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Review article

Managing patients with amyotrophic lateral sclerosis

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ABSTRACT

Amyotrophic lateral sclerosis (ALS) is the most common rapidly progressive adult-onset neurodegenerative disorder. There have been great advances in the management of patients with ALS over the past decade. It starts with the giving of the diagnosis and continues to the terminal phase of the disease. This review will examine the impact of medical and non-medical interventions on improving survival and quality of life in these patients, emphasizing the importance of a multidisciplinary approach.

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1. Introduction

Amyotrophic lateral sclerosis (ALS), interchangeably known as motor neurone disease (MND) in several countries, was originally described by the French physician Jean-Martin Charcot [1]. ALS is one of the most common adult-onset neurodegenerative diseases, and has a more or less uniform incidence of 1–2/100 000 per annum and prevalence of around 6/100 000 worldwide [2].

Great progress has been made, especially in the last decade, on the management of patients with ALS. It is a process that extends over months to years. It starts with the giving of the diagnosis to the patient and their family, and continues to the terminal phase of the disease. There are several important areas in the clinical care of patients with ALS, including medical intervention, symptomatic treatment and non-pharmacological therapies, which require the involvement of a range of health professionals. In this article, I will highlight these different strategies and pathways, emphasizing the need for a multidisciplinary approach in achieving the best results for patients.

2. Informing the diagnosis

Once the diagnosis of ALS has been firmly established, the physician needs to inform the patient of the diagnosis in a clear, honest and empathetic manner. It is crucial that positive aspects of what can be offered are stressed, and hope not completely destroyed when telling the diagnosis. Guidelines have been developed for breaking bad news to patients with ALS [3]. Carers, and usually relatives, must also be provided with comprehensive information, as the disease often evolves constantly.

3. Riluzole

Riluzole is currently the only disease-modifying drug approved for ALS. It is thought to work by multimodal inhibition of glutamatergic neurotransmission via both presynaptic (inhibition of voltage-gated sodium channels, and possibly activation of G-protein coupled transduction pathways, both leading to inhibition of glutamate release) and postsynaptic (non-competitive blockade of *N-methyl D-aspartate*[NMDA] receptors) actions. A Cochrane collaboration review showed that riluzole prolonged median survival by two to three months [4]. However, riluzole appears to be more effective in earlier onset and less severe disease: a double-blind placebo-controlled study in those over the age of 75 years or with a forced vital capacity (FVC) of less than 60% failed to show any improvement in survival [5]. Riluzole is generally well tolerated, but treatment needs to be discontinued if the liver function tests exceed five times the upper limit of normal or if neutropaenia develops.

4. Respiratory care

Ultimately, the majority of ALS patients will die of respiratory failure. Therefore, assessment and management of respiratory function and symptoms are very important. Patients may have dyspnoea at rest, orthopnoea, symptoms of nocturnal hypoventilation (e.g. morning headache and excessive daytime sleepiness) or other non-specific symptoms of respiratory insufficiency (e.g. poor concentration and fatigue).

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A randomized controlled trial has shown that in ALS patients without severe bulbar dysfunction, non-invasive ventilation (NIV) lengthens median survival by approximately seven months, more than twice the effect of riluzole. In the same trial, a significant improvement on various domains of quality of life was also reported in all ALS patients treated with NIV compared with patients on standard treatment, including those with severe bulbar impairment [6]. Current guidelines from the American Academy of Neurology suggest initiating NIV in ALS if the vital capacity falls below 50% predicted [7]. Sniff nasal inspiratory pressure test (SNIP), is a more sensitive indicator of respiratory insufficiency in ALS [8,9], although it is not routinely used despite being an easy assessment to carry out in clinic.

Tracheostomy ventilation is rare in most countries, although it is commonly offered in Japan. It may substantially prolong life [10], but is very expensive [11]. In addition, patients with tracheostomy appear to have a lower quality of life that those who use NIV [12]. Some patients and their carers may find tracheostomy ventilation acceptable, hence this option should be fully discussed with all patients.

Ethical issues frequently arise with respect to ventilation [13], but ultimately the right of the competent patient to refuse treatment overrides the doctors' desire to do what they consider is best for the patient. In the event of the patient being unable to communicate his or her wish, or being incompetent to do so, the clinician must decide what is in the patient's best interest, with the decision usually reached after discussion with family members and after taking into account any formal advance directives made by the patient. Circumstances under which ventilatory support will be withdrawn should also be discussed.

5. Nutrition

Malnutrition is an independent prognostic indicator for survival in ALS, with an almost eight-fold increased risk of death in patients who are malnourished [14]. If symptoms of dysphagia are identified, an early referral to a speech and language therapist should be made. Percutaneous endoscopic gastrostomy (PEG) has been shown to prolong survival, increase body mass index and decrease weight loss [15]. A body mass index of less than 18 to 18.5 kg/m^2 or a loss of body weight of 10% are parameters recommended as indications for PEG placement [15,16]. When PEG is performed with a vital capacity of less than 50% of normal, procedure-related mortality rises sharply [17,18]. The radiologically inserted gastrostomy tube (RIG) is increasingly being preferred over PEG as it avoids sedation, the need for a strict recumbent position, can safely be done even after the vital capacity has dropped below 50% of the predicted value and after non-invasive mechanical ventilation has been started [19,20].

6. Secretions and sialorrhoea

Patients with ALS have thin serous secretions due to cholinergic stimulation and thick secretions from beta-adrenergic stimulation [21]. The former may be reduced by an anticholinergic bronchodilator or amitriptyline [22], while the latter is decreased by beta blockers [23]. Mucolytic agents (e.g. carbocisteine) may help patients clear thick secretions from the throat.

