
Acute Exacerbation of COPD: Non-invasive Positive Pressure Ventilation

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Case Presentation

A 73-year old male smoker with a past medical history of coronary artery disease, congestive heart failure and COPD on home oxygen arrived in the emergency department with difficulty breathing. He complained of gradually increasing shortness of breath on exertion for 1 week and cough with thick yellow sputum. He denied fever, chills, chest pain, orthopnea or paroxysmal nocturnal dyspnea. He had increased the use of his bronchodilators as directed by his primary care physician. This did not improve his symptoms. The morning of admission, he woke up and was unable to catch his breath. He called EMS. Upon arrival, he was afebrile with BP 160/80, HR 130, RR 36, sPO₂ 85 % on 4 L/min O₂. Arterial blood gas (ABG) pH 7.24, pCO₂ 60, PO₂ 55, spO₂ 85 %. He was awake, yet lethargic, tachypneic and using accessory muscles of respiration. Chest auscultation revealed regular tachycardia, poor air movement, end-expiratory wheeze and no crackles. Chest x-ray demonstrated hyperinflation with no infiltrates.

Question What is the immediate approach to this patient with acute respiratory failure?

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Answer Non-invasive positive pressure ventilation.

In the absence of absolute contraindication, all patients with acute hypercapnic respiratory failure due to an exacerbation of COPD should be treated with non-invasive positive pressure ventilation (NIPPV). This patient was initiated on NIPPV with pressure support of 12 cm H₂O, PEEP 5 cm H₂O, and FIO₂ of 0.5 via a full face mask. Oxygen was titrated to maintain saturations of greater than 90 %. He was given two albuterol/ipratropium nebulized treatments in the first 30 min of his arrival, azithromycin 500 mg PO once, and solu-medrol 60 mg IV once. After 1 h, his respiratory rate decreased to 22 and he was no longer using accessory muscles. ABG on NIPPV demonstrated pH 7.33, pCO₂ 46, pO₂ 80, spO₂ 95 %. He was admitted to the intensive care unit for continued management. By hospital day 2, respiratory failure resolved and he was transferred to general care.

Principals of Management

Diagnosis

Acute exacerbations of COPD are characterized by sub-acute or acute worsening of chronic respiratory symptoms. Typical symptoms are dyspnea, cough, and increased sputum purulence and volume [1]. Severity of symptoms ranges from mild, which may improve without additional medical

treatment, to severe resulting in respiratory failure or death. The hallmark of COPD exacerbations is airflow obstruction, dynamic hyperinflation and airways inflammation, often provoked by viral or bacterial infections or environmental triggers. COPD exacerbations are associated with reductions in quality of life, progression of lung disease, and increased risk of death. In a longitudinal study of 2138 COPD patients; mortality during follow-up was significantly higher in those with one or more hospitalized exacerbations during the first year of follow-up (15%), as compared to 5% in those without an event [2]. The predicted in hospital mortality of a COPD exacerbation is 10% [3]. A severe exacerbation resulting in hypercapnic respiratory failure portends a 2-year mortality rate approaching 50% [3]. Indications for ICU admission of a COPD exacerbation are given below [4]. The approach to treatment of an acute exacerbation of COPD with hypercapnic respiratory failure requiring intensive care unit admission follows.

Indications for ICU Admission

- Severe dyspnea that responds inadequately to initial emergency therapy
- Changes in mental status (confusion, lethargy, coma)
- Persistent or worsening hypoxemia ($\text{PaO}_2 < 5.3$ kPa, 40 mmHg) and/or severe/worsening respiratory acidosis ($\text{pH} < 7.25$) despite supplemental oxygen and noninvasive ventilation
- Need for invasive mechanical ventilation
- Hemodynamic instability—need for vasopressors

