Motor Neuron Disease
Dealing with Challenging Symptoms

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Stephen Hawking death: How did physicist live so long with motor neurone disease?

'I have lived most of my life in the expectation of an early death, so time has always been precious to me,' Hawking said in 2006

Alex Matthews-King Health Correspondent | Wednesday 14 March 2018 12:15 | 9 comments

Stephen Darby: Motor neurone disease diagnosis forces Bolton full-back to retire

18 September 2018 | Bolton

New Scottish drug trial for motor neurone disease

7 August 2018
Overview

- Background
- Disease Modifying treatment
- Cramps and Spasticity
- Sialorrhoea
- Swallowing and nutrition
- Communication
- Respiratory involvement
- Cognition
- Mood disturbances and emotional lability
- Sleep Disturbance
Background

- Fatal neurodegenerative condition affecting motor neurones
- Incidence of about 1.5 per 100,000
- Male: Female 3:2; Age usually 50-70
- Onset can be spinal, truncal or bulbar
- No cure for this condition; current treatment focuses on symptomatic treatment, rehabilitation and palliative care
  - Ideally, the involvement of palliative care should occur from the time of diagnosis, throughout the course of the disease, until the eventual death of the patient and family bereavement.
- Multidisciplinary team
Anatomy of ALS
Disease Modifying Treatment

- Riluzole works on glutamate neurotransmission
- Riluzole 100 mg prolongs median survival in people with ALS by two to three months and the safety of the drug is not a major concern.
- There was a small beneficial effect on both bulbar and limb function, but not on muscle strength.
- The beneficial effects are very modest and the drug is expensive.

- Many patients resort to other treatments including alternative therapies, experimental treatment etc. but there is no evidence to support therapeutic benefit.
### Review: Riluzole for amyotrophic lateral sclerosis (ALS)/motor neuron disease (MND)

**Comparison:** riluzole 100 mg vs placebo

**Outcome:** % mortality at 12 months

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Control</th>
<th>Relative risk (fixed) 95% CI</th>
<th>Weight %</th>
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<tbody>
<tr>
<td>Bensimon 1994</td>
<td>20/77</td>
<td>33/78</td>
<td></td>
<td>18.7</td>
<td>0.61 (0.39 to 0.97)</td>
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<tr>
<td>Lacomblez 1996</td>
<td>62/235</td>
<td>90/241</td>
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<td>50.7</td>
<td>0.71 (0.54 to 0.92)</td>
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<tr>
<td>Meininger 1995</td>
<td>52/82</td>
<td>55/86</td>
<td></td>
<td>30.6</td>
<td>0.99 (0.79 to 1.25)</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>134/394</td>
<td>178/405</td>
<td></td>
<td>100.0</td>
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Test for heterogeneity $\chi^2 = 5.89$ df = 2 $p = 0.0527$

Test for overall effect $Z = -2.91$ $p = 0.00$

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**Figure 1** Forest plot resulting from meta-analysis of three randomised, placebo controlled trials of riluzole in MND (ALS). The plot shows the effect on mortality at 12 months. The result favours treatment with a risk of 0.78 (reproduced from Miller et al., with permission).
The efficacy of edaravone for the treatment of ALS was demonstrated in a six-month clinical trial conducted in Japan. In the trial, 137 participants were randomized to receive edaravone or placebo. At Week 24, individuals receiving edaravone declined less on a clinical assessment of daily functioning compared to those receiving a placebo.
Cramps and spasticity

- Quinine as first line for muscle cramps
  - Tonic water
  - Quinine sulphate 200mg at night
- If not effective then try
  - Carbamazepine or phenytoin
  - Baclofen 10-80mg daily
  - Tizanidine 6-24mg daily
  - Dantrolene 25-100mg daily
  - Gabapentin/ pregabalin
- Can also try for spasticity
- Also consider exercise programme
- ? Botox injections
Sialorrhoea

