COPD exacerbations: Management

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INTRODUCTION

- Defines an exacerbation of chronic obstructive pulmonary disease (COPD) as "an acute event characterized by a worsening of the patient's respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication" .This generally includes an acute change in one or more of the following cardinal symptoms:

Cough increases in frequency and severity

Sputum production increases in volume and/or

changes character !

Dyspnea increases

TRIAGE TO HOME OR HOSPITAL:

- An important step in the initial evaluation is to determine whether the patient needs hospitalization or can be safely managed at home .

- More than 80 percent of exacerbations of COPD can be managed on an outpatient basis, sometimes after initial treatment in the office or emergency department.

- If the exacerbation appears life-threatening or if there are indications for ventilatory support (eg, hypoxemic or hypercapnic respiratory failure), the patient should be admitted to the intensive care unit as quickly as possible.

Other criteria that might lead to a decision to hospitalizethe patient :

Onset of new signs (eg, cyanosis, altered mental status, peripheral edema)

Marked increase in intensity of symptoms over baseline (eg, new onset resting dyspnea) accompanied by

increased oxygen requirement or signs of respiratory distress

Severe underlying COPD (eg, forced expiratory volume in one second [FEV1] ≤50 percent of predicted)

History of frequent exacerbations or prior hospitalization for exacerbations !

Serious comorbidities including pneumonia, cardiac arrhythmia, heart failure, diabetes mellitus, renal failure, or liver failure

Insufficient home support

HOME OR OFFICE MANAGEMENT OF COPD EXACERBATIONS:

- Home management of COPD exacerbations generally includes intensification of bronchodilator therapy andinitiation of a course of oral glucocorticoids; oral antibiotics are added based on individual characteristics.

○ *Beta adrenergic agonists:*

- Inhaled short-acting beta (adrenergic) agonists (SABA; eg, albuterol, levalbuterol) are the mainstay of therapy for an acute exacerbation of COPD because of their rapid onset of action and efficacy in producing bronchodilation.
- For patients being managed at home, SABAs are usually administered by a metered dose inhaler (MDI), often with a spacer device, or by dry powder inhaler .
- The usual dose for relief of acute symptoms is two inhalations every hour for two to three doses and then every two to four hours based on the patient's response

○ *Muscarinic antagonists:*

- ❖ Ipratropium bromide, an inhaled SAMA (also known as a short-acting anticholinergic agent) is often used in combination with inhaled SABA.
- ❖ The usual dose of ipratropium for an acute exacerbation of COPD is two inhalations by MDI every four to six hours.
- ❖ For patients who have a history of benign prostatic hypertrophy or prior urinary retention, the addition of ipratropium to a long-acting muscarinic antagonist (LAMA; eg, aclidinium, glycopyrrolate, tiotropium,umeclidinium) may increase the risk of acute urinary retention, although data are conflicting.

○ *Oral glucocorticoid therapy:*

- ❖ For outpatients with a COPD exacerbation characterized by breathlessness that interferes with daily activities, systemic glucocorticoid therapy appears to have a small but beneficial effect with a reduction in rate of relapse.

- ❖ Our practice reflects current guidelines, which suggest using a dose that is the equivalent of prednisone 40 mg per day for 5 to 14 days.

- ❖ In addition to a lower rate of relapse, prednisone therapy was associated with decreased dyspnea and a greater improvement in forced expiratory volume in one second (FEV1) on day 10.

- ❖ Patients should be warned of potential adverse effects of systemic glucocorticoids that may require mitigation, particularly hyperglycemia (in patients with diabetes mellitus), fluid retention, and hypertension.

- ***Inhaled glucocorticoids:***

❖ High-dose nebulized budesonide (4 to 8 mg/day) had a similar effect to oral glucocorticoids in patients hospitalized for a COPD exacerbation for change in FEV1 or arterial tension of carbon dioxide (PaCO2), but was slightly inferior for oxygenation improvement.

❖ Use of the high-dose combination inhaler, budesonide-formoterol (320 mcg-9 mcg) 1 inhalation four times daily, resulted in a similar change in FEV1 compared with oral prednisolone 30 mg daily plus inhaled formoterol.

○ *Antimicrobial therapy:*

- ❖ Antibiotic therapy only for those patients who are most likely to have bacterial infection or are most ill.
- ❖ Antibiotics for outpatients with a moderate or severe exacerbation of COPD, which is defined as having at least two of these three symptoms – increased dyspnea, increased sputum volume, or increased sputum purulence.
- ❖ Do not initiate antibiotic therapy in patients whose exacerbation is mild, which we define as having only one of these three symptoms and not requiring hospitalization.

- For patients with a COPD exacerbation during influenza season, screen for influenza infection, with a preference for molecular assays over rapid antigen tests.

- If influenza infection is suspected, initiate empiric antiviral therapy without waiting for laboratory confirmation.

