Clinical concise review: Mechanical ventilation of patients with chronic obstructive pulmonary disease

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Objective: **To summarize the current literature on mechanical ventilation of patients with chronic obstructive pulmonary disease (COPD) using published data to augment commonly accepted principles of clinical practice.**

Data Source: **A MEDLINE/PubMed search from 1966 to November 2006 using the search terms mechanical ventilation, respiratory failure, noninvasive positive pressure ventilation (NIPPV), and COPD, and weaning. Subsequent searches were done on more specific issues such as heliox. Additionally, prominent researchers in this field were interviewed for knowledge of ongoing or unpublished data and their clinical practice.**

Data Extraction and Synthesis: **COPD is very common cause of respiratory failure and admission to the intensive care unit. Mechanical ventilation of patients with COPD presents a unique set of challenges compared with other patients. Care must be taken to avoid augmenting dynamic hyperinflation and acid/base disturbances resulting from chronic hypercapnic respiratory failure. Modalities such as NIPPV and helium/oxygen gas mixtures are increasingly being recognized for their ability to help prevent invasive ventilation and aid in getting patients off invasive ventilation.**

Conclusions: **Despite decades of study, most of the principles of safe mechanical ventilation for patients with COPD such as low respiratory rates that maximize expiratory time and careful attention to air-trapping still hold true to this day. NIPPV appears to be the most important new modality in reducing the mortality, morbidity and incidence of invasive mechanical ventilation. (Crit Care Med 2008; 36:1614–1619)**

KEY WORDS: chronic obstructive pulmonary disease (COPD); mechanical ventilation; noninvasive positive pressure ventilation; weaning

Worldwide over 52 million people have chronic obstructive pulmonary disease (COPD). It is currently estimated that about 16 million Americans have been diagnosed with COPD and that at least the same number have the disease but have not been diagnosed (1). It is the fourth leading cause of death in the United States but is expected to be the third by the year 2020. In 1998 COPD alone was responsible for almost 2% of all hospitalizations and a co-factor in 7% (2). Patients with COPD may require respiratory support for a variety of reasons ranging from acute exacerbations, to medical illness, to elective surgeries. In all cases, they can present a unique challenge to the personnel who manage their ventilatory support. This article will review some of the main concepts regarding mechanical ventilation of patients with COPD with emphasis on specific recommendations supported by recent literature and focus on acute respiratory failure (as opposed to chronic mechanical ventilation).

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Basic Principles

Acute respiratory failure in patients with COPD is usually multifactorial. At baseline, patients with COPD frequently have impaired oxygenation because of loss of alveolar volume and impaired ventilation from increased dead space and poor respiratory mechanics (3). Because of these baseline abnormalities, tolerance of acute pulmonary insults is poor (4, 5). As an example, consider an elderly patient with moderate COPD and a small pneumonia. The pneumonia causes new hypoxemia or worsening of hypoxemia. The patient responds by increasing minute ventilation. Emphysema-induced increase in residual volume (RV) limits tidal ventilation. Increasing respiratory rates decrease expiratory time and produce or worsen air trapping which further limits ventilation. Other factors such as chest wall mechanics, nutritional deficiencies, pulmonary hypertension, and chronic co_2 retention can make the situation worse. Eventually, the respiratory efficiency declines, the work of breathing becomes unsustainable, the patient tires, and respiratory failure ensues (6).

COPD patients with acute respiratory failure have two characteristics. First, they have fatigued their respiratory system and need rest and mechanical assistance. Second, their ventilatory support needs to be done to reduce air trapping as much as possible.

Noninvasive Positive Pressure Ventilation (NIPPV)

When patients fail conservative methods of therapy, such as bronchodilators, steroids, and oxygen therapy, NIPPV is an attractive alternative to invasive ventilatory support. NIPPV has the potential to avoid many of the pitfalls of endotracheal intubation including airway trauma, heavy sedation, and ventilation-acquired pneumonia (6, 7). Nasal or face mask support can be given with bilevel pressure support using either a conventional ventilator or a smaller made for NIPPV ventilator.

