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Management guidelines for motor neurone disease patients on non-invasive ventilation at home

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Most motor neurone disease (MND) patients die of respiratory system complications. When patients have advanced disease with symptoms of respiratory failure, management issues can become complicated by the introduction of assisted ventilatory devices. Therefore, care provision by a multidisciplinary team must be structured and co-ordinated in order to ensure that patients and their carers receive the optimal level of care. The objective of this article is to review the literature and explore the complex issues surrounding the use of non-invasive positive pressure ventilation (NIPPV) in home care MND patients as a justification for the development of a management guideline for medical practitioners. A guideline for multidisciplinary care of home ventilated MND patients will be proposed. *Palliative Medicine* 2006; **20:** 69–79

Key words: motor neurone disease; MND; non-invasive ventilation

Introduction

Motor neurone disease (MND) is a relatively rare disorder with a prevalence rate of six to eight cases per 100 000 and an incidence rate of 1.4–2.6/100 000.[1] It is an incurable, progressive, neurodegenerative condition with a variety of phenotypes and is associated with numerous complex management problems. Therefore, a high degree of expertise is required to achieve optimal patient care. The international literature supports a multidisciplinary team approach to the care of MND patients.[2–4]

MND patients prefer to be nursed and cared for in their own homes. It is in this setting that patients can focus on normalcy, maintaining control and freedom, and achieve better quality of life. There are also economic cost advantages.[5]

This article will focus on the management of MND patients with symptoms of respiratory muscle failure, as this is a phase of their illness often associated with progressive physical dependency and death within several months. It is during this period that many complicated treatment and ethical issues develop. Often, Medical specialists within hospitals and in the community, General Practitioners, nurses, allied health, volunteer staff and MND Associations are all involved in the care of the patient by this stage. Therefore, communication and care co-ordination are critically important within the multidisciplinary team. Management guidelines can be used to ensure that patients receive essential and appropriate care through a co-ordinated and structured approach.

Currently, there are no such guidelines in use within Western Australia. Based on population figures,[6] and a recent audit of referral practices to domiciliary palliative care services,[7] a number of MND patients are not receiving specialized palliative care services at home. A report from the US shows that only 47% of those MND patients who died at home, received any hospice care.[8] For a complex, life-limiting condition such as MND, it is of concern that there are patients (and their families) who do not receive the services of a domiciliary palliative care team.

The objective of this article is to review the literature and explore the issues surrounding the use of non-invasive positive pressure ventilation (NIPPV) in home care MND patients as a justification for the development of a management guideline for medical practitioners. A guideline for multidisciplinary care of home ventilated MND patients will be proposed. The discussion will adopt a palliative care perspective.

Method

A literature search was performed of the following electronic databases: Medline (1966–2004 November); EMBASE (1988–week 47 of 2004); Cochrane library of systematic reviews; gray literature (through www.caresearch.com.au). The following keywords were used: MND; ALS; motor neurone disease; ventilation; home (with all terms MeSH). All abstracts were reviewed and only relevant full-text articles in English were examined. The reference lists of key papers were hand-searched and relevant articles were included.

The opinion of local specialists in neurology, respiratory and palliative medicine, MND Association representatives and community palliative care clinical nurse consultants (Western Australian MND Reference Group)

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was obtained. The first draft of the proposed guideline was individually reviewed by each member, recommendations were discussed with the author and amendments made.

Discussion

The clinical syndrome and its natural history

MND is characterized by progressive degeneration of upper motor neurones (UMN; cortical motor neurones and corticospinal tracts) and lower motor neurones (LMN; motor neurones in the brainstem and ventral horn of the spinal cord). Clinically, there is a combination of UMN signs, including spasticity, hyperreflexia and weakness, and LMN signs, such as fasciculation, muscle atrophy, hyporeflexia, hypotonia and weakness. Involvement of brainstem motor neurones produces dysarthria and dysphagia. Fronto-temporal dementia develops in 5% of cases.[9] Deficits involving oculomotor, sensory and sphincter function are rare.[9,10]

