MOTOR NEURONE DISEASE
RESPIRATORY ISSUES

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Daw Park Repatriation General Hospital
South Australia
MOTOR NEURONE DISEASE

• Progressive weakness muscles
  – Limbs
  – Axial
  – Bulbar
  – Respiratory

• Respiratory muscle weakness
  – Breathlessness
  – Orthopnoea
  – Nocturnal hypoventilation
SYMPTOM MANAGEMENT

- Sialorrhea
- Psuedobulbar affect
- Pain
- Stiffness
- Mood
- Respiratory
  - Speech & swallow
  - Cough
- Sleep
- ADL
- Ambulation
- Fatigue
- Speech
Figure 1  Survival of Irish ALS patients according to the clinic type attended, 1996–2000.

Effect of a multidisciplinary amyotrophic lateral sclerosis (ALS) clinic on ALS survival: a population based study, 1996–2000

B J Traynor, M Alexander, B Corr, E Frost, O Hardiman
SLEEP DISTURBANCE IN MND

• Hypoventilation
  – Daytime sleepiness
  – Morning headache
  – Insomnia

• Restless legs syndrome (RLS)

• Poor sleep quality
  – In absence of respiratory dysfunction
  – Pain
  – Immobility
• 100 consecutive MND patients (60 male)
• 100 healthy controls
• Structured interview
• PSQI > 5 indicates poor sleep quality
• RLS criteria
• Epworth sleepiness score
• ALSFRS-R
• Spirometry
• Beck Depression Inventory (BDI)
• Sleep study in 12 MND patients
MND patients

- More disturbed sleep in 59%
  - 1/3 rated as mod-severe
- Nocturia
- Muscle cramps
- Prolonged sleep latency
- Reduced sleep efficiency
  - Sleep maintenance insomnia in 50%
- Not associated with FVC, oximetry
Poor sleepers
  - More advanced disease
    • Lower ALSFR-R score
  - Higher depression
  - Increased sleepiness

Polysomnogram
  - Reduced sleep efficiency
  - Fragmented sleep
  - Increased PLMs
  - Increased AHI
### Table 2  Night-time problems in patients with amyotrophic lateral sclerosis and controls

<table>
<thead>
<tr>
<th></th>
<th>Amyotrophic lateral sclerosis group, no of patients</th>
<th>Control group, no of subjects</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difficulties falling asleep</td>
<td>32</td>
<td>15</td>
<td>0.005</td>
</tr>
<tr>
<td>Difficulties staying asleep</td>
<td>48</td>
<td>18</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Unrefreshing sleep</td>
<td>29</td>
<td>12</td>
<td>0.003</td>
</tr>
<tr>
<td>Snoring</td>
<td>33</td>
<td>28</td>
<td>NS</td>
</tr>
<tr>
<td>Nocturia</td>
<td>54</td>
<td>32</td>
<td>0.002</td>
</tr>
<tr>
<td>Postural discomfort</td>
<td>14</td>
<td>2</td>
<td>0.002</td>
</tr>
<tr>
<td>Restless legs syndrome</td>
<td>22</td>
<td>8</td>
<td>0.006</td>
</tr>
<tr>
<td>Muscle cramps</td>
<td>46</td>
<td>31</td>
<td>0.029</td>
</tr>
<tr>
<td>Pain</td>
<td>8</td>
<td>9</td>
<td>NS</td>
</tr>
</tbody>
</table>
NON-INVASIVE VENTILATION

