Long term effects of non-invasive mechanical ventilation on pulmonary haemodynamics in patients with chronic respiratory failure

B Schönhofer, T Barchfeld, M Wenzel, D Köhler

Abstract

Background—It is not known whether long term nocturnal mechanical ventilation (NMV) reduces pulmonary hypertension in patients with chronic respiratory failure (CRF).

Methods—Pulmonary haemodynamics, spirometric values, and gas exchange were studied in 33 patients requiring NMV due to CRF (20 with thoracic restriction, 13 with chronic obstructive pulmonary disease (COPD)) at baseline and after 1 year of NMV given in the volume cycled mode. Patients with COPD also received supplemental oxygen.

Results—Long term NMV improved gas exchange while lung function remained unchanged. Mean pulmonary artery pressure at rest before NMV was higher in patients with thoracic restriction than in those with COPD (33 (10) mm Hg v 25 (6) mm Hg). After 1 year of NMV mean pulmonary artery pressure decreased in patients with thoracic restriction to 25 (6) mm Hg (mean change 8.5 mm Hg (95% CI –12.6 to –4.3), p<0.01) but did not change significantly in patients with COPD (mean change 2.2 mm Hg (95% CI –6.3 to 4.8)).

Conclusions—Long term NMV improves pulmonary haemodynamics in patients with thoracic restriction but not in patients with COPD.

Keywords: chronic respiratory failure; chronic obstructive pulmonary disease; non-invasive mechanical ventilation; pulmonary hypertension

Nocturnal mechanical ventilation (NMV) reverses symptoms of hypoventilation and improves pulmonary gas exchange in patients with chronic respiratory failure (CRF). The efficacy of NMV has been convincingly demonstrated in patients with CRF due to thoracic restriction and neuromuscular disease. However, in patients with chronic obstructive pulmonary disease (COPD) the data are conflicting. Preliminary results from the French and Italian multicentre trials failed to demonstrate an effect of NMV, particularly on the prognosis of COPD. It has recently been shown that an increase in mean pulmonary artery pressure was an independent predictor of hospitalisation in patients with COPD. Whether long term NMV has a beneficial effect on pulmonary hypertension in CRF is unknown. We therefore conducted a prospective study to investigate the long term effects of NMV on pulmonary haemodynamics after 1 year of NMV in patients with CRF secondary to both restrictive thoracic disorders and COPD.

Methods

Patients

In a two year period (from 1 June 1994 to 1 June 1996) all patients who were considered for NMV were approached about the study protocol. During this period a total of 45 patients with thoracic restriction and 31 patients with COPD started NMV. Informed consent to participate in the study was given by 20 patients with thoracic restriction (group A) and 13 patients with COPD (group B). All patients finished the study.

The inclusion criteria were chronic hypercapnic respiratory failure (PaCO₂ > 6.4 kPa) due to restrictive thoracic diseases (post-tuberculosis sequelae and scoliosis, group A) or COPD (forced expiratory volume in one second (FEV₁) < 1 litre and FEV₁/forced vital capacity (FVC) ratio of <50%, group B). All patients had to have received maximal medical treatment supervised by a chest physician with no hospital admission for at least 1 month before the study and to have remained free of an exacerbation during this time. No significant difference was observed between the pre-admission blood gas tensions and lung function (1 month before admission) and those obtained on admission to hospital, confirming that the patients were in a clinically stable condition.

Subjects with acute respiratory failure (requiring continuous mechanical ventilation), severe acidosis (defined as pH < 7.30), or left ventricular failure (defined as radiographically demonstrable congestion of pulmonary veins and/or an ejection fraction < 50%) were excluded in COPD (forced expiratory volume in one second (FEV₁) < 1 litre and FEV₁/forced vital capacity (FVC) ratio of <50%, group B). All patients had to have received maximal medical treatment supervised by a chest physician with no hospital admission for at least 1 month before the study and to have remained free of an exacerbation during this time. No significant difference was observed between the pre-admission blood gas tensions and lung function (1 month before admission) and those obtained on admission to hospital, confirming that the patients were in a clinically stable condition.

Anthropometric parameters, blood gas analysis, and lung function data of the two groups of patients are presented in table 1.

Measurements

Baseline measurements were performed before starting NMV. Spirometric tests and whole body plethysmography (Masterlab, Jaeger,
Würzburg, Germany) were performed. The normal values for lung function data were those of the European Respiratory Society. Resting daytime arterialised capillary blood gases were measured from the hyperaemic ear lobe while breathing room air. The criterion for the effectiveness of NMV was a decrease in PaCO₂ during the intervention.

Spontaneous unassisted ventilation was investigated during sleep using a digital pulse oximeter (mean and minimal oxygen saturation (SaO₂), Pulsoxy 7, AVL, Bad Homburg, Germany).

