to 49.1 mmHG) with NIV, despite a continued decline in VC (from 0.91 to 0.68 L) over the same period. Other studies involving smaller numbers of DMD patients within mixed NMD populations undergoing NIV have also reported trends toward improvement of daytime blood gases within the DMD subgroup (35-37).

Interestingly, few studies have attempted to specifically determine the effects of NIV on respiratory muscle function in DMD. Mellies et al (37) studied four patients with DMD and one carrying a diagnosis of Becker muscular dystrophy who received NIV for an average of 29.4 months. The MIP values were not significantly altered during the treatment period, but VC nevertheless declined by an average of 183 ml/year. Annane et al (31) found that improvements in daytime arterial pCO_2 values after nocturnal ventilation were not associated with increased respiratory muscle strength (MIP and MEP) or VC values in a mixture of neuromuscular disorders, but DMD patients were specifically excluded from their study. Nickol et al (38) also failed to find improvements in inspiratory muscle function in a group of mixed neuromuscular weakness (diagnosis not specified) patients. On the other hand, Toussaint et al (39) found evidence for short-term improvements in respiratory muscle endurance after a few hours of NIV in DMD patients suffering from dyspnea.

Effects of Long-Term Ventilation on Quality of Life and Hospitalizations

Several studies have shown that QoL in DMD patients undergoing home ventilation is comparable or better than other patient groups. Bach et al (40) found that "life satisfaction" was high in ventilated DMD patients, even in those requiring around the clock ventilatory support, and also reduced hospitalizations based on a mail and telephone survey (41). Simonds et al.

(34) obtained HRQoL data (SF-36 questionnaire) in 13 DMD patients during home ventilation (3-72 months) and found that although physical function was severely reduced, domains such as mental health, role limitation related to physical and emotional factors, and social function did not differ significantly from age matched male controls. Toussaint et al.(42) have documented improved respiratory symptom scores in DMD patients requiring mouthpiece ventilation during the day. Other studies have confirmed that patients with DMD experience a high QoL during NIV, which in certain categories is even superior to that observed in the general population (43,44). Improvements in sleep architecture during NIV have also been documented (37), which may contribute to a better sense of well-being.

Leger et al. (36) performed a retrospective review of 276 patients treated with NIV between 1985 and 1990, among whom 16 carried the diagnosis of DMD. The majority were referred for chronic respiratory failure with repeated exacerbations and hospital admissions. In the DMD group, the mean values for FVC and arterial $p\text{CO}_2$ prior to initiating NIV were 14% predicted and 55 mmHG, respectively. For all patients, NIV was used for an average of nine hours/night and 1.5 hours during the day. Nine patients with DMD were treated successfully with NIV for two years. Five required tracheostomy for different reasons such as inability to tolerate the treatment or uncontrolled hypercapnia. The remaining two patients died during NIV due to a respiratory problem. Among those DMD patients able to use NIV for 36 months, there was a reduction in the number of hospitalizations as compared the pre-NIV period.

Baydur et al (35) retrospectively analyzed patients with a mixture of musculoskeletal disorders, including 15 patients with DMD. NIV was provided for a minimum of 8 hours at night and for 2-8 hours during the day over a mean period of 22 months. NIV was initiated due to progressive dyspnea/orthopnoea, frequent waking, cor pulmonale, or headache in 12 patients; in the remaining 3 patients ventilation was initiated when arterial $p\text{CO}_2$ increased to 45 mmHG even though they were relatively asymptomatic. There was no change in hospital admission rate between the pre- and post-home ventilation periods.

Mode and Timing of NIV Initiation

Most studies in the modern era have employed a nasal interface for patients who only require nocturnal ventilation. For patients who also require diurnal ventilation, there is increasing evidence that tracheostomy can be avoided by using mouthpiece ventilation (MIPPV) in many if not most patients provided that sufficient attention is given to airway clearance measures (45-48). One recent study reported that once the VC has decreased to less than 680 ml, DMD patients are at risk for the development of diurnal hypercapnia despite seemingly adequate NIV during the night (10). However, the optimal timing for first introducing nocturnal ventilatory support, and then to eventually extending ventilatory support to the day as well as the night, has not been clearly defined.

In a recent prospective trial, Ward et al (49) identified a group of patients with chest wall or NMDs (including DMD) who had hypercapnia which was limited to sleep. The patients were randomized to receive either NIV or no ventilatory support. Nocturnal hypoventilation was defined as transcutaneous CO_2 level > 6.5 kPa (approximately 49 mmHG), and all patients had $\text{VC} < 50\%$ of predicted (0.81 versus 1.01 L in control and NIV, respectively) or symptoms suggesting nocturnal hypoventilation. Patients in the control group were switched to nocturnal NIV if preset criteria were met, such as the development of daytime hypercapnia, worsening of symptoms of nocturnal hypoventilation, recurring chest infections, failure to thrive in children, or acute ventilatory decompensation requiring hospitalization. By 12 months into the study, 70% of patients in the control group had switched over to the use of NIV, and 90% had done so at 24 months (mean of 8.3 months overall). Seven patients in the control group developed daytime

hypercapnia, three experienced worsening symptoms of nocturnal hypoventilation, and one child had poor weight gain and developed pneumonia. Although the number of DMD patients was very small in this study (3 of 10 in the controls and two of nine in the NIV group), the study is nonetheless informative. It strongly suggests that many neuromuscular patients are likely to deteriorate and require the institution of NIV within one to two years of detecting nocturnal hypoventilation.

In a group of 42 DMD patients, Toussaint et al (42) used transcutaneous CO₂ to guide the timing of introducing diurnal ventilatory support. MIPPV was introduced when transcutaneous CO₂ was greater than 45 mmHG during the last two hours of spontaneous breathing during the daytime. All patients received home respiratory therapy and cough assistance techniques. Using such an approach, MIPPV was successful in maintaining normocapnia during the daytime throughout the study period of seven years. The one, three, five, and seven-year MIPPV survival rates were 88%, 77%, 58%, and 51% respectively. Only two patients (5%) required tracheostomies. However, it is important to note that these results may not be applicable to patients with major bulbar dysfunction, who were excluded from the study and likely have a higher need for tracheostomy. In another observational cohort study by the same group, DMD patients with similar characteristics receiving tracheostomy ventilation or MIPPV were compared (50). The tracheostomy group had higher rates of tracheal injuries and spent more time in hospital, whereas the MIPPV group appeared to have more feeding problems and weight loss. However, comparable rates of survival and causes of death were observed in the two groups.

Finally, there is little data available to support a clear advantage of any particular ventilator type or mode of ventilation. In mixed groups of neuromuscular patients, both volume- and pressure-cycled devices have been used with success (51). One recent study suggested that adjusting the ventilator settings to achieve a specific target level of inspiratory muscle unloading during the daytime may improve patient-ventilator synchrony and sleep quality at night (52). This study emphasized the importance of validating the effectiveness of NIV settings during sleep.

Discussion/Conclusion

There have been very few controlled studies aimed at specifically determining the influence of long-term mechanical ventilation on survival in DMD patients. The vast majority of investigations in this field are retrospective chart reviews and observational studies, and in some cases this has included invasive as well as NIV. In addition, many of the studies involved patients with a heterogeneous group of neuromuscular or chest wall diseases, and not just DMD. Nonetheless, strong inferences regarding the benefits of long-term mechanical ventilation in DMD have been drawn from the significant improvements in survival that have coincided with the period during which NIV has come into more frequent use (24-28). Part of this survival benefit could also be related to other improvements in the care of DMD patients over this period, such as the use of aggressive airway secretion clearance techniques, treatment of infections, and the development of regional centers of excellence for the care of these patients. Indeed, meticulous attention to physiotherapy and cough assistance techniques appears to be important determinants of success in DMD patients undergoing NIV. Despite the above caveats, it is now widely accepted that long-term mechanical ventilation improves survival in DMD patients, and RCTs to definitively prove this point would be considered unethical by the medical community at this time. Nonetheless, the studies which formed the basis for recommendations about the optimal timing for initiating NIV are subject to the above limitations.

The recommendations for respiratory function monitoring in DMD are based upon a large body of observational data on the natural progression of respiratory involvement by the disease. As noted above, once VC falls to < 40% predicted, patients are at significant risk for the

development of nocturnal hypercapnia (9-11), followed within one to two years by clinical deterioration (49). Therefore, pulmonary function should be monitored at least yearly and patients should be carefully questioned about symptoms suggestive of nocturnal hypoventilation, and with increasing frequency as clinically indicated with progression of the disease. The optimal method and timing for evaluating whether significant sleep disordered breathing is present in DMD patients is open to debate. Although full polysomnography with CO₂ monitoring is generally preferred in order to distinguish upper airway obstructive events from hypoventilation and to confirm the occurrence of REM sleep, we recognize that this may not be readily available and can also represent a significant burden for some patients. Therefore, depending upon the specific circumstances and logistical constraints, alternative forms of respiratory monitoring during sleep (ideally including both oximetry and CO₂ measurements) can also be employed.

The available evidence strongly suggests that once diurnal hypercapnia has developed, QoL is reduced (42,49) and the risk of mortality within one year is high without ventilatory support (23). Under these conditions, nocturnal NIV can be effective in helping to improve daytime symptoms and reduce the degree of diurnal hypercapnia during spontaneous breathing (11,23,34,50). In addition, failure to correct isolated nocturnal hypoventilation (equivalent to transcutaneous CO₂ > 50 mmHg), even in asymptomatic patients, was shown to be a harbinger of clinical deterioration within a relatively short time frame in one randomized study of patients with a mixed group of NMDs (49). At a minimum, very close follow-up is needed in asymptomatic DMD patients with isolated nocturnal hypercapnia because it appears that many such patients could become symptomatic and require NIV within the next one to two years. In addition, we believe that nocturnal NIV should be offered to DMD patients if major hypoxemia during sleep has been documented, even when patients are asymptomatic. Our rationale is that correction of nocturnal hypoxemia could be particularly important in DMD due to the frequent co-existence of cardiomyopathy (53,54). However, it should be acknowledged that the impact of NIV on cardiac function has not been formally evaluated in any of the studies arising from our literature search, and the specific threshold values of nocturnal hypoxemia requiring treatment have not been defined.

If NIV must be extended beyond the night to include a substantial period of daytime ventilatory support for relief of symptoms and maintenance of acceptable blood gases, strong consideration should be given to the avoidance of invasive tracheostomy in favour of MIPPV. This decision should be guided by local logistical considerations and patient preference as well as other factors such as bulbar dysfunction, since the latter may preclude the use of MIPPV. Finally, it is worth noting that physicians may have an inappropriately negative view of the QoL experienced by DMD patients undergoing NIV. In this regard, physician surveys published in 1992 (55) and again in 2001 (56) reported that a substantial number of physicians did not disclose information about the possibility of long-term home ventilation to their DMD patients, although this attitude appears to be changing (57). It is important to recognize that DMD patients can and often do experience a high QoL during NIV.

Research Questions

1. NIV is usually started nocturnally. Does nocturnal ventilation with bilevel reduce phrenic nerve activity completely?
2. Is there any deconditioning with the diaphragm as a result? Does spontaneous ventilation during daytime hours compensate for (prevent) this deconditioning?
3. Patients with DMD often have associated cardiomyopathy. Ventilatory support may improve cardiac output or reduce cardiac work rate in addition to preventing hypoventilation. Does

NIV have a positive effect on cardiac function and what are the optimal NIV ventilatory parameters?

4. How do the outcomes; safety, cost, QoL, differ between 24 hour NIV in those with sufficient bulbar function and invasive tracheostomy ventilation?
5. Does prevention of nocturnal arterial hypoxemia lead to improved cardiac outcomes?
6. What are the barriers to initiation of NIV in those patients who are not offered it?

Recommendations

The following recommendations are based on evidence from the literature search and consensus of the HMV expert panel.