Weakness is progressive and affects the voluntary muscles. The involvement of specific muscle groups at presentation largely depends on the type of MND (Table 1). As the disease progresses, all patients will require increasing assistance with daily activities and mobility. Degeneration of cervical motor neurones and phrenic nerves leads to progressive diaphragmatic, chest wall and abdominal muscle weakness. The resulting atelectasis impairs ventilation by reducing vital capacity and decreasing lung compliance. A vicious cycle is created by the developing hypercapnia, which in turn, depresses central respiratory drive.[11] Diaphragmatic weakness is exaggerated by recumbancy,[11–13] which leads to sleep hypoventilation. This is can cause daytime somnolence, concentration problems, morning headaches, nervousness, and affective disorders.[14] As respiratory muscle weakness progresses, daytime hypercapnia ensues. Exertional dyspnoea is masked by immobility in MND patients with significant lower limb weakness. Hence, respiratory dysfunction can progress insidiously with symptomatic dyspnoea developing late.[15] Weakness in the respiratory muscles can impair the generation of sufficient intrathoracic pressure to enable an effective cough. Together with dysphagia from progressive bulbar muscle weakness, loss of the protective cough reflex allows mucous plugs and aspiration of food and fluids to precipitate acute respiratory crises.[13,14,16,17]

Most patients die of problems related to the respiratory system.[3,11,18,19] The rate of deterioration and prognosis is extremely variable for each individual MND patient.[19] Approximately 50% will die within three to five years of diagnosis. As few as 10% will live ten or more years.[14–16] Poor prognostic features include age of onset >60 years, predominantly bulbar involvement,[18] and a rapid rate of respiratory deterioration.[13]

Involvement of palliative care services

The involvement of a neurologist(s) is essential to confirm a diagnosis of MND.[20] A sensitive approach to communicating information in this early period is important and has been described by Miller *et al*.[21] Although General Practitioners will invariably be involved in the care of MND patients, most will lack adequate experience of this rare condition.[22,23] Therefore, early in the course of the disease, a specialist neurologist would be most equipped to co-ordinate and manage care.

Development of respiratory muscle weakness is a poor prognostic sign and usually indicates end-stage disease. Most authors recommend the involvement of specialist palliative care teams at this stage, if not earlier. This is essential if home ventilation is being used.[2,3,23–25]

Predicting respiratory failure

As respiratory failure causes significant morbidity in MND patients, a proactive approach to management is desirable. Unfortunately, symptoms and signs alone are not reliable predictors of respiratory failure. In a

Table 1 Clinical syndromes of MND[a]

Syndrome	Main features	Prognosis
Classic (Charcot) MND (ALS): 60–70% of all cases	Usually limb onset of weakness; usually with bulbar involvement. Combined UMN/LMN signs. M:F ratio 3:2	Median survival 3–4 years
Progressive bulbar palsy (PBP): 20% of all cases	Onset with dysarthria followed by progressive speech and swallowing difficulties. Limb weakness follows after months or occasionally years. M:F ratio 1:1 (more common type in older females)	Median survival 2–3 years
Progressive muscular atrophy (PMA): 10% of all cases	Almost always limb onset. >50% develop UMN signs. 85% develop bulbar weakness eventually. M:F ratio 3–4:1. Overlap with flail arm and flail leg syndromes	Median survival 5 years (can be >10 years)
Others: eg, flail arm syndrome: 10% of all cases	Predominantly LMN weakness of bilateral arms. 50–70% eventually develop UMN signs with progression. M:F ratio 9:1. More common in African or Asian patients	Usually better prognosis than other forms

[a]Adapted from Leigh *et al*.[9]

retrospective study of MND patients referred to their practice, Schiffman and Belsh found that 81% of patients did not have respiratory symptoms at diagnosis, though 86% had evidence of respiratory muscle weakness on physiologic testing.[15]

There is no single, currently described physiologic test to accurately assess the degree of respiratory muscle impairment and reliably predict impending respiratory failure in MND patients. Tests should ideally be non-invasive, technically simple, easily accessible, portable and have reference values available.[13] Forced vital capacity/vital capacity (FVC/VC), maximal inspiratory (MIP) and expiratory pressure (MEP) testing have been widely used, but have low specificity and sensitivity.[15] Some criticize the reliability and accuracy of spirometry because they are effort-dependent and are impractical for patients with significant bulbar muscle weakness. Problems arise from air leakage around the mouthpiece because of buccal and lip muscle weakness. Palatal and pharyngeal muscle laxity causes problems with pressure transduction in maximal mouth pressure tests (MEP/MIP).[13,15,17,27]

Lyall *et al*. compared invasive and non-invasive tests of respiratory muscle strength in 81 patients with MND and found that decreases in maximal sniff esophageal (sniff Poes), maximal sniff trans-diaphragmatic (sniff Pdi), and maximal sniff nasal pressure (SNP), as well as cervical magnetic phrenic nerve stimulation (CMS Pdi), were the best predictors of hypercapnia.[13] Unfortunately, these tests are impractical for routine use.

