COPD PEARLS

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Objectives

• Discuss new and emerging therapies for the management of COPD
• Identify key areas for pharmacist involvement in COPD management
• Identify key monitoring parameters and medication related adverse effects associated with COPD management
EPIDEMIOLOGY
Overview of who gets COPD
U.S. Deaths—2010

1. Heart Disease—597,689
2. Cancer—574,743
3. COPD—138,080
4. Stroke—129,476
5. Unintentional Injuries—120,859
6. Alzheimer’s Disease—83,494
7. Diabetes Mellitus—69,071
8. Kidney Disease—50,476
9. Influenza & Pneumonia—50,097
10. Suicide—38,364

Risk Factors
FEV₁ (% of value at age 25)

Age (years)

Never smoked or not susceptible to smoke

Smoked regularly and susceptible to its effects

Stopped at 45

Stopped at 65

Disability

Death

DIAGNOSIS & CLASSIFICATION
It’s more than spirometry
Clinical Presentation

• Progressive dyspnea
• Chronic productive (usually) cough
• Exposure to risk factors
A 65-year-old male was recently diagnosed with COPD. Spirometry shows a prebronchodilator FEV1 70% and postbronchodilator FEV1 74% predicted. His FEV1/FVC is 62%. After completing a questionnaire regarding his symptoms (dyspnea), his MRC grade is figured to be 2. He has had 1 COPD exacerbation in the past year. Which is the most appropriate patient group classification for him?

A. Patient group A
B. Patient group B
C. Patient group C
D. Patient group D
Spirometry’s New(ish) Role

- Required for official diagnosis
  - FEV1/FVC < 0.7
- Used in conjunction with disease impact and future risk of disease progression
- Therapy no longer based on spirometry alone
  - FEV1 poor descriptor of disease status
    - Low correlation between health-related quality of life and FEV1
Classification of Airflow Obstruction Severity

- **Mild (GOLD I):**
  - FEV1/FVC < 70%
  - FEV1 ≥ 80%

- **Moderate (GOLD II):**
  - FEV1/FVC < 70%
  - 50% < FEV1 < 80%

- **Severe (GOLD III):**
  - FEV1/FVC < 70%
  - 30% < FEV1 < 50%

- **Very Severe (GOLD IV):**
  - FEV1/FVC < 70%
  - FEV1 < 30%

Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Vancouver (WA): Global Initiative for Chronic Obstructive Lung Disease (GOLD); 2014
Evaluation of Dyspnea Severity

• Medical Research Council (mMRC) scale
  • Categorized dyspnea grades
• COPD Assessment Test (CAT)
  • Assesses effect of COPD on overall well-being
• COPD Control Questionnaire (CCQ)
  • Easy to use, but validity still being evaluated
Assessment Classification

<table>
<thead>
<tr>
<th>Group</th>
<th>Descriptive</th>
<th>Spirometry Classification</th>
<th>Exacerbations per Year</th>
<th>mMRC</th>
<th>CAT</th>
</tr>
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<tbody>
<tr>
<td>A</td>
<td>Low Risk, Less Symptoms</td>
<td>GOLD 1-2</td>
<td>1</td>
<td>0-1</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>B</td>
<td>Low Risk, More Symptoms</td>
<td>GOLD 1-2</td>
<td>1</td>
<td>2</td>
<td>≥ 10</td>
</tr>
<tr>
<td>C</td>
<td>High Risk, Less Symptoms</td>
<td>GOLD 3-4</td>
<td>≥ 2</td>
<td>0-1</td>
<td>&lt; 10</td>
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<tr>
<td>D</td>
<td>High Risk, More Symptoms</td>
<td>GOLD 3-4</td>
<td>≥ 2</td>
<td>2</td>
<td>≥ 10</td>
</tr>
</tbody>
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CAT = COPD Assessment Test; mMRC = Modified Medical Research Council (dyspnea scale)
TREATMENT

Maintenance Therapy
Smoking Cessation

• Most Important Intervention!!!!

