Motor Neuron Disease

Dealing with Challenging Symptoms

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October 2018

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 | Share

New Scottish drug trial for motor neurone disease

7 August 2018 Share

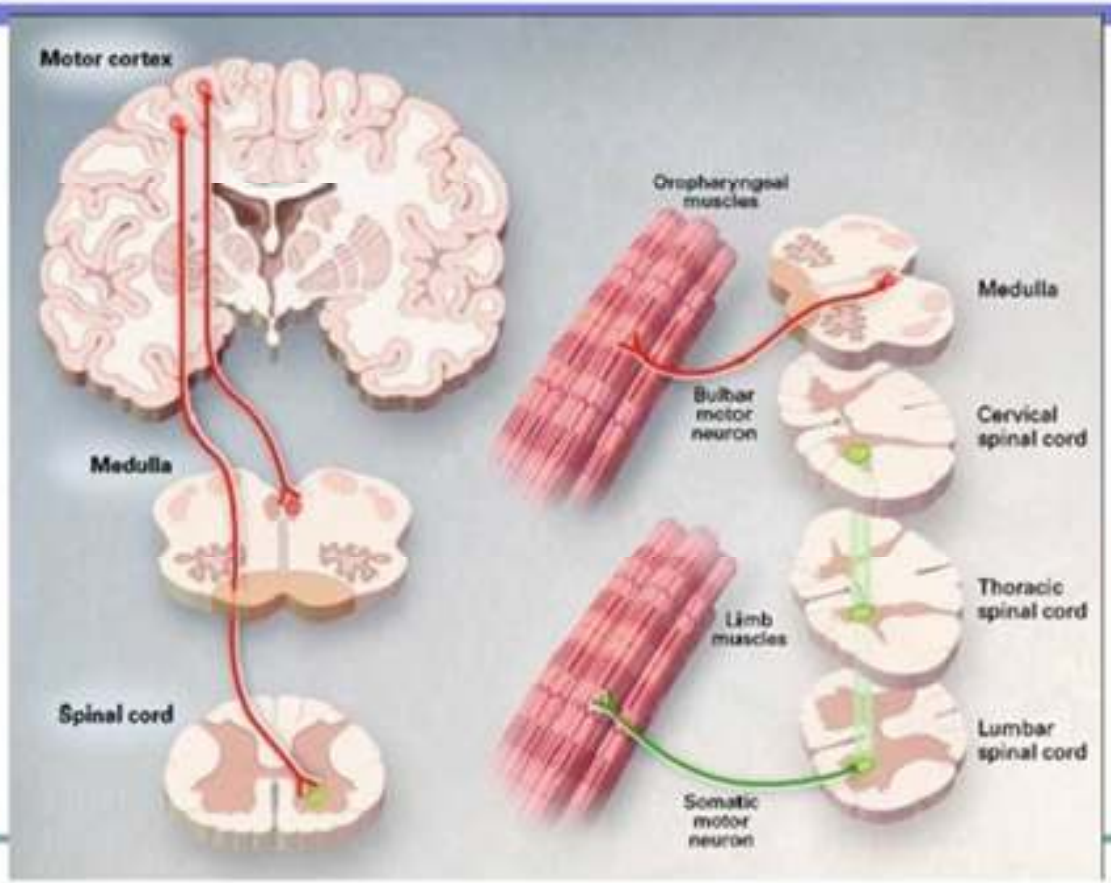
Overview

- 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



yassermetwally.files.wordpress.com

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.

