Occasional review

Ethical and clinical issues in the use of home non-invasive mechanical ventilation for the palliation of breathlessness in motor neurone disease

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Motor neurone disease (MND) is a devastating and progressive neurological disorder in which degeneration of motor neurones results in weakness and wasting of the dependent muscles. The prevalence of MND is approximately five per 100 000 and approximately 30% of patients have primary bulbar symptoms.[1] Half of the patients die within 36 months of experiencing the first symptom.

Presentation with ventilatory failure is recognised but uncommon,[2] occurring in less than 5% of cases[3]; however, abnormalities of respiratory muscle function are frequently detectable.[4 5] As the condition progresses respiratory muscle strength diminishes[4 6]; indeed, the rate of change in respiratory function is the only measurable parameter which predicts survival.[1] When the load placed on the respiratory muscle pump exceeds the capacity of the respiratory muscles, then the patient is at risk of ventilatory failure. Initially abnormalities may be present only in sleep[7] or on exercise[8] but, frequently, established ventilatory failure ensues. Ventilatory failure is usually manifest by dyspnoea which may be worse on lying flat (if diaphragm weakness is prominent) or sitting upright (if expiratory muscle weakness predominates). More commonly there is generalised weakness and then there are no clear cut postural symptoms. Direct questioning may elicit symptoms suggestive of disordered sleep architecture—for example, daytime somnolence, difficulty concentrating, or "respiratory" nightmares—or carbon dioxide retention—for example, morning headache. Examination may show paradoxical abdominal motion during respiration. This indicates substantial diaphragm weakness[9] combined with preservation of enough upper thoracic musculature to generate sufficient negative intrathoracic pressure to cause inward abdominal motion. In more advanced disease paradoxical motion may be difficult to elicit and the patient may simply appear tachypnoeic without useful rib cage movement. In established MND patients may also complain of choking symptoms; most commonly this represents swallowing difficulties. However, if unrelated to food, this symptom may be a manifestation of respiratory muscle weakness but occasionally endoscopy will show the cause to be abnormal vocal cord movement.[5]

In patients with MND in whom respiratory muscle weakness is suspected, our practice is to confirm (or refute) the diagnosis using appropriate tests[10] and to seek evidence of ventilatory failure from measurement of daytime blood gas tensions and overnight transcutaneous oxygen saturation and carbon dioxide tensions. Ideally all symptomatic patients should be considered for polysomnography, but this investigation is especially useful for patients who deny sleep related symptoms but have proven severe weakness and those with sleep related symptoms in whom strength tests fail to demonstrate severe respiratory muscle weakness. If the diagnosis of ventilatory failure due to respiratory muscle weakness is secure, the patient, his or her carers, and the clinician need to consider what treatments they wish to pursue.

What treatment options are available?

There are two possible approaches to treatment: palliation of symptoms by drug therapy or physical methods including mechanical ventilation.

Palliative measures to consider are teaching carers simple physiotherapy manoeuvres to assist expectoration, provision of home suctioning equipment, and drugs. In particular, the inability to expectorate mucus may be distressing and carers can be taught to relieve this by manually assisted coughing.[11] Expertise in the pharmacological palliation of dyspnoea is now widespread; commonly used agents are opiates, benzodiazepines, phenothiazines and anticholinergics. Acute dyspnoea can occur without warning in advanced MND and, where possible, patients and their carers should be equipped with a breathing space kit which contains drugs for home administration. The kit is a box supplied by the Motor Neurone Disease Association (MNDA) and is filled with drugs supplied by the GP for each specific patient; for this reason the contents will vary with patient and GP preference. The pack is divided into two parts; one contains diazepam suppositories for use by the carer and the second contains further drugs such as diamorphine to be administered by nurses or other health profes-

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sionals. In both chronic and acute situations these agents greatly reduce the distress associated with dyspnoea and should not be withheld where indicated. Oxygen may also provide symptomatic relief. The main disadvantage is that these drugs, including oxygen,[12] depress the spontaneous drive to breathe and consequently may exacerbate carbon dioxide retention. Thus, while this approach is justified and effective[13] for patients relatively close to death, it is not ideal for those patients with sufficient peripheral muscle strength to maintain an acceptable quality of life were it not for their ventilatory failure.

Patients with MND with normal lungs are not difficult to ventilate; indeed if, as sometimes occurs in Japan and North America, patients with MND are supported with mechanical ventilation and enteral feeding they can survive for many years after the institution of mechanical ventilation.[14 15] Such patients become effectively "locked in" as the condition progresses to involve muscles such as the oculomotor muscles which are normally relatively spared. In these patients the cause of death is usually something other than MND—for example, myocardial infarction.[14] Because of cultural and ethical differences, this management approach has not generally been adopted in the UK to date. The issue of whether to perform a tracheostomy is addressed below; in general, our practice is to avoid a tracheostomy and, instead, to offer non-invasive ventilation.