EMERGENCY DEPARTMENT AND HOSPITAL MANAGEMENT:

- For patients who are admitted to the hospital, the severity of the exacerbation is classified based on clinical signs:

No respiratory failure;
Respiratory rate 20 to 30 breaths per minute;
no change in mental status;
Pulse oxygen saturation (SpO2) 88 to 92 percent with Venturi mask 24 to 35 percent inspired oxygen (or equivalent);
no hypercapnia;

- Acute nonlife-threatening respiratory failure – Respiratory rate >30 breaths per minute; use of accessory muscles of respiration; no change in mental status; SpO2 88 to 92 percent with Venturi mask 24 to 35 percent (or equivalent); arterial tension of carbon dioxide (PaCO2) 50 to 60 mmHg or increased over baseline.

- Cute life-threatening respiratory failure – Respiratory rate >30 breaths per minute; use of accessory muscles of respiration; acute change in mental status; requiring fraction of inspired oxygen (FiO2) ≥40 percent to maintain SpO2 88 to 92 percent; PaCO2 increased compared with baseline or >60 mmHg or associated with acidosis (pH ≤7.25).

○ *Monitoring:*

- In-hospital monitoring typically includes frequent assessment of respiratory status (eg respiratory rate and effort, wheezing, pulse oxygen saturation), heart rate and rhythm, blood pressure, and also fluid status.

- Patients who require admission to the intensive care unit (ICU) should have continuous monitoring of vital signs and oxygenation. Arterial blood gas measurement is performed to assess for respiratory acidosis confirm the accuracy of pulse oxygen saturation, and to monitor known hypercapnia.

Supportive and palliative care:

- General measures
- Oxygen therapy
- Ventilatory support
- Palliative care
- Beta adrenergic agonists
- Muscarinic antagonists
- Continuing long-acting bronchodilators
- Systemic glucocorticoids
- Antiviral and antimicrobial agents

General measures

- **Cigarette smoking cessation** – Hospitalization can sometimes provide an opportunity for patients who continue to smoke to move towards cigarette smoking cessation. Nicotine replacement therapy can help reduce symptoms of nicotine withdrawal during hospitalization.

- ***Thromboprophylaxis*** – Hospitalization for exacerbations of COPD increases the risk for deep venous thrombosis and pulmonary embolism .For patients without a risk factor for bleeding who require ICU admission, recommend pharmacologic thromboprophylaxis; for those not requiring ICU admission, suggest pharmacologic thromboprophylaxis. Low molecular weight heparin is generally preferred.

Nutritional support :

- Oral nutritional supplementation may be of benefit for malnourished patients hospitalized with a COPD exacerbation.

Oxygen therapy:

- Administration of supplemental oxygen should target an SpO2 of 88 to 92 percent or an arterial oxygen tension (PaO2) of approximately 60 to 70 mmHg, to minimize the risk of worsening hypercapnia with excess supplemental oxygen

Venturi masks can deliver an FiO2 of 24, 28, 31, 35, 40, or 60 percent.

Nasal cannula can provide flow rates up to 6 L per minute with an associated FiO2 of approximately 40 percent!

simple facemasks can provide an FiO2 up to 55 percent using flow rates of 6 to 10 L per minute.

Non-rebreathing masks with a reservoir, one-way valves, and a tight face seal can deliver an inspired oxygen concentration up to 90 percent, but are generally not needed in this setting.

High-flow nasal cannula (HFNC) provide supplemental oxygen (adjustable FiO2) at a high flow rate (up to 60 L/min that results in a low level of continuous positive airway pressure. The specific indications for HFNC remain unclear.

Ventilatory support

- For patients who fail supportive therapy with oxygen and medications, ventilatory support is necessary

- NIV refers to mechanical ventilation delivered through a noninvasive interface, such as a face mask, nasal mask, orofacial mask.NIV reduces mortality and the intubation rate and is the preferred method of ventilatory support in many patients with an exacerbation of COPD.

- Patients who develop acute respiratory acidosis ($PaCO_2$ >45 mmHg [6 kPa] or pH <7.35) are the subgroup who are most likely to benefit from an initial trial of NIV

- For other patients with nonhypercapnic respiratory failure due to COPD exacerbation, a trial of NIV is also appropriate,

- Typical initial settings include an inspiratory positive airway npressure (IPAP) of 8 to 12 cm H2O and an expiratory pressure (EPAP) of 3 to 5 cm H2O.

- Invasive mechanical ventilation should be administered when patients fail NIV, do not tolerate NIV, or have contraindications to NIV.

Palliative care:

- The goals of palliative care are to prevent and relieve suffering and aid in the end-of-life care of patients with advanced disease.

- The potential outcomes of intubation/mechanical ventilation should be described to help the patient’s decision-making.