• Ability to influence natural history of COPD
  • NO MEDS DO THIS

• MOST beneficial in early stages
  • Beneficial at ANY stage
Optimization of Therapy

- Ensure patients get the meds they need
  - 60-70% are not prescribed maintenance medication
  - 5-7% SABA only
- Things to focus on:
  - Bronchodilator therapy
  - Symptom control
  - Prevention of exacerbations
- Consider individual factors
  - Inhaler technique, concomitant meds, comorbidities…

A 55-year-old male reports a persistent shortness of breath, cough and sputum production that has gradually worsened during the past year. His CAT score is 12. His spirometry showed FEV1 of 65% predicted and an FEV1/FVC of 65% after bronchodilator. No COPD exacerbations have been reported in the past year. Which medication(s) would be most appropriate to initiate?

A. Aclidinium bromide DPI
B. Fluticasone HFA
C. Tiotropium DPI
D. Salmeterol DPI
## Stable COPD Maintenance Pharmacotherapy

### GOLD Recommendations

<table>
<thead>
<tr>
<th>Group</th>
<th>First Line</th>
<th>Second Line</th>
<th>Alternative</th>
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<tbody>
<tr>
<td>A</td>
<td>SABA or SAAC (PRN use)</td>
<td>LABA alone</td>
<td>Theophylline</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LAAC alone</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>SABA + SAAC</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>LABA or LAAC</td>
<td>LABA + LAAC</td>
<td>SABA +/or SAAC Theophylline</td>
</tr>
<tr>
<td>C</td>
<td>ICS + LABA or LAAC</td>
<td>LABA + LAAC</td>
<td>SABA +/or SAAC Theophylline</td>
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<td></td>
<td></td>
<td>LAAC + PDE-4 inhibitor</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>LABA + PDE-4 inhibitor</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>ICS + LABA and/or LAAC</td>
<td>LABA + LAAC</td>
<td>SABA +/or SAAC Carbocysteine Theophylline</td>
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<td></td>
<td>LABA + LAAC + ICS</td>
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<tr>
<td></td>
<td></td>
<td>LAAC + PDE-4 inhibitor</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>LABA + ICS + PDE-4 Inhibitor</td>
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SABA = short-acting beta agonist; SAAC = short-acting anitcholinergic; LABA = long-acting beta agonist; LAAC = long-acting anitcholinergic; ICS = inhaled corticosteroids; PDE-4 = phosphodiesterase-4; GOLD 2014
Single Ingredient Therapeutic Options: Inhaled Bronchodilators

B₂ Agonists

- Short-Acting
  - Albuterol; HFA, NEB
  - Levalbuterol; HFA, NEB

- Long-Acting
  - formoterol; DPI, NEB
  - salmeterol; DPI
  - arformoterol; NEB
  - indacaterol; DPI
  - Olodaterol; RESP

Anticholinergic

- Short-Acting
  - Ipratropium; HFA, NEB

- Long-Acting
  - tiotropium; DPI
  - aclidinium; DPI

HFA = HFA metered dose inhaler; DPI = dry powder inhaler; NEB = nebulizer; RESP = Respimat inhaler
Single Ingredient Therapeutic Options: Inhaled Corticosteroids

- Beclomethasone; MDI, DPI
- Budesonide; DPI
- Fluticasone; MDI, DPI

HFA = HFA metered dose inhaler; DPI = dry powder inhaler; NEB = nebulizer; RESP = Respimat inhaler
Combination Therapeutic Options:

**SABA/SAAC**
- Albuterol / Ipratropium
  - RESP, NEB

**LABA/ICS**
- Formoterol / Budesonide
  - HFA
- Salmeterol / Fluticasone
  - DPI, HFA
- Formoterol / Mometasone
  - HFA
- Vilanterol / Fluticasone
  - DPI

