Commentary

Noninvasive positive pressure ventilation for respiratory failure caused by exacerbations of chronic obstructive pulmonary disease: a standard of care?

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Abstract

This editorial comments on a meta-analysis of the use of noninvasive positive pressure ventilation to treat patients with acute respiratory failure caused by chronic obstructive pulmonary disease (COPD) exacerbations published in the *British Medical Journal* earlier this year. Based on its analysis of seven randomized controlled trials that met pre-specified criteria, the meta-analysis demonstrated highly significant benefits of noninvasive positive pressure ventilation in COPD patients, including a reduction in a combined end-point consisting of death and endotracheal intubation. The editorial argues that, based on the strength of this and other evidence, noninvasive positive pressure ventilation to treat selected patients with acute respiratory failure due to COPD exacerbations should now be considered a standard of care.

Keywords acute respiratory failure, chronic obstructive pulmonary disease, COPD exacerbation, mechanical ventilation, noninvasive ventilation

In a recent issue of the *British Medical Journal*, Lightowler and coworkers [1] presented a meta-analysis of seven randomized controlled trials of noninvasive positive pressure ventilation (NPPV) to treat acute respiratory failure caused by chronic obstructive pulmonary disease (COPD) exacerbations as compared with 'usual care'. Their analysis showed substantial and statistically significant reductions in mortality (relative risk 0.41), intubation (relative risk 0.42) and complications (relative risk 0.32). In addition, respiratory rate, pH, and arterial carbon dioxide tension improved significantly more after the first hour of treatment, and the duration of hospital stay was approximately 3 days shorter among NPPV-treated patients. The authors concluded that 'NPPV should be considered early' to treat respiratory failure due to COPD exacerbations. In an accompanying editorial, Babu and Chauhan [2] advocated the 'timely use of non-invasive ventilation in more severe exacerbations'. The question is at what point does the weight of evidence become sufficient to establish a new standard of care, replacing 'usual' care as applied in the control groups of the randomized trials? My opinion is that we now have enough evidence to establish a new standard. The analysis by Lightowler and coworkers did not include several studies that provide further supportive evidence [3,4], and other meta-analyses have drawn similar conclusions [5]. Furthermore, consensus groups of experts advocate the routine use of NPPV for selected patients with COPD exacerbations [6,7].

The question must be asked in arguing this position – are there weaknesses in the evidence base? Lightowler and coworkers acknowledged that meta-analyses are subject to publication bias – that favorable trials are more likely to be published than are unfavorable ones. In addition, all NPPV trials in the acute setting are limited by the problem that complete blinding is virtually impossible. Even if a sham control group were included, which was not the case in any of the trials, it is quite easy for investigators and patients to tell which group they are in. Nonetheless, the consistency of the favorable findings among multiple studies reduces but does not eliminate concern about these kinds of biases.

COPD = chronic obstructive pulmonary disease; ICU = intensive care unit; NPPV = noninvasive positive pressure ventilation.

There is wide agreement that patients with COPD exacerbations who are candidates for noninvasive ventilation should be selected carefully [6,8]. Selection criteria have not been validated in prospective trials, but virtually all of the randomized controlled trials have used similar criteria. In addition, several studies have identified factors that predict the likelihood of success, which include the following [9,10]: a better neurologic score; a lower Acute Physiology and Chronic Health Evaluation score; less air leaking; a higher pH; and – the strongest predictor – a significant improvement in respiratory rate, pH or arterial carbon dioxide tension within the first hour or two. Based on studies that showed no benefit in patients with milder exacerbations [11], the standard recommendation is to select patients with more severe exacerbations as characterized by moderate-to-severe dyspnea and evidence of acute or acute-on-chronic gas exchange disturbances. In addition, patients considered to be poor candidates for noninvasive ventilation, such as those who are in respiratory arrest, medically unstable otherwise, uncooperative, and unable to protect their airway or handle airway secretions or accommodate a mask, are routinely excluded. Admittedly, these selection criteria are largely subjective and, like the decision to intubate, they require that clinicians exercise judgment.

COPD is often accompanied by comorbidity, and few studies have examined the effect of comorbid conditions on the outcomes of COPD patients treated with NPPV. However, those with concomitant congestive heart failure are likely to benefit based on studies demonstrating significant benefit of NPPV in patients with congestive heart failure [8], and a randomized controlled trial has shown that patients with COPD exacerbations complicated by community-acquired pneumonia fare better when treated with NPPV as compared with conventional therapy [12]. Caution is advised, however, when using NPPV in patients with COPD exacerbations suffering from acute myocardial infarction.

Respiratory failure due to COPD exacerbations can occur in other settings apart from at presentation to the emergency department or intensive care unit (ICU), for example postoperatively. In this setting, NPPV can be applied using the selection criteria described above, except that patients with upper airway or esophageal surgery should be excluded, and many surgeons are cautious about applications in patients who have undergone abdominal surgery requiring disruption of gastric or small bowel mucosa.

Even when patients are selected according to the above criteria, a substantial minority of patients will still fail and require intubation, ranging from 7% to 30% among the controlled trials [1]. Future studies should shift their focus from establishing the efficacy of NPPV to the refinement of selection and application techniques with the aim of minimizing the failure rate. Potential reasons for failure include selection of inappropriate candidates for NPPV, progression of the underlying disease, failure to achieve good patient–ventilator synchrony, mask intolerance, and lack of experience or skill on the part of care givers. The contributions of these factors and ways of addressing them can be tested in future studies with the ultimate aim of optimizing the application and utilization of NPPV.

At the present time, NPPV can be considered a standard of care only for selected patients with COPD exacerbations. Evidence is not sufficiently strong to support such a view for other applications of NPPV. For acute pulmonary edema, evidence clearly indicates that noninvasive positive pressure techniques are effective at promptly reducing dyspnea, improving oxygenation, and avoiding intubation [7], but it is not clear whether NPPV is superior to continuous positive airway pressure alone. There is also strong evidence to support the use of NPPV as the modality of first choice in patients with acute respiratory failure in the face of immunocompromised status, but these patients still have poor outcomes even when treated with NPPV [13] and the need to perform diagnostic procedures sometimes necessitates intubation. In other forms of respiratory failure, a trial of NPPV may be reasonable but it is difficult to argue that NPPV should be considered a standard of care. These include acute asthma, exacerbations of cystic fibrosis, various forms of hypoxemic respiratory failure, use of NPPV to facilitate weaning or to avoid extubation failure in non-COPD patients, and do-not-intubate patients. Some of these applications may become standards of care as evidence accrues from further investigations.

In a survey of NPPV utilization in European ICUs, Carlucci and coworkers [14] found that 20% of ICUs were not using NPPV at all. This is concerning because, if the use of NPPV to treat patients with acute respiratory failure due to COPD exacerbations is accepted as a standard of care, then this means that a substantial minority of institutions in Europe, and undoubtedly in the USA as well, are not offering therapy that meets current standards. Efforts must be undertaken to ensure that institutions under-utilizing or not currently using NPPV acquire the requisite knowledge and skill to offer this clearly effective therapy to their patients.

Competing interests

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