NIV in motor neurone disease

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NIV in motor neurone disease

Why does MND affect the Respiratory System?
Should NIV be offered to patients with MND?
If so when?
NIV in motor neurone disease

Why does MND affect the Respiratory System?

Should NIV be offered to patients with MND?

If so when?
Why does MND affect the Respiratory System?

• Respiratory muscle involvement
  – Inspiratory and upper airway muscles
    – Assist Ventilation
  – Expiratory Muscles
    – Required for cough

• Impairment leads to ventilatory failure
Ventilatory Failure

- Type One
  - Hypoxia
    - Pulmonary Emboli
    - Pulmonary Oedema
    - Pneumonia

- Type Two
  - Oxygenation and hypercapnia
Clinical Features of T2RF

**SYMPTOMS**
- SOBOE
- Orthopnoea
- Morning headache
- Hypersomnolence
- Disturbed sleep
- Nightmares
- Fatigue
- Impaired cognition
- Anxiety
- Poor appetite

**T2RF**

**OSA**

**Easily missed**
- Reduced chest expansion
- Tachypnoea
- Use of accessory muscles
- Weak cough
- Weak snuff
- Paradoxical movement of diaphragm

**Mistaken for depression**
Respiratory muscle function tests

- Spirometry
  - FVC <60% predicted REM hypoventilation
  - FVC < 40% predicted nocturnal hypoventilation
  - FVC < 25% predicted daytime hypercapnoea

- Lying and sitting/standing spirometry
- Overnight oximetry
  - REM hypoventilation (early sign)
Slow vital capacities on reclining

36% fall (0.95 L)
Predictors of overnight \( \text{SaO}_2 \) and \( \text{P}_{tc}\text{CO}_2 \) in primary myopathies

*Thorax* 2002;57:724-728

**Overnight \( \text{SaO}_2 \)**

**Overnight \( \text{P}_{tc}\text{CO}_2 \)**

Supine better than erect

**Supine VC**

**Supine Plmax**

\( 25 \text{mmHg} \)
Supine VC as predictor of three progressive stages of respiratory failure
Thorax 2002;57:724-728

VC 60% predicted: REM hypopnoeas

VC 40% predicted: continuous nocturnal hypoventilation

VC 25% predicted: awake hypercapnia
Respiratory muscle function tests

• Maximal Inspiratory Muscle pressure (MIP)
  – Diaphragm and inspiratory muscle strength
  – Normal > 29 cmH₂O

• Maximal Expiratory Pressure (MEP)
  – Abdominal and expiratory muscle strength
  – Normal > 59 cmH₂O

• Sniff Nasal Inspiratory Pressure (SNIP)
NIV in motor neurone disease

Why does MND affect the Respiratory System?

Should NIV be offered to patients with MND?

If so when?
Early NIV acceptance is associated with increased survival

Early treatment with noninvasive positive pressure ventilation prolongs survival in Amyotrophic Lateral Sclerosis patients with nocturnal respiratory insufficiency

Pierluigi Carratù¹, Lucia Spicuzza², Anna Cassano¹, Mauro Maniscalco³, Felice Gadaleta¹, Donato Lacedonia¹, Cristina Scoditti¹, Ester Boniello¹, Giuseppe Di Maria² and Onofrio Resta¹

Orphanet Journal of Rare Diseases 2009, 4:10

Retrospective analysis of 1yr survival of MND patients:

FVC >75% = Control group, age and gender matched (n = 44)

FVC <75% & nocturnal insufficiency (n = 28) NIV (n = 16) No NIV as declined or intolerant (n = 12)
Early NIV acceptance is associated with increased survival