When testing for hypercapnia, an alternative to arterial blood gas sampling is venous serum chloride and bicarbonate testing, described by Hadjikoutis and Wiles.[27] It is simple, cost effective and widely available. Venous serum chloride decreases (88–97 mmol/L) and bicarbonate increases (31–37 mmol/L) in patients with chronic hypoventilation. Nocturnal hypoventilation occurs early in the development of respiratory muscle dysfunction and can be detected by polysomnography,[13] and nocturnal pulse oximetry.[28–30] The latter is cost effective, simple and can be performed in the patient's own home. Regardless of which tests are used, graphs of baseline and serial test results are regarded as having the best prognostic value.[13,15,19]

Types of mechanical ventilation

There are several types of ventilatory aids. These are broadly classified in terms of invasive versus non-invasive. An in-depth discussion of ventilator types is beyond the scope of this article, but it is essential to understand the more commonly used ventilatory aids in the context of the MND patient in the home.

As its name suggests, invasive techniques require an endotracheal tube or more commonly a tracheostomy. The protected airway is then connected to sophisticated ventilators that can be adjusted to control any combination of rate, positive pressure and volume of respiration. For patients in advanced respiratory failure (ie, no respiratory muscle function), invasive ventilators can assume complete control of ventilation. This technique is commonplace in surgical and critical care settings.[31–33]

Non-invasive ventilatory aids can be divided into two groups, negative or positive pressure ventilators. Negative pressure is exerted to the chest or abdominal wall mechanically to assist inspiration. Examples of these devices are body ventilators, such as iron lungs, tank, cuirass, 'wrap' or jacket styles. Negative pressure devices were used mainly for nocturnal hypoventilation, but are cumbersome, inefficient and can aggravate upper airway obstruction during sleep. They have been superceded by positive pressure ventilators. NIPPV can be used to treat daytime as well as nocturnal hypoventilation. These ventilators deliver intermittent positive pressure via a face or nasal mask/interface. Positive pressure devices can be set to deliver variable inspiratory and expiratory pressures, triggered by spontaneous effort (eg, bilevel positive airway pressure – BiPAP). In addition, modern ventilators are set to deliver mandatory breaths if spontaneous effort is not detected within a predefined period.[31–33] Continuous positive airway pressure (CPAP) provides the same preset positive pressure during inspiration and expiration. It can be used in cases where the main problem is upper airway obstruction and not hypoventilation. For example, it can assist patients with bulbar muscle weakness by 'splinting' the upper airway lumen open with positive pressure.[34]

Mechanical insufflation–exsufflation devices have been used successfully to assist patients who have difficulty with expectoration.[31,35] These are expensive and available for home use in the UK and USA,[35] but not in Australia.

Use of home ventilation in MND

A significant proportion of end-stage MND patients choose to be treated in their own homes.[5,8,18,36] Despite the absence of randomized controlled trials in this area, much of the evidence from prospective non-randomized and retrospective cohort studies support the use of assisted ventilation in MND, particularly for symptom relief and life prolongation.

There is now increasing evidence that non-invasive ventilation can provide effective relief of respiratory symptoms and prolong life (Table 2).[37] From the research data, NIPPV is usually offered to MND patients who have respiratory symptoms or when serial test results reach certain predefined cut-offs (FVC or VC $<50\%$ predicted,[34,35,38,39] MIP ≥ 30 cm H_2O or MEP <30 cm H_2O,[39] pCO_2 >45 mmHg, [35,38] serum bicarbonate >28 mmol/L[38]). Studies of prognosis show that