- Improves survival and QoL
- Marked variation in use of NIV
- Minority of MND patients receive NIV
  - Use has increased over time
  - Practice Parameters 1999
- Lack of consensus when to initiate
- Variability of resources
  - Equipment, Ix, staff and support
<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breathlessness</td>
<td>Increased respiratory rate</td>
</tr>
<tr>
<td>Orthopnoea</td>
<td>Shallow breathing</td>
</tr>
<tr>
<td>Recurrent chest infections</td>
<td>Weak cough(^2)</td>
</tr>
<tr>
<td>Disturbed sleep</td>
<td>Weak sniff</td>
</tr>
<tr>
<td>Non-refreshing sleep</td>
<td>Abdominal paradox (inward movement of the abdomen during inspiration)</td>
</tr>
<tr>
<td>Nightmares</td>
<td>Use of accessory muscles of respiration</td>
</tr>
<tr>
<td>Daytime sleepiness</td>
<td>Reduced chest expansion on maximal inspiration</td>
</tr>
<tr>
<td>Poor concentration and/or memory</td>
<td></td>
</tr>
<tr>
<td>Confusion</td>
<td></td>
</tr>
<tr>
<td>Hallucinations</td>
<td></td>
</tr>
<tr>
<td>Morning headaches</td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td></td>
</tr>
<tr>
<td>Poor appetite</td>
<td></td>
</tr>
<tr>
<td>Forced vital capacity (FVC) or vital capacity (VC)</td>
<td>Sniff nasal inspiratory pressure (SNIP) and/or maximal inspiratory pressure (MIP) (if both tests are performed, base the assessment on the better respiratory function reading)</td>
</tr>
<tr>
<td>-------------------------------------------------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>• FVC or VC less than 50% of predicted value</td>
<td>• SNIP or MIP less than 40 cmH₂O</td>
</tr>
<tr>
<td>• FVC or VC less than 80% of predicted value plus any symptoms or signs of respiratory impairment (see recommendation 1.1.7), particularly orthopnoea</td>
<td>• SNIP or MIP less than 65 cmH₂O for men or 55 cmH₂O for women plus any symptoms or signs of respiratory impairment (see recommendation 1.1.7), particularly orthopnoea</td>
</tr>
<tr>
<td></td>
<td>• Repeated regular tests show a rate of decrease of SNIP or MIP of more than 10 cmH₂O per 3 months</td>
</tr>
</tbody>
</table>
NOCTURNAL HYPOVENTILATION

- Sleep disruption
- Morning headache
- Daytime somnolence
- Poor concentration
- Orthopnoea
- Elevated pCO2
NOCTURNAL HYPOVENTILATION

- What not to do!!!
  - Offer Clonazepam drops
  - Unfettered O2
  - Ignore role of PEG
- Assess level of function
- Explore patient goals, hopes, dreams
- Assess carers capabilities
- Advance directives/Care plan
Bi-level back up systems
Primary pump, secondary pump, one battery back up, spare masks of assorted types.

- Hybrid FFM $300
- Full face mask $300
- Pump with alarms, battery back up capacity $8500
- Lithium or acid battery $500
- Pump $8500
<table>
<thead>
<tr>
<th>Therapy Modes</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Spontaneous</strong></td>
<td>Patient in control of complete breathing profile.</td>
</tr>
<tr>
<td><img src="Image" alt="Spontaneous mode diagram" /></td>
<td></td>
</tr>
<tr>
<td><strong>Spontaneous/Timed</strong></td>
<td>Patient can over ride machine</td>
</tr>
<tr>
<td><img src="Image" alt="Spontaneous/Timed mode diagram" /></td>
<td>Machine driven back up breath rate.</td>
</tr>
<tr>
<td><strong>Timed</strong></td>
<td>Machine driven rate overrides that of patient breathing.</td>
</tr>
<tr>
<td><img src="Image" alt="Timed mode diagram" /></td>
<td>[Used when patient cannot initiate breath to trigger unit, particularly in REM sleep &amp; NREM]</td>
</tr>
</tbody>
</table>
INFLUENCING FACTORS FOR NIV

- Involvement with specialised clinic
- Male
- Married
  - Spouse support
- Social status
  - USA predominantly
- Government provision of NIV equipment
  - Local or regional service
- Cognitive impairment
- Bulbar symptoms
- Upper limb involvement
Figure 2  Deterrents to referral for non-invasive ventilation (NIV).
Positive Airway Pressure: Problems
Effects of non-invasive ventilation on survival and quality of life in patients with amyotrophic lateral sclerosis: a randomised controlled trial

Stephen C Bourke, Mark Tomlinson, Tim L Williams, Robert E Bullock, Pamela J Shaw, G John Gibson

