COPD: Update on Guidelines and Making Sense of New Inhalers
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• Kajua B. Lor, Pharm.D.
• Investigator has no conflict of interest to disclose.
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LEARNING OBJECTIVES
• Given a patient case, evaluate and apply the 2017 GOLD guidelines for classification on pharmacological management
• Describe the role of bronchodilators in the management of stable COPD.
• Determine when inhaled corticosteroids may be appropriate for use in stable COPD
• Understand differences between old and new inhalers used for COPD

OUTLINE
2017 GOLD Guidelines
• Assessment
• Combination inhalers

Making Sense of New Inhalers
• Dry Powder Inhalers
• Soft-mist inhalers

DEFINITION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)
• Chronic obstructive pulmonary disease (COPD) is “a disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually both progressive and associated with an enhanced inflammatory response of the lungs to noxious particles or gases.”
• Often encompasses CHRONIC BRONCHITIS and/or EMPHYSEMA

EPIDEMIOLOGY OF COPD
3rd leading cause of death
15 million people in the US
12 million remain undiagnosed
1.5 million ED visits per year
$42.6 billion direct and indirect cost in 2007
Primary cause: SMOKING

2017 GOLD GUIDELINES

- Global Initiative for Chronic Obstructive Lung Disease (GOLD)
  - National Heart, Lung and Blood Institute (NHLBI)
  - World Health Organization (WHO)

COPD - GOALS OF THERAPY

Reduce Symptoms
- Relieve symptoms
- Improve exercise intolerance
- Improve health status

Reduce Risk
- Prevent disease progression
- Prevent and treat exacerbations
- Reduce mortality

COPD - OLD TREATMENT ALGORITHM OF COPD

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Very Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>%FEV1 &lt; 80%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>%FEV1 &lt; 50%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>%FEV1 &lt; 30%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>%FEV1 &lt; 10%</td>
<td></td>
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</tr>
</tbody>
</table>

- Add regular treatment with one or more long-acting bronchodilators
- Add pulmonary rehabilitation
- Add L-T if repeated exacerbations
- Add L-T if chronic respiratory failure
- Consider surgical Tx

2011 ASSESSMENT OF COPD

- Symptoms
  - COPD Assessment Tool (CAT)
  - Modified British Medical Research Council (mMRC)

- Degree of Airflow Limitation (using Spirometry)

- Risk of Exacerbations

- Comorbidities

2011 COMBINED ASSESSMENT

Patient | Characteristic | Spirometric Classification | Exacerbations | Comorbidities |
--------|----------------|---------------------------|---------------|--------------|
A       | Low Risk       | GOLD 1-2                  | ≤ 1           | < 10         |
B       | Low Risk       | GOLD 3-4                  | ≥ 2           | 0-1          | < 10 |
C       | High Risk      | GOLD 3-4                  | ≥ 2           | ≥ 2          | ≥ 10 |

When assessing risk, choose the HIGHEST risk according to GOLD grade or exacerbation history.

2017 ASSESSMENT

- Diagnosis of COPD (FEV1/FVC<0.7)

- Assessment of Airflow Limitation (Spirometry)
  - Assessment of symptoms/ risk of exacerbations
    - Exacerbation History
    - Modified British Medical Research Council (mMRC)
    - COPD Assessment Tool (CAT)

- Comorbidities
**ASSESSMENT OF COPD: SPIROMETRY**

<table>
<thead>
<tr>
<th>Classification</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOLD 1: Mild</td>
<td>FEV1 ≥ 80% predicted</td>
</tr>
<tr>
<td>GOLD 2: Moderate</td>
<td>50% ≤ FEV1 &lt; 80% predicted</td>
</tr>
<tr>
<td>GOLD 3: Severe</td>
<td>30% ≤ FEV1 &lt; 50% predicted</td>
</tr>
<tr>
<td>GOLD 4: Very Severe</td>
<td>FEV1 &lt; 30% predicted</td>
</tr>
</tbody>
</table>

*Note: FEV1 = based on post-bronchodilator FEV1*

**ASSESSMENT OF COPD: SYMPTOMS**

- Modified British Medical Research Council (mMRC) – dyspnea
  - Score 0 – 1 = Less Symptoms
  - COPD Assessment Tool (CAT):
    - Score <10 = Less Symptoms
  - Clinical COPD Questionnaire (CCQ)
    - http://www.ccg.nl

**ASSESSMENT OF COPD: EXACERBATION HISTORY**

- History of Exacerbation
  - Definition: "acute worsening of the patient's respiratory symptoms that results in additional therapy"
- Classification of Exacerbation
  - Mild (treated with short-acting bronchodilators)
  - Moderate (+ antibiotics and/or oral corticosteroids)
  - Severe (all of the above + hospitalization or ER visit)

**CASE**

**DOROTHY WHITE**

DW is a 61 yo female with SOB and DOE. She smoked 1 ppd for 37 yrs, but quit 10 yrs ago. Has a persistent cough that won’t go away. Had no exacerbations in the past year.

mMRC score = 1, CAT = 18.

