

The medical management of motor neurone disease – a UK perspective of current practice

The UK MND Interest group[#]

Guidance on the management of motor neurone disease (MND), sometimes also known as amyotrophic lateral sclerosis (ALS), has previously appeared in documents including the *Practice Parameter on the Care of the Patient with Amyotrophic Lateral Sclerosis* [1] and the *Practice Advisory on the use of Riluzole in the Management of Amyotrophic Lateral Sclerosis* [2], both developed under the auspices of the American Academy of Neurology. While these documents give an excellent overview of their respective topics, this paper is aimed at hospital doctors and general practitioners looking after MND sufferers, their carers and families, in the UK. It is intended to emphasise the opportunities for symptomatic treatments which can ease the burden of suffering in this most distressing of diseases.

This document is evidence-based where possible and, where evidence is not available, it is based on expert opinion of best practice. It has been developed by the UK MND Interest Group, based on an earlier document endorsed by Council of the Association of British Neurologists in June 1999 which was widely circulated among neurologists and others but not formally published. This document has been updated to take account of developments in practice since that time as well as recent guidance from the National Institute for Clinical Excellence (NICE) [3] on the use of riluzole in MND.

Current management of MND however does not depend solely on medical treatment. The variability of symptoms and the rapid development of significant neurological disability also necessitate timely intervention from a wide range of staff in other health care disciplines. The quality of life of MND sufferers is increased when patients are managed by a multi-disciplinary team with a specific commitment to MND. Although it is not possible to provide access to such teams everywhere, it is hoped that this paper will increase awareness of the opportunities for symptomatic, as well as disease modifying, therapies among clinical colleagues.

Current status of diagnosis

The World Federation of Neurology (WFN) Research Group on Neuromuscular Diseases has recently updated the El Escorial Criteria for the Diagnosis of MND [4] [[http://www.wfnals.org/Airlie criteria/](http://www.wfnals.org/Airlie_criteria/)]. Although widely accepted these criteria were designed as an aid to clinical trials and research. They might thus be considered more restrictive than the “burden of proof” used in routine neurological practice. They do however accommodate differing levels of certainty of diagnosis and their use is encouraged.

Telling the diagnosis

- The diagnosis should be communicated by a senior doctor, in privacy, with the opportunity for an early follow-up appointment.
- Patients should be accompanied by a relative and/or health professional who would be able to provide immediate support.
- Regular feedback is essential, to ensure patients have understood the information that they have been given [5] and they should be encouraged to express their concerns.
- Written information should be available about the disease, the Motor Neurone Disease Association and other follow-up contacts.
- The diagnosis should be communicated to the General Practitioner (and family if not present when patient informed of diagnosis) without delay.

Principles of general management

A co-ordinated multidisciplinary approach is required to meet the rapidly changing physical and psychosocial needs of patients and carers throughout the course of the disease. This should be underpinned by the following principles:

- Care encompassing the whole person and those that matter to them.
- Prompt provision of treatments to secure symptom control and quality of life.
- Respect for patient autonomy.
- Open and sensitive communication,
- Planning for the future and timely liaison e.g. with the palliative care team.

Symptom management

The maintenance of optimal functional independence and well-being requires a multi-disciplinary approach:

- Drooling can be alleviated by anti-cholinergic drugs such as hyoscine (sublingual or transdermal), glycopyrrolate (subcutaneously), atropine (orally), tricyclic antidepressants (such as amitriptyline) and beta-blockers [6]. Non- pharmacological approaches such as salivary gland irradiation and duct ligation have been described.
- Dysphagia is best managed in association with speech and language therapists as well as dieticians and, as it progresses, more invasive approaches such as PEG may need to be considered in consultation with patient and carer. Expert opinion favours early PEG [7].
- Speech and language therapists also help in the management of communication difficulties. When a communication aid is needed it is essential that it is provided promptly [8].

- Muscle cramps may be treated by quinine, diazepam, phenytoin and naftidrofuryl. Quinine, diazepam and phenytoin are often usefully given at bedtime. There is considerable individual variation in levels of response to these drugs. If one does not help, others might.
- Spasticity can be helped by physiotherapy or drug treatment e.g. baclofen, dantrolene, tizanidine [9].
- The impact of increasing limb weakness may be alleviated by specific interventions ranging from low-tech equipment such as simple splints and neck support collars designed for MND sufferers to environmental control systems and computer access technology [9, 10].
- Respiratory symptoms are distressing for patients and carers. Nocturnal hypoventilation may cause early morning headache and lethargy. There is a strong suggestion that non-invasive respiratory support improves quality of life [11] and should be considered at an early stage with appropriate specialist respiratory management in discussion with patients and carers [12]. Other symptomatic treatments such as opioids can relieve dyspnoea, coughing and choking. The *Breathing Space Kit contains medication which can be used by the carer, nurse or general practitioner for the emergency treatment of the acute episodes of respiratory distress which may occur in the terminal stages [13, 14]. The use of invasive ventilation is a complex issue which, if contemplated, requires early and careful discussion with patients and carers [15].
- Depression should be differentiated from the natural sadness of disability. When present it may be treated with an appropriate antidepressant such as amitryptiline or a selective serotonin reuptake inhibiting drug (SSRI). These drugs may also relieve emotional lability and anxiety. Psychiatric advice may also be required.
- Pain is common and may be managed at all stages with anti-spasticity drugs, non-steroidal agents and analgesics [16], using the principles of the WHO ladder including opioids such as oral morphine or fentanyl transdermal patches. Significant benefits can be achieved with physiotherapy and occupational therapy.