Figure 1: Trial profile
<table>
<thead>
<tr>
<th></th>
<th>NIV (n=22)</th>
<th>Standard care (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>63.7 (10.3)</td>
<td>63.0 (8.1)</td>
</tr>
<tr>
<td><strong>Sex (male)</strong></td>
<td>14 (64%)</td>
<td>10 (53%)</td>
</tr>
<tr>
<td><em><em>Disease duration</em> (years)</em>*</td>
<td>1.9 (1.3)</td>
<td>2.0 (1.1)</td>
</tr>
<tr>
<td><strong>Riluzole</strong></td>
<td>19 (86%)</td>
<td>17 (89%)</td>
</tr>
<tr>
<td><strong>Bulbar score</strong></td>
<td>3.4 (1.7)</td>
<td>3.3 (1.8)</td>
</tr>
<tr>
<td><strong>Vital capacity (% predicted)</strong></td>
<td>55.6% (18.7)</td>
<td>48.8% (20.7)</td>
</tr>
<tr>
<td><strong>P_{max} (% predicted)</strong></td>
<td>31.1% (11.0)</td>
<td>31.0% (10.6)</td>
</tr>
<tr>
<td><strong>SNIP (% predicted)</strong></td>
<td>22.6% (11.4)</td>
<td>24.4% (10.8)</td>
</tr>
<tr>
<td><strong>PaO_{2} (kPa)</strong></td>
<td>10.0 (1.8)</td>
<td>10.2 (1.9)</td>
</tr>
<tr>
<td><strong>PaCO_{2} (mm Hg)</strong></td>
<td>6.1 (1.1)</td>
<td>6.4 (1.2)</td>
</tr>
<tr>
<td><strong>LEP</strong></td>
<td>0.34 (0.23)</td>
<td>0.36 (0.31)</td>
</tr>
<tr>
<td><strong>Body-mass index</strong></td>
<td>21.6 (3.6)</td>
<td>21.5 (3.1)</td>
</tr>
<tr>
<td><strong>Mean sleep SaO_{2}</strong></td>
<td>92.7% (4.0)</td>
<td>91.6% (7.6)</td>
</tr>
<tr>
<td><strong>% sleep SaO_{2} &lt;90%</strong></td>
<td>27.2% (40.0)</td>
<td>22.9% (36.9)</td>
</tr>
<tr>
<td><strong>Total sleep time (min)</strong></td>
<td>201 (114)</td>
<td>273 (116)</td>
</tr>
<tr>
<td><strong>REM sleep</strong></td>
<td>5.3% (6.5)</td>
<td>11.9% (9.3)</td>
</tr>
</tbody>
</table>

Data are number (%) or mean (SD). *Duration from the first onset of weakness in any muscle group to enrolment. SNIP = sniff nasal inspiratory pressure. PaO_{2} = arterial partial pressure of oxygen. PaCO_{2} = arterial partial pressure of carbon dioxide. REM = rapid eye movement.

**Table 1: Demographic and functional characteristics of patients at randomisation**
Figure 2: Survival from randomisation
A: all patients; B: patients with normal or moderately impaired bulbar function; C: patients with severe bulbar
Figure 3: Time SAQOLi symptoms domain maintained above 75% of prerandomisation assessment
A: all patients; B: patients with normal or moderately impaired bulbar function; C: patients with severe bulbar
NON-INVASIVE VENTILATION

• Increasing use
  – Postal survey UK 2000 2.6-3.5% pt’s using NIV
  – Repeat survey UK Neurologists 2009
    • 618 surveys (62% responded)
    • 3.4 fold increase patients using NIV
    • Proportion patients successfully using increased
  – Chio et al “10 year population study”
    • Increased use NIV 1995-2004 in tertiary ALS centres
• Only 38% performed any test at Dx
• Spirometry most common
  – Every visit 20%
  – Only if symptomatic
    • ABG 25%
    • Pulse oximetry 28%
• Patients with sleep disturbance
  – 62% oximetry
  – 18% respiratory sleep study ? Apnoea link
  – 6% PSG
NEUROLOGISTS PRACTICE
UK POSTAL SURVEY 2009

• Criteria for NIV referral
  – 77% used selection criteria
    • 32% relied on symptoms only
    • 43% combination symptoms, physiological