Until relatively recently the main techniques for domiciliary non-invasive mechanical ventilation were negative pressure devices[16] or the rocking bed.[17] Although both these approaches have been successfully used to treat patients with MND,[17–19] their widespread application has been limited by the size and weight of the machines and the difficulty in inserting the patient. A further problem in neuromuscular patients treated with negative pressure ventilation is upper airway obstruction[19 20] which can result in disruption to sleep architecture despite resolution of blood gas tensions.

Advances in the management of patients with obstructive sleep apnoea have also led to the development of soft nasal masks. Inspiratory application of a positive pressure to the airway via this type of mask (non-invasive positive pressure ventilation, NIPPV) provides an effective method of ventilation in neuromuscular[20] and other disorders[21] including MND. The provision of this method of ventilatory support has traditionally been confined to specialist units, but this is not always so[21] and the relative simplicity of the technique makes it potentially widely available.

King's College Hospital was the first of the six Motor Neurone Disease Association Care and Research centres to open in the UK. In 1994 our group began actively investigating patients with MND for possible respiratory muscle weakness. In those in whom the diagnosis of respiratory failure due to muscle weakness was reached, domiciliary ventilation using nasal NIPPV was offered. In 1997 our centre assessed 127 cases of MND referred from general neurologists for specialist advice and/or a second opinion and, in the same year, we offered NIPPV to 13 patients; to date 25 patients have been treated in this way. This figure is increasing year on year although we acknowledge that our special interest in ventilatory failure may have resulted in some referral bias. The mechanics of ventilating these patients proved relatively straightforward and, in all cases, symptom relief was obtained together with improvement in arterial blood gas tensions; several of our patients returned to part time work and another completed a book. Some difficult management issues emerged, however, and these are discussed below.

When should the concept of ventilation be discussed?

Ideally the concept of ventilation should be introduced relatively early, before ventilatory failure is established. Unplanned endotracheal ventilation may occur if the diagnosis of MND has not yet been reached or if emergency staff are not informed of the patient's diagnosis or wishes. In the largest study of ventilation in patients with MND 21 of 75 patients (28%) had started mechanical ventilation in an emergency despite MND having been diagnosed for an average of three years. This figure would probably be lower in the UK but this scenario is clearly undesirable and might be avoided by proper symptomatic enquiry and serial measurement of indices of respiratory muscle strength—for example, vital capacity, maximum static inspiratory pressure, or the sniff nasal inspiratory pressure.[22] Identification of respiratory muscle weakness may act as a focus for discussion and facilitate communication of patient preferences to their physicians and family. Our experience is that NIPPV is most successful in cases where the recipient has the greatest insight into his or her condition. We therefore suggest that specific enquiry about respiratory symptoms should form part of the follow up consultation in MND so that patients can be given adequate information and advice before the onset of established ventilatory failure in order to allow them to decide what treatment they would wish to receive.

Is nasal ventilation indicated prior to the onset of ventilatory failure?

In our practice most of the patients have established ventilatory failure, as demonstrated by daytime hypercapnia and bicarbonate retention, when they start on NIPPV. Nevertheless, treatable symptoms may occur before the onset of ventilatory failure because of disruption to sleep architecture[7] or severe orthopnoea due to isolated diaphragm weakness[23]; ventilatory support is indicated in these circumstances.

The concept that resting the respiratory muscles might prevent respiratory muscle fatigue and therefore delay the need for mechanical ventilation is not, to our knowledge, supported by convincing data. Indeed, such data as are available (and these were obtained in patients with muscular dystrophy) suggest that early ventilation may be harmful.[24]

Can nasal ventilation be used for 24 hour ventilatory support?

Our patients all started using NIPPV at night only and we originally considered, on the basis of our experience with NIPPV in hospital inpatients,[21] that it would not be possible to use nasal ventilation for 24 hour ventilatory support because of the well recognised problem of nasal bridge ulceration. In fact, some of our patients did manage to use 24 hour ventilatory support for many weeks by virtue of the judicious care of the nasal bridge area by relatives, the use of hydrocolloid dressings and, in one case, alternating between a conventional nasal mask and a nasal cushion system. One Californian patient is reported to have successfully used nasal pressure support for two years.[25] Interface problems can be minimised if alternative strategies are adopted during the day. Strategies to spare the nose include the use of a mouthpiece whilst awake, although this requires some strength in the facial musculature[26]; the use of intermittent abdominal pressure ventilation (IAPV) which moves the diaphragm cranially in expiration and relies on gravity to assist the subsequent descent during inspiration[27]; or a cuirass ventilator (or rocking bed) which may provide sufficient daytime support to allow the patient to have some time free of the nasal mask. These strategies are not suitable for widespread use in district general hospitals (unlike NIPPV) and usually therefore require referral to a specialist centre. This may not be considered appropriate if there has been global progression of the MND.

