Non-invasive positive pressure ventilation in patients with stable hypercapnic COPD: light at the end of the tunnel?

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Eighteen years ago in this journal, Elliott and coworkers reported on the feasibility of non-invasive positive pressure ventilation (NPPV) to improve blood gases, total sleep time and sleep efficiency in 7 of 12 patients with stable hypercapnic chronic obstructive pulmonary disease (COPD) who continued NPPV for 1 year.1 However, a meta-analysis summarising four subsequent randomised controlled trials conducted in the 1990s clearly showed that 3 months of NPPV in patients with stable COPD did not improve lung function, gas exchange or sleep efficiency.2 Moreover, descriptive long-term follow-up of patients receiving home NPPV showed that patients with thoracic restrictive and neuromuscular disorders had a favourable long-term outcome, but not patients with COPD.3 In addition, two subsequent randomised controlled trials from the beginning of the last decade demonstrated that long-term survival did not improve when NPPV was added to long-term oxygen treatment.


(LTOT) compared with those patients only receiving LTOT. Therefore, among the potentially beneficial treatment options for chronic hypercapnic respiratory failure arising from COPD, the use of NPPV remains open to question owing to a lack of convincing evidence in the literature.

One major problem in the majority of the early studies was that NPPV either did not (or was not confirmed to) improve alveolar ventilation as measured by the arterial carbon dioxide tension (PACO₂). In most randomised controlled studies, assisted forms of NPPV using low inspiratory pressures airway pressures (IPAP) ranging from 10 cm H₂O to 18 cm H₂O have been used. Despite this observation, the most recent randomised controlled trial on the long-term outcome of 144 patients with stable hypercapnic COPD receiving home NPPV published in this journal, which is the largest study to date, again used assisted NPPV with a mean IPAP of 15 cm H₂O and a mean expiratory positive airway pressure of 5 cm H₂O. There was no clear reduction in PACO₂ during spontaneous breathing in the group of patients receiving NPPV in addition to LTOT compared with those receiving LTOT alone after 12 months of treatment, although NPPV improved transcutaneous PACO₂ in patients on NPPV overnight. Interestingly, there was a slight survival benefit with NPPV. However, health-related quality of life (HRQL) as measured by the generic instrument MOS 36-Item Short-Form Health Status Survey (SF-36) deteriorated in two of the eight subdimensions (General Health and Mental Health), while specific HRQL as measured by the St George’s Respiratory Questionnaire (SGRO) did not change. Furthermore, mean adherence to NPPV for those assigned to this therapy was 4.5 h per night. Again this study showed that NPPV might have some beneficial effects, but could also have adverse effects such as reductions in HRQL.

This study underlines the importance of two issues. First, it is important that disease-specific questionnaires are used when treatment interventions are investigated in prospective trials. In this regard, HRQL measured using the highly specific and well validated Severe Respiratory Insufficiency (SRI) Questionnaire has recently been shown to be substantially increased following commencement of home NPPV in patients with stable hypercapnic COPD. In addition, in another study, HRQL was also reportedly improved when another specific questionnaire—the Maugeri Foundation Respiratory item set (MRF-28)—was used. Thus, there is no doubt that HRQL improves in stable hypercapnic COPD following commencement of home NPPV, but this is only detectable when HRQL is assessed using appropriate instruments.

The second issue of concern, however, is that NPPV using low levels of IPAP was not capable of improving blood gases during subsequent daytime spontaneous breathing following nocturnal NPPV. In contrast to this approach, Windisch and coworkers have established the concept of high-intensity NPPV for the treatment of patients with stable hypercapnic COPD. In an attempt to maximally decrease severely elevated PACO₂ levels, pressure-controlled ventilation is used with stepwise titration of IPAP up to 20–40 mbar depending on tolerance and necessity in order to achieve best respiratory function; here mean IPAP ranges around 50 mbar. High-intensity NPPV has been shown to improve blood gases during ventilation and during subsequent spontaneous breathing by an improved breathing pattern with an improved tidal volume, to increase both general and specific aspects of HRQL, to improve lung function and sleep quality and to be well tolerated over several years.

In the most recent study on NPPV published in Thorax, treatment of patients with stable hypercapnic COPD with high-intensity NPPV (mean IPAP 29 mbar) was directly compared with the conventional approach using assisted ventilation and considerably lower IPAP (mean IPAP 15 mbar), which was labelled as low-intensity NPPV. In this randomised crossover trial the mean treatment effect between low-intensity and high-intensity NPPV, both used for 6 weeks at home, was >9 mm Hg for nocturnal PACO₂ (the primary outcome) in favour of high-intensity NPPV which was therefore shown to be superior to the conventional and widely used form of low-intensity NPPV in controlling nocturnal hypoventilation. As a consequence, high-intensity NPPV but not low-intensity NPPV improved dyspnoea during physical activity, lung function and HRQL as specifically measured by the SRI.