Right heart catheterisation was performed according to the technique described by Swan et al. using a small diameter floated Grandjean catheter (5F, Angiomed, Germany). The catheter was introduced percutaneously into the antecubital vein. Mean pulmonary arterial pressure (PAPmean), pulmonary capillary wedge pressure, and thermodilution cardiac index were recorded using a polygraph (Sirecust 1260, Siemens, Erlangen). Pulmonary vascular resistance index was calculated as PAPmean – pulmonary capillary wedge pressure/cardiac index. Measurements were made at rest and during steady state exercise in the supine position. To determine the constant load, which was performed during the haemodynamic measurements, the maximal workload was defined in a pre-test protocol as the exercise intensity which the patient was able to tolerate for at least 2 minutes. The duration of the exercise test after 1 year on NMV was identical to that of the pretreatment test. In group A the work load achieved was 39.8 (20.7) W for a period of 3.3 (1.0) minutes, while in group B the corresponding values were 51.1 (20.1) W for 3.5 (1.2) minutes.

**STUDY PROTOCOL**

The protocol was approved by the ethical review committee and all subjects gave their written informed consent to participate. A run in period of 1 month without NMV was used in order to confirm clinical stability as judged by gas exchange and lung function. Pre-NMV and post-NMV blood gas analysis was performed with the patient breathing room air; oxygen therapy was discontinued 1 hour before the test.

NMV was instituted using the volume cycled mode (either Dräger EV 800 (Lübeck, Germany) or PLV 100 (Respironics, Murrysville, USA)). Details on how individual ventilator settings were obtained are described elsewhere. Hypoxaemic COPD patients received supplemental oxygen according to the guidelines of the American Thoracic Society.

Patients received 6–8 hours of daytime and nocturnal oxygen at a rate of 1 l/min if NMV alone did not correct the hypoxemia. No patient with restrictive thoracic disease required oxygen therapy during the study. Pre-study medication was not changed during the study period, except for diuretic medication which was managed according to a protocol based on the clinical condition (reduced, withdrawn if permitted, or reintroduced, depending on the incidence of peripheral oedema). Follow up was scheduled every 6 weeks. All measurements were made before (baseline) and after 1 year of NMV.

**STATISTICAL ANALYSES**

Results are expressed as mean (SD). The Wilcoxon test was used for the inrasubject comparisons within each group. A p value of <0.05 was considered significant.

**Results**

All patients completed the pre-NMV evaluation and were started on NMV. Ventilator use per day was similar in both study groups (7.1 (0.5) hours in group A and 7.3 (0.3) hours in group B) and of equal efficacy (PaCO₂ 5.2 (0.4) kPa in group A, 5.4 (0.4) kPa in group B). Oxygen use averaged 15.2 (0.7) hours/day in patients with COPD. With the additional oxygen therapy during NMV, PaO₂ increased significantly in these patients (from 7.3 (0.4) kPa to 11.7 (1.0) kPa).

In all patients in group A diuretic medication was either reduced (n=12) or discontinued.
In group B diuretic medication was reduced in two patients, continued in six, and five patients did not receive diuretic medication.

Gas exchange data at baseline and after 1 year of NMV are summarised in table 2. After 1 year of NMV both groups showed significant improvement in daytime blood gas tensions and in nocturnal SaO₂ measured during unassisted ventilation on room air. However, the increase in PaO₂, SaO₂ mean and nadir, and decrease in PaCO₂ were lower in group B than in group A (table 2). Lung function remained unchanged in both groups.

Baseline PAPmean and pulmonary vascular resistance index at rest were moderately increased in group A and only mildly increased in group B (table 3). Pulmonary hypertension was more severe in group A than in group B and worsened during exercise in both groups (table 3). Normal pulmonary capillary wedge pressures at rest and at the end of the exercise excluded left heart dysfunction in both groups. After 1 year of NMV resting PAPmean (table 3, fig 1) and pulmonary vascular resistance index at rest were unchanged in patients in group B (table 3). In both groups capillary wedge pressure and cardiac index did not change. Compared with the pre-NMV data, the degree of exercise induced worsening of pulmonary hypertension after 1 year of NMV was similar in both groups.

Discussion

After 1 year of NMV a substantial reduction in PAPmean was observed in patients in group A. This reduction may contribute to the benefit conferred by NMV in patients with CRF due to thoracic restriction.12

Pulmonary hypertension at baseline was more severe in group A patients than in those in group B, despite comparable degrees of hypercapnia and hypoxaemia. Furthermore, pulmonary hypertension did not improve in patients with COPD after 1 year of NMV.

This study has three limitations. Firstly, the ideal study design would have been a randomised controlled trial to determine whether NMV was the important factor underlying the findings. We used a prospective cohort study design as a randomised controlled trial would have been unethical in patients with thoracic restriction as there is already evidence of a marked reduction in pulmonary hypertension due to NMV.