NIPPV has been used successfully in COPD for over a decade and at least 12 published randomized controlled trials

comparing NIPPV to "standard care" have been conducted (8–19). These have been the subject of three meta-analyses (20–22). Like all studies of COPD, there is lack of uniformity across studies regarding the cause of the respiratory failure in enrolled patients and the severity of the disease. The analyses done by Lightowler et al. (21) and Peter et al. (22) concluded that the published literature show that NIPPV effectively reduces mortality and need for mechanical (invasive) ventilation in all patients with acute exacerbations of COPD. The analysis by Keenan et al. (20) took the added step of factoring disease severity on outcome and concluded while NIPPV appears to be beneficial in acute respiratory failure in more severely ill COPD patients, the treatment effect was not present in studies that included less sick patients. In a brief report, published after that study, Peter and Moran conducted further analysis of all the studies and concluded by regression analysis that patients with a serum pH of <7.37 or a pco_2 >55 mm Hg were those that were likely to benefit from NIPPV (23), implying benefit with ventilatory failure.

Patients who have COPD have multiple potential reasons for acute exacerbations producing variable degrees of respiratory embarrassment. The meta-analysis that used the least-specific entry criteria (20) and individual studies, such as one by Celikel et al. that included "mixed" causes of respiratory failure, have both showed benefit to the use of NIPPV in patients with hypercapnic respiratory failure (14).

In addition to preventing institution of invasive mechanical ventilation, NIPPV has also been used to facilitate weaning from invasive ventilation. At least five studies have looked at the use of NIPPV to facilitate liberation of patients from invasive ventilation (24–27). Two of these studies were specific for patients with respiratory failure from COPD and both showed benefit (24, 27). In the study by Nava et al., COPD patients who were screened to be potentially weanable but failed a T-piece trial after 48 hrs of conventional ventilation were randomized to either continue on traditional weaning or be extubated to NIPPV. The NIPPV group had less time in the ICU, less nosocomial pneumonia, and a better survival rate at 60 days than the control group. A meta-analysis of five randomized trials using NIPPV weaning by Burns et al. supports this finding but includes patients who do not have COPD (28). Lastly, it should be pointed out that while bilevel NIPPV is generally used in practice and was the most common mode used in the published trials, CPAP can also be used and at least two trials have demonstrated its benefits (29, 30). To our knowledge a head-to-head comparison of CPAP to bilevel ventilation in COPD exacerbations has not been published.

Invasive Mechanical Ventilation

Setting Minute Ventilation. The failure rate of NIPPV in acute exacerbations (AE) of COPD (AECOPD) remains significant and as high as 50% (31). Many COPD patients experiencing AE may have underlying chronic ventilatory failure with a baseline state of chronic compensated respiratory acidosis. The serum bicarbonate level on admission, or even better, obtained during a recent period of stability, may provide an indirect indication of the patient's baseline $Paco_2$. Assuming no acute metabolic disturbance, this should be the ventilatory target, rather than a $Paco_2$ of 40 mm Hg, as it represents the balance between the patient's central respiratory drive and the inability of the respiratory pump to maintain normal alveolar minute ventilation. Ventilator settings that produce a "normal" $Paco_2$ will likely lead to renal dumping of bicarbonate, leading to difficulty weaning from the ventilator since this level will be needed to maintain the status quo off the mechanical ventilator. "Controlled hypoventilation" should guide management, aiming for a $Paco_2$ at or above the patient's usual baseline with a pH target of 7.35–7.38 (32).

Dynamic Hyperinflation and Auto-PEEP

Worsened airway inflammation, edema, bronchospasm, and increased secretions cause patients with AECOPD to experience increased airways obstruction and greater than usual degrees of airway closure and inhomogeneous ventilation. If adequate time is not given for expiration, end-expiratory lung volume (EELV) increases beyond the normal functional residual capacity (FRC). The result is dynamic hyperinflation (DH) of the lung, with positive end-expiratory pressure in the lung due to this trapped gas, referred to as intrinsic PEEP (PEEPi), air-trapping, or auto-PEEP (32). Gas trapping and PEEPi have multiple adverse consequences (see below). A common indication that PEEPi is increasing is a rise in plateau pressures (Pplat). Regardless of the presence or absence of auto-PEEP, peak inspiratory pressures are commonly elevated in COPD patients due to increased airways resistance, however, the plateau pressure would not be expected to be increased as emphysema increases lung compliance. Elevation of Pplat supports air trapping (auto-PEEP) as the cause of decreased lung static compliance. Ventilators displaying flow-time curves provide useful information with a qualitative indication of PEEPi by demonstrating expiratory flow persisting at the onset of inspiration. This is demonstrated in Figure 1.