Table 1: Baseline Characteristics of Patients Entering the Study

<table>
<thead>
<tr>
<th></th>
<th>FVC &gt; 75%</th>
<th>FVC &lt; 75%</th>
<th>p-value between groups 2–3</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>44</td>
<td>16</td>
<td>12</td>
</tr>
<tr>
<td>male/female</td>
<td>27/17</td>
<td>9/7</td>
<td>7/5</td>
</tr>
<tr>
<td>Age</td>
<td>51.16 (7.39)</td>
<td>55.93 (5.09)</td>
<td>57.54 (6.54)</td>
</tr>
<tr>
<td>BMI</td>
<td>22.72 (3.90)</td>
<td>21.98 (4.48)</td>
<td>22.85 (3.16)</td>
</tr>
<tr>
<td>Bulbar onset</td>
<td>13/44</td>
<td>5/16</td>
<td>4/12</td>
</tr>
<tr>
<td>Spinal onset</td>
<td>23/44</td>
<td>8/16</td>
<td>6/12</td>
</tr>
<tr>
<td>FVC%</td>
<td>83.3 (11.84)</td>
<td>65.13 (13.37)</td>
<td>62.35 (12.75)</td>
</tr>
<tr>
<td>FEV1%</td>
<td>88.12 (13.98)</td>
<td>64.53 (14.17)</td>
<td>61.6 (13.8)</td>
</tr>
<tr>
<td>PaO2 mmHg</td>
<td>90.35 (9.58)</td>
<td>79.91 (12.48)</td>
<td>77.35 (9.54)</td>
</tr>
<tr>
<td>PaCO2 mmHg</td>
<td>36.43 (6.72)</td>
<td>41.83 (9.27)</td>
<td>39.48 (8.92)</td>
</tr>
<tr>
<td>ALSFRS-R</td>
<td>28.7 (6.1)</td>
<td>26.7 (7.1)</td>
<td>ns</td>
</tr>
</tbody>
</table>

Data are presented as mean (± SD); ns = not significant
Figure 1
Kaplan-Meier plots of survival in 72 patients affected by amyotrophic lateral sclerosis (ALS) from the initiation of NPPV. (Black circle) = 44 patients with ALS with FVC > 75%, (Black triangle) = 16 patients with ALS with FVC < 75% treated with NPPV, (Black square) = 12 patients with ALS with FVC < 75% not treated with NPPV. ALS patients with FVC < 75% treated with NPPV vs. patients with ALS with FVC < 75% intolerant to NPPV: $\chi^2 = 5.32, *p = 0.02$. Patients with ALS with FVC > 75% vs. patients with ALS with FVC < 75% treated with NPPV: $\chi^2 = 0.405, p = 0.5$. Patients with ALS with FVC > 75% vs. patients with ALS with FVC < 75% not treated with NPPV: $\chi^2 = 15.4, p < 0.0001$. 

FVC >75%

FVC<75%, on NIV

*p = 0.02

FVC <75%, not on NIV
Fall in %VC

FVC<75%, on NIV
VC 1.5 ± 0.3 %/mnth

FVC <75%, not on NIV
VC 2.8 ± 0.8 %/mnth

* p < 0.0001

Figure 2
Slope of FVC% in 1 year between survivors of the groups 2 and 3. Blue line: Group 2 (12) (NPPV); Red line: Group 3 (4) (no NPPV). X axis: months, Y axis: FVC%. FVC% slope change per month in group 2 (1.52 ± 0.3) and group 3 (2.81 ± 0.8); p < 0.0001.
... but does NIV just prolong suffering?

A prospective study of quality of life in ALS patients treated with noninvasive ventilation

Article abstract—Noninvasive positive pressure ventilation prolongs survival in ALS but its effect on quality of life is unknown. The authors prospectively studied quality of life using the SF-36 questionnaire in a cohort of 18 ventilated patients with ALS. Noninvasive positive pressure ventilation improved scores in the “Vitality” domain by as much as 25%, for periods of up to 15 months, despite disease progression. Noninvasive positive pressure ventilation did not cause reduced quality of life, as any fall in scores in the ventilated group were comparable to those seen in a control group. In conclusion, noninvasive positive pressure ventilation enhances quality of life when used to treat sleep-disordered breathing in patients with ALS.

