Chronic Obstructive Pulmonary Disease

Chronic obstructive pulmonary disease (COPD) is a progressive disease characterized by airflow limitation that is not fully reversible. It is caused by exposure to noxious particles or gases, most commonly cigarette smoke. It is a major cause of morbidity and mortality and a leading cause of disability in the United States. Previous definitions of COPD included chronic bronchitis and emphysema.
A suspected diagnosis of COPD should be based on the patient's symptoms and history of exposure to risk factors. **Spirometry** is required to confirm the diagnosis, using the ratio of forced expiratory volume in 1 second (FEV1) to forced vital capacity (FVC).

In advanced COPD, airflow obstruction, damaged bronchioles and alveoli, and pulmonary vascular abnormalities lead to impaired gas exchange. This results in **hypoxemia** and eventually **hypercapnia**. Hypoxemia is initially present only during exercise but occurs at rest as the disease progresses. Pulmonary hypertension develops late in the course of COPD, usually after the development of severe hypoxemia. It is the most common cardiovascular complication of COPD and can result in **cor pulmonale,** or right-sided heart failure.

TREATMENT

Desired Outcomes

The goals of COPD management include: (a) smoking cessation, (b) reducing symptoms, (c) improving exercise tolerance, (d) minimizing the rate of decline in lung function, (e) maintaining or improving the quality of life, (f) preventing and treating exacerbations, and (g) limiting complications.

General Approach to Treatment

An integrated approach of health maintenance (e.g., smoking cessation), drug therapy, and supplemental therapy (e.g., oxygen and pulmonary rehabilitation) should be used in a stepwise manner. Symptom severity and risk of COPD exacerbations can be used to guide therapy decisions.

Non pharmacologic Therapy

1. ***Smoking Cessation***

Smoking cessation slows the rate of decline in pulmonary function in patients with COPD. Stopping smoking can also reduce cough and sputum production and decrease airway reactivity. Therefore, it is a critical part of any treatment plan for patients with COPD.

2. ***Surgery***

Bullectomy, lung volume reduction surgery, and lung transplantation are surgical options for very severe COPD.

Pharmacologic Therapy of Stable COPD

Bronchodilators

Value

Bronchodilators are the mainstay of treatment for symptomatic COPD. They reduce symptoms and improve exercise tolerance and quality of life. They can be used as needed for symptoms or on a scheduled basis to prevent or reduce symptoms. Bronchodilator drugs commonly used in COPD include β2-agonists, anticholinergics, and theophylline.

Selection: long versus short

Long-acting bronchodilators are more expensive than short-acting bronchodilators but are **superior** on important clinical outcomes, including frequency of exacerbations, degree of dyspnea, and health related quality of life. Monotherapy with long-acting bronchodilators is preferred; combination therapy may be appropriate in symptomatic patients with an FEV1 less than 60% predicted, although it is unclear when combination therapy provides added benefit.

Most COPD patients need continuous bronchodilator therapy on a scheduled basis every day. For these patients, short acting β2-agonists are **inconvenient** because of the need for frequent dosing. In addition, short-acting β2-agonists have been associated with a slight, but statistically significant, **loss of effectiveness** when used regularly longer than 3 months (tachyphylaxis). Patients treated with long-acting β2-agonists should also have a short-acting β2-agonist such as albuterol available for as-needed use ("rescue" medication).

Anticholinergics Ipratropium and tiotropium are inhaled anticholinergic medications commonly used for COPD. They produce bronchodilation by competitively blocking muscarinic receptors in bronchial smooth muscle. They may also decrease mucus

secretion, although this effect is variable. Tiotropium dissociates from receptors extremely slowly, resulting in a half-life longer than 36 hours, allowing for once-daily dosing. Ipratropium has an elimination halflife of about 2 hours, necessitating dosing every 6 to 8 hours.

Tiotropium significantly decreases exacerbations and related hospitalizations, reduces symptoms, and improves quality of life compared with placebo or ipratropium. Tiotropium may be **more effective** than salmeterol for reducing exacerbations in patients with moderate to very severe COPD.