For Monitoring:

1. Carefully question and educate patients to report symptoms consistent with hypoventilation, including disturbed sleep, excessive daytime sleepiness, morning headache, and weight loss. (GRADE 1C)
2. Measure VC, MIP, MEP, PCF, and awake oxyhemoglobin saturation by pulse oximetry at least yearly; if VC < 40% predicted, also monitor awake CO₂ tension by noninvasive methods or ABG analysis. (GRADE 1C)
3. Perform an evaluation of ventilation during sleep if there are symptoms consistent with nocturnal hypoventilation or other forms of sleep disordered breathing (GRADE 1C).
4. In the absence of such symptoms, periodic screening for sleep disordered breathing should also be considered once FEV₁ or FVC < 40% predicted. (GRADE 1C)

For Treatment:

1. Offer nocturnal NIV to patients with diurnal hypercapnia (daytime arterial pCO₂ > 45 mmHg), or when there is documented nocturnal hypercapnia and the presence of symptoms consistent with hypoventilation. (GRADE 1B)
2. Institution of NIV during sleep should be offered to patients demonstrating a major degree of nocturnal hypoxemia, even if asymptomatic. (GRADE 2C)
3. When bilevel ventilation is used, back up respiratory rates are recommended during sleep while on NIV to reduce the work of breathing associated with breath initiation. (GRADE 1C)
4. Individualize the decision about the transition from nocturnal NIV to daytime ventilation by carefully evaluating patient factors (symptoms, bulbar involvement, patient preference, etc.) and available resources. In patients requiring daytime ventilation, strongly consider mouthpiece ventilation as an alternative to invasive tracheostomy. (GRADE 1B)
5. LVR manoeuvres should be introduced with declining VC. (Section I. Airway Clearance) (GRADE 1C)
6. Methods to assist secretion clearance should be initiated when PCF < 270 L/min. (Section I. Airway Clearance) (GRADE 1C)

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SECTION X.

HMV for Patients with other Muscular Dystrophies and Myopathies

Introduction

Myopathies and MDs represent a large group of diseases with different modes of inheritance and different clinical features. Many myopathies and MDs are eventually complicated by respiratory failure and death (1,2). Causes of respiratory failure may include general respiratory muscle weakness occurring together with limb weakness as in limb girdle dystrophy. There may be selective diaphragm involvement as in facioscapulohumeral dystrophy or acid maltase deficiency. There may be associated skeletal dysmorphism-like pectus excavatum and kyphoscoliosis as in Emery-Dreifuss muscular dystrophy. There may be increased chest wall impedance due to myotonia in myotonic dystrophy. There may be coexisting interstitial pulmonary involvement leading to fibrosis in the inflammatory myopathies such as polymyositis and dermatomyositis. There may be bulbar involvement increasing risk of aspiration and respiratory tract infections.

There are few studies describing respiratory failure in specific myopathies and dystrophies other than Duchenne and there are even fewer studies about long-term ventilatory support for these specific diseases.

Review of Literature

Search Strategy

Medline, Embase and other databases were explored with relevant MeSH words for long-term or home ventilation, muscular dystrophy and myopathies.

MDs and myopathies are often mixed with other NMDs and chest wall disorders in studies about long-term ventilation for patients with restrictive respiratory failure (2-6). These patients often represent only a small fraction of cases included. There is a small number of descriptive studies about long-term ventilation focussing on patients with MDs and myopathies (1,7-9,11).

Table 10-1. Summary of Literature Results

Author Year (ref)	Study Type	# of Pts	Control Group	Criteria for Ventilation Initiation	Survival	HRQOL	PFT , ABG, SDB	Cognition	Comments
Annane 2007 (3)	Meta-analysis 8 Randomised Controlled Trials	144 NMD and chest wall dis.	yes	Usually daytime hypercapnia or night time hypoventilation sx.	↑ survival (ALS)	May ↑ HRQoL ↓ ST +LT hypoventilation Sx.	↑ ST night SaO ₂ ↓ STdaytime PaCO ₂	NR	Only one relevant study Cf Ward S below No difference between volume vs pressure-cycled ventilation
Howard 1993 (1)	Retrospective (1978-1991)	84	none	Acute hypercapnic respiratory failure 3 DM with chronic invasive ventilation	NR	NR	NR	NR	Descriptions sorted by specific diseases
Howard 2003 (2)	Expert opinion and literature review	none	none	NR	NR	NR	NR	NR	Physiopathology and NIV management in NMD
Ward 2005 (4)	Randomised Controlled Trial	48 (26 randomised)	yes	normal daytime PaCO ₂ but nocturnal hypoventilation confirmed by a peak TcCO ₂ >6.5 kPa	Nine of the 10 controls failed non-intervention by fulfilling criteria to initiate NIV after a mean (SD) of 8.3 (7.3) months	NR	↓ mean (SD)% of the night during which TcCO ₂ was >6.5 kPa ↑ Mean(SD) SaO ₂ increased in the NIV group	NR	NIV vs not in limited nocturnal hypoventilation
Mellies 2003 (7)	Prospective	30 (12.3±4.1 yrs)	none	daytime ventilatory insufficiency (n=14) or symptomatic SDB (n=16).	No patient died or experienced life threatening complications during the study period	↑ HRQoL	sustained improvement in daytime gas exchange and nocturnal hypoxemia and hypercapnia. Suppressed SDB and improved sleep	NR	Impact of NIV on children PFT, ABG and sleep

Author Year (ref)	Study Type	# of Pts	Control Group	Criteria for Ventilation Initiation	Survival	HRQOL	PFT , ABG, SDB	Cognition	Comments
Ragette 2002 (9)	Prospective	42	none	NR	NR	NR	SDB onset (IVC <60%, PImax <4.5 kPa), SDB with continuous hypoventilation (IVC<40%, PImax <4.0 kPa), and SDB with diurnal respiratory failure (IVC <25%, PImax <3.5 kPa).	NR	Day time PFT as predictors of SDB
Lopez-Campos 2008 (13)	Observational prospective study	115 18 NMD	none	NR	NR	HRQoL of patients receiving HMV is influenced by many factors, especially by dyspnea and the number of admissions. An obstructive pattern in the PFT also influences HRQoL.	Factors influencing QoL		

Abbreviations: PFT: Pulmonary Function Test, ABG: Arterial Blood Gas, SDB: Sleep Disordered Breathing, NMD: Neuromuscular Disorders, ST: short-term, LT: long-term,
NR: not relevant

Treatment of chronic ventilatory failure with NIV is standard practice in adults and children with hypercapnic respiratory failure secondary to neuromuscular and chest wall disorders. Application of nocturnal NIV when these individuals become hypercapnic during the day prolongs survival (11,12), improves nocturnal and diurnal ABG tensions, normalizes sleep patterns (7) and enhances HRQoL (12).

Ward et al (4) reported an RCT examining whether nocturnal hypoventilation is a valid indication for NIV in patients with NMD and chest wall disorder. Forty eight patients aged 7 to 51 years and VC <50% predicted underwent overnight respiratory monitoring. Few patients had MDs other than Duchenne or myopathies (eight congenital muscular dystrophy; one Becker muscular dystrophy; one limb girdle muscular dystrophy; and one spinal muscular atrophy type 2). Twenty six of 48 patients with daytime normocapnia but nocturnal hypercapnia were randomised to either nocturnal NIV or to a control group without ventilatory support. Nine of the 10 controls failed non-intervention by fulfilling criteria to initiate NIV after a mean (SD) of 8.3 (7.3) months. The authors concluded that patients with NMD with nocturnal hypoventilation are likely to deteriorate with the development of daytime hypercapnia and/or progressive symptoms within two years and may benefit from the introduction of nocturnal NIV before daytime hypercapnia ensues.

Indications for NIV in thoracic cage disorders and chronic NMD reported by Consensus Conference of American Chest Physician (10) are: symptoms of hypoventilation and one of the following: $PaCO_2 \geq 45\text{mmHG}$ or nocturnal oximetry demonstrating oxygen saturation $\leq 88\%$ for 5 consecutive min (suggesting nocturnal hypoventilation) or MIP $\leq 60\text{ cmH}_2\text{O}$ or FVC $\leq 50\%$ of predicted.

Many experts agree on the importance of identifying nocturnal hypoventilation and nocturnal hypoxemia (or SDB) in the evaluation of patients with NMD however, polysomnography is time consuming, expensive and not universally available. Ragette et al.(9) looked for relationships between nocturnal respiratory variables and daytime lung function. They studied 42 patients with primary myopathies: 10 with Duchenne muscular dystrophy, 10 with congenital muscular dystrophy, seven with limb girdle dystrophy, one with nemaline myopathy, one with myotonic dystrophy and one with a non-classified myopathy. They reported that VC correlated with respiratory muscle function and gas exchange by day and night. They noted that SDB evolved from REM hypopneas, to non-REM hypopneas with REM hypoventilation, to REM/non-REM hypoventilation, and then diurnal respiratory failure (7-9). The authors concluded that bedside spirometric testing at 6 to 12 month intervals provides a low cost, reproducible way to separate patients into distinct risk groups.

Patients with VC >60% are unlikely to have SDB, indicating good respiratory reserve and minimal risk of respiratory complications. Those with VC <60% are predisposed to SDB, indicating reduced respiratory reserve and the need for polysomnography or alternative means of assessing nocturnal gas exchange. At VC <40% continuous hypercapnic hypoventilation becomes the major concern and blood gas analysis is warranted for proper evaluation. As continuous hypercapnic hypoventilation indicates barely compensated respiratory failure and a high risk of acute respiratory deterioration, accordingly NIV must be considered at this point.

The same group of investigators also performed a prospective study of home ventilation for a child and adolescent population. Mellies, Ragette et al. (7) investigated the long-term impact of nocturnal NIV on sleep, SDB, and respiratory function in 30 children and adolescents with progressive NMD. Indications for NIV were daytime ventilatory insufficiency (n=14) or symptomatic SDB (n=16): nine with congenital muscular dystrophy, five with DMD, 11 with Spinal Muscular Atrophy (SMA) type I-II, two juvenile type of acid maltase deficiency, one with

hereditary motor and sensor neuropathy type I, one with centronuclear myopathy and one with nemaline myopathy. The authors concluded that home ventilation is also indicated in children and adolescents with symptomatic SDB or chronic ventilator insufficiency.

Discussion

As noted by Annane et al. (3), further larger randomised trials are needed to confirm long-term beneficial effects of nocturnal mechanical ventilation on QoL, morbidity and mortality, to assess its cost-benefit ratio in MDs and myopathies. However, there is much, although not ideal, supportive evidence for a beneficial effect on survival. Accordingly whether controlled trials are ethical at this stage will make these trials unlikely to occur.

As is the case for other causes of restrictive respiratory failure and based on a small number of non-randomized prospective studies, retrospective studies and expert opinion home ventilation for MDs and myopathies should be considered for patients with chronic hypercapnic respiratory failure or symptoms and signs of nocturnal hypoventilation. Since HRQoL in patients with chronic respiratory failure is influenced by dyspnea, the number of hospitalizations, and the number of emergency room admissions (13), management strategies must target these issues. Periodic evaluation before and after initiation of NIV is essential and must include assessment of respiratory muscle weakness, dyspnea, daytime somnolence, morning headaches, speech and swallowing difficulties, ability to cough and to clear secretions and recurrent respiratory infections.

Objective assessment must include VC (preferably both erect and supine as an indicator of diaphragmatic involvement), chest radiograph and ABG. Additional tests must be used as needed such as maximal mouth inspiratory and expiratory pressures, PCF, nocturnal oximetry, polysomnography, and direct evaluation of diaphragmatic function. Patients with VC <60% are predisposed to SDB, indicating reduced respiratory reserve and the need for identification of nocturnal hypoventilation. At VC <40% diurnal hypercapnia becomes the major concern and PaCO₂ measurement is warranted.

Benefits of eventual long-term ventilation must be discussed with patients and their relatives. Noninvasive techniques of airway clearance must be explained and applied even before institution of long-term ventilation. Initiation of HMV must be made according to patient willingness and availability of technical and human resources.

Regular assessment of the efficacy of mechanical ventilation is important. Follow up ABGs, and nocturnal oximetry or ambulatory polysomnography will provide important feedback. Data retrieved from some new generation ventilators after days, weeks or months of treatment may also give important information about compliance and treatment efficiency.

Conclusion

Based on few studies about HMV for patients with myopathies, miscellaneous MDs, expert opinion and recommendations made for other groups of NMD; long-term ventilatory support for these patients must also be considered when there is daytime hypercapnia or symptoms and signs of nocturnal hypoventilation.

