Updates in Chronic Obstructive Pulmonary Disease Maintenance Therapy

Sarah Petite, Pharm.D., BCPS
Assistant Professor of Pharmacy Practice
University of Toledo College of Pharmacy and Pharmaceutical Sciences
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Learning Objectives

• Review current guideline recommendations for chronic obstructive pulmonary disease (COPD) management

• Analyze current literature evaluating various bronchodilator treatment options for COPD

• Apply literature to specific COPD patient cases in clinical practice
Case

• JR is a 64 YOM seen at an ambulatory care family medicine clinic. He reports increased shortness of breath, sputum production and sputum color change. He is diagnosed with a COPD exacerbation. Last exacerbation was 6 months ago

• PMH: COPD (diagnosed 1 year ago, spirometry unknown)

• Home medications: Albuterol/ipratropium inhaler prn

• COPD Assessment Test Score: 14
What COPD maintenance medication therapy is appropriate for JR?
GOLD 2017 Guidelines

- Released January 2017
- Last update 2011
- Additional reports yearly from January 2013

GOLD 2017 Guideline Revisions

- Treatment Categories
- First Line Therapy Options
- Second Line Therapy Options

Diagnosis

- Evaluate symptoms and risk factors
- Spirometry assessment to confirm diagnosis
  - Post-bronchodilator FEV$_1$/FVC < 0.7
- Airflow limitation severity

<table>
<thead>
<tr>
<th>Grade</th>
<th>Classification</th>
<th>Spirometry</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOLD 1</td>
<td>Mild</td>
<td>FEV$_1$ ≥ 80% predicted</td>
</tr>
<tr>
<td>GOLD 2</td>
<td>Moderate</td>
<td>50% ≤ FEV$_1$ &lt; 80% predicted</td>
</tr>
<tr>
<td>GOLD 3</td>
<td>Severe</td>
<td>30% ≤ FEV$_1$ &lt; 50% predicted</td>
</tr>
<tr>
<td>GOLD 4</td>
<td>Very Severe</td>
<td>FEV$_1$ &lt; 30% predicted</td>
</tr>
</tbody>
</table>

FEV$_1$, Forced Expiratory Volume over 1 second
FVC, Forced Vital Capacity

Symptom Assessment

- Modified Medical Research Council (mMRC) dyspnea scale

- Complete symptom assessment recommended
  - St. George’s Respiratory Questionnaire (SGRQ)
  - COPD Assessment Test (CAT)

2011 ABCD Assessment Tool

Exacerbation History

- ≥ 2 OR ≥ 1 hospitalization
- 0-1 AND no hospitalizations

Symptoms

- mMRC 0-1 CAT < 10
- mMRC ≥ 2 CAT ≥ 10

Refined ABCD Assessment Tool

Exacerbation History

≥ 2 OR
≥ 1 hospitalization

0-1 AND
no hospitalizations

Symptoms

mMRC 0-1
CAT < 10

mMRC ≥ 2
CAT ≥ 10

Why Revise the Tool?

• Accuracy of pulmonary function tests
  ▫ Airflow limitation used to classify 77% Group C and D
  ▫ Symptomatic patients = worse prognosis
    • Group B ↑ mortality and hospital admissions vs. Group C

• Spirometry use inconsistent in clinical practice
  ▫ 30%-59% of patients undergo assessment

Han MK, et al. CHEST 2007;132:403-409
Lee TA, et al. CHEST 2006;129:1509-1515
Soriano JB, et al. CHEST 2013;143:694-702
## Pharmacologic Options

<table>
<thead>
<tr>
<th>Medication Class</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short-acting bronchodilators</td>
<td></td>
</tr>
<tr>
<td>• Short-acting beta$_2$-agonist</td>
<td>Albuterol, Ipratropium</td>
</tr>
<tr>
<td>• Short-acting muscarinic antagonist</td>
<td></td>
</tr>
<tr>
<td>Long-acting bronchodilators</td>
<td></td>
</tr>
<tr>
<td>• Long-acting muscarinic antagonist (LAMA)</td>
<td>Tiotropium, Umeclidinium, Glycopyrrolate</td>
</tr>
<tr>
<td>• Long-acting beta$_2$-agonist (LABA)</td>
<td>Salmeterol, Indacaterol, Vilanterol</td>
</tr>
<tr>
<td>Inhaled corticosteroids (ICS)</td>
<td>Fluticasone</td>
</tr>
<tr>
<td>Combination Products</td>
<td></td>
</tr>
<tr>
<td>• LABA/ICS</td>
<td>Salmeterol/Fluticasone</td>
</tr>
<tr>
<td>• LAMA/LABA</td>
<td>Umeclidinium/Vilanterol, Glycopyrrolate/Indacaterol</td>
</tr>
<tr>
<td>Oral phosphodiesterase enzyme inhibitors</td>
<td>Roflumilast, Theophylline</td>
</tr>
</tbody>
</table>

First Line Therapy Recommendations

<table>
<thead>
<tr>
<th>Group</th>
<th>2017 GOLD</th>
<th>2016 GOLD Update</th>
</tr>
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<tbody>
<tr>
<td>A</td>
<td>Bronchodilator (short or long)</td>
<td>Short-acting bronchodilator</td>
</tr>
<tr>
<td>B</td>
<td>Long-acting bronchodilator</td>
<td>Long-acting bronchodilator</td>
</tr>
<tr>
<td>C</td>
<td>LAMA</td>
<td>LABA/ICS OR LAMA</td>
</tr>
<tr>
<td>D</td>
<td>LAMA/LABA preferred</td>
<td>LABA/ICS AND/OR LAMA</td>
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### Group C: LAMA Evidence

