Who benefits from home mechanical ventilation?

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The ability to support patients with chronic respiratory failure (CRF) in the home has been one of the major advances of respiratory medicine. The delivery of ventilatory support has progressed from negative pressure devices, introduced as a consequence of the poliomyelitis epidemics in the 1940s and 1950s, through ventilation via tracheostomy to non-invasive ventilation (NIV) via face or nasal masks. NIV has expanded from its initial role within the intensive care unit to the respiratory ward and subsequently to the home setting. The provision for home mechanical ventilation (HMV) in the UK has expanded but the clinical benefit to differing diagnostic groups is far from clear. Clinical practice is based on a combination of physiological studies, randomised controlled trials (RCT) and clinical experience.

Obstructive lung disease

The evidence for using NIV for the management of acute hypercapnic respiratory failure (AHRF) in patients with chronic obstructive pulmonary disease (COPD) is established in both the critical care and ward setting. However, the evidence for HMV is controversial. There is evidence that long-term oxygen therapy (LTOT) improves survival in patients with severe COPD, but fails to improve nocturnal hypoventilation and is required for more than 15 hours a day. In addition, sleep disordered breathing, prevalent in COPD patients, contributes to morbidity so a rationale to use nocturnal NIV to manage CRF is appropriate. Three physiological mechanisms of action for NIV have been proposed:

- improved hypercapnic ventilatory response (HCVR)
- enhanced pulmonary mechanics
- increased respiratory muscle strength (RMS).

These mechanisms were investigated by Nickol et al in COPD patients using HMV for three months. The study confirmed the improvement in arterial blood gas parameters shown previously and investigated these mechanisms in detail. HCVR is a simple test measuring changes in ventilation in response to breathing carbon dioxide (CO₂): the relationship between changes in ventilation and CO₂ reflects central chemoreceptor sensitivity. There was an increased HCVR at five days but no further increase at three months, highlighting the importance of ensuring an adequate initial set up of HMV in these patients (Fig 1). Hyperinflation was reduced over the course of the intervention, indicating enhanced pulmonary mechanics. RMS was unchanged.

Despite a paucity of RCT evidence in support, these and other physiological data have directed clinicians to use HMV for COPD patients with CRF, in particular those with frequent admissions with AHRF. An early double-blind RCT conducted using negative pressure ventilation showed no differences in any of the clinical and physiological outcome variables measured. However, as with a number of the subsequent studies using positive pressure ventilation, there was a high rate of non-compliance; thus this study can be criticised for only demonstrating that domiciliary negative pressure ventilation has limited feasibility in the home setting. There has been improved tolerance with positive pressure NIV but all the RCTs to date are limited by poor study design.

The most common critique of the current evidence is that the trials used sub-optimal inspiratory pressures and...
therefore failed to ventilate patients effectively.\(^8\) Other trials had poor ventilator compliance or did not select patients with CRF (which seems counterintuitive). Clini et al\(^9\) assessed performance of NIV against LTOT in a multicentre RCT in hypercapnic patients. A small improvement in gas exchange and health-related quality of life (HRQL) was demonstrated, but without hospitalisation or mortality benefit. The NIV settings were titrated to comfort with inspiratory pressures that would be considered low in comparison with today’s clinical practice. Furthermore, the patients selected would now be classified as severe ‘end-stage’ disease. Positive outcomes were shown in a randomised crossover trial with hypercapnic COPD patients treated for three months with LTOT alone or plus HMV.\(^10\) The latter group showed improved gas exchange, sleep quality and exercise capacity.\(^10\) Further RCTs are required focusing on optimisation of ventilator settings and patient compliance to clarify the role of HMV in COPD patients with CRF.