Table 2 Summary of important studies

	Lyall *et al.*[38]	Moss *et al.*[43]	Kleopas *et al.*[34]	Aboussoun *et al.*[41]	Moss *et al.*[24]	Kaub-Wittemer *et al.*[42]	Cazzolli *et al.*[39]
Study type	Prospective case/control – UK	Case series. California Kaiser Permanente Program. Interviews/ Questionnaire	Retrospective Chart Review (USA)	Observational study – tertiary referral centre	Case study – interviews (IL, USA)	Cross-sectional survey – questionnaire in Germany	Prospective study – interviews (USA)
Patients enrolled	Sixteen consecutively referred. Three out of 16 bulbar patients	Fifty patients: 36 at home; 14 institutionalized	All MND patients attending specialist clinic 1993–1997. $n=122$. Bulbar and limb patients	Bulbar and limb patients. $n=39$	355 MND patients. Sixteen patients TV at home. Three patients institutionalized	52 patients. NIV = 32 patients. TV = 21 patients	75 patients. TV = 50, NIPPV = 25 (five with bulbar onset).
Types of assisted ventilation	NIPPV – domiciliary home ventilators	Seven out of 50 NIPPV; 43 out of 50 TV	NIPPV –?face mask or nasal not stated	NIPPV or volume ventilators via face/nasal mask. ±Insufflation/ exsufflation device or suction	Tracheostomy ventilation	NIPPV – nasal (88%), full face (9%) masks	Nasal NIPPV – 23 at home, two in nursing homes. TV – 25 at home, 25 in nursing facility
Enrolment criteria	Symptoms: dyspnoea, orthopnea, sleep disturb. Tests: hypercapnia, FVC < 50%, increased serum bicarb, abnormal polysomnogram	All MND patients on long term mechanical ventilation. 42% started in acute setting. 42% agreed to use before respiratory crisis	FVC < 50%, rapid decrease in FVC > 15% in three months. Symptoms of respiratory failure	New orthopnea, worsening CO_2 > 44 mmHg, FVC < 60%, abnormal blood gases, abnormal MIP/MEP	Emergency TV. 74% gave consent. 37% thought it was temporary	TV started in emergency setting. NIV started for management of symptoms of chronic hypoventilation	NIPPV – started electively when new onset of: sleep disruption, orthopnea, dyspnoea, daytime somnolence, poor cough. FVC < 50%, abnormal MIP/MEP. TV started in emergency
Review interval	Three-monthly		Three-monthly	Three to six monthly in clinic. One to two monthly spirometry			
Patient's opinion	Improved 'vitality' (SF-36) and sleep	QOL score = 6 out of 10. Happy to be alive. Better for those at home. QOL – NIPPV better than TV	Not studied	Not studied	90% would choose it again. Glad to be alive. 37% considered stopping	QOL scores same in NIPPV and TV groups. 94% of NIPPV and 81% of TV patients would choose it again. >80% patients would recommend it to others	No QOL instrument. NIPPV –100% satisfied if tolerated. TV – 72–92% satisfied (glad to be alive). Better satisfaction in those at home than in institution
Carer's opinion	Not studied	Very stressed. Significant burden. Life changing	Not studied	Not studied	80% would encourage patient to choose it again. Best thing was continued family life. 50% would choose it for themselves	97% would encourage patient to have NIPPV again. 94% would choose NIPPV for themselves	TV group – suctioning greatly increased burden. 80% used nurses. NIPPV – nil carers needed external nursing
End stage respiratory failure	Palliation. All refused TV when symptoms worsened			All refused tracheostomy in terminal stage	73% doctors would withdraw ventilation at patient's request	97% NIPPV patients refused TV	93% NIPPV patients refused TV
Additional comments	Need careful adjustment and fitting when starting NIPPV. Optimize comfort	Insurance essential for home care patients, otherwise unaffordable. Issues on informed consent and advanced directives	FVC <50% = poor prognosis, survival six months. Improved tolerance of NIPPV with better mask fit. Better tolerance = longer use of NIPPV = better survival	Bulbar patients less likely to tolerate NIPPV – mask discomfort, air leaks, nasal congestion, nasal bridge pressure. Survival advantage in NIPPV patients versus non-NIPPV patients even when statistically corrected for bulbar/ limb onset	Only 5% MND patients on TV. Insurance essential for care at home (otherwise unaffordable). Nursing care most costly. Low prevalence of home ventilation due to cost/ insurance factors. Patients need to be more informed, advanced directives	Small patient numbers due to resource limitations. Domiciliary NIPPV/TV fully government funded in Germany. 52% response rate – long questionnaire. Selection bias	Five of five bulbar patients did not tolerate NIPPV. MND patients do not want TV if discussed in advance. TV is associated with high costs, burdensome to family. Patients need to be more informed

MND, motor neurone disease; TV, tracheostomy ventilation; NIPPV, non-invasive positive pressure ventilation; FVC, forced vital capacity; QOL, quality of life; MIP, maximal inspiratory pressure; MEP, maximal expiratory pressure.

below these cut-offs, patients have significant respiratory muscle weakness and an average life expectancy of six months.[34] NIPPV is used to treat respiratory symptoms of dyspnoea, orthopnoea, sleep disturbance, daytime somnolence, fatigue and its associated complications.