<table>
<thead>
<tr>
<th>Study</th>
<th>Interventions</th>
<th>Outcomes (LAMA vs. LABA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vogelmeier, et al</td>
<td>Tiotropium (n=3707) Salmeterol (n=3669)</td>
<td>Time to 1st exacerbation: 187 vs. 145 days (P &lt; 0.001)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AECOPD rate: 0.64 vs. 0.74 (P=0.002)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 36.5% of patients had AECOPD</td>
</tr>
<tr>
<td>Decramer, et al</td>
<td>Tiotropium (n=1721) Indacaterol (n=1723)</td>
<td>AECOPD rate: 0.73 vs. 0.9 (P &lt; 0.001)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• ~33% of patients had AECOPD</td>
</tr>
</tbody>
</table>

- No difference in COPD exacerbation rates with tiotropium vs. salmeterol/fluticasone


AECOPD, Acute Exacerbation of COPD
# First Line Therapy Recommendations

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Glycopyrronium/Indacaterol vs. Salmeterol/Fluticasone: LANTERN Study

**Study Design**
- Randomized, double-blind, double-dummy
- 26 week study duration
- Inclusion: ≤ 1 COPD exacerbation in past year

**Outcomes**
- 1°: Changes in FEV₁
- 2°: COPD exacerbation rate, adverse events (infection)

**Results**
- COPD exacerbation rate per year: 0.3 vs. 0.46 (P < 0.05)
  - Less than 20% of patients had COPD exacerbation
- Pneumonia: 0.8% vs. 2.7% (P-value not reported)

Glycopyrronium/Indacaterol vs. Salmeterol/Fluticasone: FLAME Study

Study Design

• Randomized, double-blind, double-dummy
• 52 week study duration

Inclusion

• ≥ 1 COPD exacerbation in previous year
• mMRC ≥ 2

Outcomes

• 1°: Annual COPD exacerbation rate
• 2°: Time to first exacerbation, adverse events (infection)

FLAME Results

- **Pneumonia Incidence:** 3.2% vs. 4.8% (P=0.02)
- **Annual COPD exacerbation rate:** 3.59 vs. 4.03 (P=0.003)

FLAME Conclusions

- Glycopyrronium/Indacaterol is more effective for exacerbation prevention
  - Patients with a history of COPD exacerbation
    - 75% of patients Group D
  - Lower infection risk compared to salmeterol/fluticasone

- Limitations
  - 52 week duration
  - Mild exacerbations occurred most frequently
    - Diaries used to track symptoms
  - Dosage form differences in United States
    - Glycopyrrolate/Indacaterol

Patient Case

- JP is a 75 YOF admitted to your hospital’s internal medicine service for a COPD exacerbation. She denies significant symptoms at home. Last COPD exacerbation was 5 years ago.

- PMH: COPD (x 5 years), GERD (x 2 years)

- Home medications:
  - Albuterol 90 mcg inhaler 2 puffs Q4H prn
  - Tiotropium 18 mcg inhaled daily
  - Omeprazole 20 mg daily
Refined ABCD Assessment Tool

Exacerbation History

≥ 2 OR ≥ 1 hospitalization
0-1 AND no hospitalizations

Symptoms

mMRC 0-1 CAT < 10
mMRC ≥ 2 CAT ≥ 10

GOLD 2017 Guideline Revisions

Treatment Categories

First Line Therapy Options

Second Line Therapy Options

# Second Line Therapy Options

<table>
<thead>
<tr>
<th>Group</th>
<th>First Line</th>
<th>Further Exacerbations</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Bronchodilator (short or long)</td>
<td>Continue therapy OR Alternative bronchodilator</td>
</tr>
<tr>
<td>B</td>
<td>Long-acting bronchodilator</td>
<td>LAMA/LABA</td>
</tr>
<tr>
<td>C</td>
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What is the role for ICS?

- Asthma-COPD overlap syndrome

- Consider ICS withdrawal in stable patients
  - No difference in exacerbation rates on tiotropium/salmeterol

- LAMA/LABA vs. LAMA/LABA/ICS research is ongoing

Case

- JR is a 64 YOM seen at an ambulatory care family medicine clinic. He reports increased shortness of breath, sputum production and sputum color change. He is diagnosed with a COPD exacerbation. Last exacerbation was 6 months ago.

- PMH: COPD (diagnosed 1 year ago, spirometry unknown)

- Home medications: Albuterol/ipratropium inhaler prn

- COPD Assessment Test Score: 14
# Refined ABCD Assessment Tool

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<th>Exacerbation History</th>
<th>Symptoms</th>
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<tr>
<td>≥ 2 OR ≥ 1 hospitalization</td>
<td>mMRC 0-1 CAT &lt; 10</td>
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<td>0-1 AND no hospitalizations</td>
<td>mMRC ≥ 2 CAT ≥ 10</td>
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Case Question

• Based on the 2017 GOLD Guidelines, what is the most appropriate therapy for JR?

  • A. Continue albuterol/ipratropium prn
  • B. Initiate salmeterol
  • C. Initiate glycopyrrolate/indacaterol
  • D. Initiate salmeterol/fluticasone
Summary

- COPD treatment focused on presence of symptoms and exacerbation history
  - Airflow limitation not recommended to determine maintenance therapy

- Bronchodilators preferred for first line therapy
  - LAMA monotherapy (Group C)
  - LAMA/LABA (Group D)

- Role of ICS therapy in COPD is changing
  - Further research ongoing in Group D COPD
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