• 10% early intervention
  – Physiological impairment, no symptoms

• Symptoms to trigger referral
  – Morning headache
  – EDS
  – Orthopnoea
<table>
<thead>
<tr>
<th></th>
<th>2000</th>
<th>2009</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>New patients</td>
<td>1719</td>
<td>1695</td>
<td>−1.4</td>
</tr>
<tr>
<td>Review patients</td>
<td>2280</td>
<td>3077</td>
<td>+35</td>
</tr>
<tr>
<td>NIV referrals</td>
<td>234</td>
<td>612</td>
<td>+262</td>
</tr>
<tr>
<td>Success rate</td>
<td>54%</td>
<td>72%</td>
<td>+33</td>
</tr>
<tr>
<td>Patients currently receiving NIV</td>
<td>126</td>
<td>431</td>
<td>+342</td>
</tr>
</tbody>
</table>

NIV, non-invasive ventilation.
Table 6  Palliative measures used by neurologists in patients with motor neurone disease

<table>
<thead>
<tr>
<th></th>
<th>Oxygen (%)</th>
<th>Benzodiazepines (%)</th>
<th>Opioids (%)</th>
<th>Opioids and benzodiazepines (%)</th>
<th>Other* (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>End of life</td>
<td>44</td>
<td>46</td>
<td>53</td>
<td>43</td>
<td>11</td>
</tr>
<tr>
<td>Prior to end of life (NIV not tolerated/inappropriate)</td>
<td>42</td>
<td>41</td>
<td>41</td>
<td>33</td>
<td>11</td>
</tr>
<tr>
<td>Prior to end of life (before NIV trial)</td>
<td>26</td>
<td>19</td>
<td>15</td>
<td>13</td>
<td>5</td>
</tr>
</tbody>
</table>

*Antidepressants, antisecretory agents (hyoscine hydrobromide, glycopyrrhonium), steroids, physiotherapy, complementary therapies. NIV, non-invasive ventilation.
ITALIAN REGION NIV USE

- 10 year prospective epidemiology register
- 1260 new diagnosis (687 male (54%))
- Mean age diagnosis 65.6 years
- Spinal presentation 787 (62.5%)
- Bulbar presentation 473 (37.5%)
- Incidence: 2.9/100 000 population
- NIV use 259 patients (20.6%)
- NIV in tertiary ALS centre 37.2% vs 8.8% (p=0.0001)
MND bi-level at the RGH 2012

- RGH MND Clinics data base = 52 MND patients registered.
- MND patients found to be suitable and commenced Bi-level
- $N = 9 = 17\%$

Suitable MND patients on Bi-level therapy

<table>
<thead>
<tr>
<th>RGH MND Clinics, 52 patients registered</th>
<th>On Bi-level, 9, 15%</th>
</tr>
</thead>
<tbody>
<tr>
<td>RGH MND Clinics</td>
<td>On Bi-level</td>
</tr>
</tbody>
</table>

= 85%
2011 total AISI
Bi-level cohort at home with a pump.

MND pts = 13 [not concurrent pts]
Other patients in RF = 70 patients
Site of current MND patients (10/2011)
2011 comparison of Bi-level issue rate ..... workload.

2011 all patients issued with non invasive ventilation Bi-level or AutoServo Ventilation

- MND
- Other NIV group

Pie chart:
- 39% MND
- 61% Other NIV group
Duration of Bi-level usage [28 patients]

Survival time on Bilevel therapy.
All MND NIV deaths 2005 to end 2011, n= 28
Duration of Bi-level usage [28 patients]

- 46% remained on therapy 1 - 6 months [13pts].
- 78% bi-level for 1 - 12 months [13+9 pts].
- 14% patients continued between 18 & 30 months.
- Two patients on therapy > 4 to 6 years.
The human face of MND and Bi-level

- Mr T.; Divorced
- 64 years age,
- diagnosed with MND 2004,

2006, commenced Bi-level

- Lower limb weakness, bilateral dexterity loss, slurred speech, occasional choking, headaches on waking,
- $PCO_2$ 51, $PaO_2$ 72
- Supportive carer but also deaf
2006 to 2008

• Regular out patients visits translating to eventual nurse home visits.
• Peg inserted.
• Patient underwent embryonic stem cell therapy in China [unproven therapy for MND].