Sialorrhoea results from inability to swallow saliva properly. It puts patients at risk of aspiration and causes social embarrassment. Treatment options include anticholinergic agents (e.g. amitryptyline, transdermal scopolamine, atropine) [7], botulinum toxin [24] and, as a last resort, radiation therapy to the salivary glands [25].

7. Pseudobulbar affect

Pseudobulbar affect or emotional lability, usually characterised by inappropriate or disproportionate crying, or pathological laughing, is present in up to half of ALS cases [26]. It is commonly treated with tricyclic antidepressants or selective serotonin reuptake inhibitors (SSRIs) [27,28].

8. Cramps, spasticity and pain

Pain can occur in up to 70% of patients with ALS [29]. Pain may be due to cramping, spasticity or immobility of joints. Quinine sulphate helps relieve cramps [30]. Physiotherapy and muscle relaxants such as baclofen or tizanidine, are used to treat spasticity [31]. Intrathecal baclofen or botulinum toxin injections into specific muscle groups may be effective in severe cases of spasticity [32,33]. Joint immobility may be helped by nonnarcotic analgesics such as nonsteroidal anti-inflammatory drugs. Narcotic analgesics are beneficial in severe pain [29].

9. Physical and occupational therapy

Stretching and passive mobility exercises decrease spasticity, prevent contractures, maintain function and reduce pain [34]. There is no clear benefit, and potential harm, with vigorous physical activity and high-resistance exercise [35]. Occupational therapy enables the patient to learn functional techniques and obtain adaptive equipment to perform activities of daily living.

10. Fatigue

Fatigue is common in neuromuscular diseases. Modafinil has been shown to benefit patients with ALS in an open-label pilot trial [36].

11. Communication

About four-fifths of ALS patients will suffer from speech impairment during the course of their disease [37]. Therefore, speech and language therapists are important to encourage patients to maintain communication, sometimes with the help of communication aids. Augmentative and Alternative Communication (AAC) devices to aid communication have been shown to benefit ALS patients [38].

12. Depression and anxiety

Depression and anxiety are common in ALS, with prevalence rates reported to be up to 44% and 30% respectively [39]. Psychological intervention with cognitive behavioural therapy may be helpful in conjunction with pharmacological treatment. There are no clinical drug trials of depression and anxiety in ALS. Drugs that are commonly used in depression include tricyclic antidepressants and SSRIs, while benzodiazepines can be used in anxiety.

13. Euthanasia and physician-assisted suicide

A Dutch study reported that 20% of patients with ALS died from euthanasia or physician-assisted suicide [40]. Another study from Washington and Oregon showed that 56% of ALS patients would consider assisted suicide, although only 11% of the patients in that series were depressed [41]. It is suggested that hopelessness, which is negative outlook about the future, is a better predictor of suicidal intent or suicide than depression [42–44]. Non-pharmacological approaches are usually needed in these cases to help patients maintain hope in the future [41].

14. Advance directives

Advance directives help patients to communicate their wishes about the end-of-life care to health professionals, family and friends. They are very common in the USA, but much less so elsewhere. It has been suggested that physicians should be encourage to discuss advance directives with patients [45].

15. Terminal care

Pain and suffering during the terminal phases of the disease can be helped by pharmacological approaches to palliative sedation. These include giving opioids and benzodiazepines. Titrating sedation for symptomatic treatment of dyspnoea or pain rarely causes respiratory depression. Short dyspnoeic episodes can be managed by sublingual lorazepam, while more prolonged dyspnoea can be treated initially with oral morphine, then later with subcutaneous or inhaled morphine, or intravenous midazolam [7,21,29]. Hospice services provide comfort and dignity to patients and relatives in these difficult times, although these services are not universally available [46].

16. Quality of life

Ultimately, it is the quality of life that is often the most important factor in the management of patients with amyotrophic lateral sclerosis. The World Health Organization (WHO) recognizes that quality of life is dependent on more than just the health status of a patient, and includes '… psychologic state, level of independence, social relationship, personal beliefs and their relationship to salient features of their environment' [47]. In this context, quality of life does not correlate with measures of physical strength and function, and does not always deteriorate with progressing disability [48,49]. Psychological, existential or religious factors, and support systems appear to have a major effect on quality of life [48,50,51]. Attention must also be paid to the quality of life of carers, as the burden of looking after patients with ALS can be substantial [52,53].

17. Conclusion

The management of patients with ALS is complex and benefits from a multidisciplinary approach, which leads to increased survival [54,55] and a better quality of life (in terms of social functioning and mental health) [56]. There is now a wealth of experience and knowledge on how to manage these patients to a high standard. Therefore, it is important that the treating physician considers pharmacological and non-pharmacological interventions, in collaboration with other health professionals, and relatives and carers of patients, when treating patients with this devastating disease.

18. Learning points

- Management of patients with amyotrophic lateral sclerosis (ALS) starts with the giving of the diagnosis and continues to the terminal phase of the disease.
- Riluzole, the only approved disease-modifying drug in ALS, prolongs median survival by two to three months.
- Non-invasive ventilation improves survival of ALS patients without severe bulbar dysfunction more than that of riluzole, and improves quality of life in all ALS patients.
- Nutritional status predicts survival in ALS, hence is important to maintain.
- A multidisciplinary approach improves both the survival and quality of life of patients with ALS.

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