Research Questions

1. What is the ideal venue for initiation of elective NIV; outpatient setting, sleep lab, inpatient bed, ICU or home? What are the differences in outcomes, cost and QoL for patients and families?
2. Does commencing NIV when nocturnal hypercapnia alone is present improve outcomes?

Recommendations

The following recommendations are based on limited evidence from few studies about long-term ventilation in general NMDs and consensus of the HNV expert panel.

1. Obtain periodic clinical assessment and spirometry at six to 12 month intervals, including sitting (plus supine if diaphragmatic weakness is suspected) spirometric testing. (GRADE 1C)
2. Consider monitoring for sleep disordered breathing in patients with VC <60%. (GRADE 1C)
3. Consider ABGs or nocturnal measure of CO₂ in patients with VC <40% to exclude hypercapnia. (GRADE 1C)
4. NIV should be offered when there is daytime hypercapnia or symptomatic nocturnal hypoventilation. (GRADE 1C)
5. Assess airway clearance ability with PCFs and implement cough assistance strategies (Section I. Airway Clearance). (GRADE 1C)

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SECTION XI.

HMV for Patients with Myotonic Dystrophy (Steinert's Muscular Dystrophy)

Introduction

Myopathies and MDs represent a large group of diseases with different modes of inheritance, different ages of onset, different muscle weakness distributions but many of them are eventually complicated by respiratory problems, respiratory failure and death (1, 2):

Dystrophia Myotonica (DM) or Myotonic Dystrophy or Steinert's disease is of special interest because of its relatively high incidence in Canada and even more so in Québec. It is the most frequent adult onset MD, with a worldwide prevalence of 14 per 100,000 population and 189 per 100,000 population in Saguenay-Lac-Saint-Jean (3) region of Québec. It is an autosomal dominant disorder resulting from an unstable myotonin kinase gene (19q13.3).

DM is characterized by muscle weakness and myotonia. The weakness distribution includes facial and anterior neck muscles, distal muscles of the limbs which progresses to involve proximal muscles. Other features include frontal balding, cardiac conduction defects, cataracts, testicular atrophy and intellectual and emotional problems (3).

Patients with DM may have an irregular awake respiratory pattern as well as SDB (4). Hypoventilation may occur, related to reduced response to CO₂, upper-airway obstruction, respiratory muscle weakness, or reduced chest wall compliance (5). SDB may be observed with central and obstructive apneas (6). Hypercapnia is more prevalent in advanced DM at time that proximal limb muscle weakness is recognized. Weakness of the inspiratory muscles is usually severe when proximal limb weakness is clinically evident. But unlike other types of proximal myopathies, hypercapnia in DM may be present even with relative preservation of VC and maximal breathing capacity (5).

Daytime sleepiness and abnormal REM sleep distribution in DM have generated the hypothesis of a dysfunction of the hypothalamic hypocretin system as seen in patients with narcolepsy. However, the pathophysiologic basis is distinct from narcolepsy, as patients with DM do not have a consistent defect of hypocretin release or receptor function (7,8).

Cognitive impairment and personality disorders are commonly described among the symptoms of myotonic dystrophy. In contrast, only a small percentage of patients show low intelligence and this may in fact be more prevalent in patients with maternal inherited DM (9). Many patients show dependant tendencies, depressed attitude and difficulties in establishing relationships in social life (3, 9).

Respiratory failure is a major cause of death among DM patients. These patients have high prevalence of chronic respiratory failure. Aspiration pneumonia and perioperative pulmonary complications are common. In a cohort of 375 DM patients followed for 10 years, Mathieu J. et al. reported 32/75 (42%) deaths related to respiratory problems (10). The estimated ratio of observed to expected deaths was significantly increased (56:1) for respiratory disease. Deaths related to cardiac problems were also frequent (conduction defects and coronary disease).

Very few articles address long-term ventilatory support for patients with chronic respiratory failure related to myotonic dystrophy. A literature search was completed to support any evidence-based recommendations.

Review of Literature

Few studies of populations of NMDs included DM patients (1). Only one relevant study dedicated to long-term ventilation for DM patients was found (14).

Nugent et al (14) did a descriptive analysis of retrospective clinical data about 16 DM patients referred for assisted ventilation between 1989 to 1997. They prospectively assessed the efficacy of ventilatory support in 10 patients, non-randomly and without a control group. Post-polio myelitis patients were selected as an historical control group because there were enough patients in their database to obtain age- and sex-matched control subjects with complete records of compliance for comparison.

Patients were home ventilated for a mean period of 27 months, starting on average eight years after DM diagnosis. Five of the ten patients were ventilated more than two years. Reasons for initiating ventilation included; poor quality sleep, daytime sleepiness and morning headaches, daytime hypercapnia $p\text{CO}_2 > 49$ mmHg or night rise of transcutaneous $p\text{CO}_2 > 54$ mmHg. Mean PFTs values at beginning showed FVC less than 30% predicted, P_{Imax} 29 cm H₂O and P_{Emax} 45 cm H₂O. The majority of patients were ventilated noninvasively, with volume or pressure preset ventilators, with full-face or nasal masks.

Table 11-1. Summary of Literature Search Results

Author ^{Ref} (Year)	Study Type	# of Pts (Myotonic D)	Control Group	Criteria for ventilation initiation	Survival	HRQoL	PFT, ABG, SDB	Cognition	Comments
Nugent (14) (2002)	Descriptive analysis of retrospective (1989-1997) and prospective clinical data (1997-1998)	16(16)	post-polio group from same center data base	chronic hypercapnic respiratory failure (n = 11) nocturnal hypoventilation (n=1) respiratory arrest (n=1)	3 deaths Survivors ventilated for 2 to 72 months	SF36 ↓ compared to control group BDI 4 patients with depression	ST+ LT day + night ↑ PaO ₂ ↓ PaCO ₂	NR	NIV compliance less than post-polio group
Howard (1) (1993)	Retrospective (1978-1991)	84 (13)	none	Acute hypercapnic respiratory failure 3 DM with chronic invasive ventilation	NR	NR	NR	NR	Description sorted by specific disease

Abbreviations: PFT: Pulmonary Function Test, ABG: Arterial Blood Gas, SDB: Sleep Disordered Breathing, SF36: Short Form 36 HRQoL questionnaire, BDI: Beck Depression Inventory, SRI: Spanish Respiratory Insufficiency questionnaire, ST: Short -Term, LT: Long-Term

Physiologic Responses to Assisted Ventilation

ABG analysis before the start of ventilatory support showed hypoxemia (mean PaO₂ , 53.0 mmHG) and carbon dioxide retention (mean PaCO₂ , 64.3 mmHG). There was a significant improvement before discharge, with an improvement in mean PaO₂ to 65.3 mmHG and a reduction in mean PaCO₂ to 53.8 mmHG. At reassessment in the survivors, these improvements were maintained. Pulmonary function tests showed a restrictive pattern initially with a reduction in maximal mouth pressures in keeping with respiratory muscle weakness. At reassessment, there had been no significant change in FVC, or maximal mouth pressures, to suggest that treatment may have had an effect on the decline in respiratory function.

Compliance with Assisted Ventilation

The number of hours used per 24/h on the ventilator was significantly lower for patients with myotonic dystrophy compared with the historical control group of post-poliomyelitis patients; mean, 6.3 h (SEM, 1.2 h) compared with 8.8/h (SEM, 0.4 h), respectively (p < 0.05). Reasons for poor compliance included difficulty sleeping with the ventilator, nasal blockage, and lack of improvement in daytime symptoms. The lack of improvement in daytime symptoms may be because primary sleepiness is a clinical feature independent of SDB in DM (18).

Quality of Life

Compared with age- and sex-matched control subjects, the results of the SF-36 survey demonstrated the greatest differences were in physical function and role limitation, which were both 72% lower in DM patients. The smallest differences were in mental health and role limitation caused by emotional problems. In the Hospital Anxiety and Depression scale (15) questionnaire, where a score > 10 suggests clinically relevant anxiety or depression, no patient reached that level of anxiety. Two patients had elevated scores for depression. In the

Beck Depression Inventory (16), four patients had a score > 15, suggesting moderate-to-severe depression.

However, the impact of home ventilation on these variables can not be interpreted from the data reported in the study because questionnaires were only completed after ventilation had been initiated

Discussion

Chronic hypercapnic respiratory failure is a common finding in patients with myotonic dystrophy and can occur with minimal signs of peripheral muscle weakness. As with other NMDs, periodic assessment of symptoms (dyspnea, daytime sleepiness, morning headaches, etc) and pulmonary function test including FVC, MIP, MEP must be made. Because pCO₂ may be elevated without severe reductions of FVC in DM, measurement of ABGs should be considered earlier. Signs of chronic respiratory failure must be sought and will be found in the majority of patients with proximal limb muscle weakness.

Similar to other NMDs, long-term ventilatory support must be considered for patients with daytime hypercapnia and those with symptoms and signs of nocturnal hypoventilation.

There are few reports of long-term use of NIV support in this condition. In previous studies which included patients with different NMDs (1), all patients with myotonic dystrophy required tracheostomy for long-term ventilation. However, NIV is preferable because a tracheostomy tube reduces cough efficiency, promotes secretions, and may increase the frequency of respiratory infections.

The study of Nugent et al (14) supports the contention that most patients with myotonic dystrophy can be treated with prolonged ventilatory support at home with immediate and sustained improvements in physiologic parameters. There seems to be good survival on assisted ventilation with more than one-half of the patients receiving treatment for >two years. Nevertheless, without an RCT, increasing survival related to ventilatory support cannot be proven.

Selection of an appropriate ventilator and interface for each patient is an important aspect of management in this group of patients. Because of facial muscle weakness, oral leakage of air when using a nasal mask is common and an oronasal mask may be required.

Depressive tendencies as well as intellectual impairment and personality disturbances have been noted in patients with myotonic dystrophy. It is unclear whether the depression is a direct result of brain dysfunction or a secondary reaction to the physical disability. These patients often appear to be poorly motivated. Repeated education with both patient and family or the caregiver regarding treatment is essential especially for long-term home ventilation. Because of the low compliance with treatment and limited motivation, patients or physicians and caregivers sometimes decide not to initiate long-term home ventilation. In one of the world's largest DM cohorts located in Saguenay-Lac-St-Jean region of Québec, very few DM patients are home ventilated despite high rate of respiratory failure as cause of death and despite resource availability (10). This observation emphasizes difficulties of initiating HMV for DM patients who may lack the motivation and the capacity to direct their own care.

It is beyond the scope of this review, but as the second cause of death in Myotonic Dystrophy patients, cardiopathies with arrhythmias and sudden death cannot be forgotten. Cardiac conduction tissue involvement is the most frequent feature, characteristically in a variably

progressive and asymptomatic form. Significant abnormality on the ECG may include rhythms other than sinus, PR interval of 240 msec or more, QRS duration of 120 msec or more, or second-degree or third-degree atrioventricular block (16). A severe ECG abnormality (relative risk, 3.30; 95% confidence interval [CI], 1.24 to 8.78) and a clinical diagnosis of atrial tachyarrhythmia (relative risk, 5.18; 95% CI, 2.28 to 11.77) are independent risk factors for sudden death (17). Though, regular follow up by cardiology is warranted with periodic ECGs (even ambulatory ECGs), it is unclear whether ventilatory support has an ameliorative effect on arrhythmias or cardiac function in patients with DM.

Conclusion

Based on one specific study of home ventilated DM patients, expert opinion and recommendations made for other groups of neuromuscular disorders, long-term ventilatory support for patient with myotonic dystrophy must be considered when there is daytime hypercapnia or symptoms and signs of nocturnal hypoventilation. Because of some biopsychosocial issues, compliance with long-term ventilatory support may be lower in DM patients so they may need extra support from caregivers, RTs and physicians.

Research Questions

1. What are the best methods to encourage adherence with positive pressure therapy in patients with Myotonic Dystrophy?
2. Are there any improvements in cognitive function or cardiac status as a result of the initiation of PPV?