August 2008
• Compliance 19 hours per day,
• Reducing mask free time,
• Has full complement of two pumps, a battery and various masks.
2009 to 2010

• < 30 minutes capacity mask free.
• Mobility = only able to use finger to write text on mobile phone. Total care needs.

• Numerous urgent calls = re failed pumps, masks, tubing etc, requiring immediate attention
  – Tearing of electric cables from pump while performing transfer from bed into wheel chair.
  – Flooding of pump with water during transfer movement.
  – Failures of battery back up system due to carer shorting it out.

• Last abg July 2009 PaC02 38, Pa 02 98.

• Patient goes on car trip around Australia with carer
Urgent equipment calls continue

Zero mask free time.

Limited or no oral hygiene...... fetid breath.

Minimal communication from patient, carer deaf.

Mask abrasion to nose.

July 2011 patient carries out Advanced Directive at home

Palliative sedation
Quality of life

- Total time on Bi-level 5yrs 6 months.
- Time with approximately < 1 hour mask free capacity = 2 yrs 6 months.
- Extensive burden on carer.
- Patient had family oriented goals to live for.
Equipment costs

Costs of equipment provision for Mr T

• 1 pump scrapped due to water damage = $6,500
• 3 pumps scrapped = $20,500
• Mask cost = usually six masks of various types = $1600.
• Batteries = one damaged beyond repair, $400,

• **Total equipment cost = approximately $29,000**
Nursing time cost

- Initial be-level set ups are often urgent and time consuming,
- Regular urgent equipment requests,
- Short notice home visits,
- Rapidly changing patient needs require frequent overseeing by OPD or home visiting.
- Current nursing provision under funded.
ISSUES WITH VENTILATION

• Deterioration
  – Disease continues to progress
  – Reduced ability for communication
  – “Locked in”

• Family concerns
  – Massive impact, particularly when NIV 24/7

• Discussion regarding withdrawal NIV
  – Should commence at initiation

• Staff concerns
WITHDRAWAL OF NIV

• When not 24 hour dependent
  – May choose not to use NIV
  – Breathlessness, anxiety
  – Symptom management

• Total dependence on NIV
  – Death within a short period of time
  – Symptom management
  – Adequate staffing
ISSUES AROUND WITHDRAWAL

• When to discuss
• Finality
• Conflict
  – Mixed emotions
• Staff issues (MDT)
  – Ethics
  – Religious
• Practical
• Consent and testamentary capacity
  – FTD
“PREEMPTIVE PALLIATIVE SEDATION”

• PS guidelines
  – Intolerable and refractory symptoms
  – Degree of sedation proportionate to symptoms
  – Treatment of last resort
  – Terminal prognosis
    • How close to death?

• Withdrawal NIV
  – 1st resort not last
  – Presume symptoms may be severe
  – ? Existential distress; Fear of symptoms

Cough assist machine

Diaphragm pacing
SOUTH AUSTRALIAN MND CLINIC

• Respiratory assessment
  – Spirometry at diagnosis or initial visit
  – ABG initial visit
  – 3-4 monthly review with Spiro/ABG
  – Flail limb variant ? 6 month or none

• Symptom assessment
  – Including mood

• Swallowing & speech disorders

• Allied health referral

• Advanced care planning

• Palliative care
  – Co-ordination with local service
Practice parameter: The care of the patient with amyotrophic lateral sclerosis (an evidence-based review)

- Principles of management
- Breaking bad news
- Symptom management
  - Sialorrhea
  - Pseudobulbar affect
- Nutrition
- Respiratory management
- Palliative care
Only EBM recommendations

- Multi-D clinic increases survival by 47%
- Sialorrhea
  - Anticholinergic agents
  - Botulinum toxin
- Pseudobulbar affect
  - DM/Q 30mg BD (USA FDA only)
• No RCT for pain or dyspnoea, NIV withdrawal, hospice care

• NIV withdrawal consensus
  – Counselling
  – Symptom control
    • Benzo, opioids, anticholinergic