Not all MND patients will tolerate NIPPV. The interface (mask) and positive pressure causes discomfort and skin ulceration. Respiratory secretions can accumulate and compromise the upper airway. These factors adversely influence patient tolerability and compliance. Problems should be anticipated and patients observed closely and reviewed regularly whilst receiving treatment. Therefore, NIPPV should be managed by trained personnel. Adjustments to optimize comfort are essential and initiation of treatment should ideally be performed in an inpatient setting by an experienced respiratory team.[39,40] Skin ulceration can be minimized by using different interfaces (rotate nasal and face masks), colloid dressings on the nasal bridge and respite from NIPPV. Sialorrhoea can be treated with anticholinergic medications. The literature describes NIPPV as being well-tolerated and efficacious in patients with predominantly limb weakness rather than bulbar weakness.

Cazzolli and Oppenheimer performed a prospective study of 75 home care MND patients on intermittent positive pressure ventilation (IPPV) in America. Twenty-five patients were on NIPPV. Twenty had predominantly limb weakness and experienced good relief of respiratory symptoms. Five had significant bulbar symptoms (dysphagia, dysarthria, excessive oral secretions) and found the treatment ineffective.[39] Aboussouan *et al*. also found that patients with predominantly bulbar dysfunction failed to tolerate BiPAP.[41] Bach studied factors leading to the successful use of non-invasive ventilatory aids in a prospective trial. All those who could tolerate NIPPV via face/nasal mask, found it effective. As their VC deteriorated, their dependence on NIPPV for symptom relief increased until they were on continuous, 24-hour assisted ventilation. Another group that had significant bulbar muscle weakness did not tolerate NIPPV for a variety of reasons. These included air leaks around the mask interface (due to laxed/atrophic buccal muscles) and poor control of upper airway secretions.[35] In general, most MND patients who tolerated NIPPV, found it an effective treatment modality with negligible adverse effects.

In a large retrospective chart review of 122 patients seen at their specialist ALS clinic, Kleopa *et al*. studied the effect of BiPAP on patient survival. All patients were assessed at three-monthly intervals and had pulmonary function tests performed. BiPAP was offered when FVC was $<50\%$ predicted, when $>15\%$ fall in FVC between clinic reviews, or the new onset of dyspnoea. Not only did patients experience symptomatic improvement, but there was also a statistically significant improvement in survival with increasing duration of BiPAP use. Furthermore, there was evidence that patients with bulbar onset disease not only tolerated BiPAP, but showed greater clinical improvement than the limb onset patients. This was illustrated by a greater than proportionate slowing of the rate of FVC decline in the bulbar onset patients.[34] For any treatment that prolongs survival, one would hope that quality of life is improved.

A well-designed prospective study by Lyall *et al*. showed that quality of life was improved on NIPPV. Using the SF-36 assessment tool, the authors showed that there was improvement ($P<0.05$) in the 'vitality domain' of NIPPV-treated patients compared to matched, non-ventilated controls. More importantly, results showed quality of life was not made worse on NIPPV. Responses to questions related to 'well-being' were similar in both NIPPV and control groups, and scores were equivalent to the normal population. Epworth Sleepiness Scores improved significantly after commencement of NIPPV, indicating symptomatic improvement.[38]

In the study of Kaub-Wittemer *et al*., 52 German patients were satisfied with home ventilation. Patients commenced NIPPV via a nasal mask for palliation of symptoms of chronic hypoventilation. Very high satisfaction with treatment was indicated by 94% of NIPPV patients, who would choose to have the procedure again or recommend it to other patients.[42] Several studies showed that very few patients on NIPPV would electively have tracheostomy ventilation (TV) when their disease progressed to the point that NIPPV was ineffective.[35,41,42] Unlike the US and Japan, TV is rarely an option for MND patients in Australia and the UK.[26]

Tracheostomy ventilation can prolong a patient's life for many months to years provided there is adequate nursing and medical support.[2,24,39,42,43] Traditionally, TV would be initiated in an emergency setting when MND patients presented with acute respiratory collapse. Patients who were intubated/tracheostomized and ventilated in this setting were rarely successfully weaned off the ventilator and had to endure long-term institutionalized care or return home if there was suitable full-time care.[2,44] A cuffed tracheostomy protects the airway and prevents aspiration pneumonitis, a frequently fatal event in end-stage MND.[2] MND patients on TV encounter many problems including: swallow and speech impairment, immobility, bronchospasm, tracheomalacia, haemorrhage and fistula formation.[32] Socioeconomic problems include: few long-term residential facilities equipped to manage TV patients, enormous carer burden, likely progression to a 'locked in' state,[37] and high economic costs. For these reasons, initiation of TV is discouraged in Australia and the UK.