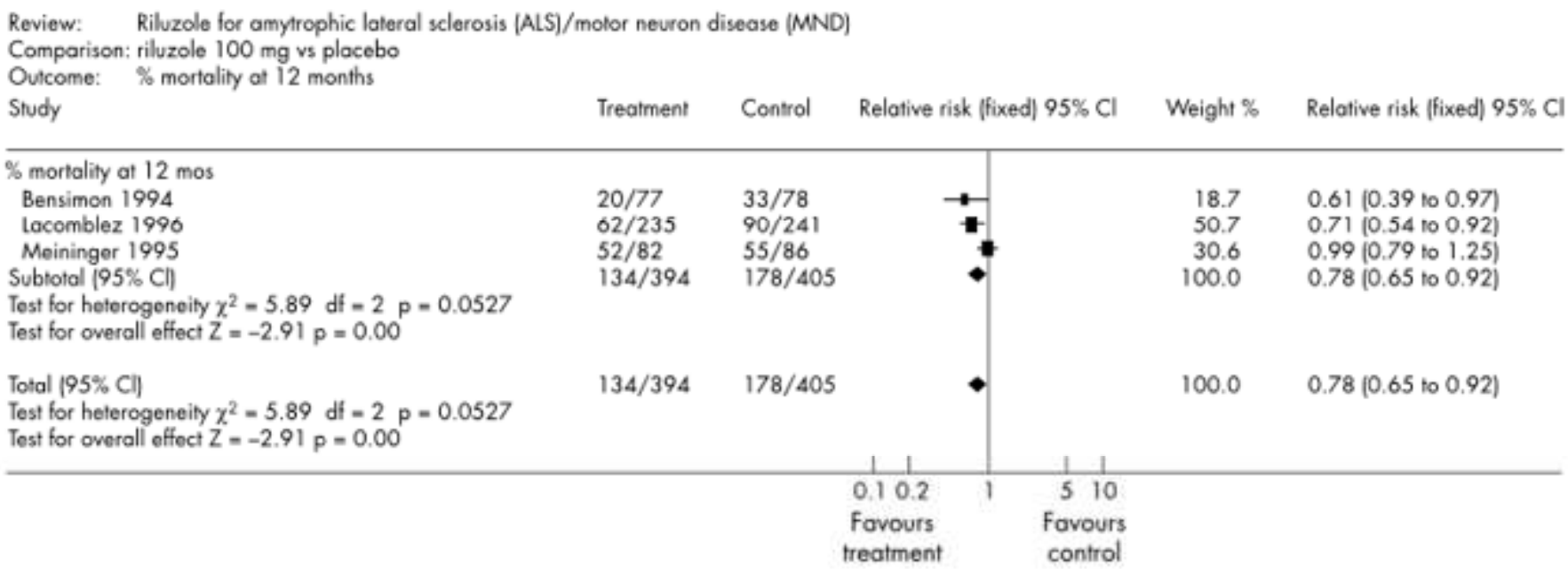


Figure 1 Forest plot resulting from meta-analysis of three randomised, placebo controlled trials of riluzole in MND (ALS). The plot shows the effect on mortality at 12 months. The result favours treatment with a risk of 0.78 (reproduced from Miller *et al*,[21] with permission).

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Articles

Safety and efficacy of edaravone in well defined patients with amyotrophic lateral sclerosis: a randomised, double-blind, placebo-controlled trial

The Writing Group*

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on behalf of the
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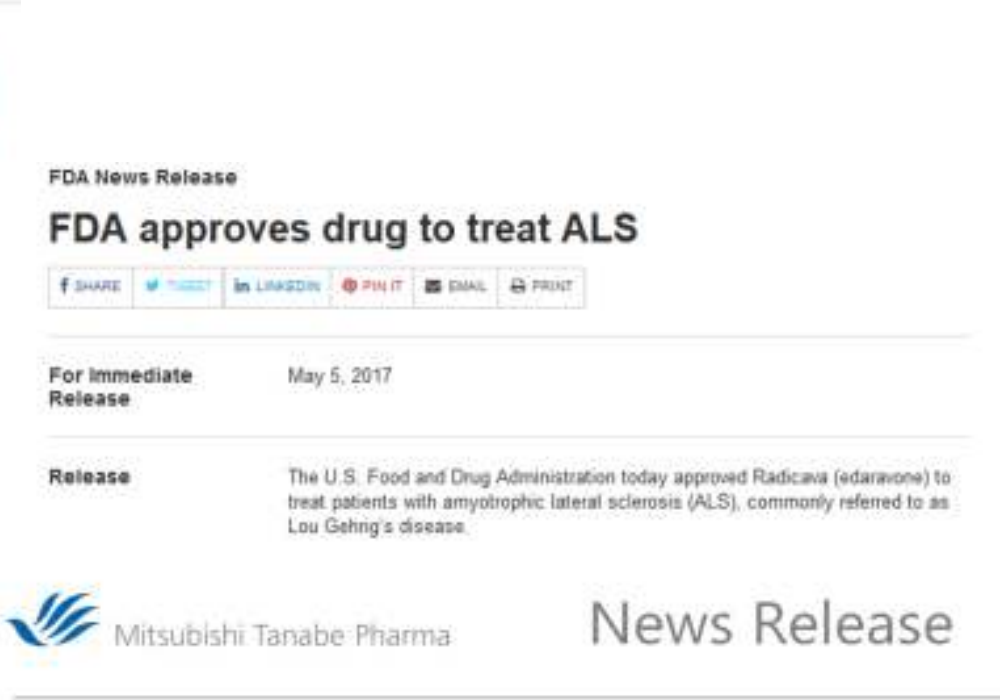

FDA News Release

FDA approves drug to treat ALS

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For Immediate Release: May 5, 2017

Release: The U.S. Food and Drug Administration today approved Radicava (edaravone) to treat patients with amyotrophic lateral sclerosis (ALS), commonly referred to as Lou Gehrig's disease.