**LABA/LAAC**
- Vilanterol / Umeclidinium
  - DPI

HFA = HFA metered dose inhaler; DPI = dry powder inhaler; NEB = nebulizer; RESP = Respimat inhaler
Oral Therapeutic Options

- Methylxanthines
  - Aminophylline
  - Theophylline

- Phosphodiesterase Inhibitor
  - Roflumilast
New Inhaled Products

- **Tudorza®** (aclidinium bromide)
  - Twice daily dosing
  - Simple administration technique
  - AWP $153.64 (one inhaler)

- **Breo Ellipta®** (fluticasone/vilanterol)
  - Once daily dosing
  - AWP $103.10 (one inhaler)

- **Anoro Ellipta®** (umeclidinium/vilanterol)
  - Once daily dosing
  - AWP $337.14 (one inhaler)

- **Combivent Respimat®**
  - No longer MDI
  - AWP $334.76 (one inhaler)

Tudorza Pressair®

1. Remove Cap
2. Push and release green button
3. Check control window for green
4. Breathe out completely (away from device)
5. With closed lips around device use a quick, deep breath
6. Hold breath
7. Breathe out from nose
8. Control window (red)
Breo Ellipta®

1. Packaged in a foil tray
2. Check counter
3. Open cover (audible click)
4. Breathe out away from device
5. Inhale with one long, steady, deep breath
6. DO NOT COVER AIR VENT
7. Hold breath
8. Breathe out slowly and gently
9. Rinse mouth and spit
Anoro Ellipta®

- Same technique as Breo Ellipta®
- No rinse/spit after inhalation
Combivent Respimat®

Cartridge installation
1. Pull off clear base to install cartridge (base will be visible)
2. Discard date is 3 months from cartridge installation
3. Replace clear base

Priming
1. Turn clear base in direction of arrows (click)
2. With orange cap open, press dose release button
3. Repeat previous steps until visible spray
4. Repeat step 1→2 a total of 3 times

Dose
1. Activate dose
2. Breathe out slowly away from device
3. While breathing in slowly and deeply, press dose-release button and continue to breathe in slowly
4. Hold breath
Adverse Effects

- Beta agonists
  - Arrhythmia
  - Tremor
  - Hypokalemia
- Antimuscarinics
  - Dry mouth
  - Metallic taste
  - Cardiac effects
- Glucocorticoids (inhaled)
  - Local infection
  - Cough, hoarseness
  - Skin bruising
  - Pneumonia
Inhaled Corticosteroids & Pneumonia

Cochrane Review

• 43 studies including more than 30,000 patients
• Compared each ICS against control
• Indirect comparison of budesonide and fluticasone
• Results:
  • Fluticasone and budesonide can increase “serious” pneumonias
  • No increased risk of mortality compared to non-ICS therapy
  • Fluticasone associated with higher risk of any pneumonia

Prophylactic Antibiotics

Cochrane Review

- Seven RCTs involving 3170 patients
  - Azithromycin, erythromycin, clarithromycin & moxifloxacin
- Continuous daily antibiotics reduced exacerbation frequency
  - NNT = 8
- Limited effect on death, hospitalization, or loss of lung function
- Drawbacks
  - Antibiotic resistance
  - Permanent hearing loss
  - QTc prolongation

Herath SC, Poole P. Prophylactic antibiotic therapy for chronic obstructive pulmonary disease (COPD). Cochrane Database of Systematic Reviews 2013, Issue 11
Beta Blockers and COPD

Cochrane Review

• Assessed the effect of cardioselective beta-blockers on respiratory function of patients with COPD
• 22 trials analyzed
• Results:
  • No changes in FEV1 or respiratory symptoms compared to placebo
  • No effect on treatment response to beta agonists

Etminan, et al.

• Systematic review assessing beta-blocker use and COPD mortality
• Relative risk of COPD related mortality with beta-blocker use was 0.69 (95% CI: 0.62-0.78)
TREATMENT

Acute Exacerbation Therapy
A 60-year-old man with COPD presents with a 3-day history of worsening SOB and cough. He complains of increased sputum when he coughs, which is mostly clear. In addition to bronchodilator therapy, which of the following would be appropriate?