- Palliative care consultation can help explore the patient's understanding of their illness and prognosis, assess and manage symptoms (eg, dyspnea, anxiety, panic, depression), discuss the patient's goals of care, place of death preferences, and advance directives, and help implement end-of-life care.

Initial pharmacologic therapy

- **Beta adrenergic agonists**

- all patients with an exacerbation of COPD receive prompt treatment with an inhaled short-acting beta (adrenergic) agonist (SABAs; eg, albuterol, levalbuterol) because of their rapid onset of action and efficacy in producing bronchodilation in COPD

- Typical doses of albuterol in this setting are 2.5 mg by nebulizer or one to two inhalations by MDI with a spacer every one hour for two to three doses and then every two to four hours as needed, guided by the response to therapy.

- Combination therapy with albuterol and ipratropium is clearly superior to albuterol alone in stable COPD, but studies in acute exacerbations are limited .

- Nonetheless, it is common practice to use the combination for COPD exacerbations.

- Subcutaneous injection of SABAs (eg, terbutaline, epinephrine) carries a high risk for inotropic and chronotropic adverse effects, such as arrhythmias or myocardial ischemia, and is virtually never used for COPD exacerbations.

Muscarinic antagonists:

- Combination ipratropium-albuterol soft mist inhaler (SMI) can be used, 1 inhalation, approximately every hour for two to three doses and then every two to four hours as needed, guided by the response to therapy.

- Ipratropium is also available in an MDI that can be used with a spacer, 2 inhalations every 4 to 6 hours.

- However, in stable COPD, the combination of SAMA plus SABA provides superior bronchodilation compared with SABA alone. Thus, this combination is often used to treat COPD exacerbations.

Systemic glucocorticoids:

- For patients requiring emergency department or hospital-based treatment for a COPD exacerbation, recommend a course of systemic glucocorticoids.

- Intravenous glucocorticoids are typically administered to patients who present with a severe exacerbation, who have not responded to oral glucocorticoids at home, who are unable to take oral medication, or who may have impaired absorption due to decreased splanchnic perfusion (eg, patients in shock)

- The optimal dose of systemic glucocorticoids for treating a COPD exacerbation is unknown

- Frequently used regimens range from prednisone 30 to 60 mg, once daily, to methylprednisolone 60 to 125 mg, two to four times daily, depending on the severity of the exacerbation

- The optimal duration of systemic glucocorticoid therapy is not clearly established and often
  depends on the severity of the exacerbation and the observed response to therapy.

- The GOLD guidelines suggest that glucocorticoids (eg, prednisone 30 to 40 mg/day) be given for five days ,while the European Respiratory Society/American Thoracic Society guidelines suggest a course of
  therapy up to 14 days in duration .Thus, a range of 5 to 14 days appears reasonable.

- At the end of the treatment course, glucocorticoid therapy may be discontinued rather than tapered, if the patient has substantially recovered.

- Systemic glucocorticoids, when added to the bronchodilator therapies described above, improve symptoms and lung function, and decrease the length of hospital stay.

- Even short courses of systemic glucocorticoids are associated with an increased risk of harm, such as hyperglycemia, pneumonia, sepsis, venous thromboembolism, and fracture.

Antiviral and antimicrobial agents

- Most clinical practice guidelines recommend antibiotics for patients having a moderate to severe COPD exacerbation that requires hospitalization.

- The optimal antibiotic regimen for the treatment of exacerbations of COPD has not been determined.

- Use a "risk stratification" approach when selecting initial antibiotic therapy, providing a broader antibiotic regimen for patients at risk for resistant organisms.

- Antiviral therapy is recommended for patients with clinical and laboratory evidence of influenza infection who require hospitalization for an exacerbation of COPD.

- Because of the risk of acute bronchoconstriction with inhalation of zanamivir, oseltamivir is preferred unless local resistance patterns suggest a likelihood of oseltamivir-resistant influenza.

Discharge planning

- It is hoped that comprehensive discharge planning will help speed symptom resolution and reduce readmissions for COPD exacerbations.

- However, the optimal components of discharge planning have not been determined, so discharge-related decision-making is largely guided by good medical practice.

TREATMENTS WITHOUT DOCUMENTED BENEFIT:

- Mucoactive agents, methylxanthines, and mechanical techniques to augment sputum clearance have not been shown to confer benefit for patients with a COPD exacerbation.
- Some mucoactive agents may worsen bronchospasm.
- The methylxanthines, aminophylline and theophylline, are considered second-line therapy for exacerbations of COPD.
- While intravenous magnesium has a bronchodilator effect in acute severe exacerbations of asthma, intravenous magnesium does not appear to have a substantial effect in exacerbations of COPD based on limited evidence

- Mechanical techniques to augment sputum clearance, such as directed coughing, chest physiotherapy with percussion and vibration, intermittent positive pressure breathing, and postural drainage, have not been shown to be beneficial in COPD and may provoke bronchoconstriction.