Recommendations

The following recommendations are based on limited evidence and consensus of the HMV expert panel:

1. Obtain six to 12 monthly clinical assessment of symptoms of daytime or nocturnal hypoventilation. (GRADE 1C)
2. Obtain yearly VC and consider daytime PaCO₂ measurement, even with mild reductions of VC when patients exhibit symptoms of hypoventilation. (GRADE 1C)
3. Consider overnight oximetry or polysomnography when there are symptoms of nocturnal hypoventilation. (GRADE 1C)
4. Long-term NIV should be offered to patients with daytime hypercapnia or symptomatic nocturnal hypoventilation as for other NMDs. (GRADE 1C)
5. Carefully assess motivation and ability to adhere to treatment with patients and their caregivers before initiating long-term ventilatory support. (Consensus)
6. Reassess every six months to verify treatment adherence and provide extra help and motivation as needed. (Consensus)
7. Assess airway clearance ability with PCFs and implement cough assistance strategies (Section I. Airway Clearance). (GRADE 1C)

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SECTION XII.

HMV for Patients with Post-Polio Syndrome

Introduction

Post-polio syndrome (PPS) is the occurrence of progressive weakness with a constellation of other manifestations (including fatigue, pain, sleep disturbance and cold intolerance) with onset several decades after surviving acute poliomyelitis (1). Due to the nonspecific nature of the symptoms and lack of definitive testing, it can be a difficult diagnosis to confirm. In 1997, the Post-Polio Task Force, by consensus, confirmed diagnostic criteria to include: a prior episode of paralytic poliomyelitis, followed by a period of neurologic recovery and then an interval of neurologic and functional stability, which is then, followed by either an abrupt or gradual onset of new weakness or abnormal muscle fatigue, muscle atrophy or generalized fatigue. Other causes of these symptoms must be excluded (2,3). Although the exact prevalence of PPS is unknown, studies report from 22.4- 64% of polio survivors being affected (1). However, in industrialized countries where wild virus polio cases have been eradicated, the proportion of patients using HMV because of PPS will be diminishing (4,5).

Late-onset of respiratory problems in PPS often occurs in individuals who initially exhibit respiratory muscle involvement and in one survey, 42% of PPS patients had new breathing-related problems (6,7). Chronic hypoventilation may lead to respiratory failure in some patients who tend to have lower baseline vital capacities and more rapid annual decline in VC has been documented (6,8), but one longitudinal study showed that a decline in VC of 40 ml per year in those with a poor prognosis (who progressed to respiratory failure) did not statistically differ from the 30 ml per year in those who had a good outcome (9). The presence of concurrent scoliosis was associated with lower VC and worse blood gas derangements but the annual decline in VC was not accelerated (9). Several series have shown an increased risk of respiratory failure with VCs < 50% predicted (7,9,10). Deterioration may be precipitated by acute respiratory infections which may be related to expiratory muscle weakness and poor airway secretion clearance. Scoliosis, respiratory infection, obesity and concurrent lung disease may play a role in the respiratory deterioration (1); however, the onset of nocturnal hypoventilation is often insidious (6,9,11).

Initially, negative pressure ventilators and tracheostomy with invasive positive pressure ventilation (IPPV) were the modes of HMV commonly used but increasingly since the 1980s noninvasive positive pressure ventilation has been employed with Bach reporting on successful use of mouth IPPV in severely affected PPS patients and subsequently using oronasal or nasal masks with IPPV. (8,12,13). Bach noted that the amount of time free from ventilatory support correlated with VC but no data was provided (13). Relief from the symptoms of chronic hypoventilation and reversal of signs of cor pulmonale have been described elsewhere (13,14,15,16).

Review of Literature

Study Characteristics

There are no RCTs on the initiation of HMV in PPS with most of the information coming from descriptive retrospective and prospective series of mixed populations of patients, with PPS being one cause of chronic hypoventilation. Survival data is obtained from observational case series (17,18,19). Descriptions of timing and location of initiation of HMV are lacking. Information on QoL is available from one center both in a prospective observational study and a case-control study (20,21).

Outcomes

Survival and Morbidity

Based on the published mainly retrospective series, there appears to be alleviation of symptoms and reversal of signs of hypoventilation regardless of type of mechanical ventilation instituted (8,13,14,16,17). A Cochrane Systematic Review of nocturnal mechanical ventilation for chronic hypoventilation secondary to neuromuscular and chest wall disorders only included a few post-polio patients in the mixed population of patients. Although the evidence of therapeutic benefit was weak, it supported the suggestion that the symptoms of chronic hypoventilation were alleviated (15).

Survival has been reported in two large series of HMV with subpopulations of PPS patients, with 100% five-year survival in 30 PPS patients and a five-year survival of 75% in the other study (18,19). A smaller series with only 12 PPS patients had a 45% five-year survival (17). Although no trials clearly demonstrate the effectiveness airway clearance in PPS there is little doubt that these individuals remain at risk for pneumonia and respiratory failure as a result of impaired cough effectiveness. Until more specific evidence is available it remains prudent to monitor cough capacities and introduce airway clearance techniques when PCFs fall near or below 270 L/min.

Quality of Life

Two publications, one an observational study and the other a cross-over study, from the same investigators in Sweden, have demonstrated larger dysfunctions in the sleep-related parameters of the Sickness Impact Profile and Health Index Questionnaires in Nasal NIV PPS patients than in tracheostomy ventilated PPS patients. They surmise this finding is due to possible increase in arousals from mouth leaks in the NIV group although this has not been directly measured (20,21).

Work of Breathing

Two cross-over studies of NIV during sleep have demonstrated that bilevel pressure support ventilation is associated with a decreased oxygen cost of breathing compared with continuous volume-cycled mandatory ventilation (23,24).

Sleep Quality

Three types of SDB have been described in 35 symptomatic PPS patients who had sleep studies – OSA, hypoventilation and a mix of both. Those with just OSA had normal lung function and were obese, while the hypoventilation group had features of restricted lung function, decreased maximal respiratory pressures, and cor pulmonale. Scoliosis was present in over two-thirds with some component of hypoventilation (25). Dalmage et al noted increased apnea-hypopnea index in polio survivors only in those with scoliosis but not in those with respiratory muscle involvement at the time of acute polio, however, those with previous respiratory muscle involvement had abnormal lung volumes, respiratory muscle dysfunction and ABG derangements. Those who survived bulbar polio had essentially normal respiratory function and sleep parameters (26). Steljes et al performed sleep studies to assess sleep quality in 13 patients with PPS and initiated NIV with volume cycle home ventilators in the sleep laboratory when hypoventilation was present. A subgroup of 5 patients using rocking beds during sleep had poor sleep quality and respiratory abnormalities that reversed with the institution of nasal NIV (27). A further 4 PPS patients had mixed or OSA that responded well to CPAP therapy. Hypersomnolence is a commonly reported symptom in presentations with nocturnal hypoventilation or OSA (27,28). Bach performed polysomnograms in 13 patients (eight PPS, five chronically ventilated acute polio survivors) who used mouth NIV and showed leakage was

a frequent occurrence that could be limited by use of lip seals and/or nasal occlusion. They did not report arousal data but other studies have suggested leakage is associated with arousals and oxygen desaturations (22). Bach suggests the evaluation of signs and symptoms of chronic hypoventilation should include VC and overnight oxygen saturation trending and that polysomnography is only helpful in those with symptoms who do not have significant restriction, subnormal mean nocturnal oxygen saturations or nocturnal hypercapnia (22).

Table 12-1. Literature Search Results of HMV for Individuals with PPS

Author Year (Ref)	Study Type	# of Pts	OUTCOMES		
			Lower vital capacity linked to respiratory failure	Reversal of symptoms of chronic hypoventilation	Sleep studies + for obstructive sleep apnea
Bach (6) 1995	Retrospective	73	Yes		
Bach (8) 1987	Retrospective	31	yes		
Migren(9) 1997	Prospective Cohort	31	yes		
Perhrsson (10) 1992	Retrospective	47	yes		
Annane (15) 2007	Cochrane Review			yes	
Hsu (25) 1998	Retrospective	35			yes
Dolmage (26)	Prospective Cohort	50			yes
Steljes (27) 1990	Prospective Descriptive	13			yes

Discussion/Conclusion

There is little evidence to suggest that patients with PPS who develop respiratory insufficiency should be treated differently from other patients with slowly progressive NMD. Most of the papers that informed the recommendations are studies in which groups of slowly progressive NMD patients and chest wall disorders are combined. When VC falls below 50%, evaluation for possible hypoventilation should be considered (or sooner if symptoms are present); however, this is based on low-quality evidence (observational studies- see table 12-1). The only caveat would be that the presence of symptoms of sleep disturbance or hypersomnolence, in the absence of indicators of hypoventilation, may be the harbinger of OSA syndrome and a polysomnogram would be required.

Research Questions

1. Do patients with PPS using ventilation benefit from a back-up respiratory rate or is a spontaneous mode of ventilation equally effective?
2. Is overnight oximetry alone sufficient to identify nocturnal hypoventilation and candidates for NIV?

Recommendations

The following recommendations are based on limited evidence and consensus of the HNV expert panel:

1. Yearly assessment of VC is recommended from the time of presentation of PPS. (GRADE 1C)
2. If VC >50% with symptoms of hypoventilation, perform measurements of daytime ABGs, overnight oximetry and consider polysomnography. (GRADE 1C)
3. When VC <50%, perform ABG analysis and/or nocturnal oximetry yearly. (GRADE 2C)
4. With confirmation of the presence of chronic hypoventilation, offer NIV. (GRADE 1C)
5. Assess airway clearance ability with PCFs and implement cough assistance strategies (Section I. Airway Clearance). (GRADE 1C)

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SECTION XIII.

Ethical Issues in the Care of Home-Ventilated Patients

Introduction

This chapter provides an exploration of the pressing professional, ethical and legal issues involved with the care and treatments of adult ventilated patients in their home environments. It examines the characteristics of the home setting and the unique ethical, professional and legal issues that arise from providing care in this environment. Finally, this chapter offers a validated decision-making framework to assist with both systematically and critically working through ethical dilemmas and for negotiating through conflicts in perspectives, values and decisions at the end of life. It also recommends a validated process for disclosing 'bad news' to patients and their families.

Consider Case One: A 21 year-old patient, Mr. Smith, is suffering from DMD. He has had experience with a temporary tracheostomy in the past when he urgently needed relief from an anaphylaxis incident. He has clearly stated that he does not want to receive a tracheostomy again, even though it means that when NIV is no longer effective, he would likely die as a consequence. He also has a younger brother with DMD. Mr. Smith's close family, currently caring for him at home, wishes him to consider receiving a tracheostomy when it could potentially extend his life for many years. How would you approach this situation in light of its inherent ethical, professional and legal considerations? What justification would you provide for your decisions?

Consider Case Two: A 48 year-old patient, Mrs. Doe is suffering from Amyotrophic Lateral Sclerosis, and is living at home fully assisted by a mechanical ventilator. She is a widow with three adult children living either at home or in the neighbourhood. Mrs. Doe is at the stage of her rapidly progressing illness such that her only means of communication is through the use of two of her fingers. Mrs. Doe is increasingly teary, and her three children, though very caring and supportive of her, seem to disagree about what future medical interventions would be appropriate for their mother. How would you approach this situation, and what rational justification might you provide to support your position?

Patients, their families and health care professionals continue to grapple with value-laden issues and dilemmas related to the phenomenal development of medical technology that provides options to sustain and extend life, previously unimaginable. For debilitating diseases and trauma that severely and permanently compromise patients' ability to breathe without ventilatory support, the provision of optimal holistic care in a hospital setting poses extensive and far-reaching ramifications. Not surprisingly, therefore, caring for such patients in their home environments creates quite unique dilemmas and challenges.

Review of literature

A survey of the literature pertaining to home-ventilated patients showed that there is relatively little written about these important ethical (or value-laden issues), with most of the published papers focusing on the care and treatments of paediatric patients.

It is very important to note that the community environment is quite distinct from the hospital setting in many significant ways. The usual processes for identifying and addressing medico-ethical issues in the context of the patient's home environment naturally require some significant modification and customization in order to be respectful of ethical principles, professional standards, legal duties and obligations. For example, the home care culture changed the

traditional concept of the physician's role from being the primary authority in an acute care setting to a collaborator in the patient's treatment in his/her home environment (1).