Bronchodilators

Short-acting beta adrenergic agonists (albuterol, levalbuterol) are potent bronchodilators with rapid onset of action and are first line therapy for acute exacerbation of COPD [5]. Typically, these are combined with short acting anticholinergic agents such as ipratropium bromide. Both drugs can be administered with equal efficacy via

metered dose inhaler or nebulizer; however nebulized delivery is often preferred during an acute exacerbation of COPD due to ease of administration for persons in respiratory distress. Albuterol should be dosed at 2.5 mg/3 mL via nebulizer every 1–4 h or 4–8 puffs (90 mcg per puff) via MDI. Ipratropium bromide is dosed at 500 mcg by nebulizer every 4 h or 2–4 puffs (18 mcg per puff) via MDI every 4 h. There is no advantage to increasing the dose of nebulized albuterol to 5 mg and continuous nebulized beta-agonists are not recommended [6]. Side effects of beta-adrenergic agonists include tachycardia, anxiety, tremors, hypokalemia, and rarely lactic acidosis. Side effects of short acting anti-cholinergic agents include dry mouth, urinary retention and exacerbation of narrow-angle glaucoma. There is no role for methylxanthines such as aminophylline for treatment of hospitalized patients with COPD exacerbations [7, 8].

Systemic Corticosteroids

When added to bronchodilator therapy, systemic corticosteroids improve lung function, decrease treatment failure rates, prevent relapse, and decrease length of hospitalization [9–11]. There is no significant difference in clinical outcomes in hospitalized patients with a COPD exacerbation treated with oral versus intravenous corticosteroids [12]. The dose of corticosteroids and length of treatment varies widely in clinical trials. A randomized controlled trial (RCT) in patients with acute exacerbation of COPD treated in the emergency department randomized patients to either a 5 day course or a 14 day course of prednisone 40 mg daily. The study concluded that patients randomized to 5 days of treatment had similar rates of relapse within 6 months and this was non-inferior to a longer course [13]. Given the short and long term side effects of systemic corticosteroids, a reasonable approach to treatment is a 5 day course of 40 mg of prednisone for most patients [5]. In critically ill patients clinicians often prescribe higher doses with little evidence to support this practice. In an observational study of ICU patients with COPD exacerbations, doses of methylprednisolone < 240 mg daily compared

to >240 mg daily resulted in a slightly shorter hospital and ICU length of stay and duration of mechanical ventilation [14]. There was no mortality difference. There is not enough data to recommend an optimal dose of corticosteroids in the ICU setting.

Antibiotics

The majority of COPD exacerbations are due to bacterial or viral infections. There is evidence that viruses and bacteria act synergistically to provoke airways inflammation and exacerbation [15]. Additionally, new strains of airway bacteria have been shown to trigger a significant inflammatory response and resultant exacerbation [16]. GOLD and European Respiratory Society guidelines recommend antibiotics for all patients with a moderate to severe COPD exacerbation and for those requiring hospitalization [5, 17]. Antibiotics reduce the risk of treatment failure and length of hospital stay in persons with severe exacerbations [18]. For example, in a RCT of patients requiring intubation and mechanical ventilation, ofloxacin was compared to placebo and was found to decrease mortality (4% vs 22%), duration of mechanical ventilation and length of hospital stay [19]. The antibiotic regimen prescribed should target common bacterial pathogens, local patterns of resistance and risk factors for *P. aeruginosa* infection should be considered [20, 21]. Treatment courses of 3–7 days are appropriate in most cases. A meta-analysis comparing 5 days to greater than 7 of antibiotics (beta-lactams, macrolides, and fluoroquinolones) demonstrated no difference in outcomes and fewer drug related adverse events in those with 5 day course [22].

Non-invasive Positive Pressure Ventilation (NIPPV)

NIPPV refers to positive pressure ventilation through a nasal or oral interface as opposed to endotracheal tube or tracheostomy tube. NIPPV can be delivered through standard ICU ventilators or a variety of portable devices. Indications for NIPPV in COPD exacerbations are given