Secondly, the number of recruited patients was relatively small, despite a 3 year study period. Between 1 June 1994 and 1 June 1996 all patients with COPD and with thoracic restriction who began NMV in our hospital

Table 3 Mean (SD) values of the haemodynamic parameters at baseline and after 1 year NMV in patients with thoracic restriction (group A) and patients with COPD (group B)

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>P value</th>
<th>Max</th>
<th>Group B</th>
<th>P value</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before exercise</td>
<td></td>
<td></td>
<td>Before exercise</td>
<td></td>
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<tr>
<td>PAPmean (mm Hg)</td>
<td>33.2 (10.0)</td>
<td>#</td>
<td>55.1 (14.4)</td>
<td>25.3 (6.0)</td>
<td>#</td>
<td>44.8 (14.1)</td>
</tr>
<tr>
<td>PCW (mm Hg)</td>
<td>9.0 (5.0)</td>
<td>#</td>
<td>16.4 (5.5)</td>
<td>8.7 (3.2)</td>
<td>#</td>
<td>15.5 (4.6)</td>
</tr>
<tr>
<td>PVRI (dyn/cm²/m²)</td>
<td>606 (200)</td>
<td></td>
<td>654 (172)</td>
<td>410 (127)</td>
<td>#</td>
<td>474 (143)</td>
</tr>
<tr>
<td>After 1 year NMV</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>PAPmean (mm Hg)</td>
<td>24.8 (6.2)</td>
<td>#</td>
<td>46.9 (13.9)</td>
<td>27.5 (6.0)</td>
<td>#</td>
<td>47.8 (10.2)</td>
</tr>
<tr>
<td>PCW (mm Hg)</td>
<td>9.2 (3.4)</td>
<td>#</td>
<td>16.4 (5.5)</td>
<td>9.2 (2.8)</td>
<td>#</td>
<td>16.5 (5.0)</td>
</tr>
<tr>
<td>PVRI (dyn/cm²/m²)</td>
<td>432 (158)</td>
<td>#</td>
<td>508 (169)</td>
<td>408 (92)</td>
<td>#</td>
<td>471 (111)</td>
</tr>
<tr>
<td>Mean change (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PAPmean (mm Hg)</td>
<td>–8.5 (–12.6 to –4.3)**</td>
<td>#</td>
<td>–8.2 (–14.6 to –1.7)*</td>
<td>2.2 (–0.3 to 4.8)</td>
<td>#</td>
<td>3.0 (–2.6 to 8.6)</td>
</tr>
<tr>
<td>PCW (mm Hg)</td>
<td>0.2 (–2.3 to 2.7)</td>
<td>#</td>
<td>–0.1 (–4.6 to 4.3)</td>
<td>0.5 (–0.9 to 2.0)</td>
<td>#</td>
<td>1.0 (–0.8 to 2.8)</td>
</tr>
<tr>
<td>PVRI (dyn/cm²/m²)</td>
<td>–174 (–239 to –61)**</td>
<td>#</td>
<td>–146 (–239 to –53)*</td>
<td>–2 (–99 to 95)</td>
<td>#</td>
<td>–3 (–46 to 40)</td>
</tr>
</tbody>
</table>

PAP = pulmonary arterial pressure; PCW = pulmonary wedge pressure; PVRI = pulmonary vascular resistance index.

*Mean change in haemodynamic parameters (95% confidence interval, CI) from baseline to 1 year NMV (*p<0.05, **p<0.01, Wilcoxon test).

#Comparison of the values before and at the end of maximal load (max) (0p<0.05, ###p<0.001, Wilcoxon test).

Figure 1 Individual values of mean pulmonary artery pressure (PAPmean) before and after 1 year of NMV in patients with thoracic restriction (group A) and patients with COPD (group B). **p<0.01 (Wilcoxon).
Effects of non-invasive mechanical ventilation on pulmonary haemodynamics

The effects of non-invasive mechanical ventilation on pulmonary haemodynamics have been investigated in various patient populations. In patients with chronic obstructive pulmonary disease (COPD), non-invasive mechanical ventilation (NMV) has been shown to improve gas exchange and reduce hypoxaemia and hypercapnia. In a study involving patients with COPD, NMV was associated with an increase in PaO2 and a decrease in PaCO2, indicating an improvement in gas exchange. Furthermore, NMV led to a reduction in pulmonary hypertension at rest, as evidenced by a decrease in pulmonary artery pressure.

In patients with chronic respiratory failure (CRF), treatment with NMV has been shown to improve gas exchange and reduce hypoxaemia and hypercapnia. A study involving patients with CRF showed that NMV caused a significant improvement in gas exchange and a reduction in pulmonary hypertension.

The benefits of NMV in COPD and CRF are well-documented, but the extent to which these findings can be generalised to other patient populations is uncertain. Future studies are needed to identify predictive parameters for response to NMV and to determine the long-term effects of this intervention.
The authors thank M Polkey and M Pfeifer for their critical remarks and B Ragette for the linguistic advice on the article.

The data in this study have already been presented at a workshop of the German study group on Home and Long Term Mechanical Ventilation held on 26–28 March 1998 and published as a non-peer reviewed paper in a Supplement of Pneumologie (Schönhofer B, Barchfeld T, Wenzel M, Kohler D. Auswirkungen der intermittierenden Selbstbeatmung auf die pulmonale Hypertonie bei chronisch ventilatorischer Insuffizienz. Pneumologie 1999;53:S113–5).