Non-invasive positive pressure ventilation

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In the late 1980s non-invasive positive pressure ventilation (NPPV) was developed for the domiciliary management of chronic hypercapnic ventilatory failure, in preference to negative pressure ventilation. As confidence in the technique grew, patients with acute-on-chronic ventilatory failure were ventilated in hospital. This article reviews the uses of NPPV in both chronic and acute respiratory failure (RF).

Chronic respiratory failure due to neuromuscular disease or chest wall deformity

In general, hypercapnic RF worsens during sleep because of a normal physiological drop in respiratory drive. Initially, patients develop RF only at night, managing to maintain a normal carbon dioxide tension during the day. At this stage, an otherwise unexplained rise in base excess in the blood may be a clue to the presence of nocturnal hypoventilation. As the disease progresses, however, abnormal blood gas tensions develop during the day. Symptoms are non-specific and may be mistaken for a 'normal' part of the underlying disease; they include lethargy, sleepiness, morning headache, neuropsychiatric symptoms, dyspnoea and ankle oedema (which may be mistaken for heart failure). In addition, these patients are at risk of sudden life-threatening deterioration, for example with a trivial chest infection. Unfortunately, patients with chest wall deformity (CWD) or neuromuscular disease (NMD) not infrequently present as an emergency, sometimes requiring intubation and mechanical ventilation, with a history typical of nocturnal hypoventilation going back over many months. Because symptoms are so non-specific, it is important to have a high index of suspicion in 'at risk' individuals (Table 1) and a low threshold for further investigation.

Investigation

Patients at risk of developing nocturnal hypoventilation should be assessed at an early stage by a respiratory physician, since the need for assisted ventilation can often be anticipated by observing trends in physiological measurements. Patients should be warned of the symptoms of nocturnal hypoventilation, and those with a weak cough can be taught how to maximise secretion clearance.

Table 1. Causes of chronic type II respiratory failure22.

| Cause                                      |
|--------------------------------------------|
| Chest wall deformity:                      |
| ● early-onset scoliosis                     |
| ● thoracoplasty/sequeulae of tuberculosis  |
| Non- or slowly progressing neurological conditions: |
| ● central hypoventilation syndrome         |
| ● Ondine's curse                           |
| ● spinal cord injury — tetraplegia         |
| ● pellomycetitis                           |
| ● diaphragmatic paralysis                  |
| ● metabolic myopathies                     |
| ● spinal muscular atrophy                  |
| ● congenital myopathies                    |

Progressive neuromuscular disorders:

- Duchenne muscular dystrophy
- Amyotrophic lateral sclerosis (motor neuron disease)

Obstructive lung disease:

- chronic obstructive pulmonary disease
- bronchiectasis, cystic fibrosis

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Suggested investigations are listed in Table 2.

**Key Points**

- patient selection, staff training and expertise are crucial for successful non-invasive positive pressure ventilation (NPPV) in both acute and chronic disease.
- NPPV has a clear role in the management of patients with acute exacerbations of chronic obstructive pulmonary disease (COPD).
- endotracheal intubation and complications are reduced.
- survival is improved.
- there are some data to support the use of NPPV to facilitate weaning and in non-hypercapnic respiratory failure.
- NPPV is well established in the domiciliary treatment of chronic ventilatory failure due to neuromuscular disease and chest wall deformity.
- a high index of suspicion is needed for possible nocturnal hypoventilation in at-risk patients.
- objective measurement is useful in predicting need for assisted ventilation.
- patients should be referred early for specialist assessment.
- progressive disease (eg motor neuron disease. Duchenne muscular dystrophy) is not a contraindication.
- the use of NPPV in patients with COPD is less clear-cut and should be reserved for those who are hypercapnic and have clearly failed with standard therapy.

**Treatment**

There are no large prospective randomised controlled trials (RCTs) to support the use of NPPV in patients with CWD or NMD, but the benefits are such that most people would now consider it unethical to enter patients into an RCT with survival or quality of life as an endpoint. Several case series report excellent results with NPPV in patients with severely deranged blood gas tensions who would have been expected to have a poor prognosis. Simonds and Elliott reported a five-year actuarial survival for patients with previous polio of 100%, sequelae of tuberculosis 95%, NMD 81% and early-onset scoliosis 79%. Health status amongst those ventilated compared favourably with UK population norms and patients in the USA with chronic disorders. Leger et al. reported similar results in 276 patients from a number of centres in France, and showed a reduction in hospital charges once NPPV was instituted. However, there are questions to be answered regarding the timing of institution of NPPV. Although symptomatic and blood gas deterioration occurs rapidly each time ventilatory support is withdrawn in some patients, in others it is much less clear-cut. Protriptyline, a non-sedating tricyclic antidepressant used in low dose as a rapid eye movement sleep suppressor, may obviate the need for domiciliary ventilation in some patients with mild disease. The indications for starting home NPPV are shown in Table 3.