<table>
<thead>
<tr>
<th>Pre-Albuterol</th>
<th>Post-Albuterol</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1 (L)</td>
<td>2.00 L</td>
</tr>
<tr>
<td></td>
<td>28% predicted</td>
</tr>
<tr>
<td>FEV1/FVC%</td>
<td>53%</td>
</tr>
<tr>
<td>FEF25-75% (L/sec)</td>
<td>0.75</td>
</tr>
<tr>
<td></td>
<td>0.88</td>
</tr>
</tbody>
</table>

**What is this patient’s GOLD stage?**

**According to the 2017 guidelines, to which GOLD patient group would DW belong to?**
COMPONENTS OF GOLD COPD MANAGEMENT

1. Reduce risk factors
2. Assess and Monitor Disease
   - Spirometry, Risk of Exacerbation, Symptoms + Comorbidities
3. Manage stable COPD
   - Non-pharmacologic
   - Pharmacologic
4. Manage acute exacerbations

2017 PHARMACOLOGIC TREATMENT

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Preferred treatment</th>
<th>Escalation/de-escalation strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Bronchodilator</td>
<td>Evaluate effect and continue, stop or try alternative class of bronchodilators if needed</td>
</tr>
<tr>
<td>B</td>
<td>Long-acting bronchodilator</td>
<td>If persistent symptoms combo LA anticholinergic + LABA</td>
</tr>
<tr>
<td>C</td>
<td>LA anticholinergic monotherapy</td>
<td>If further exacerbations combo LA anticholinergic + LABA</td>
</tr>
<tr>
<td>D</td>
<td>LA anticholinergic + LABA</td>
<td>If further exacerbations triple therapy LA anticholinergic + LABA + ICS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Consider roflumilast (FFV &lt; 50% predicted and pt has chronic bronchitis)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Consider macrolide (in former smokers)</td>
</tr>
</tbody>
</table>

2011 GOLD GUIDELINES

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Recommended First Choice</th>
<th>Alternative Choice</th>
<th>Other Possible Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>LA anticholinergic prn</td>
<td>LABA prn</td>
<td>Theophylline</td>
</tr>
<tr>
<td>B</td>
<td>LA anticholinergic prn</td>
<td>LABA</td>
<td>SABA and/or SA anticholinergic</td>
</tr>
<tr>
<td>C</td>
<td>ICS + LABA</td>
<td>LA anticholinergic</td>
<td>Carbocysteine</td>
</tr>
<tr>
<td>D</td>
<td>ICS + LABA + LA anticholinergic</td>
<td>LA anticholinergic + PDE-4 inhalator</td>
<td>Theophylline</td>
</tr>
</tbody>
</table>

DOROTHY WHITE

DW is a 61 yo female with SOB and DOE. She smoked 1 ppd for 37 yrs, but quit 10 yrs ago. Has a persistent cough that won't go away. Had no exacerbations in the past year. mMRC score = 1. CAT = 18. Pt has Humana insurance.

Current medications:
- Albuterol (Proventil®) 90 mcg/hr 1 puff q 4 - 6 hours as needed for shortness of breath
- Tiotropium (Spiriva Respimat) 2.5 mcg/actuation inhale 2 puffs once a day

What is the best recommendation for DW?

A) Start indacaterol (Arcapta Neohaler®)
B) Start mometasone and formoterol (Dulera®)
C) Start roflumilast
D) Stop tiotropium. Start combination tiotropium and olodaterol (Stiolto Respimat®)
SUMMARY OF 2017 GOLD GUIDELINES

- Revised assessment
- Spirometry – GOLD Grade 1 – 4
- ABCD groups are based on...
  - History of Exacerbations
  - Symptom Control
- Long acting bronchodilators are preferred over short acting agents except for patients with only occasional dyspnea
- Escalation and de-escalation strategies have been added

OUTLINE

2017 GOLD Guidelines
- Assessment
- Combination inhalers

Making Sense of New Inhalers
- Dry Powder Inhalers
- Soft-mist inhalers

PHARMACOLOGIC TREATMENT

- Bronchodilators
  - Beta-2 Agonists
  - Short-acting (SABA)
  - Long-acting (LABA)
- Anticholinergics
  - Short-acting: ipratropium
  - Long-acting: tiotropium
- Combinations
- Theophylline
- Corticosteroids
  - Inhaled (ICS)
- Phosphodiesterase-4 inhibitors: Roflumilast