In order to provide some context, the introduction of PPV by tracheostomy in the latter half of the 20th century succeeded in reducing mortality from bulbar poliomyelitis from 90% to 20% within a 30-year period. One by-product of this success was the creation of a 'population of survivors' dependent on prolonged life-sustaining technology (1). Transitional care became increasingly important for patient care, as technological advances allowed for patients to not only live longer, but potentially recover enough to persist without assistance. Units were created to educate family members on how to care for their loved ones in order to transition patients into a home setting (1). Arguably, the current interest in mechanical ventilation beyond the intensive care unit (ICU) likely originated through the need to find solutions to the prospect of indefinite hospitalization for such patients.

Long-term noninvasive mechanical ventilation provided at home was developed as an alternative to the institutionalization of polio survivors. Initially focused on patients with hypoventilation due to NMDs, respiratory disorders and skeletal abnormalities, NIPPV is now broadly applied across clinical settings, as well as in the home environment.

In 1995, Goldstein and colleagues noted that clinically stable patients requiring ongoing ventilatory support could be maintained at lower cost in the community than in the ICU, with less disruption to family life and greater opportunity for rehabilitation and independence, while intensive care beds could, as a result, be released for other patients (2). Furthermore, extended periods of time in the ICU also, "lacks a rehabilitative focus, fosters dependence and may disrupt family life" (2).

Perhaps the first significant motivating force for shifting ventilation from the ICU setting to the community-based or home setting is the issue of scarce health care resources. Increasingly, ICUs are occupied with patients who are chronically ventilated for a number of complex reasons, and the wait list for long-term care for chronically ventilated patients is several years, varying from one jurisdiction to another. Affordability, in the context of the ethical duty of responsible stewardship and the allocation and use of scarce resources, creates extensive ethical issues relating to justice and fairness. For example, the actual cost in the U.S. for 24-hour domiciliary ventilation is estimated at \$7,250 per month and for nocturnal NIV at \$1,600 per month. However, the cost of maintaining a patient in hospital may exceed \$80,000 per month (3).

Goldberg argues that the provision of HMV to patients is selected according to "predetermined medical, psychosocial, environmental, technological, organizational and financial criteria" can dramatically improve QoL, simplify the provision of care and reduce inpatient costs (3). Individuals with impairments may reach their optimal functional level in society with the help of HMV (2).

In other words, the second major argument for home ventilation is based on the philosophy of reintegration of patients in their own home environments – with their families and familiar surroundings, wherein personal, cultural and religious/spiritual values, beliefs, rites and rituals are more readily appreciated and honoured. This home-based health care delivery process, therefore, promotes patient and family-centredness, as well as respect for patient autonomy (a cardinal ethical principle in Western bioethics today).

However, the population requiring ventilatory support is diverse, and the clinical conditions necessitating ventilation extend across a range of severity. Ventilatory support is required for both obstructive disease, such as COPD, and various non-obstructive conditions, including kyphoscoliosis and NMDs such as ALS, DMD and SCI. A number of patients with NMD require invasive ventilation via tracheostomy.

In Goldstein's 1995 study of 98 HMV users, of whom 47% were ventilated invasively, 28% reported independence in self-care, with a further 33% able to care for themselves partially. Thirty-eight percent of the participants had made an informed choice about first starting mechanical ventilation or opting for it on a permanent basis. 87% of individuals receiving ventilator support responded that the overall experience of mechanical ventilation had been positive rather than negative, indicating that they viewed mechanical ventilation as sustaining life, improving physical symptoms and facilitating greater mobility and freedom. Those who responded negatively focused on problems relating to limited mobility, dependence on caregivers, a lack of social acceptance and difficulties with equipment (2).

Generally, persons with neuromuscular conditions reported an increase in life satisfaction as a result of HMVs (2). Many individuals receiving ventilator support stressed the need for more information related to their situation, both for their own education and as part of the continuing education of physicians and health care providers, especially those living in smaller communities. In 2002, Cano and colleagues conducted a study of the QoL of 52 French patients with DMD ventilated at home (4). Ninety-two percent of patients reported feeling positive about their QoL more than 50% of the time, with no difference in satisfaction between patients with different types of ventilation (4).

Institution/Hospital as Compared with Home Environment Setting

Evidence-based practice is crucial to the creation of best practice guidelines. Specifically as it applies to ethical issues and home ventilation, the following should be noted:

1. There is a paucity of empirical evidence on safety and risk, as well as on ethics in home/community-based care, and this naturally includes issues relating to home-ventilation. Existing literature indicates caution regarding the generalization of evidence derived from hospital-based settings to community-based settings.
2. A review of the evidence identified the limited applicability of institutionally derived patient safety frameworks to the home care sector and calls for a rethinking of the underlying assumptions and guiding frameworks that have been used to systematically identify and critically examine pressing ethical issues encountered in the community setting.
3. In this regard, a modified version of an ethical decision-making framework to better capture safety/risk prompts (Appendix II) and its validation as an effective problem-solving tool for safety and risk issues in the community setting should be thoroughly explored.

Context

The home environment is rapidly becoming the preferred milieu for delivering care to patients. Home care is increasingly being recognized as a key element for the continuum of care in the health care system, and Roy Romanow, in his landmark report on the Future of Health Care in Canada, calls home care the "next essential service" (5).

There are numerous reasons for this shift in health care delivery. These include: scarce health care resources (including manpower) and, consequently, limited in-patient beds, medical technology which makes it possible to deliver selective care in patients' homes, and a

philosophical shift toward patients achieving a much improved QoL experience when they are cared for at home. The latter advantage of being cared for at home is certainly not unqualified, and many resources, systems and processes are necessary to ensure the safe and effective delivery of patient care in their environments.

There needs to be capacity-building, a smooth and well-integrated continuum of care, a reasonable degree of sustainability, noting that there is a natural decline in patients' health over time, and well-defined recourse for patients and their families in the event that they can no longer manage in the home environment.

However, an aging population, smaller family size, shifting social and cultural values, economic deprivation, an acknowledgement of the tremendous impact of caregiver burden and compassion-fatigue all contribute to the reducing capacity for families to provide care (albeit with medical technology in the home) and a meaningful and effective restructuring of the traditional health delivery system.

People are being discharged from hospital into the community earlier, and with greater need for support. New technologies mean that caregivers are caring for increasingly acute illnesses at home. This raises the question of quality and safety – for the client/family caregiver and service provider. Arguably, this increasing shift of care from the institutional sector to the community is resulting in increased demand, but without concomitant resources. This could potentially translate into a loss of a high standard of care, increased burdens to families, safety concerns, and moral distress for both health care professionals and families. Furthermore, it may lead to the situation where our system may not be able to effectively provide care and treatments for patients in their homes despite having the medical technology to enable this option.

From the perspective of the available evidence, there is little Canadian literature on quality in-home care, although it is recognized that there are quality related issues in the industry. They include poor or no data on the outcomes of care and inadequate communications among home care agencies and other parts of the health care delivery system. Some quality issues are hampered by lack of agreement about what constitutes quality of care in home care programs, others by the lack of research on reliable and valid indicators of home care quality (6). Health care standards and quality metrics have, for the most part, been developed in acute care settings, and further work is still required to translate these in to community based environments and to develop relevant and meaningful quality measures.

There is little evidence on patient/client safety in the community-based setting. However, of note is the paper entitled “Safety in Home Care: Broadening the Patient Safety Agenda to Include Home Care Services” (7). The report identifies that “overwhelmingly, research on patient safety is focused on institutions and largely absent from the patient safety literature is a discussion of the non-institutional environment. The overall state of patient safety in home care in Canada is relatively unknown.” Research on patient safety in home care in Canada is in its infancy. However, arguably, it is urgently required if we are to address many medico-moral issues related to home care and ventilation in particular. Furthermore, “there is a general consensus that safety in home care must be viewed through a different lens than the traditional way patient safety in hospital settings has been conceived” (7).

The findings in this paper regarding factors that influence safety and other challenges in care delivery in the home environment are congruent with the contributing factors identified in another study (8). These considerations are:

- family is the unit of care
- safety of client, family caregiver and provider are inextricably linked
- the unregulated and uncontrolled setting of individual homes
- the multiple dimensions of safety – physical, emotional, social and functional
- autonomy and choice for clients, families and caregivers; client acceptance of care responsibilities
- isolation, vulnerability, lack of support – clients living alone and caregivers/providers working alone
- communication issues on many levels; errors, gaps, delays
- maintaining and developing knowledge, skills and competence; training
- diminishing focus on prevention, health promotion and chronic care
- human resources challenges – magnified in home care
- complexity of client medical condition (multiple conditions with multiple medications)
- clients and informal caregivers assuming responsibility for medical procedures
- delays in service implementation
- inadequate/incomplete client/caregiver education prior to discharge
- equipment management, use or misuse
- failure to identify and control risk

Furthermore, there is a paradigm shift in the health care delivery model from the hospital-based 'medical model' to a more appropriate 'home care model.' These two models (Table 13-1) reflect quite different philosophies, and it is important to ensure that the more fitting and relevant approach is utilized in the home care environment.

Table 13-1: Health Care Models

	Medical Model	Home Care Model
Process:	Command/Control	Collaboration
Focus:	Professional focus	Person-centered
	Patient-focus	Family-centered
Emphasis:	Illness (episodic)	Health-wellness (continuous)
		Health promotion/prevention
Goal:	Curing	Caring
Fosters:	Dependency	Independence
Decisions:	Receptive	Participatory
Communication:	One-way	Two-Way
Response:	Reactive	Proactive
Respect:	Professional wisdom	Person/family insights
Environment:	Clinical, invasive	Dignified, private
Ethical foundation:	Beneficence	Autonomy

Specific ethical issues involved in the care and treatments of home-ventilated patients include the following. Here is an overview of some of the significant ethical issues involved. Each of these pressing value-laden issues will be explored from ethical, professional and legal perspectives, with the intention of providing clarity, coherence, consistency and adequacy for the practical application of an ethically sound standard of practice in Canada.

Decisions around Withdrawing Mechanical Ventilation

The decision to withdraw ventilatory support often creates a great deal of moral angst amongst patients, their families and health care professionals, and the entire process of decision-making is especially challenging for home-ventilated patients. This is particularly problematic and anxiety-provoking when the patient could continue to survive on HMV. This raises many ethical, professional, spiritual and legal questions around notions (and misconceptions) of assisted suicide, euthanasia, consent and the patient's right to self-governance.

Some health care practitioners are comfortable withdrawing ventilatory support in the patient's home, while others argue that this is best achieved in a hospital setting. There are compelling moral arguments on both sides of this discussion. Many health practitioners feel obliged to honor the Hippocratic maxim "first, or above all, do no harm," and withdrawing life-sustaining interventions, which invariably lead to death, can pose a significant ethical dilemma for them. In this case the "harm" done is in not respecting the patient's autonomy and subjecting them to further suffering.

In recent times, these principles have come into conflict with patient autonomy or the right to self-governance, making the division between beneficence (the commitment to benefit the patient) and non-maleficence (the obligation to not cause harm to the patient) less clear. In honoring both patient autonomy and professional autonomy, it is recommended that a clear, coherent and accountable process be consistently taken to address these challenging issues. Please refer to Appendix II for an integrated, objective and inclusive ethical decision-making framework that incorporates collective wisdom through patient (and family)-centredness and interdisciplinary discernment.

A study conducted by Wenger et al. illustrates how there is a great misunderstanding between physicians and patients with respect to the withdrawal of treatment. The study revealed that in over 5,000 acutely ill patients, of whom a third had acute respiratory failure, approximately 64% wished to receive CPR, while 36% wished to refrain from receiving CPR. Physicians were 86% correct in understanding those patients who wished to receive CPR. However, only 46% of physicians correctly understood that patients did not wish to receive CPR. The disparity between physician and patient wishes with respect for treatment may be a reflection of the lack of meaningful communication of the patient's values and care preferences.

It is crucial to remember that patients, if mentally capable, have the fundamental moral, human and legal right to self-governance, in keeping with the ethical principle of "respect for autonomy" and the legal principle of "informed consent/informed refusal." Informed consent only has true meaning, value and leverage if capable patients have the right to forego or withdraw medical interventions, including those that will lead to their death. In respecting capable patients' wishes, values and beliefs – derived from their right to self-determination – patients are treated with respect and dignity.