- Once patient complains of problems with saliva, assess respiratory function, swallowing, diet and oral care
- Symptom of bulbar dysfunction
  - Home suction device
  - Atropine (may try atropine eye drops given sublingually)
  - Antimuscarinics such as benzhexol (but issues with cognition especially in elderly)
  - Amitryptilline
  - Hyoscine as tablet or patch
  - Glycopyrrolate can also be given via PEG/RIG
  - Other considerations would be Botulinium Toxin A to salivary glands or salivary gland irradiation (? safety)
Swallowing is a complex phenomenon

- Assess appetite and thirst
- GI symptoms such as nausea and constipation
- Look for causes of reduced oral intake and weight loss
  - Swallowing problems
  - Limb weakness
  - Mood
  - Social issues
• Importance of Nutrition

• EARLY speech and language therapy involvement +/- nutritionist

• Discuss gastrostomy early and do not delay

• Radiologically inserted gastrostomy (RIG) vs Percutaneous Endoscopic Gastrostomy (PEG)
  • The European and North American experience of PEG is similar. If the VC is greater than 50%, the risk of death in the month after gastrostomy is small.
  • RIG can be performed safely in patients with VC below 50% predicted, and in those using non-invasive ventilation. We now perform RIG as the intervention of choice in all MND patients if possible.
Summary of Assessment for PEG/RIG procedures

A. Indications for considering PEG or RIG
- Poor dietary intake and dehydration
- Patient with bulbar symptoms requests early gastrostomy
- Significant difficulty swallowing with evidence of aspiration (unsafe swallow)
- Evidence of failing nutrition (>10% loss of baseline body weight despite nutritional supplements) and/or hydration

B. Relative or absolute contraindications for PEG or RIG
- Patient unlikely to survive more than 3 months
- Patient unable to give informed consent
- Unable to manage feeds; no carer available

C. Assessment before PEG or RIG
- Discuss with patient and family in the context of end of life issues to ascertain that the patient and family understand the procedure, its risks, and place within palliative care
- Assess for evidence of respiratory insufficiency (symptoms; VC >50% predicted; sniff nasal pressure >40 cm water; overnight oximetry shows no significant desaturations; morning blood gases normal)
- If no evidence of respiratory insufficiency, proceed to PEG or RIG
- If evidence of respiratory insufficiency, offer and try non-invasive ventilation (NIV) before gastrostomy
- Delay RIG for 2–4 weeks while patients becomes accustomed to NIV. If swallowing unsafe and/or nutrition and hydration poor, use fine nasogastric tube for feeding/hydration
- Once NIV established, proceed to RIG
- Set whole process in the context of palliative and end of life care

SNP, sniff nasal pressure; VC, vital capacity
Communications

- Early involvement of SLP and Occupational Therapists
- Use of both low-level technologies, for example, alphabet, word or picture boards and high-level technologies, for example, PC or tablet-based voice output communication aids may be helpful.
  - Always tailor according to individual
- Review the person's communication needs during multidisciplinary team assessments.
  - With time and deteriorating mobility and hand function, needs may change
Respiratory problems

- Main cause of death in patients with MND and most feared symptom
- Need proper assessment and discussion of treatment options
- Once respiratory function deteriorates or if patient is admitted with a pneumonia and type 2 respiratory failure is more complex and complications significantly higher
### Symptoms and signs of potential respiratory impairment

<table>
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<th>Signs</th>
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<tr>
<td>Breathlessness</td>
<td>Increased respiratory rate</td>
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<tr>
<td>Orthopnoea</td>
<td>Shallow breathing</td>
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<tr>
<td>Recurrent chest infections</td>
<td>Weak cough(^1)</td>
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<tr>
<td>Disturbed sleep</td>
<td>Weak sniff</td>
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<tr>
<td>Non-refreshing sleep</td>
<td>Abdominal paradox (inward movement of the abdomen during inspiration)</td>
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<tr>
<td>Nightmares</td>
<td>Use of accessory muscles of respiration</td>
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<tr>
<td>Daytime sleepiness</td>
<td>Reduced chest expansion on maximal inspiration</td>
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<tr>
<td>Poor concentration and/or memory</td>
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<tr>
<td>Confusion</td>
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<tr>
<td>Hallucinations</td>
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<tr>
<td>Morning headaches</td>
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<td>Fatigue</td>
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<td>Poor appetite</td>
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Respiratory function tests