below [4]. The most commonly used mode of ventilation employed in acute hypercapnic respiratory failure associated with COPD exacerbation is bilevel positive airway pressure (BPAP) where an inspiratory positive airway pressure (IPAP) and expiratory positive airway pressure (EPAP) is set. Pressure support, assist control and proportional assist ventilation are other options depending on the available device. There are few studies directly comparing NIPPV modes in acute hypercapnic respiratory failure. The goals of NIPPV are to reduce work of breathing, improve minute ventilation, correct hypercapnia and avoid endotracheal intubation while maximizing patient comfort. There are several available patient interfaces, full face mask, oronasal mask, nasal mask, and nasal pillows [23]. In a randomized trial of 26 patients with COPD exacerbations, NIPPV via full face mask, nasal mask or nasal pillows were compared [24]. The nasal mask was best tolerated while the full face mask provided the greatest physiologic improvement. A larger study comparing the nasal to orofacial mask found that more than half of patients with the nasal mask needed to be changed to the face mask most often due to air leak [25]. Based upon these studies, when initiating NIPPV for acute hypercapnic respiratory failure, full face mask or oronasal mask are the preferred approach. NIPPV should be initiated as soon as possible as delays may increase the likelihood of failure and need for endotracheal intubation [26]. Indications for invasive mechanical ventilation are shown below and include: cardiac/respiratory arrest, altered mental status, inability to clear secretions and protect the airway, non-respiratory organ failure, facial deformity or trauma, high risk of aspiration, recent esophageal surgery, anticipation of prolonged need for mechanical ventilation [4, 27]. Need for emergent intubation is an absolute contra-indication to NIPPV. Altered mental status due to hypercapnia is an exception. These patients should be closely monitored. Improved pH and PaCO₂ within 30 min to 2 h predicts NIPPV success [28, 29]. If there is no improvement in mental status or physiologic variables within this time frame, the patient should be intubated or consider withdrawing NIPPV to oxygen therapy alone. There is high quality evidence that NIPPV for the

treatment of acute hypercapnic respiratory failure in COPD improves important clinical outcomes. A meta-analysis including 14 randomized controlled trials and greater than 700 patients comparing standard therapy to NIPPV plus standard therapy in acute COPD exacerbation concluded that NPPV decreased mortality (11 % vs. 21 %), intubation rate (16 % vs. 33 %) and reduced hospital length of stay and complications related to treatment [30].

Indications for Noninvasive Mechanical Ventilation

At least one of the following:

- Respiratory acidosis (arterial pH < 7.35 and/or PaCO₂ > 6.0 kPa, 45 mmHg)
- Severe dyspnea with clinical signs suggestive of respiratory muscle fatigue, increased work of breathing, or both, such as use of respiratory accessory muscles, paradoxical motion of the abdomen, or retraction of the intercostal spaces

Indications for Invasive Mechanical Ventilation

- Unable to tolerate NIV or NIV failure
- Respiratory or cardiac arrest
- Respiratory pauses with loss of consciousness or gasping for air
- Diminished consciousness, psychomotor agitation inadequately controlled by sedation
- Massive aspiration
- Persistent inability to remove respiratory secretions
- Heart rate, 50 min 21 with loss of alertness
- Severe hemodynamic instability without response to fluids and vasoactive drugs
- Severe ventricular arrhythmias
- Life-threatening hypoxemia in patients unable to tolerate NIV

Evidence Contour

NIPPV Use in Individuals with Do-Not-Intubate Orders

A majority of the randomized controlled trials demonstrating efficacy of NIPPV in acute respiratory failure excluded persons with do-not-intubate (DNI) orders. In clinical practice, NIPPV is routinely used in such individuals. Typically, this requires treatment in a high level care area such as an intensive care unit utilizing resources in persons where this therapy has unclear benefit. Observational studies have concluded however that many individuals with acute respiratory failure and DNI orders do survive hospitalization when treated with NIPPV, particularly in those with a primary diagnosis of COPD or cardiogenic pulmonary edema. Hospital survival rates vary from 35 to 43 % in published studies [31, 32]. One prospective, observational study of 37 patients with acute hypercapnic respiratory failure due to acute exacerbation of COPD, DNI orders, and NIPPV use demonstrated a 1-year survival of 30 % [33].

NIPPV After Extubation

In an unselected patient population, the use of NIPPV after extubation as a rescue therapy for respiratory failure did not prevent the need for re-intubation or reduce mortality [34]. Individuals with high risk of extubation failure, such as those with COPD and hypercapnia during spontaneous breathing trials do benefit from early use of NIPPV after extubation [35–37]. Compared to standard medical therapy, those receiving NIPPV at the time of extubation were less likely to require re-intubation and 90 day survival was greater. NIPPV should be applied routinely and immediately after extubation of COPD patients with hypercapnia. The benefits of NIPPV after extubation or as a weaning strategy have not been replicated in other conditions.

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