Patients using tiotropium as maintenance therapy should be prescribed albuterol as their rescue therapy. The combination of ipratropium and tiotropium is **not recommended** because of the risks of excessive anticholinergic effects.

Side effects

Inhaled anticholinergics are well tolerated with the most common adverse effect being dry mouth. Occasional metallic taste has also been reported with ipratropium. Other anticholinergic adverse effects include constipation, tachycardia, blurred vision, and precipitation of narrow angle glaucoma symptoms. Urinary retention could be a problem, especially for those with concurrent bladder outlet obstruction.

Methylxanthines

Place in treatment

Theophylline is a nonspecific phosphodiesterase inhibitor that increases intracellular cAMP within airway smooth muscle resulting in bronchodilation. It has a modest bronchodilator effect in patients with COPD, and its use is limited due to a narrow therapeutic index, multiple drug interactions, and adverse effects. Theophylline should be reserved for patients who cannot use inhaled medications or who remain symptomatic despite appropriate use of inhaled bronchodilators.

Adverse effects and monitoring

Theophylline's bronchodilatory effects depend on achieving adequate serum concentrations, and therapeutic drug monitoring is needed to optimize therapy because of wide interpatient variability. The most common adverse effects include heartburn, restlessness, insomnia, irritability, tachycardia, and tremor. Dose-related adverse effects include nausea and vomiting, seizures, and arrhythmias. Smoking leads to increased clearance and subsequently decreased plasma levels of the drug. Because most patients with COPD are current or past smokers, it is important to assess current

tobacco use and adjust the theophylline dose as required based on altered plasma theophylline levels if tobacco use changes.

Corticosteroids

Role

Inhaled corticosteroids improve symptoms, lung function, quality of life, and exacerbation rates in patients with an FEV1 less than 60%.They do not appear to modify the rate of decline in pulmonary function or improve mortality.

Indication

Inhaled corticosteroids are recommended for patients with severe and very severe COPD and frequent exacerbations that are not adequately controlled by long-acting bronchodilators.

Side effects and comparison with combination therapy

Monotherapy with inhaled corticosteroids is less effective than when combined with a long-acting β2-agonist and is therefore not recommended. Combination inhaler devices (Advair [fluticasone/salmeterol], Symbicort [budesonide/ formoterol], and Dulera [mometasone/formoterol]) are convenient and ensure patients receive both medications.

Upon discontinuation of inhaled corticosteroids, some patients may experience deterioration in lung function and an increase in dyspnea and mild exacerbations. Long-term use of oral corticosteroids should be avoided due to an unfavorable risk-to-benefit ratio. The steroid myopathy that can result from long-term use of oral corticosteroids weakens muscles, further decreasing the respiratory drive in patients with advanced disease.

Combination Therapy

Indication

For patients who remain symptomatic on monotherapy, a combination of bronchodilators can be used. Combining albuterol plus ipratropium, a long-acting β2-agonist plus theophylline, or a long-acting β2-agonist plus tiotropium, produces a greater change in spirometry than either drug alone. Administering a long-acting β2-agonist plus ipratropium leads to fewer exacerbations than either drug alone. Some

studies have found an increase in adverse events without added benefit when combinations of bronchodilators are used.

Example combination

Triple therapy with inhaled corticosteroid, long-acting β2- agonist, and tiotropium is commonly used. Triple therapy appears to improve lung function and quality of life but may not further reduce exacerbations or dyspnea. Further studies are needed to determine if the benefits of triple therapy outweigh the increased risk of adverse effects and added cost.

Potential benefits and risks of any combination therapy should be considered on a case-by-case basis. Patients should be monitored closely and therapy should be changed if the combination is not more effective.

Immunizations

Serious illness and death in COPD patients can be reduced by about 50% with annual influenza vaccination. The optimal time for vaccination is usually from early October through mid-November. A onetime pneumococcal polysaccharide vaccine should be administered to all adults with COPD.

Patients older than 65 years should be revaccinated if it has been more than 5 years since initial vaccination and they were younger than 65 years at the time.

Drugs to be reviewed in BNF

1. Salbutamol
2. Prednisolone
3. montilukast
4. levofloxacin
5. clarithromycin
6. amoxicillin