

Precipitating Causes and Strategies to Reduce Frequency of Exacerbations

A variety of stimuli may result in the final common pathway of airway inflammation and increased symptoms that are characteristic of COPD exacerbations. Studies suggest that acquiring a new strain of bacteria is associated with increased near-term risk of exacerbation and that bacterial infection/superinfection is involved in over 50% of exacerbations. Viral respiratory infections are present in approximately one-third of COPD exacerbations. In a significant minority of instances (20–35%), no specific precipitant can be identified.

The role of pharmacotherapy in reducing exacerbation frequency is less well studied. Chronic oral glucocorticoids are not recommended for this purpose. Inhaled glucocorticoids reduce the frequency of exacerbations by 25–30% in most analyses. The use of inhaled glucocorticoids should be considered in patients with frequent exacerbations or those who have an asthmatic component, i.e., significant reversibility on pulmonary function testing or marked symptomatic improvement after inhaled bronchodilators. Similar magnitudes of reduction have been reported for anticholinergic and long-acting β -agonist therapy. The influenza vaccine has been shown to reduce exacerbation rates in patients with COPD. As outlined above, daily azithromycin administered to subjects with COPD and an exacerbation history reduces exacerbation frequency.

Patient Assessment An attempt should be made to establish the severity of the exacerbation as well as the severity of preexisting COPD. The more severe either of these two components, the more likely that the patient will require hospital admission. The history should include quantification of the degree of dyspnea by asking about breathlessness during activities of daily living and typical activities for the patient. The patient should be asked about fever; change in character of sputum; any ill contacts; and associated symptoms such as nausea, vomiting, diarrhea, myalgias, and chills. Inquiring about the frequency and severity of prior exacerbations can provide important information.

The physical examination should incorporate an assessment of the degree of distress of the patient. Specific attention should be focused on tachycardia, tachypnea, use of accessory muscles, signs of perioral or peripheral cyanosis, the ability to speak in complete sentences, and the patient's mental status. The chest examination should establish the presence or absence of focal findings, degree of air movement, presence or absence of wheezing, asymmetry in the chest examination (suggesting large airway obstruction or pneumothorax mimicking an exacerbation), and the presence or absence of paradoxical motion of the abdominal wall.

Patients with severe underlying COPD, who are in moderate or severe distress, or those with focal findings should have a chest x-ray. Approximately 25% of x-rays in this clinical situation will be abnormal, with the most frequent findings being pneumonia and congestive heart failure. Patients with advanced COPD, those with a history of hypercarbia, those with mental status changes (confusion, sleepiness), or those in significant distress should have an arterial blood-gas measurement. The presence of hypercarbia, defined as a $P_{CO_2} > 45$ mmHg, has important implications for treatment (discussed below). In contrast to its utility in the management of exacerbations of asthma, measurement of pulmonary function has not been demonstrated to be helpful in the diagnosis or management of exacerbations of COPD.

There are no definitive guidelines concerning the need for inpatient treatment of exacerbations. Patients with respiratory acidosis and hypercarbia, significant hypoxemia, or severe underlying disease or those whose living situation is not conducive to careful observation and the delivery of prescribed treatment should be admitted to the hospital.

ACUTE EXACERBATIONS

Bronchodilators Typically, patients are treated with an inhaled β agonist, often with the addition of an anticholinergic agent. These may be administered separately or together, and the frequency of administration depends on the severity of the exacerbation.

Patients are often treated initially with nebulized therapy, as such treatment is often easier to administer in older patients or to those in respiratory distress. It has been shown, however, that conversion to metered-dose inhalers is effective when accompanied by education and training of patients and staff. This approach has significant economic benefits and also allows an easier transition to outpatient care. The addition of methylxanthines (such as theophylline) to this regimen can be considered, although convincing proof of its efficacy is lacking. If added, serum levels should be monitored in an attempt to minimize toxicity.

Antibiotics Patients with COPD are frequently colonized with potential respiratory pathogens, and it is often difficult to identify conclusively a specific species of bacteria responsible for a particular clinical event. Bacteria frequently implicated in COPD exacerbations include *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*. In addition, *Mycoplasma pneumoniae* or *Chlamydia pneumoniae* are found in 5–10% of exacerbations. The choice of antibiotic should be based on local patterns of antibiotic susceptibility of the above pathogens as well as the patient's clinical condition. Most practitioners treat patients with moderate or severe exacerbations with antibiotics, even in the absence of data implicating a specific pathogen.

Glucocorticoids Among patients admitted to the hospital, the use of glucocorticoids has been demonstrated to reduce the length of stay, hasten recovery, and reduce the chance of subsequent exacerbation or relapse for a period of up to 6 months. One study demonstrated that 2 weeks of glucocorticoid therapy produced benefit indistinguishable from 8 weeks of therapy. The GOLD guidelines recommend 30–40 mg of oral prednisolone or its equivalent for a period of 10–14 days. Hyperglycemia, particularly in patients with preexisting diagnosis of diabetes, is the most frequently reported acute complication of glucocorticoid treatment.

Oxygen Supplemental O_2 should be supplied to keep arterial saturations $\geq 90\%$. Hypoxemic respiratory drive plays a small role in patients with COPD. Studies have demonstrated that in patients with both acute and chronic hypercarbia, the administration of supplemental O_2 does not reduce minute ventilation. It does, in some patients, result in modest increases in arterial P_{CO_2} , chiefly by altering ventilation-perfusion relationships within the lung. This should not deter practitioners from providing the oxygen needed to correct hypoxemia.

Mechanical Ventilatory Support The initiation of noninvasive positive-pressure ventilation (NIPPV) in patients with respiratory failure, defined as $P_{aCO_2} > 45$ mmHg, results in a significant reduction in mortality rate, need for intubation, complications of therapy, and hospital length of stay. Contraindications to NIPPV include cardiovascular instability, impaired mental status or inability to cooperate, copious secretions or the inability to clear secretions, craniofacial abnormalities or trauma precluding effective fitting of mask, extreme obesity, or significant burns.

Invasive (conventional) mechanical ventilation via an endotracheal tube is indicated for patients with severe respiratory distress despite initial therapy, life-threatening hypoxemia, severe hypercarbia and/or acidosis, markedly impaired mental status, respiratory arrest, hemodynamic instability, or other complications. The goal of mechanical ventilation is to correct the aforementioned conditions. Factors to consider during mechanical ventilatory support include the need to provide sufficient expiratory time in patients with severe airflow obstruction and the presence of auto-PEEP (positive end-expiratory pressure), which can result in patients having to generate significant respiratory effort to trigger a breath during a demand mode of ventilation. The mortality rate of patients requiring mechanical ventilatory support is 17–30% for that particular hospitalization. For patients age > 65 admitted to the intensive care unit for treatment, the mortality rate doubles over the next year to 60%, regardless of whether mechanical ventilation was required.