Ethical issues with using assisted ventilation

Autonomy and informed consent. Studies from the US have shown that many patients (or family members) had to decide whether to accept TV in the setting of acute respiratory collapse. In some cases, informed consent was not obtained.[2,24,39,42,43] This situation is far from ideal. As all MND patients are competent to make their own decisions in the early stages of illness, it would be opportune to discuss issues regarding future treatment at this time.[2,18,21,44]

In a prospective, longitudinal study by Silverstein *et al*. in 1985, 70% patients wanted to be involved in the decision-making processes. Only 55% felt that general information about the disease was satisfactorily provided and 39% needed more information for better understanding. A total of 81% wanted to know as much information as possible. They desired specific details on how the disease would progress with regards to limb weakness, dysphagia, speech problems and sexual dysfunction. Specific information about the use of ventilators was requested.[45] Cross-cultural differences exist and it is essential for clinicians to acknowledge each individual's preferences.[26,46]

Although there is currently no legislation in Western Australia to recognize advanced directives or health care proxies,[47] early discussions and the use of documented health directives are essential for patient-focused treatment decision making.[2,48] However, international studies have shown that these management plans have been under-utilized.[26] The German study of Kaub-Wittemer *et al*. in 2003 found only 33% of TV patients had been informed of the possibility of respiratory failure before the event and 19% did not give informed consent for TV. Despite being an elective procedure, only 66% of NIPPV patients in this study felt that they were given adequate information.[42] A US survey of 121 MND patients by Albert *et al*. found only 10–15% of patients had advanced directives (although legally binding) and even fewer had verbal discussions with their doctors or documentation. Furthermore, only around half of patients had assigned a Power of Attorney or Health Care Proxy. These patients were surveyed within two years of their diagnosis and most were not ventilated.[49] In another US study of 50 patients on long term TV who had been diagnosed for an average of five years, Moss *et al*. found that 42% did not have documented resuscitation orders, but 79% did make family members aware of when to cease TV. Only half of these had made their wishes known to their doctors.[43] Neudert *et al*. noted six cases of relatives who attempted resuscitation.[4] Therefore, there is clearly a need for doctors to communicate more effectively with their MND patients and families.

Some essential discussion topics could include: the diagnosis and prognosis, symptom development, treatment options and desire for palliation or life prolongation with nutritional or ventilatory support, when to start (eg, at onset of respiratory symptoms) or stop these treatments (eg, unacceptable quality of life; when unable to communicate by any means or 'locked-in'), and resuscitation orders. These discussions should ideally be initiated by an appropriate physician (neurology, respiratory or palliative care specialist) and documented – advanced directives.

It is the doctor's role to initiate discussions about future care directives,[21,24,43] but the ideal timing of these conversations is unclear. Only 58% of physicians in northern Illinois felt it was appropriate to discuss home ventilation around the period of diagnosis.[24] It would be reasonable not to discuss these sensitive issues too soon after diagnosis as it can cause unnecessary distress and hopelessness. Clinically significant respiratory problems are rare within a year of diagnosis.[49] Therefore, it would be reasonable to delay discussions for six to 12 months, but preferably no longer. Furthermore, regularly reviewing treatment options and decisions on a six-monthly basis is recommended, as patients' views can and do change with disease progression.[21,45]

Carer stress – issues of carer burden. In MND, the burden of the disease falls heavily upon family members.[4,24,39,42,43,50–52] TV is significantly more burdensome to carers than NIPPV. Patients on TV generally have more advanced disease, survive longer (longer period of care),[42] and require more intensive care, such as frequent suctioning of the tracheostomy.[39] Regardless of ventilator type, most carers felt stressed, socially isolated, restricted and financially strained. Some carers felt that their own quality of life was worse than the patient's quality of life.[42] Despite these burdens, most family carers did not regret the decision to undertake home ventilation and would choose it again if they needed to. Furthermore, many ($>90\%$) carers would choose NIPPV for themselves. Continued family life at home was the most often cited advantage of home ventilation.[24,42]