Do patients receiving ventilatory support have a poor quality of life?

NIPPV could not be expected to influence the progression of MND and, given the likelihood of increased longevity, it is not surprising that Pinto and co-workers found the treatment group to encounter greater disability than the untreated group towards the end of their illness.[28] Moss and colleagues examined the burdens and benefits of home mechanical ventilation in a group of 24 patients with MND in Northern Illinois, the majority of whom were using 24 hour a day ventilation via a tracheostomy.[29] The activities that these patients could pursue were relatively limited and most considered that the best thing about ventilation was that it kept them alive. However, 90% of patients were glad they had chosen mechanical ventilation and said they would do so again. Interestingly their carers, while glad that the patient had used ventilation, said they were much less likely to choose it for themselves in the same situation. When assessed using a battery of psychological tests encompassing depression, hopelessness, stress, loneliness, and overall quality of life, ventilator dependent MND patients were not significantly different from non-ventilator dependent MND patients.[30] Further evidence of patient satisfaction with mechanical ventilation may be inferred from the finding that 42% of such patients would wish to undergo cardiopulmonary resuscitation.[31]

How much does it cost?

The cost of providing domiciliary ventilation depends in large part on the level of support required. Moss and colleagues estimated the median cost (in 1993) of 24 hour a day domiciliary ventilation to be US$7250 per month and for nocturnal NIPPV to be US$1600[29]; however, the annual cost of maintaining a patient in hospital may exceed US$1 000 000.[31] In the UK costs may also vary[32] but the cost of using NIPPV with a palliative intent is essentially the cost of the machine (approximately £3000–5000) and consumables (maximum £300 per quarter). The machine may of course be reused after the death of the patient. Nevertheless, we have experienced a variable response from purchasers. Further costs are associated with the need for an inpatient stay of about a week to initiate treatment. In our practice these and other costs such as staff time are currently absorbed into the overall cost of providing the respiratory service. As discussed earlier, it is acknowledged that the patient is likely to live longer with greater disability; in the UK system the indirect cost of this is borne by the carer(s), usually the family. When assessing these costs it is necessary to consider both financial costs such as missed employment opportunities as well as the enormous emotional burden inherent in the domiciliary ventilation of a severely disabled relative.

What are the contraindications?

Since the aim of treatment is palliative, contraindications are relative if NIPPV results in symptomatic improvement. However, use of NIPPV will be more difficult for patients who dislike wearing a mask or for those with local problems such as anatomical abnormalities of the nose or upper airway. Patients without a carer will have practical problems applying the mask, particularly if the disease has involved the upper limbs. One of our patients has spent a year in a hospice because he had no relative at home who could apply the mask at night and attend to other domestic needs. Bulbar[33 34] or vocal cord[5] dysfunction may increase the risk of aspiration and make successful NIPPV more difficult, but is not in our view a contraindication. NIPPV is simply one tool in the palliative care of patients with MND; care must be taken to ensure that the use of NIPPV does not delay input from palliative care teams. We have been fortunate that our local hospices have been enthusiastic about patients receiving NIPPV.

Risks of increased longevity

Domiciliary rocking bed and negative pressure ventilation are not thought to cause prolongation of life,[17 18] but recent data suggest that NIPPV may do so. Pinto and colleagues provided NIPPV to nine consecutive patients with MND and disturbance of arterial blood gas tensions, while the nine preceding patients seen in their unit received palliative therapy and served as controls.[28] At one year all of the controls were dead but eight of the nine treated patients were alive. Cazzolli and Oppenheimer reported eight living patients (average duration

of NIPPV 25 months) and six dead patients (average duration of NIPPV 21 months) in a group of patients successfully adopting NIPPV.[25] In patients prescribed NIPPV but who were not using it at the time of death (from choice, lack of effect, or intolerance of the machine) the average survival time was 5.5 months. Similar data were recently reported from the Cleveland Clinic; patients intolerant of NIPPV had a relative risk of death of 3.1 compared with patients who were able to tolerate NIPPV.[35] The median survival in patients treated at King's College Hospital is 10 months. It therefore seems likely that patients with MND with ventilatory failure treated with NIPPV do live longer, and the magnitude of the survival benefit may exceed that conferred by the use of Riluzole.[36]

Should patients with bulbar symptoms be managed differently?