- Initially or soon after diagnosis, baseline respiratory function should be established
  - Single measurement of SPO2 at room air
  - One or both of
    - Forced Vital Capacity (FVC) or Vital Capacity
    - Stiff nasal inspiratory pressure and/or maximal inspiratory pressure

- Assessment should be repeated every 2-3 months but may vary depending on rate of progression, symptoms or patients wishes
- Arterial blood gas if SPO2 is <92-94%

Refer early to respiratory physicians for consideration of sleep studies and discussion of ventilatory options
Sleep Study with capnography
• Non-pharmacological measures to minimise dyspnoea involve upright positioning and careful planning of the day (ie spacing out activities that trigger dyspnoea, such as toileting and showering)

• Influenza vaccine should be taken

• Regular physiotherapy and treatment with antibiotics as needed

• Consider benzodiazepines to deal with breathlessness associated with anxiety – diazepam, midazolam, lorazepam

• Also consider opioids to relieve symptoms associated with breathlessness
  • 2.5mg morphine QDS
Non invasive ventilation

- Discuss non invasive ventilation
  - Does not stop underlying disease progression but improves quality of life and prolongs survival
- Always respect patients wishes
- Discuss issues related to stopping ventilation and end of life care
Different types of Interfaces for NPPV (Nava Lancet 2009)

- Nasal mask
- Nasal pillow
- Mouthpiece
- Full face mask
- Total face mask
- Helmet

CHEST® Journal
Cough assist device
Cognition

- Usually relatively preserved
- Fronto-temporal dementia has been associated with MND in 5-10% of cases
- More common in pseudobulbar type rather than predominantly limb-affected
- Often goes undetected due to poor speech and communication problems
- May refer for formal neuropsychological assessment
Mood disorders

- Patient support groups for patients and carers
- Depression and Anxiety should be treated appropriately, and not viewed as unavoidable consequences of a progressive disease.
- The drugs of choice for depression in this context include serotonin reuptake inhibitors, for example fluoxetine.
- Tricyclic antidepressants and benzodiazepines may also be used for anxiety
  - Lorazepam 0.5-4mg/ diazepam
Emotional Lability

- Upper motor neuron involvement causes pseudobulbar palsy; emotional lability
- May involve inappropriate laughing, excessive crying or involuntary emotional expression
- Affects 20-50% of patients
- Treatment usually with antidepressants – SSRIs or amitryptilline
- One class 1 study found combination of dextromethorphan (DM)/quinidine (Q) (30 mg DM/30 mg Q BID) but side effects were limiting.
Insomnia and sleep disturbance

- One of the earliest indicators of respiratory insufficiency is sleep disturbance
  - During REM sleep, ventilation becomes more dependent on the diaphragm, which is disadvantaged by the supine position. Episodes of hypoventilation occur during sleep with recurrent arousal and disturbed sleep.
  - Patients may attribute the awakenings to urinary problems and complain of nocturia.

- May relate to physical discomfort or anxiety
- If sleep remains disturbed after relief of pain then sedatives may help. Amitriptyline is preferable to hypnotics
Conclusion

- Motor Neuron Disease is a treatable condition
- Patient centred approach through multidisciplinary team
- Riluzole offers very modest survival benefit
- RIG/PEG offer should be offered early on
- Both survival and quality of life is improved by NIV
- Maintaining communication is vital for autonomy

- Palliative care should be offered throughout the course of disease not just as end of life care
References


- NICE Guideline - Evidence-based statements to deliver quality improvements in the assessment and management of motor neurone disease (MND) 2016