Adequate support for carers is essential if ventilated MND patients are to remain at home. Carers require information, education and assistance. Studies have identified that carers desire information on symptoms and prognosis, strategies on how to care for patients and knowledge of social and financial services or resources.[4,22] In Western Australia, the MND Association Care Advisors are an indispensable resource. They offer a comprehensive range of education and support services for patients, carers and health professionals. In particular, they hold meetings, training and respite activities for carers. Treating physicians need to be aware of all available health and social services because they can be powerful advocates for patients and carers who require assistance.[4,50]

Stopping treatment – withdrawing ventilation. Once life-prolonging treatment, such as NIPPV or TV, has commenced, stopping treatment is one of the most difficult decisions a physician will have to make.[53] Deontological ethicists say that life must be preserved at all costs,[54] but also that an autonomous patient has the right to refuse unwanted treatment.[55] When a patient requests that ventilation be stopped, continuing to do so against a patient's will would be ethically and legally indefensible.[54] For the ventilated MND patient, continued treatment brings no hope of recovery, but instead life prolongation in the face of worsening physical symptoms and high social, emotional and financial cost to carers, family and the community.

The importance of advanced directives must be reiterated, as communication becomes exceedingly difficult in end-stage MND. Decisions may have to be made by family members or a surrogate. Generally, doctors would consider withdrawal of ventilation upon the request of the patient.[24,56] Ventilator withdrawal becomes more difficult when a patient is using it continuously, 24 hours a day. In the context of MND, it is exceedingly rare for the patient to have the capability of removing the mask or switching off the ventilator independently. The doctor would usually have to 'actively' withdraw ventilation.

Elective withdrawal must be carefully discussed and planned, as it is emotionally and ethically sensitive. A multidisciplinary team approach should be adopted, with the patient, primary carer, and family central to discussions. Palliative care services should be involved. If referrals to domiciliary palliative care are made at the point of onset of respiratory symptoms, as suggested in this guideline, patients and families would already have developed rapport and working relationships with staff by the time ventilation is withdrawn. These relationships are extremely important in such serious end-of-life management practices. Patients should be counseled against unplanned attempts at withdrawing ventilation in the absence of medical support.

It must be emphasized to the patient that they are significantly dependent upon the ventilator once they are using it for prolonged periods throughout the day. Therefore, severe and undesirable dyspnoea may result if NIPPV is withdrawn without adequate supervision and pre-medication.

Most of the experience in elective withdrawal of ventilation has come from the intensive care setting, on invasively ventilated non-MND patients. It is also referred to as terminal weaning. Studies advocate rapid withdrawal of ventilatory assistance over several minutes to hours by reducing pressure support or oxygen flow.[53,57–60] In conscious individuals, pre-medication with opioids and sedatives (morphine and midazolam) is recommended. Dosages should be administered parenterally (intravenous/subcutaneous) and titrated according to each individual's symptoms and responses.[61] Prescribing a continuous infusion of morphine and midazolam and additional bolus doses for intermittent distress are appropriate. Close supervision by professional staff and immediate treatment of symptoms during the period of terminal weaning are essential. When closely supervised and managed appropriately, most patients rapidly become unconscious from hypercapnia and die peacefully.[3] There is no evidence that appropriate use of opioids, anxiolytics or sedatives will hasten death, and thus the principle of 'double effect' may not apply.[25,53,57,58,60]

Palliative care of patients who choose not to have ventilation

A large proportion of MND patients do not elect to use ventilatory devices.[24] Common problems encountered by patients in the terminal phase include dyspnoea, anxiety, choking on secretions, coughing and diffuse pain.[3,36] Hospice studies from the UK indicate that 88–98% of patients die peacefully without choking.[3,25] Management by a specialized domiciliary palliative care team is essential. Holistic care of patients with respiratory dysfunction includes: control of respiratory secretions with anticholinergic drugs (eg, glycopyrrolate); appropriate use of morphine and anxiolytics; domiciliary oxygen; nutritional and psychological support; inpatient hospice respite.[10,23] End-of-life care planning is also important and involves counseling, dispelling myths,[25] and exploring issues relating to death (eg, preferred place of death). Bereavement counseling for families is important.