NPPV is appropriate for some patients with progressive NMD. Simonds et al. reported a five-year survival of 73% in hypercapnic patients with Duchenne muscular dystrophy (DMD) treated with NPPV. Pinto et al. compared the outcome from NPPV in motor neuron disease in 10 patients and 10 control patients who had refused NPPV. Although the forced vital capacity of the NPPV treated patients was worse, suggesting more severe respiratory muscle weakness, 50% were alive at two years whereas all control patients had died within eight months. However, a prospective RCT of NPPV in patients with DMD, as prophylaxis to delay the onset of ventilatory failure, showed no advantage from NPPV – and indeed there was a trend towards higher mortality in the NPPV treated patients. None of the patients, however, had evidence of daytime hypercapnia or nocturnal hypoventilation, so the absence of benefit is not surprising. Although NPPV is not appropriate for all patients with progressive NMD, the option should at least be discussed with most patients and their families.

**Table 2. Investigation of patients at risk for nocturnal hypoventilation.**

**Minimum:**
- spirometry (lying and sitting if NMD)
- mouth pressures (if NMD)
- arterial blood gas tensions
- overnight monitoring of oxygen saturation ± transcutaneous CO$_2$

**Additional:**
- more detailed pulmonary function tests
- measurement of oesophageal, gastric and transdiaphragmatic pressures during a sniff and following electrical or magnetic stimulation of the phrenic nerves
- more detailed monitoring during sleep in patients in whom obstructive sleep apnoea is suspected

CO$_2$ = carbon dioxide; NMD = neuromuscular disease.

**Table 3. Indications for domiciliary non-invasive positive pressure ventilation (NPPV).**

NPPV should be considered in patients with extrapulmonary restrictive disorders who have:
- I been admitted as an emergency with acute RF
- II chronic symptoms with any of the following:
  - FVC <1 litre
  - abnormal overnight oximetry/capnography
  - daytime hypercapnia with or without hypoxia

FVC = forced vital capacity; RF = respiratory failure.
Obstructive lung diseases

Successful NPPV in chronic obstructive pulmonary disease (COPD) has been reported in uncontrolled studies. There have been few controlled trials, mostly with small numbers of patients followed over a short period and with variable results. Two longer-term uncontrolled studies have shown five-year survival rates comparable to the oxygen treated patients in the Nocturnal Oxygen Therapy Trial and Medical Research Council study. Most of the patients were hypercapnic and thus less likely to benefit from long-term oxygen therapy (LTOT). Until further data are available, a trial of NPPV can be justified only for patients who have failed with or cannot tolerate LTOT, and effective control of nocturnal hypoventilation during NPPV should be confirmed.

Acute and acute-on-chronic respiratory failure

There is such pressure on intensive care unit (ICU) beds in the UK that assisted ventilation is considered for only a small proportion of patients with COPD, and then usually only when they are in extremis. A number of case reports highlighted the fact that it is possible to ventilate patients with acute exacerbations of COPD non-invasively. This brought the possibility of providing ventilatory support at an earlier stage to a group of patients who, in the UK, would not normally be offered assisted ventilation. Although invasive mechanical ventilation (IMV) is regarded as the gold standard for the treatment of life-threatening RF, it is associated with a range of complications, including ventilator-associated pneumonia and difficulties with weaning. There are theoretical advantages in avoiding endotracheal intubation (ETI), but concerns have been voiced that NPPV, by delaying ETI, may lead to a worse outcome. Also, 13–29% of patients are unable to tolerate the mask, and the procedure may be very time-consuming. The upper airway is not protected and the lower airway cannot be accessed, limiting the applicability in those who are unconscious or have secretion retention.

Five prospective RCTs of NPPV, predominantly in patients with acute exacerbations of COPD, have been published (Table 4). The two studies performed in the ICU show that NPPV is feasible and that the ETI rate is substantially reduced. In the study of Brochard et al., most of the excess mortality and complications, particularly pneumonia, were attributed to intubation. These data suggest that NPPV may be superior to IMV, but this was a highly selected group of patients, with the majority excluded from the study. There is no direct comparison between IMV and NPPV: the two techniques should be viewed as complementary, with NPPV considered as a means of obviating the need for ETI rather than as a direct alternative. Furthermore, in the UK, where NPPV is usually performed on general wards, the general application of these results is uncertain.

Three prospective RCTs of NPPV outside the ICU have shown varying results:

1. In the first trial, research staff supernumerary to the normal ward complement initiated NPPV. On an intention-to-treat analysis there was no difference between the two groups of patients, but a significant survival benefit was seen in the NPPV group when those unable to tolerate NPPV were excluded.