Disease modifying therapy in MND

Reviews of some of these therapies are currently registered with the Cochrane Collaboration [<http://www.cochrane.co.uk>]. It is hoped that coverage of this area will become more comprehensive in the future. These comments are based on clinical effectiveness only and do not consider the issue of cost.

Riluzole is the only drug currently licensed in the UK for the treatment of MND. Riluzole is a disease-modifying therapy. It does not cause symptomatic improvement and does not prevent death. Patients and carers need to be informed of the implications of the trial data before starting

treatment. Evidence for its efficacy comes from two randomised placebo-controlled trials (RCT's) [17,18] see footnote⁺. The NICE (National Institute for Clinical Excellence) guidance [3] states that “1.1 Riluzole is recommended for the treatment of individuals with the amyotrophic lateral sclerosis (ALS) form of motor neurone disease (MND)” and “1.2 Riluzole therapy should be initiated by a neurological specialist with expertise in the management of MND. Routine supervision of therapy should be managed by locally agreed shared care protocols undertaken by general practitioners”. The Cochrane Systematic Review [19] concluded that “Riluzole 100mg per day is reasonably safe and probably prolongs survival by about two months in patients with ALS. More studies are needed, especially to clarify its effect in older patients (over 75 years) and those with more advanced disease.” Riluzole treatment is appropriately discussed with MND patients as soon as a working diagnosis has been made, although RCT evidence only exists currently for patients with definite or probable MND within the El Escorial Criteria [4]. Patient choice or adverse effects such as fatigue and nausea, may lead to cessation of therapy. Efficacy evidence from placebo-controlled randomised clinical trials only extends to 18 months of therapy. Nonetheless it is reasonable to continue therapy for longer than 18 months when considered appropriate by the clinician, patient and carers. However, it is not appropriate to start patients with advanced disease on riluzole or to prolong treatment into the terminal phase. .

- Although there is published evidence from one placebo-controlled RCT [20] that insulin-like nerve growth factor (rhIGF-I) slows disease progression, this was not confirmed in a second RCT [21]. This drug is not licensed.
- Many other putative disease-modifying therapies for MND have been investigated but have not shown to be effective in RCT's.

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Conflict of interest

The UK MND Interest Group is funded by unconditional educational grants from Aventis, the manufacturers of riluzole, and Amgen. Members of the group have accepted speakers honoraria from several pharmaceutical firms, including Aventis, the manufacturer of riluzole. Some members of the group were also investigators in the second large trial of riluzole in MND, but only PNL participated in the data analysis and manuscript preparation. The Association of British Neurologists has received financial support from the pharmaceutical industry including the manufacturers of medications for motor neurone disease.

*Obtainable on medical request through the Motor Neurone Disease Association, David Niven House, PO Box 246, NORTHAMPTON, NN 1 2PR. (Telephone 01604-250505, fax 01604-24726). Kit includes suggestions for the management of acute respiratory symptoms. It is then stocked with drugs through prescription by the GP. The following contents are suggested:

Diazepam	enema (Stesolid) 10mg x 3	(for use by carers)
Diamorphine	for injection 5mg x 3	(for use by nurse or doctor)
Midazolam	for injection 10mg in 2 ml	(for use by nurse or doctor)
Hyoscine hydrobromide	for injection 400µg x 3	(for use by nurse or doctor)
Water	for injection 5mls x 3	(for use by nurse or doctor)

Chlorpromazine 25mg x 3 for injection is suggested as a possible alternative to Midazolam.

Glycopyrronium bromide 200µg x 3 is suggested as a possible alternative to Hyoscine hydrobromide.

[†]These RCT's report a modest decrease in risk of tracheostomy or death with riluzole (relative risk riluzole 100mg/day= 0.66 (95% confidence interval 0.42-1.02), p = 0.05 over 12 months treatment, [17]; relative risk, riluzole 100mg/day (Cox model) = 0.65 (95% confidence interval 0.50-0.85), p =

0.002 over 18 months treatment, [18]. It has been calculated [22] that the number of patients needed to treat with riluzole 100mg/day to prevent one death or tracheostomy after one year (based on [18]) is 9.2 (95% confidence interval 5.2-38). A post-hoc analysis of the data from the dose-ranging trial [23] has suggested that riluzole delays the progression of the disease to severe disability. The findings of this preliminary study require confirmation.

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