A. Burst dose of oral corticosteroid for 14 days
B. Burst dose of oral corticosteroid for 5 days
C. Burst dose of oral corticosteroid for 10 days and antibiotic therapy
D. Antibiotic therapy alone should be sufficient
Oral Corticosteroids—Less is More

• Previous recommendation 10-14 day duration
• REDUCE trial
  • Compared 5-day course to 14-day course of steroids
  • 5-day therapy associated with shorter hospital stay
  • No difference in exacerbation rate
• Observational data
  • Low-dose corticosteroids as good as high-dose in hospitalized and ICU patients with COPD in terms of exacerbations
  • Low-dose associated with shorter ICU and hospital length of stay

Antibiotics Role

- Use remains controversial
- Best evidence supporting use in exacerbations when clinical signs of bacterial infection exist
- Antibiotics should be given only if patients have:
  - All 3 cardinal symptoms (dyspnea, sputum volume & sputum purulence)
  - 2 cardinal symptoms with one being increased purulence
  - Mechanical ventilation

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COMORBIDITIES
A respiratory illness with systemic complications
Assessment of Comorbidities

Occur in any stage of disease and influence mortality and hospitalizations independently:

- Cardiovascular disease (CVD)
- Osteoporosis
- Depression
- Skeletal muscle dysfunction
- Metabolic syndrome
- Lung cancer
CVD

• Heart failure
  • COPD shown to be a predictor of mortality in HF with 5-year survival as low as 31% compared to 71% in those without the comorbidity

• Arrhythmias
  • Afib has been shown to be an independent predictor of increased mortality and QOL

• Interventions to reduce CV complications
  • Smoking cessation
  • Effective management of COPD
  • Beta-blocker therapy
  • Statins (In regards to CV risk reduction)
  • ACE/ARB therapy

Sekine Y et al. COPD may increase the incidence of refractory supraventricular arrhythmias following pulmonary resection for non-small cell lung cancer. Chest 1002;120:1783-90
Osteoporosis

- Often associated with decreased BMI
- Prevalence between 4% and 59%
- Inhaled corticosteroid debate
  - Variable results for inhaled corticosteroids in regards to bone mass
  - Epidemiological evidence demonstrating association with fractures
- Interventions
  - Calcium and vitamin D with or without diagnosed osteoporosis
  - Bisphosphonate with reduced BMD
Anxiety and Depression

- Generalized anxiety disorder in patients with COPD ranges between 10% and 33%
- Panic attacks range from 8% to 67%
- Depression in COPD patients ranges from 6% to 60%
  - Thought to be a predictor of mortality
  - Correlated with HRQoL
- Successful management of psychological disorders is key to successful management of COPD
REVIEW QUESTIONS
A 60 yo male reports persistent shortness of breath, cough and sputum production that has gradually worsened over the last few months. His COPD CAT score is 11. His medications currently consist of albuterol HFA 2 puffs multiple times daily for shortness of breath. Current spirometry shows FEV1 70% and FEV1/FVC of 65%. He reports no COPD exacerbation in the past year. Which is the best medication to initiate?

A. Beclamethasone MDI  
B. Fluticasone plus salmeterol MDI  
C. Tiotropium DPI  
D. Umeclidinium and vilanterol DPI
Which of the following COPD treatment options provide dual bronchodilator therapy?

A. Anoro Ellipta®
B. Breo Ellipta®
C. Spiriva®
D. Symbicort®
The following patients would require antibiotics when treating an acute exacerbation of COPD, EXCEPT:

A. A patient with increased dyspnea, increased sputum volume, and increased sputum purulence
B. A patient with increased dyspnea, increased sputum purulence, and no change in sputum volume
C. A patient with increased dyspnea, increased sputum volume, and no change in sputum purulence
D. A patient with increased dyspnea with an oxygen saturation requiring mechanical ventilation