COPD

Bronchodilators
- Short acting
- Long acting

Combinations
- LAMA/LABA
- LABA/ICS

Others
- Long term oxygen
PHARMACOLOGICAL MANAGEMENT OF COPD

- Bronchodilators are central to symptom management in COPD
- Inhaled bronchodilators are preferred over oral bronchodilators
- Short-acting bronchodilators are given PRN – do not give on a regular basis
  - Albuterol or ipratropium can be used as “quick-relievers”
- Combination of short-acting bronchodilators are superior compared to either medication alone in improving FEV1 and symptoms
- Combining bronchodilators (LABA/LAMA) may improve efficacy and decrease side effects
- LABA monotherapy is seen in COPD
- Inhaled corticosteroids are used in combination and recommended for treatment in Group C or D


TYPES OF INHALERS

<table>
<thead>
<tr>
<th>Metered Dose Inhalers (HFA)</th>
<th>Dry Powder Inhalers</th>
<th>Soft Mist Inhalers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Examples: albuterol, beclomethasone, albuterol/salmeterol, fluticasone/salmeterol, ipratropium</td>
<td>Diskus</td>
<td>Respimat</td>
</tr>
</tbody>
</table>

METERED DOSE INHALERS

- Examples: albuterol, beclomethasone, albuterol/salmeterol, fluticasone/salmeterol, ipratropium
- Clean at least once a week, check when empty if it doesn’t have a counter
- Spacers may help

<table>
<thead>
<tr>
<th>METERED DOSE INHALERS</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prime 3 – 4 times</td>
<td>Shake</td>
<td>Exhale</td>
<td>Inhalate slow and deep</td>
<td>Hold breath</td>
</tr>
</tbody>
</table>

DRY POWDER INHALERS

- Examples: salmeterol, salmeterol/fluticasone, aclidinium, fluticasone/valenterol, indacaterol
- Breath activated
- Dry powder inhalers with internal blister packs should be discarded 6 weeks after opening

<table>
<thead>
<tr>
<th>DRY POWDER INHALERS (Cont’d)</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose indicator</td>
<td>Pressair</td>
<td>Neohaler</td>
<td></td>
</tr>
</tbody>
</table>
DRY POWDER INHALERS
1. Hold inhaler in correct position
2. Exhale away from inhaler
3. Inhale fast and deep
4. Hold breath

SOFT MIST INHALER - RESPIMAT
- Some say the respimat is the optimal delivery system

SOFT MIST INHALER - RESPIMAT
1. Prime at least 4 times
2. Exhale away from inhaler
3. Inhale slow and deep
4. Hold breath

NEW INHALERS
- 2014 Inhalers: Seebri Neohaler* (glycopyrrolate) LAMA
  Tudorza Pressair* (aclidinium) LAMA
  Striverdi Respimat* (olodaterol) LABA
  Anoro Ellipta* (umeclidium/vilanterol) LAMA/LABA
- 2015 Inhalers: Seebri Neohaler* (glycopyrrolate) LAMA
  Utibron Neohaler® (glycopyrrolate/indacaterol) LAMA/LABA
  Stiolto Respimat* (tiotropium/olodaterol) LAMA/LABA

NEW INHALERS
- 2015 Inhalers: Seebri Neohaler* glycopyrrolate and Utibron Neohaler* glycopyrrolate/indacaterol
- Contain long-acting anticholinergic: glycopyrrolate
  - Recall other long-acting anticholinergics – tiotropium, aclidinium – Tudorza Pressair®, umeclidium – Incruse Ellipta®
  - Combination long-acting anticholinergic and LABA – umeclidium/vilanterol – Anoro® or tiotropium/olodaterol – Stiolto®
- Advantage
  - Similar lung function and side effect profile as tiotropium
- Disadvantage
  - Used BID (Seebri* and Utibron*) vs qday (Anoro* and Stiolto*)
- Medication access

MEDICATION ACCESS
- Wisconsin Medicaid
- United (individual plans vary)
- Humana

Incruse Ellipta* (umeclidium) LAMA
- Not preferred – preferred LAMA is Spiriva Respimat/handihaler
Tudorza Pressair* (aclidinium) LAMA
- Not covered
Seebri Neohaler® (glycopyrrolate) LAMA
- Not covered – preferred LAMA is Spiriva Respimat/handihaler
Striverdi Respimat* (olodaterol) LABA
- Not preferred – preferred LABA is Serevent
Anoro Ellipta* (umeclidium/vilanterol) LAMA/LABA
- Not covered

Utibron Neohaler® (glycopyrrolate/indacaterol) LAMA/LABA
- Not covered – preferred LAMA/LABA covered
Tiotropium/olodaterol
- