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Mechanical ventilation in amyotrophic lateral sclerosis: a cross-cultural perspective

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Abstract Mechanical ventilation is known to be an effective means of relieving symptoms of chronic hypoventilation and prolonging life in patients with amyotrophic lateral sclerosis (ALS). Various methods of mechanical ventilation are available to patients with ALS. However, attitudes towards mechanical ventilation in ALS vary widely across different cultures, and even within a given medical system. This article describes differences and similarities between a North American, a European and a Japanese approach, based on the respective medical and cultural traditions. The common goal is to provide optimal palliative care to patients with ALS.

Key words Amyotrophic lateral sclerosis · Motor neurone disease · Palliative care · Cross-cultural comparison · Mechanical ventilation

Introduction

Amyotrophic lateral sclerosis (ALS) is a progressive degenerative motor neurone disease with an estimated global prevalence of about 6–8/100,000 population per year. The worldwide incidence of ALS is 1.5–2/100,000 population per year and is increasing, although the reasons for this are as yet unknown [1].

In recent years, a number of factors have contributed to a surge of interest in ALS. Advances in the scientific understanding of the pathophysiology of the disease, especially in its inherited form, together with the first small successes in therapeutic trials, have raised hopes that in the future medical interventions, which significantly slow the course of the disease, may be available [2, 3]. In addition, palliative therapy in ALS has become a major focus of attention, in part as a result of the increasing influence of patient support groups and improved patient education [4].

All patients with ALS develop symptoms of respiratory insufficiency during the course of their disease. Respiratory failure is responsible for the majority of deaths owing to ALS, which usually occur within 3–5 years of disease onset. However, symptoms of chronic nocturnal hypoventilation can severely compromise the quality of life of patients with ALS long before respiratory failure ensues. Various modes of mechanical ventilation can be used to palliate these symptoms and also to prolong the lives of patients. However, attitudes towards ventilation for patients with ALS vary both between and within different countries. In this paper, we review the various methods of mechanical ventilation available to ALS patients and discuss current practices from a North American, a European and a Japanese perspective.

Indication and modes of ventilation

Patients with ALS often present with symptoms of chronic hypoventilation while external signs are still quite modest. Often, forced vital capacity (FVC) may appear adequate, and arterial blood gas measurements may remain normal. The earliest signs of respiratory compromise typically occur during sleep, particularly rapid eye movement (REM) sleep [5]. Patients may complain of frequent nocturnal awakenings, daytime fatigue and/or somnolence and general malaise.

Patient self-reported symptoms are key indicators for the possible use of mechanical ventilation. Symptoms of chronic respiratory insufficiency [4] include:

- Daytime fatigue and sleepiness, concentration problems
- Difficulty falling asleep, frequent awakenings, nightmares
- Morning headache
- Nervousness, tremor, increased sweating, tachycardia
- Depression, anxiety
- Tachypnoea, dyspnoea, hypoventilation
- Visible efforts of auxiliary respiratory muscles
- Reduced appetite, weight loss, recurrent gastritis
- Recurrent or chronic upper respiratory tract infections
- Cyanosis, oedema
- Vision disturbances, dizziness, syncope
- Diffuse pain in head, neck and extremities

Although sensitive, such symptoms may not be specific for chronic respiratory insufficiency. A standing FVC of approximately 1.5 l or a significant drop in vital capacity when measured in the supine position may help indicate chronic hypoventilation as the aetiology of patient symptoms. In some cases, however, patients may have symptoms at an FVC of > 50% of the predicted value. A helpful test when the FVC appears to be adequate is transcutaneous nocturnal oximetry. With this method, the oxygen saturation is measured throughout the night via transcutaneous finger electrodes. Saturations of < 93% or desaturations of > 3% lasting 20–30 s are indicative of nocturnal hypoventilation. These typically occur during REM sleep but may be further exacerbated by increased upper airway resistance, profuse secretions or even gastro-oesophageal reflux [6].

Respiratory therapeutic interventions

In recent years, a variety of modes of mechanical ventilation have become available. The correct choice of ventilator options for a patient with ALS is dependent upon a range of factors, which include availability, cost, patient preference and the presence of other symptoms such as upper airway obstruction or heavy bronchial secretions.

One major challenge in the management of patients with ALS is to determine the appropriate time at which to commence mechanical ventilation. Ideally, it should be offered before the onset of respiratory failure in order to allow the patient sufficient time to become familiar and competent with the device before it becomes essential.

Modes of mechanical ventilation

Ventilators may be either invasive (administered via a tracheostomy or endotracheal tube) or non-invasive (applied directly to the face or body).

Invasive ventilators offer the advantage of bypassing the upper airway and thus can be used in patients with upper airway obstruction as a result of bulbar involvement or heavy secretions. Tidal volume and positive end-expiratory pressure can be selected to reduce dead space and prevent the collapse of peripheral airways and subsequent atelectasis. Patient survival can thus be extended indefinitely, although the disease course will progress unabated with the probable eventual loss of all patient communication and independence.

Invasive ventilation has a number of major drawbacks, including the exorbitant costs involved, the need for 24-h nursing care and its often detrimental long-term impact on the quality of life of both the patient and caregiver. Indeed, in many countries invasive ventilation is not available to patients with ALS owing to the progressive, incurable nature of their illness, and even in countries where it is available, it is seldom used [7, 8].

Non-invasive mechanical ventilators can be categorised as either negative- or positive-pressure devices. Negative-pressure devices passively expand the chest, thereby increasing the inspiratory volume. The best-known historical example of this type of ventilator is the ‘iron lung’, in which patients were placed in an air-tight cylinder with the head protruding. Air was then pumped out of the cylinder, causing the chest wall to expand, thus simulating the action of the diaphragm. However, this type of ventilator is large and confining, and does not afford ease of movement or hygiene for the patient. Thus, it tends to be unpopular and is not widely used.

Other more patient-friendly negative-pressure devices are the chest shell, also known as the cuirass, and the pulmo-wrap. The cuirass is a rigid shell that is applied to the chest from the neck down to the bottom of the ribcage and adheres to the thorax by negative-pressure suction. A seal around the edge of the cuirass allows air to be pumped out from under the shell, creating negative pressure and expanding the lungs like a smaller, more mobile version of the iron lung. Since the patient’s limbs are outside the cuirass, greater mobility is possible. The pulmo-wrap is an airtight body suit that covers the chest and is sealed at the neck, shoulders and hips. It tends to be more comfortable than the cuirass, but much more difficult to apply.

A disadvantage with all negative-pressure ventilators is the possibility of exacerbating upper airway obstruction by creating negative pressure in the glottis and further

narrowing the upper airway. However, even patients with severe bulbar involvement have occasionally used the cuirass with success.

Non-invasive positive-pressure ventilators (NIPPVs) administer pressurised air to the lungs through the naso-oropharynx. This allows greater air volumes to enter the lungs and, similar to invasive ventilation, can halt or even reverse micro-atelectasis. Many varieties of NIPPV exist; however, not all are appropriate for patients with ALS.

Continuous positive airway pressure (CPAP) is commonly used for otherwise healthy patients with sleep apnoea, but is entirely inappropriate for patients with ALS, since it applies a constant pressure during both the inspiratory and expiratory phases, thus increasing the work of breathing. In contrast, bi-level positive airway pressure (BIPAP) applies a lighter expiratory than inspiratory pressure, thus reducing the work of breathing. BIPAP may be administered via a mask or nasal pillow and is typically used for 6–8 continuous hours during sleep, although it can be used for longer periods according to patient needs. It is a very effective method of treating the signs and symptoms of chronic hypoventilation in ALS, increasing pO_2 and tidal volume and decreasing pCO_2. However, the major limitation to BIPAP is that patients with considerable bulbar involvement experience difficulty in learning how to use the device [9].