Mitsubishi Tanabe Pharma

News Release

May 28th, 2018

For the ALS patients in the world,
we hope to deliver Japan-originated ALS treatment
EMA accepts our filing for Edaravone to treat ALS

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

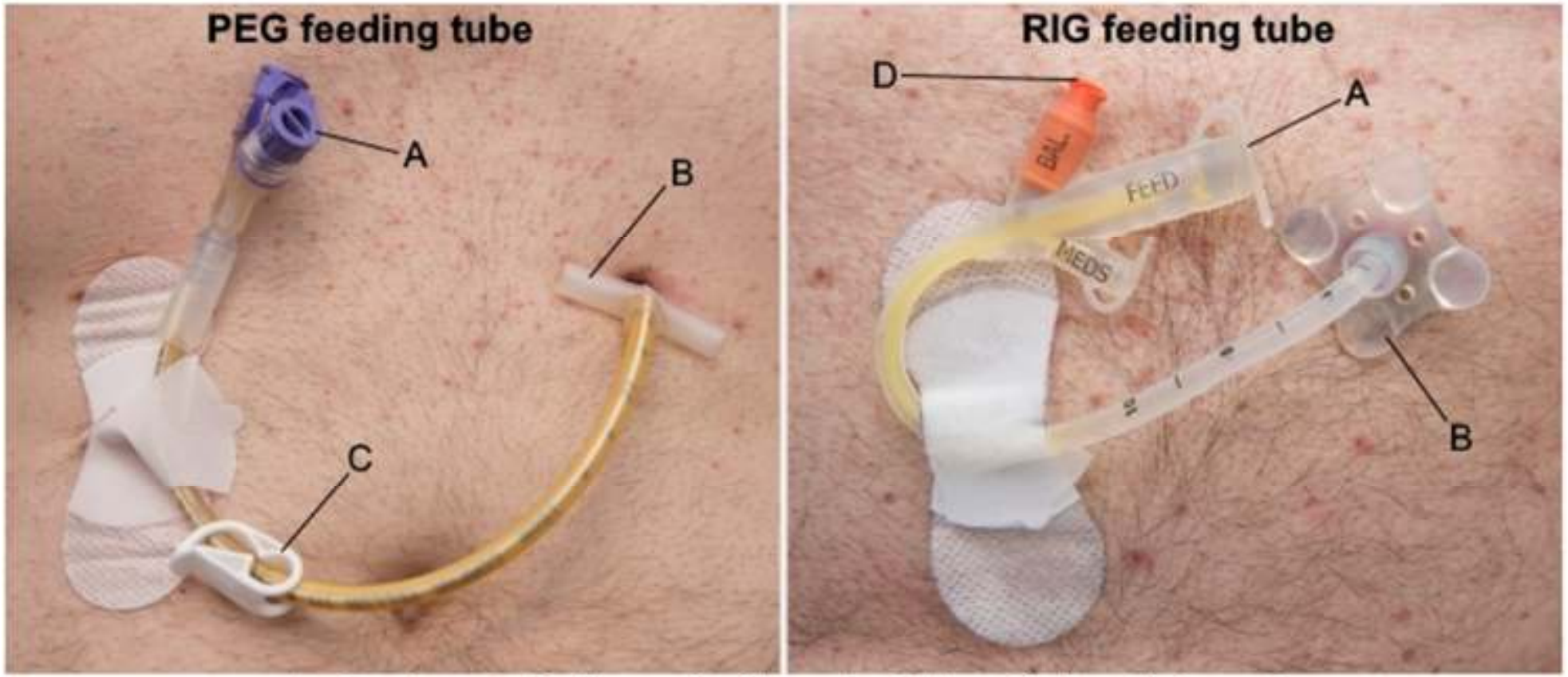
- Other considerations would be Botulinium Toxin A to salivary glands or salivary gland irradiation (? safety)

Swallowing and nutrition

- 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.