NEUROLOGY 2001;57:153–156

R.A. Lyall, MBBS; N. Donaldson, PhD; T. Fleming, BSc; C. Wood, HND; I. Newsom–Davis, DClinPsy; M.I. Polkey, PhD; P.N. Leigh, PhD; and J. Moxham, MD

NIV group: Sleepiness, poor appetite, am headaches, orthopnoea & dyspnoea
RMW, hypoventilation and SDB
All pt offered NIV, and those accepting it entered into study

Control group: Age and sex matched
Normal diaphragm function & similar levels of generalised disability
No symptoms of hypoventilation
No SDB, normal CBG, normal bulbar function
<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>NIV 3 mths</th>
<th>9 mths</th>
<th>Baseline</th>
<th>Control 3 mths</th>
<th>Control 9 mths</th>
</tr>
</thead>
<tbody>
<tr>
<td><code>n</code></td>
<td>16</td>
<td>16</td>
<td>4 (11 RIP)</td>
<td>11</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>VC (%)</td>
<td>53 (22)</td>
<td>63 (14)</td>
<td>-</td>
<td>95 (15)</td>
<td>106 (10)</td>
<td>88 (20)</td>
</tr>
<tr>
<td><code>PcCO₂</code> (kPa)</td>
<td>6.8 (1.2)</td>
<td>5.6 (0.4)</td>
<td>5.6 (0.1)</td>
<td>4.7 (0.4)</td>
<td>4.8 (0.1)</td>
<td>5.1 (0.1)</td>
</tr>
<tr>
<td><code>PcO₂</code> (kPa)</td>
<td>9.9 (1.3)</td>
<td>11.2 (1.3)</td>
<td>9.7 (0.8)</td>
<td>11.5 (1.3)</td>
<td>11.3 (1.5)</td>
<td>10.8 (0.7)</td>
</tr>
<tr>
<td>Bicarb (mM/l)</td>
<td>33 (3)</td>
<td>27 (2)</td>
<td>28 (2)</td>
<td>24 (2)</td>
<td>25 (1)</td>
<td>26 (1)</td>
</tr>
<tr>
<td>ESS (/24)</td>
<td>9.3 (5)</td>
<td>4 (3)</td>
<td></td>
<td>5 (3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitality</td>
<td>27 (12)*</td>
<td>46 (16)</td>
<td>45 (17)</td>
<td>61 (26)*</td>
<td>60 (28)</td>
<td>45 (13)</td>
</tr>
<tr>
<td>Role physical</td>
<td>20 (33)*</td>
<td></td>
<td>12 (14)</td>
<td>32 (39)*</td>
<td>8 (14)</td>
<td></td>
</tr>
<tr>
<td>Role emot¹</td>
<td>75 (37)*</td>
<td></td>
<td>83 (33)</td>
<td>70 (41)*</td>
<td>67 (58)</td>
<td></td>
</tr>
<tr>
<td>Social funct</td>
<td>56 (28)*</td>
<td></td>
<td>44 (28)</td>
<td>59 (29)*</td>
<td>50 (33)</td>
<td></td>
</tr>
<tr>
<td>Gen health</td>
<td>39 (25)*</td>
<td></td>
<td>37 (41)</td>
<td>42 (17)*</td>
<td></td>
<td>44 (21)</td>
</tr>
</tbody>
</table>

* Significantly low compared to population normal values

SF36 well-being scores (bodily pain and mental health scores) were not significantly reduced in the NIV and control groups cf normal population values.
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

121 assessed for eligibility

19 did not meet criteria
10 refused to participate

92 clinical review every 2 months

51 did not meet criteria for randomisation during surveillance period

41 randomised

21 assigned NIV
22 analysed

19 assigned standard care
19 analysed

Orthopnoea ± MIP < 60% or symptomatic hypercapnia

Minimisation by bulbar function, VC, age, BMI and rate of progression

FU 12 M

Lancet Neurol 2006; 5: 140–47
Total \( n = 41 \)

- **Orthopnoea, \( n = 38 \) (20 with normal \( \text{CO}_2 \))**
- **No orthopnoea but symptomatic hypercapnia, \( n = 3 \)**
- **Normal to moderate bulbar impairment, \( n = 20 \)**
- **Severe bulbar impairment, \( n = 21 \)**