Other positive-pressure ventilation methods include intermittent percussive ventilation (IPV) and insufflation-exsufflation. IPV involves the delivery of pressurised, intermittently vibrating, nebulised saline, bronchodilators and/or expectorants through the mouth for 10- to 15 min periods in order to aid clearing of pulmonary and bronchial secretions and decrease mucous plugging. The insufflator-exsufflator (or cufflator) delivers air under positive pressure and then sucks the air back out, thereby assisting patients' cough and decreasing mucous plugging. For patients who are able to use this device without gagging or prolonged coughing, it can be very effective. Many ALS patients, however, are unable to use this, especially if they have significant bulbar involvement.

The North American experience

In North America, and especially the United States, the provision of medical care has a strong tradition of being patient-driven, and this has had a considerable impact on the respiratory care given to patients with ALS. Economic considerations have generally been less important.

In major ALS centres, non-invasive mechanical ventilation is typically offered to patients with chronic hypoventilation, since it provides effective symptom relief, requires minimal nursing support, and is compatible with good quality of life [10]. The use of invasive mechanical ventilation, although routinely offered in many ALS centres, is not generally encouraged because of the tremendous emotional burden that is placed on both the patients and their families. Even in large ALS centres, many physicians feel that invasive mechanical ventilation is not compatible with a good quality of life for most patients [8].

Furthermore, depending upon home-nursing requirements, invasive mechanical ventilation can be associated with mean financial costs as high as US $ 15,000/month. In contrast, the costs of non-invasive ventilation are estimated at about US $ 400/month. The majority of patients in the United States and Canada have private or national health insurance (Medicaid for indigent populations and Medicare for those > 62 years in the US). Most health insurance policies will fully reimburse the costs of non-invasive ventilation, but not those of invasive ventilation, as 24-h home-nursing care is seldom covered. Thus, health insurance coverage can impact on the type of care available to patients with ALS.

In a recent retrospective review (D.F. Gelinas, unpublished data) of 60 patients with ALS participating in therapeutic drug trials at the Forbes/Norris ALS Center, San Francisco, United States, during 1996–1997, 20 patients used non-invasive mechanical ventilation for relief of their symptoms of chronic hypoventilation. Although no asymptomatic patient received mechanical ventilation, chronic hypoventilation was substantiated by a low FVC alone in 39% of patients and by nocturnal desaturations in 61%. The majority of those patients on non-invasive support used a BIPAP machine (72%); a further 6% used a chest cuirass, while the remaining 22% used a variety of intermittent positive-pressure devices. Successful use of non-invasive ventilation was related to patient motivation, respiratory education and the ability to control the upper airway (i.e. less bulbar involvement). All patients who used non-invasive ventilation experienced an improvement in their symptoms of insomnia, fatigue and dyspnoea.

At present, the American Academy of Neurology is attempting to standardise ALS respiratory management by formulating a series of evidence-based reviews on which to base recommended clinical practice guidelines.

The European experience

Traditionally, European neurologists have been reluctant to recommend, or even consider, the use of mechanical ventilation for patients with ALS. However, in recent years, many neurologists in northern Europe, especially the United Kingdom, have started to consider ventilation as a genuine option in ALS. This attitude is now gradually spreading southwards, accompanying the shift from a traditional paternalistic attitude (*salus aegroti suprema lex*) to a more patient-centered approach (*voluntas aegroti suprema lex*), which has become increasingly prevalent in European medicine in recent years.

A number of factors have contributed to the widespread reluctance among European neurologists to use

mechanical ventilation in patients with ALS. These include an inadequate understanding of the distinction between non-invasive, intermittent home mechanical ventilation (NI-HMV) via a mask and invasive, 24-h ventilation via tracheostomy [11] and concerns over progression from non-invasive ventilation to tracheostomy. In addition, there has been a disinclination to employ expensive, time-consuming technical equipment in patients with a short life expectancy.

Data from a small series of 24 German ALS patients receiving non-invasive ventilation do not support these concerns [12]. A total of 11 patients with an average non-invasive ventilation duration of 12 months died. Of these, 4 chose to end non-invasive ventilation after periods varying from 2 to 56 months. All 4 patients reported good to excellent symptomatic relief with non-invasive ventilation, the reason for discontinuation being a poor overall quality of life as a result of disease progression. The average duration of ventilation for the 13 remaining patients was 16 months. The palliation of symptoms was good to excellent in 17 out of 24 patients (70%), and no patients progressed to tracheostomy. Monthly costs for non-invasive ventilation equipment amount to about US $ 200–300, although costs for nursing care can be much higher. Interestingly, for 20 out of 24 patients, the primary caregiver was either the wife or another female relative (mother, daughter).

NI-HMV is offered to the patients as a palliative treatment for symptoms of chronic nocturnal hypoventilation. Therefore, NI-HMV should be discussed with the patient as soon as these symptoms start to appear [13]. NI-HMV is not primarily intended to prolong life, although it may do so dramatically in some cases [14, 15]. Although the European attitude towards ventilation in ALS is slowly becoming more open, many problems still persist. The main difficulty lies in the increasing care requirements of a ventilated ALS patient with progressive disability. The lack of sufficient financial provision to meet these needs and of adequate facilities for patients who cannot be cared for at home are major obstacles. Furthermore, in many European countries, caring for a patient with ALS who is receiving mechanical ventilation becomes a financial burden for the physician, as a result of inadequate cost-reimbursement schemes for home visits.

Recently, the European ALS study group has initiated efforts to formulate standards of care for patients with ALS, which will include guidelines for the use of mechanical ventilation [16]. It is to be hoped that this will help increase awareness and the use of mechanical ventilation among European patients with ALS in the future.

The Japanese experience

There is considerable debate among neurologists in Japan as to whether or not to recommend mechanical ventilation for patients with ALS. In the past, mechanical ventilation was not generally advised because of quality of life concerns. However, in recent years, physicians in Japan have been becoming increasingly likely to advocate the use of ventilators. Despite this, there is considerable variation in their use.

A recent development in Japanese health care is the requirement of physicians to explain treatment options in detail to patients and their families in order to obtain informed consent. Traditionally, decision-making in health care in Japan has been largely left to the physician, with the patient being given little opportunity to express any preference. Paradoxically, as the use of mechanical ventilators for patients with ALS is becoming more accepted among physicians, increased patient education and choice has led to some patients with ALS declining ventilation.

In Japan, ALS has been designated an intractable disease by the Ministry of Health and Welfare and, as such, medical costs are completely covered by medical insurance and government support. Thus, the quality of available medical services is irrespective of any insurance coverage and includes the loan of mechanical ventilators and regular visits by medical staff. In some cases, patients with ALS may not be registered because the physician or the patient's family may not wish to disclose the true nature of the disease to the patient. In these instances, 70–90% of costs are still covered by medical insurance.

The use of ventilators among patients with ALS in Japan is reflected in three nationwide surveys that have been performed: one of hospital neurologists and two of patients who were members of the Japanese ALS Association and their families.

The Research Committee of CNS Degenerative Diseases, Ministry of Health and Welfare, conducted a survey on the natural history of ALS in 1995 [17]. Documentation on 696 deceased ALS patients who had died between 1985 and 1994 were collected from 47 neurological institutions. The mean age at onset of ALS was 59.0, SD 10.7 years and mean duration of disease to time of death was 41.8, SD 34.6 months. A total of 171 patients (24.5%) used mechanical ventilators. The mean duration of disease for patients using ventilators was 54.0 months compared with 35.5 months for those not receiving ventilation. Mechanical ventilation primarily involved invasive ventilation with tracheostomy. In some institutions, its use was preceeded by non-invasive negative-pressure devices.