**Restrictive lung disease**

The demographics of HMV users with restrictive lung disease are changing. The original indication was related to the sequelae of poliomyelitis epidemics as well as post-tuberculosis chest wall disease. These diseases are decreasing but, although other neuromuscular disorders (eg motor neuron disease and Duchenne muscular dystrophy) are increasingly treated with HMV, there has been a significant rise in obesity hypoventilation syndrome (OHS).\(^11\)

**Neuromuscular disease**

Early studies showed that the cause of death in most patients with progressive neuromuscular disease was respiratory failure,\(^12\) identifying HMV as a potential useful treatment in patients such as those with Duchenne muscular dystrophy and motor neuron disease. The physiological data investigating the modes of action showed improved gas exchange and Epworth Sleepiness Score at three months.\(^13\) As with COPD, the mechanism of action was associated with improvements in HCVR, with limited changes in pulmonary mechanics and RMS.\(^13\) In addition, a dose-response effect of NIV on arterial \(\text{CO}_2\) (\(\text{PaCO}_2\)) was demonstrated, supporting a true treatment effect.\(^13\)

Initial data from observational trials showed HMV was associated with improved HRQL, fewer inpatient hospital days and improved survival (Table 1).\(^14\)–\(^16\) However, these results should be interpreted with caution as no control or sham groups were used, the comparisons being made with historical

### Table 1. Summary of outcome data for trials involving home mechanical ventilation (HMV) in patients with neuromuscular disease (NMD).

<table>
<thead>
<tr>
<th>Ref</th>
<th>Design/Participants</th>
<th>Intervention</th>
<th>Outcomes</th>
<th>Summary</th>
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| 18  | Prospective RCT, 41MND patients | Usual care (n=19) or HMV (n=22) followed for 12 months or to death | Survival, symptoms, HRQL, daytime somnolence | • Improved survival in HMV arm without bulbar symptoms  
• Overall improved symptoms of dyspnoea, HRQL and ESS |
| 16  | Prospective/restrictive lung disease (total n=6, DMD n=2) | Withdrawal of NIV for 1 week | ABGs, symptoms, sleep quality | • No significant change in ABGs  
• Worsening dyspnoea, morning headaches, daytime somnolence, reduced subjective sleep quality, overnight oximetry |
| 15  | Retrospective/mixed cohort of 276 patients, including 16 DMD analysed separately | Analysed results comparing before and after treatment over 2-year period | ABGs, hospital admissions, PFTs, HRQL | • Trend to reduced \(\text{PaCO}_2\) and increased \(\text{PaO}_2\)  
• Reduced hospital inpatient days in long-term users compared with pre-initiation of HMV  
• No significant changes in PFTs  
• HMV well tolerated and improved subjective sleep quality |
| 14  | Prospective/restrictive lung disease (total n=20, NMD n=12) | Before and after treatment (3 months) | ABGs, HCVR, pulmonary mechanics, respiratory muscle strength, daytime somnolence symptoms | • Improved ABGs, HCVR  
• Unchanged dynamic compliance, respiratory muscle strength, spirometry, lung volumes, transfer factor  
• Reduced ESS  
• 1- and 5-year survival rates 85% and 73%, with good levels of tolerability  
• Significant improvement in ABGs with reduced \(\text{PaCO}_2\) and increased \(\text{PaO}_2\)  
• Similar HRQL improvements to other groups receiving NIV |
| 17  | Prospective, 23 consecutive DMD patients | Before and after NIV | Survival, ABGs, HRQL | • Improved survival in HMV arm without bulbar symptoms  
• Improved ABGs, HCVR  
• Unchanged dynamic compliance, respiratory muscle strength, spirometry, lung volumes, transfer factor  
• Reduced ESS  
• 1- and 5-year survival rates 85% and 73%, with good levels of tolerability  
• Significant improvement in ABGs with reduced \(\text{PaCO}_2\) and increased \(\text{PaO}_2\)  
• Similar HRQL improvements to other groups receiving NIV |

