COPD Pharmacology

University of Hawai‘i Hilo Pre-Nursing Program
NURS 203 – General Pharmacology
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Objectives

• Understand the epidemiology and pathophysiology of COPD
• Understand the pharmacologic reasoning behind first choice medications for COPD vs asthma
• Know the general pharmacologic characteristics of medications used to treat COPD
Definition

“Chronic Obstructive Pulmonary Disease (COPD), a common preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients.”

- The GOLD Report
Epidemiology and Etiology

- Epidemiology
  - Difficult to determine
    - Leading cause of morbidity and mortality worldwide
    - 4th leading cause of death in U.S.
    - Lack of standardization
    - Under diagnosed
    - Under reported

- Etiology
  - Smoking
  - Pollution
  - Occupational exposures
  - Age
  - Alpha 1-antitrypsin deficiency
  - Airway hyper-responsiveness
  - Lung growth and development
Additional risk factors

• Socioeconomic status
  • Poverty - Exposures, pollution, crowding, poor nutrition, infections, or other

• Asthma/bronchial hyper-reactivity
  • Asthmatics at higher risk of contracting COPD after adjusting for smoking (12 fold)
  • Asthmatics more likely to present with irreversible airflow limitation
  • BHR second only to smoking in COPD risk factors
  • Excess loss in FEV1
  • Smoking vs asthmatics – similar reduced lung function

• Chronic bronchitis
  • May or may not be associated with lung function decline
  • Smokers with CB are even more likely to contract COPD

• Infections
  • Exacerbations & Development
Symptoms of COPD

- Defining symptoms
  - Chronic and progressive cough
  - Dyspnea
  - Sputum production
- Some patients may experience other non-specific symptoms
  - Wheezing
  - Chest tightness
  - Weight loss
  - Fatigue
  - Anxiety and depression
Pathophysiology

- Changes in tissue
  - Airways
  - Parenchyma
  - Pulmonary vasculature
- Airway remodeling
  - Repeated injury and repair
- Idiopathic inflammation in non-exposed patients
Airflow limitation and air trapping

- Airflow limitation
  - Caused by
    - Inflammation
    - Fibrosis
    - Mucus secretion

- Air trapping
  - Decrease in ability to inspire created by hyperinflation due to air trapped in the lungs
  - Leads to
    - Decrease in functional residual capacity
    - SOB
  - Reduced by the use of bronchodilators
Gas exchange & mucus hyper-secretion

- Gas exchange
  - Reduction in gas exchange
    - Produces
      - Hypoxemia
      - Hypercapnia

- Mucus hyper-secretion
  - Mucus producing goblet cells
    - Increased number
    - Increased size
Stable/Chronic COPD—Short-acting bronchodilators

**Beta$_2$-agonists**
- Fenoterol, Levalbuterol, Albuterol, terbutaline
- MDI, DPI, nebulizer solution, oral, & injection
- Rapid onset (5 mins) of effects & wears off in 4-6 hours
- ADR’s –
  - Tachycardia, arrhythmia, tremor, hypokalemia

**Anticholinergics**
- Ipratropium bromide, oxitropium bromide
- MDI
- Onset 15-20 mins & effects may last up to 9 hours
- ADR’s
  - Dry mouth, bitter (metallic) taste, nausea
### Stable/Chronic COPD

**Long-acting bronchodilators**

#### Long acting Beta2 agonists (LABA)
- Salmeterol, formoterol, arformoterol, indacaterol, tolbuterol, vilanterol
- Dry powder inhalers, MDI, transdermal, and nebulizer solutions
- Dosed Q12 hrs or Q24 hrs
- ADRs
  - Headache, neuromuscular and skeletal pain, HTN, dizziness, rash

#### Long-acting Anticholinergics
- Tiotropium, aclidinium, glycopyrronium, umeclidinium
- Inhaled dry powder inhaler (Handihaler with capsules), SMI
- Onset 30 mins, duration 12 to greater than 24 hours
- Dosed daily
- ADRs
  - Dry mouth, constipation, urinary retention, tachycardia, blurred vision, glaucoma
Stable/Chronic COPD—Short-acting & Long-acting bronchodilators

- Improve FEV$_1$, improve emptying of lungs, reduce hyperinflation at rest and during exercise
- May be given scheduled or as needed
- Drug selection may determined by comorbid conditions, individual patient response, side effects, or convenience/cost
- Inhaled preferred over oral
- Recommended in all COPD patient groups
- Combinations provide better efficacy when used in patients with no symptom improvements on monotherapies
Stable/Chronic COPD - Methylxanthines

- Theophylline and aminophylline
  - Due to low efficacy and low tolerability, generally no longer recommended – used for patients who or are not able to coordinate inhaled therapy or the unavailability / affordability of inhaled therapy
  - Oral and parenteral
- 200 mg BID, titrated to target dose every 3-5 days to achieve 8-15 mcg/ml
- Requires serum concentrations 1-2 times per year once steady state is achieved
  - Toxicity may be seen in therapeutic ranges
- Factors that decrease clearance – age, pneumonia, liver dysfunction, ventricular failure, drugs (cimetidine, macrolide abx, & fluoroquinolone abx)
- ADRs
  - Gastrointestinal – dyspepsia, nausea, vomiting, diarrhea
  - Cardiovascular - tachycardia
  - CNS – headache and dizziness
Stable/Chronic COPD – PDE-4 inhibitors

- Roflumilast – Reduce inflammation, no direct bronchodilator effects, but lowers FEV₁ when combined with other medications and should always be used with a long-acting bronchodilator
  - Oral (pill)
  - Q 24 hour dosing
  - ADR’s
    - Nausea, reduced appetite, abdominal pain, diarrhea, weight loss and headache
  - Do not use with theophylline
## Stable/Chronic COPD - Corticosteroids

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<tr>
<th>Inhaled</th>
<th>Oral</th>
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<tr>
<td>- Beclomethasone, budesonide, fluticasone</td>
<td>- Prednisone &amp; methyl-prednisolone</td>
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<td>- Recommended in severe or very severe COPD in combination with long-acting bronchodilator(s) alone or with PDE4 inhibitors</td>
<td>- Oral (pill)</td>
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<td>- DPI, MDI, &amp; solution for nebulizer</td>
<td>- Not recommended in the treatment of chronic stable COPD</td>
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<td>- Improved symptoms and quality of life</td>
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<td>- ADRs</td>
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<td>- Locally – well tolerated (hoarseness, sore throat, candidiasis), may increase risk of pneumonia and fracture</td>
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COPD - Exacerbation

- Definition
  - “an acute event characterized by a worsening of the patient’s respiratory symptoms that is beyond normal day-to-day variations leads to a change in medication”

- Differentiation between daily variations and exacerbation is important

- Prognosis is poor
  - 5 year mortality rate of 50%

- Successful prevention
  - Understand how to use medications
Questions