In those situations where the patient's condition is such that he or she could continue to survive on HMV and the patient expresses a desire to have the HMV withdrawn, it would be prudent to ensure that the patient is indeed mentally capable to consent to, or refuse, ventilatory support. To honour an incapable patient's desires would constitute negligence, and the physician could be sanctioned by his/her college and also be held liable for the harms that befell the patient.

With respect to HMV, the core of the definition of "capacity" in most provincial (and international) legislation includes the ability to understand the information that is relevant to making a decision about the treatment and the ability to appreciate the reasonably foreseeable consequences of a

decision or lack of decision. It is important to remember that patients are presumed to be mentally capable, and the burden of proof for incapacity lies with the health care professional. Furthermore, capacity is not global; rather it is task and time-specific. In other words, a patient may lack capacity regarding one medical intervention yet possess capacity for other interventions. Furthermore, capacity can fluctuate depending on time specific situations.

In keeping with procedural justice, due process and the inherent right to recourse, patients have the right to challenge a finding of incapacity, and this would normally be processed through a Consent and Capacity Board in many jurisdictions. Therefore, health care professionals have a duty to inform their patients of this right when they inform them of the finding of incapacity to consent to, or refuse, specific medical interventions.

In responding to a request to have the HMV withdrawn in the event that the patient could potentially continue to survive for a reasonable time longer on the HMV, it would also be prudent to determine if the patient may suffer from depressive thoughts or may be actively suicidal. If there were reasonable grounds to believe that this may be the case, it would be judicious to have the patient more thoroughly assessed by a psychiatrist. It may be the case that the patient is clinically depressed and could benefit from psychiatric interventions. The physician is not obliged to honour the desire to withdraw life-supports from a patient who is actively suicidal.

On the other hand, should the patient's consistent and capable evaluation of his experience be that the burdens of medical interventions are disproportionate to any perceived benefits, the treating team should thoroughly explore the option of HMV withdrawal with the patient (and his/her family if the patient so desires). In this case, arguably, the intention is not to facilitate or hasten death; rather the intention is to prevent further disproportionate burdens. This would be consistent with the principle of "double effect." According to the principle of "double effect", four criteria must be met (9). These are (a) the action is good in itself, (b) the good and not the bad effect is intended, (c) the production of the bad effect is not a means to the good effect, and (d) there is a good/proportionate reason to risk the bad effect to bring about the good effect. The principle of double effect allows for physicians and staff to aid the patient in achieving a "good death," which adheres to traditional ethical principles in medicine, such as symptom management, relief of burden to the patient and strengthening relationships with family members.

There are circumstances when the patient and/or his/her family are non-adherent to prescribed medical interventions surrounding the use of HMV, and these create significant safety issues in particular. As a first step, it is prudent and reasonable to determine the source or rationale of the non-adherence. These may be numerous, for example, a misunderstanding of previously shared information, a lack of therapeutic trust, or a sense of false security/wishful thinking that all will be well irrespective of strict compliance with procedures. Having determined what the exact non-adherence issues might be, the care team would, in collaboration with the patient and his/her family, decide on the most appropriate and reasonable corrective measures. This may include clarification and further teaching around the procedures and protocols, or even increasing resources, and closely monitor for a trial period. Or, indeed, the patient's safety may require transferring him or her back to an acute care setting.

Should the patient be incapable of consenting to, or refusing HMV, the physician and care team would need to collaborate with the appropriate substitute decision-maker or decision-makers (SDM/s) and receive informed consent for ongoing therapeutic interventions. A SDM may be designated by default or as specified in legal documentation that the capable patient developed in appointing a substitute proxy. It would be wise for the physician to counsel the SDM with

respect to what his/her role and responsibilities entail. These include respecting the incapable patient's prior expressed capable wishes or advance care directives, where known, or his/her "best interests" as defined by applicable legislation (10).

There are circumstances when requests are made by a SDM to continue to have the patient on HMV, despite the clinical observation that the continuation of the HMV is medically "futile." That is, it is not only no longer achieving any overall medical benefits or meeting any of the goals of medicine, but it is causing the patient disproportionate or undue burdens. This often causes clinicians much moral distress, because of the ethical principle of "non-maleficence". In these unfortunate circumstances, it would be prudent to remind the SDM of his/her responsibilities and the legal criteria for substitute decision-making, and every attempt should be made to negotiate a decision that is legally, ethically and professionally acceptable. The aim or goal of this process is to form a consensus between the patient, family and staff – directed at the best approach to treat the patient with respect and dignity (10). These discussions would incorporate the patient's cultural and religious (and secular) values and beliefs. Some religious systems, such as certain sects of Judaism, forbid the withdrawal of life supports such as HMV.

Palliative Care

There is an ongoing debate whether a patient, who is maintained on HMV is an appropriate recipient of palliative care services. In many jurisdictions, the definition of "palliative" excludes many home-ventilated patients, who would otherwise benefit enormously from appropriate support and services. Part of the dilemma lies, on the one hand, with the fact that some home-ventilated patients may well be sustained for over a decade while on the other hand, patients' conditions may rapidly deteriorate, leading to death and much family grief and suffering.

If palliative care could be provided proactively, it could serve to establish trust and, when needed, provide invaluable supports and services to patients and their families (even after the death of the patient). It is, therefore, important to monitor the patient's condition closely and to plan ahead as best one can under the circumstances. Advance care planning is an exceedingly important dimension of providing holistic care to patients. Studies show that patients are very interested in participating in advance care planning. Patients welcome the notion of having their wishes respected, which provide them with a sense of comfort and reassurance (10).

In anticipation of the progression of the patient's condition, it would be prudent to explore in a sensitive, caring and compassionate manner, with the patient and his/her family/SDM, treatment options and philosophy of care. For instance, when it would be reasonable to not provide the patient with cardio-pulmonary resuscitation (No-CPR/DNR), and to become actively involved with a palliative care team. The focus of the conversation should be on the support and service that would be provided to address the common perception that patients are usually "abandoned" once they have a No-CPR/DNR order or when they are categorized as being under "palliative" care.

Disclosing "Bad News" to Patients and Their Significant Others

It is important to recognize that disclosure of medical or personal health information to capable patients is crucial to ensure that informed consent occurs in a rigorous manner. In North America, the general "rule of thumb" is: what information would a lay/average person in the patient's circumstances expect to know in order to enable him/her to make an informed decision? This information must include: (a) the nature of the treatment, (b) the expected benefits of the treatment, (c) the material risks of the treatment, (d) the material side effects of the treatment, (e) alternative courses of action, and (f) the likely consequences of not having the treatment (11).

Some physicians choose not to distress patients and their families regarding questionable medical interventions such as long-term ventilation under some circumstances, especially where the goals and objectives for care are either difficult to articulate or difficult to be processed by the family. On the other hand, some clinicians simply find it stressful to break “bad news.” Excellent guidelines for breaking “bad news” have been developed to assist clinicians in this important area (12).

Furthermore, sometimes the decision not to inform some patients or their families is based on arguments surrounding the concepts of withholding and withdrawing life-sustaining medical interventions. This is often apparent in individuals (patients, their families and health practitioners alike) from certain cultural and religious affiliations. In a rights-driven Canadian society, this approach is open to the criticism of being paternalistic, potentially bearing professional, moral and legal sanctions. This issue of not informing patients or families often presents itself prior to the implementation of ventilation.

It is important to remember that capable patients have a right to forego knowing personal health information. For example, sometimes patients from a variety of cultures may choose not to discuss end-of-life issues. However, there are occasions when the capable patient’s family request that the patient not be informed about certain personal health information. The prudent physician will confirm with the capable patient how much information he/she wishes to know and, indeed, whether he/she intends to continue to make health care decisions or to relinquish decision-making in favour of a SDM. This would be consistent with respect for autonomy and informed consent.

Quality of Life Experience

QoL considerations naturally constitute an exceedingly important dimension of the patient’s experience, including a sense of meaning and purpose. Despite many attempts to measure QoL constructs, it is important to remember that it is primarily subjective and personal, and it may vary not only from individual to individual but also from one time of day to another. This illustrates the need to be collaborative, sensitive and broad-minded in one’s approach, re-assessing the capable patient’s desire and need for ongoing ventilation and, indeed, other medical interventions on an ongoing basis.

Conducting this evaluation in the home setting can pose a challenge for the physician by reason of a lack of resources, infrequent visits, and family members being present. Still, it is the care team’s responsibility to monitor the patient’s bio-psycho-socio-spiritual determinants in a manner that is comfortable to the patient, and to provide him/her with appropriate and timely supports. Therefore, every effort should be made to assess the patient’s experience and changes to his/her sense of well-being.

Philosopher Paul Ricoeur commonly uses a phenomenological-hermeneutic process to describe experience. This notion can be applied to the QoL of patients living at home on ventilators. An application of Ricoeur’s philosophy is described as, “experiencing home as a safe and comfortable space from which to reach out... striving to live in the present, surrendering oneself to and trusting others, and experiencing technology as a burden and a relief to the lived body” (13).

Furthermore, despite claims that individuals who use ventilators have a poor QoL, there are many positive reports that ventilator usage at home allows for many more opportunities to participate in activities that are not available in a hospital setting (14). In a study by Brooks and

colleagues, the results showed that ventilatory support at home allowed a wide range of activities to be possible, such as, “involvement with family and friends, social activities, homemaking, volunteerism, advocacy, education and employment” (15). Due to these additional opportunities, individuals receiving treatment at home reported a very high QoL.

Additionally, a study by McDonald et al. indicates that individuals who were ventilator-dependent considered themselves more spiritual than others and the study revealed that there were no significant differences in their general, “feelings of competency or of being at peace with dying” (16). Although there are many possibilities for individuals who are ventilated to have an acceptable QoL, there are several socio-material barriers as well. For example, Goldstein and colleagues found that 81% of ventilator users were unemployed in a survey that they conducted (2). And, some ventilator users prefer to be accompanied when leaving their residences due to limitations in transportation. Other barriers in living for individuals who use ventilators include restrictive employment and limited housing options (16). All of these issues must be taken into consideration when creating an atmosphere to support the best possible QoL for an individual living at home on a ventilator.

Caregivers' Burden

Caregivers' burden is a significant moral issue in the care of the HMV patient, both adult and children. Disclosure of clear, coherent and forthright medical information to patients and their families (usually caregivers) is necessary to allow them to collectively make informed and realistic decisions throughout the continuum of care – from hospital to home. Advocating for, and offering, practical and effective supports for both patients and their families is crucial if home ventilation is to be successful; otherwise, studies show that the ventilated patient's experience and QoL is reduced substantially and caregivers' burden and distress increases significantly.

In a study by Moss et al (17) the following consequences resulted from caregivers: “Eleven (58%) caregivers noted that ‘being tied down’ was the major burden of home ventilation; seven (37%) cited the stress of dealing with nurses, insurers, and suppliers; and four (21%) mentioned the financial strain on the family. Nine (47%) reported that their own health had suffered as a result of caring for their family member”. The preceding quotation reveals some of the burdens that caregivers tend to feel when looking after a family member who requires a ventilator and lives at home.

There are numerous options to provide support to caregivers, and these include respite, self-support groups, and ready accessibility of community service providers and excellent co-ordination of the patient's care. It is not uncommon to find that concerns and ambivalence around the continuation of HMV are correlated in some situations to caregivers' own experience of well-being. In providing active ongoing support to caregivers through a family-centred approach, clinicians are, in effect, facilitating the QoL experience of their patients.

Advance Care Planning

Advance care planning is crucial in proactively determining what care and treatment decisions would be most appropriate for the patient over time, given his/her values, preferences and beliefs. This would necessarily include discussions about resuscitation, artificial nutrition and hydration, treatment for infections, kidney failure and other relevant conditions. These decisions ought to be re-visited regularly with capable patients – as they have every ethical and legal right to change their minds.

It is noteworthy that SDMs are generally not permitted to create advance care directives on behalf of incapable patients. However, they are expected to actively collaborate with health care professionals to generate a care plan that would reflect the incapable patient's prior expressed capable wishes, values and beliefs and, indeed, best interests.

However, as active participants in the decision-making process, patients need to be involved in the development of care plans and to provide the care team with informed consent – based on the criteria discussed above. There is sometimes a cultural dimension to the receptivity of patients and their families to participating in advance care planning, and it would be prudent of the care team to be sensitive to this consideration.