2. In the second trial, the lack of difference between the two groups is not surprising because, given the

Table 4. Published randomised controlled trials of non-invasive positive pressure ventilation in acute exacerbations of chronic obstructive pulmonary disease.

| RCT                | No. | No. with COPD | Mean pH at study entry | Setting          | Outcome (NPPV group first) |
|--------------------|-----|---------------|------------------------|------------------|-----------------------------|
| Bott et al          | 60  | All           | 7.33                   | General ward     | Survival: 27/30 vs 21/30, NS |
| Kramer et al        | 31  | 23            | 7.28                   | ICU              | ETI: All: 31 vs 73%, p <0.05; COPD: 9% vs 67%, p <0.05 |
| Brochard et al      | 85  | All           | 7.28                   | ICU              | Survival: 15/16 vs 13/15, NS |
|                     |     |               |                        |                  | Hospital stay and charges unaffected |
|                     |     |               |                        |                  | ETI: 26 vs 74%, p <0.001 |
|                     |     |               |                        |                  | Survival: 91 vs 71%, p = 0.02 |
|                     |     |               |                        |                  | Complication rate: 16 vs 48%, p = 0.001 |
|                     |     |               |                        |                  | Hospital stay: 23 vs 35 days, p = 0.005 |
| Barbe et al         | 24  | All           | 7.33                   | Emergency room/ General ward | None required ETI or died |
| Wood et al          | 27  | 6             | 7.35                   | Emergency room   | ETI: 45.5% vs 43.8%, NS |
|                     |     |               |                        |                  | Survival: 75% vs 100%, NS |

ETI = endotracheal intubation; RCT = randomised controlled trial; ICU = intensive care unit.
modest level of acidosis at presentation, most patients were likely to improve with standard therapy.

Wood et al.\(^\text{2}\) found a non-significant trend towards higher mortality in those given NPPV (4/16 vs 0/11; \(p = 0.123\)), which was attributed to delays in intubation. It is difficult to draw many conclusions from this study as the two groups were poorly matched and the numbers small.

In preliminary reports we have recently described a multicentre RCT of NPPV in acute exacerbations of COPD (\(n = 236\)) on general respiratory wards in 13 centres\(^\text{7}\). NPPV was applied by the usual ward staff according to a simple protocol. 'Treatment failure', a surrogate for the need for intubation, defined by \textit{a priori} criteria, was reduced by NPPV as was in-hospital mortality. Subgroup analysis\(^\text{18}\) suggested that the outcome in patients with pH below 7.30 after initial treatment was inferior to that in the studies performed in the ICU. These patients are probably best managed in a higher dependency setting with individually tailored ventilation. Staff training and support are crucial wherever NPPV is performed, and operator expertise more than any other factor is likely to determine its success or otherwise. Table 5 shows factors to be considered when deciding where NPPV should be performed\(^\text{19}\).

Inevitably, some patients will require intubation, and NPPV has a role in weaning\(^\text{20}\). Furthermore a recent RCT\(^\text{21}\) has shown a significant reduction in complications, but not in mortality or hospital stay, in patients with type I RF. The indications for NPPV may be widened still further.

Summary

NPPV is a major advance in respiratory and critical care medicine. In the acute setting, it has a clear role in the management of patients with COPD who are acidic, and in weaning from IMV. NPPV in hypoxic RF shows promise for selected patients, but further studies are required. For domiciliary use, NPPV is effective in both the short and long term for the management of extrapulmonary restrictive disease, but further research is required for COPD.

Table 5. Factors to be considered in deciding the location for non-invasive positive pressure ventilation for a patient with acute exacerbations of chronic obstructive pulmonary disease\(^{11,13,16}\):

- Staff expertise
- Staff/patient ratio
- Patient's other nursing needs
- Clinical condition
  - Severe acidosis at presentation
  - Coma or confusion
  - Significant comorbidity
  - Radiological evidence of consolidation
  - Orofacial abnormalities that interfere with the fitting of the nasal or face mask
- Failure of improvement in pH and other physiological variables in first hour

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High-resolution computed tomography and diffuse lung disease

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New drug treatments in psychiatric disease

Table 1. Roles of high-resolution computed tomography

- to detect diffuse lung disease in patients with a normal or near normal chest radiograph and/or normal lung function tests
- to narrow the differential diagnosis or make a confident histspecific diagnosis in patients with obvious but non-specific radiographic abnormalities
- to investigate patients with suspected bronchiectasis or unexplained severe obstructive airways disease
- to guide the type and appropriate site of lung biopsy
- to assess disease reversibility, particularly in patients with fibrosing lung disease

CME Respiratory medicine – II

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