One might speculate that high-intensity NPPV with controlled ventilation and high IPAP levels would not be nearly as well tolerated as low-intensity NPPV with assisted ventilation and almost 50% lower IPAP levels. Interestingly, however, this study revealed the opposite to be true as patients spent an average of 3.6 additional hours/day on NPPV when using high-intensity NPPV compared with the average time spent on low-intensity NPPV. In addition, dropouts occurred only while on low-intensity NPPV. Thus, more effective ventilation achieved by more aggressive forms of NPPV results in better patient adherence, which could result in improved HRQL and better symptom control even though significant side effects must not be ignored. However, it should also be mentioned that more time in hospital (on average, 2.5 days) was needed to get patients acclimatised to high-intensity NPPV. This, however, seems to be justified given the clear advantages of high-intensity NPPV. For this reason, high-intensity NPPV offers a new and promising therapeutic option in the treatment of patients with COPD with chronic hypercapnic respiratory failure. Clearly, future long-term randomised controlled trials are needed to determine whether high-intensity NPPV can also improve long-term survival. It is, however, debatable whether the improvement in long-term survival should be regarded as the most important aim of treatment once chronic hypercapnic respiratory failure has developed in patients with end stage COPD; improvement of sleep quality, dyspnoea, HRQL and physical activity are probably as important.

NPPV has also been used during physical activity. High-intensity NPPV when applied during walking using a rollator with the same settings as used during night, in addition to oxygen, produced substantially better oxygenation, dyspnoea and walking distance than oxygen alone in a randomised crossover trial. In addition, a 3-month randomised controlled trial published in this journal showed that NPPV also augmented the benefits of pulmonary rehabilitation in patients with COPD with chronic hypercapnic respiratory failure. NPPV was performed with a mean IPAP of 20 cm H₂O, a mean expiratory positive airway pressure of 6 cm H₂O and a mean respiratory rate of 18 breaths/min, which is not as aggressive as high-intensity NPPV but is considerably more aggressive than the conventional approach of low-intensity NPPV. As a consequence, the addition of NPPV to rehabilitation significantly improved gas exchange compared with rehabilitation alone. This resulted in an improvement in functional status and several measures of specific HRQL as assessed by the SRI and MRF-28. Based on these results, the addition of NPPV to rehabilitation offers a promising new treatment indication although long-term results are awaited.

In summary, the time has now come to open a new chapter in the discussion on if...
Lung Alerts: promoting education and encouraging new authors

Angshu Bhowmik,¹ Jenni Quint²

Lung Alerts were introduced by Wisia Wedzicha, Editor-in-Chief in 2003 to increase the educational content of the journal. The aim was to commission brief summaries of papers on respiratory topics published in non-respiratory journals, thereby attracting a broader interest particularly among doctors in training. It was also intended to allow readers to keep abreast of publications in journals to which Respiratory Specialists are less likely to subscribe.

At the time of writing, 572 Lung Alerts have so far been published from 2003 until June 2010 at an average of 4.25 per month. A further 15 are in press.

Of the 387 Lung Alerts we have edited, looking at contributors from a regional perspective, the largest proportion (44%) were from London and the Kent, Surrey and Sussex Deaneries. 8% of contributors have been from outside the UK. The North Western (6%), South West Peninsula (5%), Eastern (5%) and LNR (Leicestershire, Northamptonshire and Rutland) (4%) Deaneries have been the other major sources of authors of Lung Alerts.

Fifty per cent have been written by Specialist Registrars or equivalent, 20% by doctors in various grades which previously fell under the category of ‘Senior House Officer’, 10% by ‘Research Fellows’, 7.5% by Consultant or equivalent doctors, 1.6% by Foundation 1 doctors and three of the Alerts have been written by students. The remainder were written by doctors of various other grades including Specialty doctors and Associate Specialists. We are hopeful that the experience of being able to publish in Thorax will have led to many of those who were not already committed to careers in Respiratory Medicine and Science being drawn to this specialty!

Over the years, 70 journals have provided the sources for the papers summarised in Lung Alerts. The largest number has been from the New England Journal of Medicine (99) with other major contributors being the Lancet (48) and...

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and when NPPV should be applied in patients with stable hypercapnic COPD. Recent research indicates that the technique of how NPPV is applied is the crucial issue regarding the acceptance and effectiveness of NPPV. Here, the new concept of high-intensity NPPV has provided promising results with respect to gas exchange, lung function, treatment compliance, dyspnoea and HRQL. In addition, NPPV applied during physical activity and rehabilitation has emerged as a new potential indication for NPPV aiming to improve gas exchange, functional status and exercise-induced dyspnoea. Although the importance of proven NPPV-associated improvements in gas exchange, symptoms, functional status and HRQL is undisputed, we need an answer as soon as possible to the question: ‘Are these new approaches also capable of improving long-term survival?’

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