Quantitating auto-PEEP is more difficult and prone to error. Increasing extrinsic PEEP (PEEPe) to the point that Pplat increases with volume-cycled ventilation or tidal volume decreases with pressure-limited ventilation provides a quantitative estimate of the PEEPi. Alternatively, one can directly measure PEEPi by occluding the expiratory port for 1–3 seconds at end expiration to allow redistribution of volume and equilibration of pressure throughout the lung before reading the airway pressure, or using built-in PEEPi measurement provided on many newer ventilators. Unless the patient is paralyzed, obtaining an accurate estimate of end-expiratory pressure with an end-expiratory pause is unreliable. Error will occur in these measurements by even the smallest patient inspiratory or expiratory efforts, and any quantitative assessment of auto-PEEP should be considered an estimate only (34).

Consequences of Dynamic Hyperinflation

The air-trapping that results from impaired exhalation has multiple negative consequences. Excessive gas trapping can overdistend lung regions, compressing adjacent, more functional lung regions leading to hypoxia. With increasing hyperinflation as minute ventilation increases, a paradoxic increase in $Paco_2$ results, producing the loss of the normal relationship between $Paco_2$ and minute ventilation. In the patient who is not adequately sedated, the discomfort associated with increasing hyperinflation and hypercarbia may also lead to patient/ventilator asynchrony ("bucking the ventilator") with resultant greater increases in airway pressures, co_2 production, and hypercarbia. Less dramatic but no less important, air-trapping increases the inspiratory work for the patient by increasing the negative intrathoracic pressure

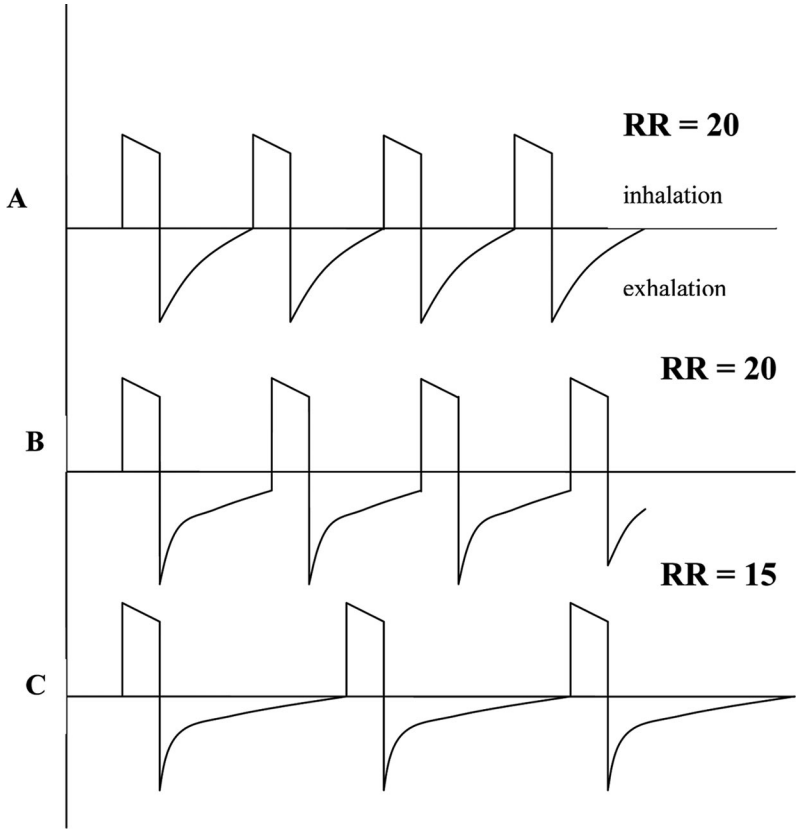

Figure 1. The use of flow/time waveforms to guide ventilator settings in chronic obstructive pulmonary disease. Flow-time waveform with bidirectional flow rate on the X axis and time on the Y axis. The midline represents zero flow. *A*, illustrates a normal wave form demonstrating full exhalation to functional residual capacity by the flow rate reaching zero prior to the next breath. *B*, illustrates a patient with airway obstruction at the same respiratory rate (*RR*) with air trapping as demonstrated by expiratory flow not reaching zero. *C*, illustrates the same patient with a lower respiratory rate and no air-trapping.