A – Feeding port. B – Flange. C – Clamp. D – Balloon inflation-deflation port.

Summary of Assessment for PEG/RIG procedures

- PEG: patients with minor bulbar symptoms and without significant respiratory muscle weakness (that is, VC >50%; SNP >40%; normal overnight oximetry and morning arterial blood pCO_2)
- RIG: patients with pronounced bulbar symptoms and/or respiratory difficulties

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

Communication

- 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

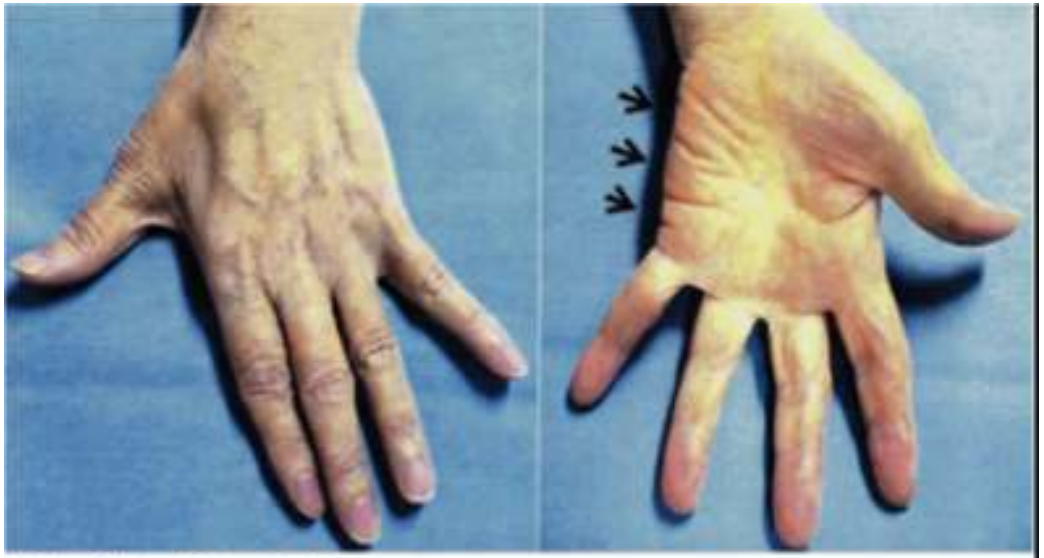


Abb. 1: „Split hand" bei der ALS

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

Symptoms
Breathlessness
Orthopnoea
Recurrent chest infections
Disturbed sleep
Non-refreshing sleep
Nightmares
Daytime sleepiness
Poor concentration and/or memory

Poor concentration and/or memory
Confusion
Hallucinations
Morning headaches
Fatigue
Poor appetite