Proposed guidelines

In the US, the ALS CARE database was established in 1996 and currently collects information on more than 2014 enrolled patients. When it was established, the objective of the database was to enable neurologists to evaluate diagnostic and therapeutic decisions.[8,36] It is currently being used to assess the impact of evidence-based guidelines, such as the Practice Parameter, on medical practice and patient care.[8]

The Practice Parameter by the American Academy of Neurology was established in 1999. It produced a number of recommendations and guidelines of care in several different areas of MND management (eg, nutrition, pain, sialorrhoea treatment).[21] Unlike the Practice Parameter, the focus of this article is on the use of non-invasive ventilation at home and expanding on the important aspects of its management. The following guideline has been formulated from the pertinent issues raised in this literature review and the author's experiences in domiciliary palliative care. It is to be used as a guide for medical practitioners who care for MND patients on non-invasive home ventilation.

Guidelines for multidisciplinary care of MND patients on non-invasive ventilation at home

At presentation:

- Patient is seen by General Practitioner and should be referred to a specialist neurologist.

Neurologist's appointments:

- To confirm the diagnosis.
- Offer referral to another neurologist for a second opinion.
- Discuss diagnosis, offer information/literature and referral to MND Association.
- Forward patient details (with consent) to the national MND Registry.[8,36,62]
- Obtain baseline respiratory function testing (eg, VC, FVC, SNP, serum chloride and bicarbonate, nocturnal oximetry).
- Consider referral to paramedical services – occupational/speech/ physiotherapy (as appropriate).
- Ensure all correspondence is copied to General Practitioners, community nurses or MND Association Care Advisors (if available), ie, those who may have frequent dealings with the patients in between specialist appointments.
- Consider scheduled neurology appointments at a frequency of two to three monthly depending on the rate of deterioration.

Multidisciplinary management – GP/neurologist/respiratory/paramedical

- Review of symptoms (in particular sleep disturbance, dyspnoea, respiratory infections, morning headaches, daytime somnolence etc.) and new problems.
- Consider discussing the following topics: natural history, symptom progression, treatment options, prognosis, respite care, carer support resources (when appropriate).
- Treatment specific respiratory disorders (eg, infection/secretions).
- Pneumococcal vaccination.
- Serial spirometry/SNP/serum bicarbonate/nocturnal oximetry etc. and graph results.

Respiratory care planning – multidisciplinary (over several appointments):

- Referral to respiratory physician within six to 12 months of diagnosis (earlier if respiratory function parameters are deteriorating rapidly or symptoms of nocturnal hypoventilation). Discuss rationale for proactive management/care planning.
- Offer information (written) to patient and carer about symptom monitoring and advice about future care.
- Explore/discuss issues regarding use of NIPPV for symptom management, life prolongation and quality of life.
- If patient elects NIPPV, consider appropriate timing of commencement – ie, based on symptoms or investigation results.
- Encourage discussion and documentation of advanced directives: resuscitation status, treatment end points for NIPPV (when to stop), use of antibiotics for chest infection, attitude towards intubation/TV.

Starting NIPPV:

- Significant respiratory symptoms or serial test measurements reach threshold values (see discussion).
- Refer to domiciliary palliative care service (important).
- Suggest admission into inpatient respiratory unit to set up and optimize settings for NIPPV.
- Instruct family and carers regarding use of positive pressure ventilator.
- Discharge home.

MNDA advisors/palliative care/GP/respiratory and neurology teams:

- Involvement of domiciliary palliative care service ($\pm$in hospital/hospice specialist) at onset of respiratory insufficiency – for symptomatic support and management of NIPPV at home.
- Palliative care physician to co-ordinate multidisciplinary team's activities (unless alternative specified).
- All correspondence regarding patient management to be copied to every specialist/MNDA advisors/ community palliative care service/GP. A copy to be offered to the patient for their 'own file'.
- Review written advanced directives regularly – at least six monthly.
- Discuss end-of-life care (if appropriate).
- Withdrawal of NIPPV – rationale, set date, time, place (home/hospice), people involved. Preferable that palliative care doctor initiates withdrawal process. Prescribe continuous infusion of opioid and sedatives plus boluses prn. Closely monitor for distress – doctor/nurse/carer.
- Bereavement service.

Conclusion

A guideline for the management of home-based MND patients with respiratory problems has been proposed in this article. It is intended to assist multidisciplinary teams achieve a co-ordinated and comprehensive service to these patients. Future research should be directed towards the practice of withdrawal of assisted ventilation specifically in MND patients and the development of specific practice guidelines in this area.

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