the patient must generate to trigger a breath from the ventilator. This may lead to tachypnea, ineffective inspiratory efforts, increased agitation, and patient/ventilator asynchrony. This affect can be reduced by the careful application of PEEPe and ventilators that are flow-triggered, as opposed to pressure-triggered, can reduce this problem as well (33). Additionally, increases in mean airway pressure associated with auto-PEEP impair venous return reducing cardiac output (34). The combination of PEEPi, sedation, and possible use of paralytic agents, and the poor fluid intake and increased insensible loss of dyspneic tachypnic patients all combine to result in the hypotension frequently seen following intubation. Finally, dynamic hyperinflation increases the likelihood of pneumothorax (35).

Reducing Dynamic Hyperinflation

Other than treating the underlying condition with bronchodilators and anti-inflammatory agents, the primary method by which DH is reduced is through increasing expiratory time. This is accomplished best by reducing the respiratory rate but can also be treated by altering the inspiratory to expiratory (I:E) ratio. Two studies found the decelerating waveform resulted in the lowest peak inspiratory pressure, physiologic deadspace ratio, and $Paco_2$ compared to square and sine wave patterns of inspiratory flow when tidal volume, rate, and inspiratory time to total respiratory cycle time were kept constant. However, this was associated with an increase in the alveolar to arterial Po_2 gradient (A-a gradient).

In cases of severe air-trapping that have led to profound hypoxemia or hemodynamic compromise, short periods of "air dumping" may be required. With the use of volume control mode in some ventilators, the choice of decelerating waveform produces prolongation of inspiratory time and would likely worsen auto-PEEP. During this maneuver, the respiratory rate (RR) is lowered to a rate sufficient to let most of the trapped air escape (36, 37). This commonly requires lowering the RR to extremely low levels for a very short period and thus careful monitoring and heavy sedation or paralytics are necessary. An increase of the tidal volume (in pressure-cycled ventilation) or a decrease in the Pplat (in volume-cycled ventilation) are a good indication that the maneuver is working.

Somewhat more controversial is the application of PEEPe to decrease airtrapping in patients with COPD. As previously mentioned, PEEPe can be used to improve triggering in situations of increased PEEPi. Many studies have evaluated the role of PEEPe in reducing DH and the results are mixed. Two studies found no significant effect of PEEPe until levels reached 85% to 90% of PEEPi, at which point it had negative effects on gas exchange and hemodynamics (38, 39). One study by Caramez et al. showed three different responses to incremental increases in PEEPe in their small group of patients: a) no change in isovolume-expiratory flows and lung volume until PEEPe crossed a threshold value following which over inflation occurred; b) stepwise decrease in isovolume-expiratory flows with progressive over inflation, and; c) paradoxic drop in EELV with decreased Pplat and total PEEP, with increased isovolume-expiratory flow. The latter pattern occurred in five of eight patients during at least one of four different combinations of tidal volume and respiratory rate (40). They found no predictors of the patient's response and suggested a therapeutic trial for patients in whom measures to maximize expiratory time were inadequate to sufficiently reduce hyperinflation and PEEPi. These patterns have been duplicated by other investigators who showed some beneficial effects to setting PEEPe at ~80% of PEEPi (32, 37, 41–44).

The main difficulty for clinicians is to accurately determine what PEEPi is and not to exceed it. Several methods exist and entail significant complexity to perform well. The two most commonly used in studies are the airway occlusion technique and the use of an esophageal balloon. A detailed comparison of these two methods can be found in a paper by Zakynthinos et al. (45). A more detailed examination of this entire literature can be found in a review by Gladwin and Pierson, who conclude that there is little evidence that PEEPe "stents" open the airways but may be helpful in patient-assisted modes of breathing to reduce work of breathing and aid triggering (32).

Other Adjunctive Measures

Many other technologies have been applied to the ventilation of patients with COPD. Perhaps the most widely studied is the use of helium/oxygen (heliox) mixtures. Heliox allows increased air flow in states of increased airways resistance and thus improves ventilation. Proven effects include reducing PEEPi and work of breathing (46–49), decreasing intrathoracic pressure and airways resistance (31), improving hemodynamics (50), and assisting in weaning (49, 51). Additional studies have shown it can reduce hospital stay length and costs (31) and is useful when used in concert with NIPPV (31, 52).