In general, patients are very interested in advance care planning, especially if this is approached by framing the initial conversation toward patient empowerment in times when he/she may not be able to provide care direction and family and care teams are left struggling with doing the “right thing.” Advance care planning also improves communication between patients and family members/caregivers. Furthermore, enhanced communication improves the QoL for patients and produces greater satisfaction. On a 10-point scale, patients in a home environment rated their QoL higher than those living in a hospital environment. Similarly, as described earlier in this paper, their yearly costs were also reduced (3).

Allocation of Scarce Health Care Resources

Issues relating to the allocation of scarce health care resources are certainly important considerations in providing care and treatments for home ventilated patients. The ethical principle of distributive justice would require the systematic sifting out of biases, prejudice and discrimination and the inclusion of morally significant considerations in a fair, transparent, inclusive and accountable decision-making process, as we strive to honour and safeguard our patients' best interest while seriously considering the legitimate medical needs of others.

Clinicians have a “fiduciary” or trust relationship with their patients, and developing therapeutic alliance through reasonable loyalty is an important aspect of the clinician-patient encounter. While physicians have multiple roles in society (for example, with respect to risk of serious harms they are expected to protect not only their patients but others as well), their primary duty is to the patients with whom they have an established therapeutic relationship. Therefore, decisions to ventilate patients should be based on the particular patient's medical condition and prognosis, as well as his/her wishes, values, beliefs and best interests. There is, of course, a professional advocacy responsibility for increased health care resources when it is believed that this would better meet patients' holistic care needs and contribute to a more just and fair health care system. The micro-allocation of scarce resources is likely to be of lesser concern once the decision has been made for HMV.

Confidentiality

Given that the care setting is the patient's home, and likely the home of others as well, members of the care team need to take special precautions around issues relating to confidentiality and privacy. The hospital environment is comparatively much more controlled in this regard. The care team should ensure that conversations about the capable patient's personal health in the presence of others should only occur with consent from the patient.

Similarly, examination of the patient should take his/her privacy into consideration. While family members are generally voluntary informal caregivers to the patient, this does not automatically entitle them to personal health information. It would be prudent to establish ahead of time, say at the beginning of the HMV relationship, the person or persons whom the capable patient

consents to share personal health information with. Naturally, the SDM for the incapable patient is entitled to personal health information to enable him/her to make informed decisions. In Ontario, the Personal Health Information Act (2004) (11) provides clear guidance regarding clinician-patient confidentiality.

Conclusion

In the context of HMV, patients, their families and clinicians face numerous pressing ethical issues and dilemmas, and health care professionals need to identify and address these in an effective and reflective manner. This chapter provides clear, coherent, prudent guidelines to enable clinicians to manage these challenges reasonably and consistently. They serve to promote professional virtues of compassion, trust, integrity, sensitivity and truthfulness, which compliment moral principles, professional standards and legal maxims in this unique therapeutic alliance and fiduciary relationship.

It is also important to note several key recommendations that will assist the patient-physician relationship and aim towards respecting patients' values, beliefs and autonomy. It is highly recommended that physicians work collaboratively with key stakeholders involved in the delivery of care and decision-making process. This naturally includes the patient, family members and other health professionals, bearing in mind that consent is required from capable patient to include family members.

One must also make every attempt to establish clear and meaningful advanced directives with patients, ensuring that they fully understand and appreciate the nature of refusing or allowing specific medical care. It is also important to note that values may conflict when faced with complicated decisions in health care, and one ought to work with the patient to help prioritize these values and interests in accordance with the patient's desires and preferences.

When considering the most appropriate location for a patient requiring ventilation, one must think about a number of significant factors. First and foremost, the patient's values and beliefs ought to be seriously considered and respected if practically possible. One should aim to allow for optimal independence, respect for patient autonomy and work with the patient to achieve an increased and optimal QoL for the patient. It must be emphasized that clinicians must focus on the desires, values and beliefs of the capable patient, as opposed to paternalistic intervention, thereby imposing the physician's desires and preferences upon the patient. Correspondingly, one must recognize one's own biases and predilections and endeavor to participate in a collaborative and fair decision-making process that primarily addresses, reflects and respects the values and wishes of the patient.

Similarly, when developing a plan of care with a patient on ventilation, it is crucial to have a clear and coherent strategy that will allow members who are participating in the care of the patients to be accountable for their particular roles in the patient's care. This process will also involve full-disclosure necessary to make full and free informed decisions. Furthermore, one ought to consider the health of caregivers. Often, caregivers' burden can negatively influence not only the caregiver, but the patient as well. Hence, it is necessary to consider supporting caregivers, educating them with regard to healthy coping strategies, and providing them with some form of respite care whenever possible and desirable.

Recommendations

1. Physicians must actively work collaboratively with the patient, family members and other health professionals involved in the health care decision-making process, while at all times maintaining respect for patient autonomy, dignity and confidentiality. (Consensus)
2. It is important to proactively counsel capable patients and establish clear advanced directives (regarding issues such as crisis management and end-of-life care) in a timely manner, ensuring that patients fully understand and appreciate the reasonably foreseeable outcomes of their decisions. Physicians must work with patients to help prioritize their values, interests and preferences. (Consensus)
3. When considering the most appropriate location for on-going ventilation issues relating to safety and the patient's values, beliefs and preferences must be the primary considerations for making such decisions providing optimal independence, respect for patient autonomy and increased QoL. (Consensus)
4. In the event that the patient lacks decisional capacity regarding specific treatments, substitute decision-makers and clinicians must incorporate the patient's advance care directives in the decision-making process or, where there are no known advance care directives, to act in the patient's 'best interests.' (Consensus)
5. One must recognize one's own biases and endeavor to participate in a collaborative and fair decision-making process that primarily addresses, reflects and respects the values and wishes of the patient. (Consensus)
6. A plan of care should involve full-disclosure of pertinent information and a clear and coherent strategy, which would enable the patient to make fully informed decisions. This will allow any members participating in the patient's care to be held accountable for their duties and obligations. (Consensus)
7. Given the reality of scarce resources, any process of allocating limited care resources must be in accordance with distributive justice and due process. (Consensus)
8. The well-being of caregivers and the exhausting responsibilities of care must be considered. Caregivers should be supported, educated with regard to healthy coping strategies, and provided with some form of respite care whenever possible and desirable. (Consensus)

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SECTION XIII. APPENDIX I – Making Sound Ethics Decisions: An Integrative Ethical Decision-Making Process



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ETHICAL DECISION-MAKING PROCESS

“But in order to pave the way for such a sentiment (that is, one that forms the basis of a moral judgement) and give a proper discernment of its object, it is often necessary, we find, that much reasoning should precede, that nice distinctions be made, just conclusions drawn, distant comparisons formed, complicated relations examined, and general facts fixed and ascertained.” David Hume

The process starts with disequilibrium in the integrity of the milieu.

In practice, a member of the team, the client or a member of his/her family, perceives disequilibrium in the *milieu* – seemingly a dilemma has arisen. A member of the team is uncertain as to what the next course of action should be, or someone is unhappy/distressed with a particular situation, and appropriate help is sought – a concern or complaint is lodged, officially or unofficially. The situation has no clear alternatives, has far-reaching implications, involves a number of people (directly and indirectly), and has a perception of unresolvability through an identifiable clinical solution. The specific nature of the problem may or may not be identified at this point.

The matter is taken to the team for discussion. The lodger of the concern should be accorded full respect for his/her feelings and opinions. The situation should be treated with a sense of urgency and with full confidentiality. The primary person who lodged the concern/complaint should provide a description of the perceived difficulty to the team. Either the team offers a reasonable and ready explanation or solution to the satisfaction of the individual, or identifies the existence of a medico-ethical dilemma. If the existence of a dilemma is confirmed, then the team proceeds to the First Stage in the Ethical Decision-Making Process. Team involvement is a nothing less than a collective and collaborative process.

Stage One: Recognition of Dilemma & Comprehensive Information Gathering, Including Personal Values and Contextual Constraints.

Gather as much information as possible and, in so doing, ensure that nothing relevant gets missed. All judgements should be suspended, and members ought not to rush to conclusions. Moral intuitions play a great part at this stage. Brainstorming is very important in order to explore and generate a wide variety of possibilities and options. Professional and personal values, opinions, ideas, and feelings are voiced. It is imperative to foster an atmosphere of mutual trust, respect and co-operation. Remember that there may be ambiguity, uncertainty and perhaps fear, anxiety and resentment. Moral judgements made in a professional capacity would affect one's conscience, one's private sphere. Ideally, the team aims at arriving at consensus in decision, and this is only attainable when team players are satisfied that their respective positions have been heard, appreciated, and critically evaluated in the process, and they have in front of them a decision that they could live with.

1. DILEMMA

Q: Why is there disequilibrium in the client-treatment team relationship or dissension amongst team members with regard to client care and treatment?

Q: What is causing the qualm, uneasiness, or apprehension?

Note: Confirm that a dilemma exists. Something is amiss, and the team doesn't really know what to do. It probably doesn't even know exactly what is the problem. The team perceives *at least* two alternatives from which to choose, but cannot agree on a choice.

2. STAKEHOLDERS

Q: Who are the legitimate stakeholders, and what has each at stake?

Note: The primary stakeholder is invariably the client. Other stakeholders might include significant others, health care professionals, the organization, others (co-clients, society, insurance company, employer, etc.)

3. CLIENT'S VALUES, WISHES AND PREFERENCES

Q: What are the client's values, wishes and preferences?

Note: If the client is suicidal or homicidal or unable to care for himself/herself (as defined in the Mental Health Act), then there is need to honour the duty to rescue and/or protect.

Q: Are there reasons to suggest that the client may not be mentally competent to consent to, or refuse, care and treatments?

Note: The assumption is always that the client is mentally competent. If the client is unable to provide consent or lacks 'capacity', then one needs to follow an Advance Directive, substitute proxy/Power of Attorney for Personal Care. If none of these exist, then elect a proxy (in accordance with current legislation). It is important to remember that a client's seemingly irrational decision does not, by itself, constitute incompetence.

Q: Are there rationally justifiable reasons why the client's preferences might be overridden?

Note: The onus is always on the health care professional(s) to justify any overriding of clients' values, wishes and preferences. This is medical paternalism!

4. TIME

Q: Does this constitute an emergency situation (as defined in the legislation), and how much time is there to arrive at a decision?

Note: If classified as an emergency, then act with prudence to rescue and protect (using best interests principle) if unable to secure consent from the client or Substitute Decision Maker, and if no Advance Directives are available. Further deliberation is required after the initial intervention in order to determine an ethically acceptable course of action. How might another reasonable clinician/treatment team act under similar circumstances? Casuistry can be extremely useful in an emergency situation, because it provides the team with past precedent-setting cases and their outcomes.

5. RESOURCES

Q: What are the relevant resources at the team's disposal?

Note: If the resources (expertise/competency or material) are inadequate or unavailable resources then a consultation and perhaps transfer to an appropriate clinician and/or facility might be necessary.

6. INFORMATION GATHERING

Note: There is a need to have a thorough case description (includes culture, religion, language, etc); medical and mental illness (includes history, investigations, severity, prognosis, etc); all therapeutic alternatives available to manage the condition, including probabilities of each with its risks and benefits, as well as the ramification of non-intervention. Clarify what information is factual and what is uncertain/undetermined.

7. PROFESSIONAL CODE OF ETHICS

Q: What guidance, if any, is provided by the applicable code(s) of ethics?

8. THE LAW

Q: What guidance, if any, does the law provide under these circumstances?

Note: It's usually very helpful to have a knowledge of precedent-setting cases (casuistry)

9. ORGANIZATION'S POLICY & PRACTICES

Q: What are the institution's current policy and practices in these situations?

Assuming that the client's care is being coordinated and supported by a care team from a health care organization

Stage Two: Attempt to Separate the Clinical, Legal and Ethical Components

Having gathered as much pertinent information as possible, the team proceeds to identify the nature of the difficulty. There are usually clinical, legal, social, policy and procedural considerations that are intricately interwoven with the ethical component in medico-moral dilemmas. Serious attempts should be made to tease these apart, within reason, in order to ensure clarity of consideration.