Although approximately 30% of patients with MND present with bulbar symptoms, trunk or limb signs are often present in such patients; indeed, MND should be diagnosed with great caution on the basis of signs in the bulbar region alone.[37] Only a minority (7.5%) of patients who present with primary bulbar disease remain with primarily bulbar disease through the course of their illness.[1] Thus, it is unsurprising that "bulbar patients" with established MND may have substantial ventilatory muscle weakness[5] and, in our view, merit a similar investigative pathway to non-bulbar patients. Nevertheless, it is acknowledged that patients with bulbar disease are at increased risk of aspiration and this may require appropriate investigations and treatment/prophylaxis. Bulbar patients are less likely to be able to tolerate NIPPV but, if they can, they derive equal benefit.[35] As with non-bulbar patients who are intolerant of NIPPV, the question of tracheostomy may arise but, because (statistically) these patients are older, their prognosis is, if anything, worse than that of patients with non-bulbar disease[1] and the same reservations therefore apply (see below).

Should a tracheostomy be used?

In patients who are starting long term domiciliary ventilation, tracheostomy may have advantages in preventing aspiration, especially in patients with bulbar disease.[15] Similarly, for patients whose expiratory muscle weakness precludes effective cough,[38] tracheostomy permits convenient suctioning. However, tracheostomised patients seem to be more likely to be dissatisfied with their quality of life than patients treated with NIPPV.[25] Such patients are also, in the UK, likely to experience greater difficulty in establishing care at home. A third disadvantage of tracheostomy is that patients risk continuing to indefinite 24 hour ventilatory support without a fully informed discussion of the implications of this progression. A standard cuffed tube prevents the patient from talking, but fenestrated cuffed tubes may allow speech and still increase protection against aspiration. An alternative strategy is to have the cuff up at night and down during the day. Occasionally, after a period of unplanned endotracheal ventilation, patients may present with a tracheostomy in situ.[25] Our policy in these circumstances is still to attempt extubation, but this may prove impossible. With this exception our practice has not been to offer tracheostomy because our goal is to palliate symptoms rather than extend longevity. Thus, even in bulbar patients, if effective palliation can be achieved using NIPPV we regard this as a satisfactory outcome.

Management of the terminal phase in patients receiving NIPPV

Occasionally patients die of a non-respiratory cause—for example, gastrointestinal bleeding—whilst receiving ventilation; however, in general, patients die of respiratory causes. Approximately half of our patients have succumbed to a chest infection either at home or in a local hospice. This may be a welcome development and withholding antibiotic therapy may be reasonable. Other patients progress to become continually dyspnoeic during the day, requiring an increased duration of ventilator use. If this can be achieved without nasal ulceration this may be acceptable to patients; if not, drugs may be required for symptom control.

Patients with MND who receive mechanical ventilation (whether non-invasively or via a tracheostomy) may reach a stage where they find their quality of life intolerable. Under these circumstances the patient may occasionally, despite palliative measures, request discontinuation of mechanical ventilation. This situation is clearly potentially distressing for both relatives and staff and requires sensitive handling with the emphasis on preserving patient dignity and autonomy. However, mechanical ventilation is a medical therapy and, if a mentally competent patient desires it, there is no ethical reason why it should not be discontinued either immediately or on a date decided by the patient.[15 39 40]

The management of terminal ventilator withdrawal is controversial and should ideally be dictated by patient preference. Essentially the choice lies between an abrupt discontinuation of ventilatory support or a gradual withdrawal (sometimes called terminal weaning). Some lay people and health care professionals might incorrectly view the former approach as euthanasia, but the notion that there is a distinction between the two approaches cannot be supported by ethical argument.[41]

If the patient is to have ventilatory support suddenly removed, dyspnoea is likely. As with any medical process, the clinician has a responsibility to execute the patient's request in a compassionate and humane manner.[42] Specifically, discomfort must be anticipated and rapid titration of medications (usually opiates and benzodiazepines) to maintain comfort is essential.[41] Oxygen may also be useful but we have not resorted to anaesthetic agents as reported by Goldblatt and Greenlaw.[39]

If the patient is to come off the ventilator gradually (by reducing the efficacy of the venti-

lator), this will allow the gradual development of hypercapnia and provide terminal coma.[43] Anxiolytic and opiate drugs may still be required with this approach.

Conclusion

Symptomatic ventilatory failure occurs in MND and can frequently be effectively palliated using non-invasive mechanical ventilation (NIPPV). Patients and their carers should be warned that this treatment carries a risk of increased longevity at the cost of increased disability. Clinical trials to measure the health economic aspects of NIPPV and the impact of NIPPV on quality of life are urgently needed to define the role of NIPPV in the routine management of patients with MND.

Note: Dr Davidson has made a video for patients and relatives explaining various modes of ventilatory support which is available from him at the Lane-Fox Unit, St Thomas' Hospital, London SE1 7EH, but it is not specific for MND.

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