Less well-studied are therapies such as "transtracheal open ventilation" in which the patient receives a cuffless small bore tracheostomy tube for ventilator assistance (53). One study showed significant reductions in time required on the ventilator, intensive care unit days, and complications in the transtracheal open ventilation group. A small trial to evaluate nitric oxide in patients with AECOPD showed no benefit (54). Another small trial looked at prone positioning in AECOPD patients with severe hypoxia (>60% F_{IO_2}) and found oxygenation increased and the volume of aspirated secretions increased (55). The study was not powered to show outcome differences.

Weaning

Considerable literature exists describing modalities that assist in weaning COPD patients from invasive ventilation. As previously mentioned several studies have shown a benefit of early extubation to NIPPV. Heliox use has also been shown to decrease re-intubation in at least two studies. Jaber et al. studied 18 patients without COPD following extubation and found reductions in transdiaphragmatic pressure, the pressure-time index, and improved patient comfort while breathing helium-oxygen rather than air immediately after extubation (51). Diehl et al. demonstrated reduced work of breathing without a change in breathing pattern by using helium-oxygen rather than air-oxygen in 13 AECOPD patients just before extubation, and in the five patients they were able to re-test following extubation (49).

For the patient failing initial weaning attempts, the choice of a weaning strategy arises. Vitacca et al. published a study specifically examining difficult to wean COPD patients transferred to a long-term weaning unit following tracheostomy (56). They found no difference between pressure support weaning vs. spontaneous breathing trials in terms of success, complications, or duration of weaning efforts. Both groups did better than historical controls, suggesting the most important aspect of their weaning was having a well-defined protocol in place for staff to follow. Reissmann et al. demonstrated that 5–7.5 cm H_2O of continuous positive airway pressure (CPAP) in spontaneously breathing intubated AECOPD patients resulted in fewer spontaneous breathing trial failures, less dyspnea, and a slower breathing pattern than in control patients without CPAP (57). The addition of PEEPe may be useful for patients failing to wean by T-piece, and it suggests that patients who have failed an extubation attempt should have a trial of CPAP or bilevel positive airway pressure with 5–7.5 cm H_2O of expiratory positive airway pressure following the next extubation.

Many investigators have searched for predictors of weaning success or failure. Alvisi et al. looked at 28 patients who failed to meet extubation criteria on a standardized weaning trial and subjected them to multiple analyses of respiratory mechanics after failing the trial. Respiratory mechanical data were subsequently compared to the same patient's data at the time they successfully completed a spontaneous breathing trial. They found no parameter, either individually or as part of a composite score, accurately predicted success as defined by passing a 2-hr spontaneous breathing trial and remaining extubated for 48 hrs (58). A study by Zanotti et al. also measured multiple respiratory system mechanics but only showed that higher vs. lower static compliance (62.7 ± 17.% vs. 111.6 ± 18.0 mL/cm H_2O). with a threshold value of 88.5 mL/cm H_2O measured in the first 24 hrs of intubation correlated with extubation failure (59). Another study showed that abnormal gastric tonometry, defined as an intramucosal pH ≤7.30 during mechanical ventilation, was predictive of failure of spontaneous breathing trial or extubation (60).

Patients failing to wean from mechanical ventilation should have an evaluation for neuromuscular disease. In a small group of patients, Amaya-Villar et al. found over one third of patients (9/26) admitted to their ICU with AECOPD requiring greater than 48 hrs of mechanical ventilation and ≥ 240 mg/d of methylprednisolone developed acute quadriplegic myopathy (61). They identified total dose of administered steroid, severity of illness at onset, and development of sepsis as risk factors for this common complication. Surprisingly, use of neuromuscular blocking agents was not associated with the development of acute quadriplegic myopathy in this study.

CONCLUSIONS

In summary, the ventilation of patients with COPD represents one of the greatest challenges for ICU clinicians. It is clear that many, if not most, of these patients with acute respiratory failure will benefit from a trial of NIPPV. If invasive ventilation ensues, great care should be taken to avoid augmenting the forces at work that lead to air-trapping in these patients. Often the best strategy is a very passive one, doing not much more than resting the patient in a state of sedation and waiting for the acute problems to resolve while resting the patient.

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