Q: What is the legal dimension to the dilemma?

Note: Consider if the law of the land has been, or stands to be, violated; for example: does the client meet the criteria for dangerousness or is seriously vulnerable; has there been an allegation of child abuse or sexual misconduct; or does it involve a client who is impaired to drive a vehicle/fly a plane? In medical practice, laws usually have qualifying phrases that allow for value judgements. Concepts like 'reasonable', 'sufficient', 'lawful excuse', and 'unwarranted' are duly considered in courts of laws, "in an effort to give substance to the moral convictions of reasonable or common-sense people." This is especially relevant in the discipline of psychiatry, because of the extensive usage of elusive and ill-defined terms and concepts. If the dilemma involves a predominantly legal issue, seek direction from organization policy, Risk Manager, or legal counsel, and act with team consensus ideally.

Q: What is the clinical dimension to the dilemma?

Note: Consider current medico-scientific data as they apply to the case. It is very important to heed Howard Brody's caution that "With an ethical dilemma, we can have all the data in the world, and we still cannot arrive at an answer until we come to grips with our values and make some value judgements." If the dilemma involves a predominantly clinical issue, collaboratively (team and client and/or Substitute Decision-Maker) determine the most appropriate course of action. Consider if you might benefit from a medical/psychiatric consultation. Act with team consensus ideally.

Q: What is the ethical dimension to the dilemma?

Note: It is important to remember that anything associated with values – rights and entitlements, duties and obligations, as well as justice and fairness – are inherently ethical. If the dilemma involves a predominantly ethical (value) issue, then progress to Stage Three. Consider a consultation with a Bioethicist.

Stage Three: Pertinent Ethical Duties & Obligations

Specify the ethical duties and obligations that pertain to the case, noting how they apply. It is important to remind oneself that it is the client who usually has most at stake. Values are only meaningful in a context of duties and obligations. Pertinent ethical principles include: (1) **Respect for autonomy** – to respect the individual's right and liberty to make choices in accordance with his personal wishes, values and cherished goals in life. (2) **Non-maleficence** – to not cause harms/evils to the client (on balance with benefits). (3) **Beneficence** – to actively benefit the client by protect and promote the client's well-being and welfare, primarily as perceived by him/her. (4) **Distributive justice** – pertains to the just and fair distribution of finite health resources.

Please note the **prima facie** nature of these duties and obligations. This means that it is possible to override a certain duty by another, provided that there are rationally justifiable reasons to believe that the latter should have priority under the circumstances.

Q: What is the role of each stakeholder?

Note: The role of each stakeholder should be identified in order to ensure clarity and consistency.

Q: What are the treatment team's duties and obligations to the client, the client's immediate family, potential clients, and society in general?

Note: Health care professionals' *primary* obligation is to their clients.

Q: Likewise, what are the organization's duties and obligations to each of the above?

Q: What are the client's special responsibilities in his/her care and treatment process?

Note: Responsibilities accompany rights, and these should be identified as they pertain to the issue at hand.

Q: What obligations exist to legitimate third party stakeholders (such as society and significant other/s) as they pertain to this case?

Stage Four: Identification of Specific Conflict

Having determined the specific duties and obligations that are pertinent, it becomes necessary to specify, as clearly as possible, what conflict exists, or whether there is a perception that someone is failing to discharge his/her obligations adequately and effectively.

Q: What is the nature of the conflict – might it be interpersonal or even institution-based?

Note: Consider if the dilemma might have resulted from personal conflicts within the interdisciplinary team, between the client/significant other and the treatment team, or between the treatment team and the institution itself.

Q: What ethical principles or interests are in conflict in this situation?

Note: Consider if there might be a conflict between beneficence and respect for the client's autonomy, or between respect for client autonomy and a perceived obligation to society.

Q: Might the situation be such that a team member (or the organization) is simply failing to honour a specific ethical obligation to a legitimate stakeholder?

Note: Health care professionals are generally very well meaning, but it is conceivable that sometimes they might fail to identify and honour specific duties and obligations to their clients, albeit unwittingly.

Stage Five: Critical Analysis & Viable Alternatives

Stages 5 and 6 are closely related. The team progresses to a critical analysis of the implicated duties and obligations. Further information gathering and clarification might become necessary. One needs to employ rationally justifiable means of 'prioritizing' those ethical principles that conflict.

Individuals from the team share their rationales for the positions that they tend to favour. Following this, a brief re-examination of these rationales is crucial because, not surprisingly, they might very well become modified in the process.

Examine all viable alternatives, including the option of delayed and non-intervention. Take into account the foreseeable consequences, short and long term, of all viable possibilities. These necessarily include all anticipated goods/benefits as well as all anticipated harms/evils. The probabilities of these are also crucial considerations.

It would be easier to initially exclude the alternatives that are totally unacceptable. Develop a list of all ethically justifiable resolutions from the most desirable to the least. In so doing, juxtapose selected viable alternatives with pertinent ethical duties and obligations or principles.

Caution: Scrutinize for clarity, congruence, consistency, coherence, and adequacy.

Exclude deficient alternatives. The team needs to reach consensus. Dissenters might wish to drop out of the team at this stage of the process if their moral positions are hopelessly irreconcilable with the preferred alternatives.

Stage Six: Resolution Strategies with Preferential Scale

Rank the list of viable alternatives according to those choices that appear most desirable (according to the criterion already specified). This is a particularly important stage.

Q: What choice is most congruent with the client's wishes, values, and preferences, and what reasons, if any, exist to suggest that these should not be honoured?

Q: What harms/evils should one be avoiding/preventing/ removing? How realistic is this?

Q: What benefits should one be aiming towards? How realistic is this?

Q: Have any promises been made (that require honouring)?

Q: Would staff be acting paternalistically, and is this rationally justifiable?

Q: Would anyone be exploited in the process and, if so, exactly whom and why, and how can this be avoided?

Q: What choice is most likely to offer the best overall consequences, short and long term?

- Q: What choice is most likely to prevent the most harm, short and long term, to stakeholders, especially the client who invariably has most at stake?**
- Q: Would any of the proposed choices violate the institutional policies and values, the law and professional codes of ethics?**
- Q: What choice would all stakeholders be most willing to live with?**
- Q: What choice would serve as a good example for others in a similar situation to follow?**
- Q: What choice is most justifiable by appealing to universal ethical principles rather than personal preferences?**
- Q: What do you honestly believe another reasonable group of individuals would choose given the same circumstances?**
- Q: What if the staff and client roles were reversed?**
- Q: Is there consensus that the anticipated end justified the proposed means in this particular case?**

Juxtapose each chosen and ranked alternative with the client's values, beliefs and goals as determined directly from the client (or from a duly elected substitute decision-maker). Rank order those alternatives that are most congruent with the client's own moral position. It is important to remember that in health care practice most care and treatments involve some harms/evils, for example, adverse effects. One must always weigh these anticipated harms/evils against anticipated benefits, before implementing a course of action.

Sometimes, a reasonable compromise is to undertake an acceptable course of action for a trial period, then reassess and re-evaluate efficacy and sentiments held by major stakeholders.

There should be a fair process for stakeholders to resolve intransigent disagreements and conflicts, and this usually involves an ethics committee, ethicist, or mediator.

Documentation is of paramount importance. Very careful documentation of the content of all meetings and proceedings, including names and roles of all participants should be undertaken.

Caution: Examine for clarity, coherence, consistency, congruence, and adequacy. Briefly check over the process to ensure that nothing pertinent was excluded.

Stage Seven: Action Implementation

Before you attempt to implement the consensually-arrived at decision, it is important to answer the following questions:

- Q: Who is most appropriate to implement the choices arrived at, and why?**
- Q: When is the best time to implement the decision, and why?**
- Q: When do you expect to see anticipated results?**

Under most circumstances, no person should be expected to implement a decision that he/she cannot live with. However, this maxim must be tempered by the principle that no immediate harms/evils would befall the client by one's non-participation. You do have certain duties and obligations to your client, and these must be carefully considered when attempting to make a personal appeal to your conscience.

Stage Eight: Evaluation of Effectiveness

Q: Were the effects from the intervention those that were expected, and did the decision resolve the specific dilemma that one was faced with?

Q: Did the results occur within the time frame anticipated?

Q: Are there other consequences that were unforeseen, and were new difficulties created? Might these require further deliberation and intervention?

Q: Was this decision the most ethically justifiable under the circumstances?

It is important to remember that the care team ought to (holistically) support the client and her loved ones throughout the therapeutic relationship.

Stage Nine: Preventative Strategies

This is perhaps one of the most important stages in the process of ethical decision-making.

Q: What can be learnt from the dilemma (through open and honest dialogue by members of the care team in an 'operational debriefing session')?

Q: What factors contributed to the dilemma?

Q: Are there problematic policies and procedures?

Q: Is there a need to modify current policies/procedures/ guidelines in order to prevent a recurrence in future?

Q: Would it be helpful to hold an 'emotional debriefing' session for the care team in order to validate their feelings/emotions and to offer support.

It would be folly to believe and expect that the facility, clinician, or care team could foresee every problematic situation. Because we are dealing with rather elusive and changing phenomena such as values, convictions, expectations and desires, ethical quandaries will arise in the delivery of health care. However, once a dilemma occurs, we must deal with it ethically, promptly and adequately. We must then critically examine the entire circumstances of the situation in order to determine the best strategy to prevent a recurrence. In this regard, the client's input would be invaluable.

Editorial Independence

The CTS receives unrestricted grants, which are combined into a central operating account to facilitate knowledge translation activities of all CTS Guideline Committees. Sources include the Canadian Institutes of Health Research, AstraZeneca Canada, GlaxoSmithKline Inc., Pfizer, Talecris and Boehringer Ingelheim Canada. Funds were specifically donated for the HMV Committee by: ALS Society of Canada, Muscular Dystrophy Canada, Respironics, Rick Hansen Foundation / Laval University, VIASYS Healthcare, VitalAire Canada Inc. and West Care Medical. No sponsors played a role in the collection, review, analysis or interpretation of the scientific literature or in any decisions regarding the key messages presented in this document. As such, the CTS Home Mechanical Ventilation Committee is functionally and editorially independent from any funding sources of the CTS, and is accountable to the CTS Respiratory Guidelines Committee and the CTS Board of Directors.

Conflicts of Interest

Members of the CTS Home Mechanical Ventilation Committee declared potential conflicts of interest at the time of appointment, and these were updated throughout the development process, in accordance with the CTS Conflict of Interest Disclosure Policy. Individual member conflict of interest statements are posted at <http://www.respiratoryguidelines.ca/guideline/home-mechanical-ventilation-disease>.

Acknowledgments

The authors thank the CTS for their invaluable administrative support, including specifically Director Janet Sutherland, and Guidelines Coordinators, Elena Goubanova, Stella Muthuri, and Candice Brown. This guideline was developed under the aegis of the CTS Canadian Respiratory Guidelines Committee (CRGC), and we specifically thank the Chair, Dr. Louis-Philippe Boulet, for his expertise and guidance throughout the guidelines process. Tom Oliver was instrumental with advice on guideline and consensus methodological issues. We thank our Canadian and International HMV Expert Peer Reviewers: Anita K Simonds MD FRCP, Royal Brompton and Harefield NHS Trust, United Kingdom; Emilio Servera MD FCCP, Hospital Clínico Universitario, Spain; Joao Carlos Winck MD PhD, Hospital São João, Portugal; Michael J. Kampelmacher MD PhD, University Medical Centre Utrecht, The Netherlands; Nicholas Hart, St. Thomas' Hospital, Guy's and St. Thomas' NHS Foundation Trust, United Kingdom; Roger S. Goldstein MB ChB FCCP, West Park HealthCare Centre, Canada; Mark Herzog RRT, Canadian Society of Respiratory Therapists, Canada; David J. Leasa, Critical Care & Respiriology, London Health Sciences Centre, Canada; Franz R. Michel MD, Switzerland; R.T. M. Sprooten, MD, Centre of Home Ventilation, Maastricht University Medical Centre, The Netherlands; The Canadian Association of Physical Medicine & Rehabilitation Spinal Cord Injury Special Interest Group; the Canadian ALS Clinical Trials and Research Network.