<table>
<thead>
<tr>
<th></th>
<th>NIV (( n=22 ))</th>
<th>Standard care (( n=19 ))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>63.7 (10.3)</td>
<td>63.0 (8.1)</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>14 (64%)</td>
<td>10 (53%)</td>
</tr>
<tr>
<td>Disease duration* (years)</td>
<td>1.9 (1.3)</td>
<td>2.0 (1.1)</td>
</tr>
<tr>
<td>Riluzole</td>
<td>19 (86%)</td>
<td>17 (89%)</td>
</tr>
<tr>
<td>Bulbar score</td>
<td>3.4 (1.7)</td>
<td>3.3 (1.8)</td>
</tr>
<tr>
<td>Vital capacity (% predicted)</td>
<td>55.6% (18.7)</td>
<td>48.8% (20.7)</td>
</tr>
<tr>
<td>( P_{\text{max}} ) (% predicted)</td>
<td>31.1% (11.0)</td>
<td>31.0% (10.6)</td>
</tr>
<tr>
<td>SNIP (% predicted)</td>
<td>22.6% (11.4)</td>
<td>24.4% (10.8)</td>
</tr>
<tr>
<td>( \text{PaO}_2 ) (kPa)</td>
<td>10.0 (1.8)</td>
<td>10.2 (1.9)</td>
</tr>
<tr>
<td>( \text{PaCO}_2 ) (mm Hg)</td>
<td>6.1 (1.1)</td>
<td>6.4 (1.2)</td>
</tr>
<tr>
<td>LEP</td>
<td>0.34 (0.23)</td>
<td>0.36 (0.31)</td>
</tr>
<tr>
<td>Body mass index</td>
<td>21.6 (3.6)</td>
<td>21.5 (3.1)</td>
</tr>
<tr>
<td>Mean sleep ( \text{SaO}_2 )</td>
<td>92.7% (4.0)</td>
<td>91.6% (7.6)</td>
</tr>
<tr>
<td>% sleep ( \text{SaO}_2 ) ( \leq 90% )</td>
<td>27.7% (40.0)</td>
<td>27.9% (36.9)</td>
</tr>
<tr>
<td>Total sleep time (min)</td>
<td>201 (114)</td>
<td>273 (116)</td>
</tr>
<tr>
<td>REM sleep</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. \( \text{PaO}_2 \)=arterial partial pressure of oxygen. \( \text{PaCO}_2 \)=arterial partial pressure of carbon dioxide. REM=rapid eye movement.

**Table 1: Demographic and functional characteristics of patients at randomisation**
All patients

Survival with NIV versus BSC:

All patients 219 (75-1382) versus 171 (1-878)
Better bulbar 216 (94-681) versus 11 (1-283)
Poorer bulbar 222 (75-1382) versus 261 (6-878)

Greater benefit than chemotherapy for lung cancer
All patients

Quality of life >75% BL with NIV versus BSC, SF 36:

SA QLI

All patients 192 (48-1357) versus 46 (0-703)
Better bulbar 205 (69-629) versus 4 (0-143)
Poorer bulbar 143 (48-1357) versus 100 (2-703)

Signif improvement for:
CRQ dyspnoea
SA QLI daily function
Social isolation
NIV use

Mean NIV adherence through duration of use:

- Better bulbar group 9.3 hrs (final use/ use at 1 mnth = 277%)
- Poorer bulbar group 3.8 hrs (final use/ use at 1 mnth = 98%)

*Poorer outcome in bulbar patients due to lack of efficacy or poorer use? May be the former as no correlation between hours of use and survival*

Mean I+E pressures = 15 + 4 cmH₂O

IPAP tolerated 23% higher in the better bulbar group
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Why does MND affect the Respiratory System?
Should NIV be offered to patients with MND?
If so when?
When should NIV be offered to patients with MND?

Early! Diagnosis to respiratory failure often < 1 year

May be offered with any one of:

- Orthopnoea* (*greatest benefit and subsequent adherence*)
- Daytime sleepiness/ unrefreshing sleep
- Daytime hypercapnia or raised bicarb/ BE
- Nocturnal desaturation
- Reduced VC or significant VC postural drop

Respiratory review for consideration for NIV

• History and focused examination
• CBG, VC and cough peak flow
• Discussion of pros- and cons- of NIV
• Set up with modest pressures (e.g. starting at 12+4 cmH₂O)
• NIV machine: battery back-up/ 2 machines/ power priority
• Cough assistance?
• Follow-up: visits minimised ± home visits
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