**Notes:**  
1. \(\text{ABG} = \) arterial blood gases; \(\text{DMD} = \) Duchenne muscular dystrophy; \(\text{ESS} = \) Epworth Sleepiness Score; \(\text{HCVR} = \) hypercapnic ventilatory response; \(\text{HRQL} = \) health-related quality of life; \(\text{MND} = \) motor neuron disease; \(\text{NIV} = \) non-invasive ventilation; \(\text{PaCO}_2 = \) arterial carbon dioxide tension; \(\text{PaO}_2 = \) arterial oxygen tension; \(\text{PFT} = \) pulmonary function test; \(\text{RCT} = \) randomised controlled trial.
To investigate the effect of HMV on survival and HRQL, Bourke et al. performed an RCT of patients with motor neuron disease randomised to receive NIV or standard care. Criteria for initiation of HMV were symptomatic hypercapnia or orthopnoea with a maximum inspiratory pressure below 60% predicted. The patients were followed up for 12 months or until death. HMV improved HRQL and survival in all patients; in particular, the subgroup with better bulbar function had a median survival benefit of 205 days with maintained HRQL. HMV also improved HRQL in those with poor bulbar function but without any survival benefit.

These data have been used to support the provision of HMV in neuromuscular disease but the optimum timing for initiation of ventilation has not yet been established. Most trials used symptomatic daytime hypercapnia or evidence of profound respiratory muscle weakness as markers for initiation. One multicentre RCT18 showed that early intervention in Duchenne muscular dystrophy prior to the development of CRF showed no benefit in delaying progression to ventilatory failure, and alarmingly demonstrated higher mortality in the HMV arm.

A more structured approach was adopted in a study of neuromuscular disease and chest wall disease patients with daytime normocapnia but nocturnal hypoventilation, randomising them to either early or delayed treatment.19 Within 24 months, 90% of patients required initiation of HMV, 70% within the first 12 months. The earlier initiation of HMV to reduce risk of acute decompensation needs to be balanced against its inconvenience.

**Chest wall disease**

Many of the studies of patients with neuromuscular disease include patients with chest wall disease. Data from small retrospective studies or uncontrolled trials show improvement in gas exchange.20 Again, like other groups, these patients have an improvement in HCVR.13,20 Survival data from observational cohorts show a survival advantage with HMV over standard care with oxygen (Fig 2).13,21

**Obesity hypoventilation syndrome**

The obesity epidemic has driven obesity-related respiratory problems. Obstructive sleep apnoea has a standard diagnostic and treatment algorithm but OHS, despite its high mortality, is underdiagnosed with limited understanding of the pathophysiology of CRF.22 The diagnosis of OHS is an overlap of obesity (body mass index (BMI) ≥ 30 kg/m²), daytime hypercapnia (PaCO₂ >6 kPa) and sleep-disordered breathing. The population prevalence is unknown but it is more common with increasing BMI, occurring in approximately 25% of patients with a BMI over 40.23

Nowbar et al.22 showed that survival rates are poor without NIV (as with other areas of HMV), but there are no RCTs of treatment with NIV compared with sham or standard care. The only prospective RCT compared NIV with continuous positive airways pressure (CPAP) in a highly selected subset of OHS patients without severe nocturnal hypoventilation. Not unsurprisingly, this study showed no advantage of NIV over CPAP.24 A number of studies have demonstrated improvement in physiological parameters, including gas exchange, sleep quality, daytime vigilance and HRQL.24 Again, NIV improves the HCVR.25

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**Fig 2.** Survival curves of kyphoscoliotic patients treated with long-term oxygen therapy (LTOT) or LTOT plus non-invasive ventilation (NIV).
Conclusions

Current practice is to start HMV for stable hypercapnic COPD patients who have recurrent admissions with AHRF requiring NIV and for symptomatic neuromuscular, chest wall deformity and OHS patients. Future trials need to have an emphasis on COPD and OHS patients, for whom physiological improvements have not been substantiated, by well-designed RCTs demonstrating clinical effectiveness in terms of improving HRQL, exercise capacity and survival.

References

10 Meecham Jones DJ, Paul EA, Jones PW, Wedzicha JA. Nasal pressure support ventilation plus oxygen compared with oxygen therapy alone in hypercapnic COPD. Am J Respir Crit Care Med 1995; 152:538–44.