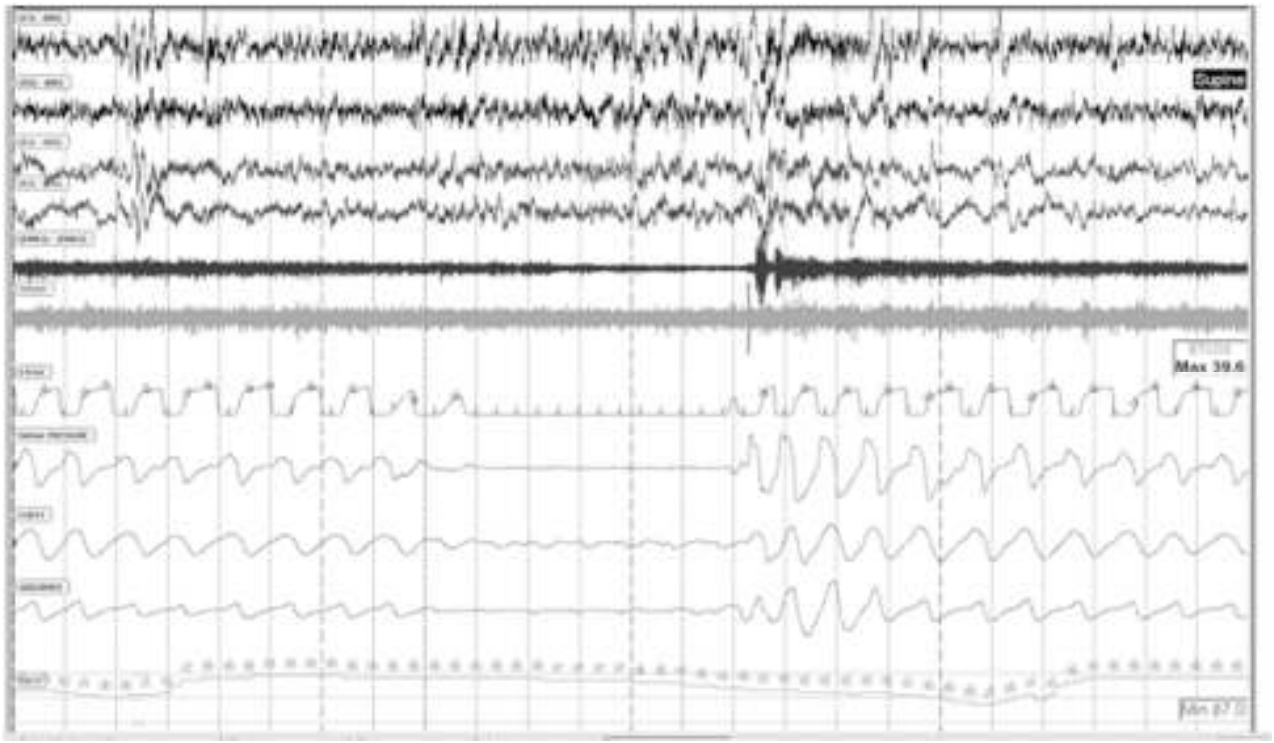
Signs
Increased respiratory rate
Shallow breathing
Weak cough[1]
Weak sniff
Abdominal paradox (inward movement of the abdomen during inspiration)
Use of accessory muscles of respiration
Reduced chest expansion on maximal inspiration

Respiratory function tests

- Initially or soon after diagnosis, baseline respiratory function should be established
  - Single measurement of SPO_2 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 SPO_2 is <92-94%

Refer early to respiratory physicians for consideration of sleep studies and discussion of ventilatory options

Sleep Study with capnography



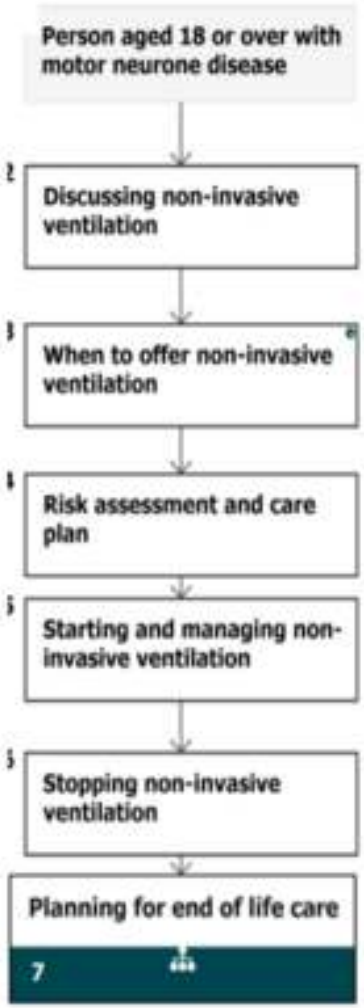
- Non-pharmacological measures to minimise dyspnoea involve upright positioning and careful planning of the day (ie spacing out activities that trigger dyspnoea, such as toileting and showering)
- Influenza vaccine should be taken
- Regular physiotherapy and treatment with antibiotics as needed

- 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)

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

- Miller RG, Mitchell JD, Moore DH. **Riluzole for amyotrophic lateral sclerosis (ALS)/motor neuron disease (MND**). Cochrane Database of Systematic Reviews 2012, Issue 3. Art. No.: CD001447.
- P N Leigh, S Abrahams, A Al-Chalabi, M-A Ampong,L H Goldstein, J Johnson, R Lyall, J Moxham, N Mustfa, A Rio, C Shaw, E Willey, and the King's MND Care and Research Team. **The Management of Motor Neuron Disease.** J Neurol Neurosurg Psychiatry 2003; 74 (Suppl IV):iv32–iv47
- Howard RS, Orrell RW **Management of motor neuron disease** Postgraduate Medical Journal 2002:78;736-741
- NICE Guideline - **Evidence-based statements to deliver quality improvements in the assessment and management of motor neurone disease** (MND) 2016