A questionnaire survey of members of the Japanese ALS Association (patients, family members and relatives of deceased patients) regarding the use of mechanical ventilation was performed in July 1993 [18]. In total, 902 questionnaires were distributed, of which 677 (75%) were completed and returned. Of these, 379 were from patients and their families and 298 from relatives of deceased patients.

Mechanical ventilation was used by 46% of patients with ALS, a considerably higher proportion than was ex-

pected. A total of 24% of patients who were at home received ventilation, compared with 76% of patients who were in hospital. Among patients who received ventilation, 21% did so on the recommendation of their physician, while only 10% did so at their own wish. A further 12% of patients were ventilated at the request of their family. In addition, 15% of patients were provided with a mechanical ventilator after discussion between the patient and their family. In the remaining 42% of patients, mechanical ventilation was used as an emergency procedure without any detailed informed consent being given by the patient.

Among patients who did not use mechanical ventilation, 35% declined on the basis of their own personal preference. In 25% of cases, the decision to refuse ventilation was taken by the family. Of these, 69% of families stated concerns over the patient's future as the primary reason. In only 7% of cases was the decision not to use a ventilator based on the physician's recommendation. Of the others, 23% were not in time because of acute deterioration, 7% did not think that disease was sufficiently severe, 1.5% were not aware of the option and < 1% could not be admitted to hospital.

In Japan, mechanical ventilators are usually installed when patients show apparent respiratory distress. Oxygen by mask may be given on occasions of hypoventilation in patients with insomnia or headache. As respiratory distress progresses, invasive ventilation with tracheostomy is commonly used, rather than non-invasive negative-pressure devices. The type of mechanical ventilation was not specified in either the Research Committee of CNS Degenerative Diseases or Japanese ALS Association surveys; however, invasive ventilators with intubation or tracheostomy are the most likely methods to have been used.

Surveys of ALS patients and their families provide a basis by which to predict the future use of mechanical ventilation by ALS patients in Japan. The decision to implement mechanical ventilation appears to be principally made by families, including in emergency cases, supported by the clinicians' recommendations. Previously, a paternalistic approach by clinicians was considered to be the most influential factor in the choice of medical therapeutic procedures. However, it appears that this may be less dominant than suspected, with patients and their families having a significant role in the decision-making process. Since these surveys were conducted, the Japanese Ministry of Health and Welfare has decided to introduce medical insurance to cover the costs of mechanical ventilation at home and home visits by medical staff for ALS patients. Despite this, however, patients do not appear to be encouraged to use mechanical ventilation because of the fear of a long-lasting disease course culminating in a 'locked-in' state.

Conclusion

Any discussion of mechanical ventilation in patients with ALS on a worldwide level must take place within the broader context of significant cross-cultural differences in the balance between a paternalistic, prescriptive attitude towards decision-making in medicine and a more autonomous, patient-centered approach.

In this regard, several reports have highlighted a global west-to-east gradient [19]. Thus, in North America there is a strong tradition of patient autonomy and freedom of choice, while in Japan decisions are usually taken by the physician, who is generally committed to a life-prolonging approach. In Europe, the situation is more heterogeneous and lies somewhere between the American and Japanese positions. However, an important consideration in offering mechanical ventilation to patients with ALS throughout the world is that although symptoms of chronic hypoventilation may be alleviated and survival extended, the underlying disease continues unabated, which may lead to an eventual 'locked-in' state.

On a global basis, neurologists are attempting to provide patients with ALS the optimal available care within the framework of their respective medical and cultural traditions. Many factors have a significant impact on the care that can be provided, including the wishes and expectations of patients and their families, ethical and legal considerations, and resource allocation problems. No single approach to the management of patients with ALS can be described as superior to another; the common goal is to provide an optimal level of palliative care that emphasises the chance of a meaningful life for the patient even in the wake of severe and progressive physical impairment.

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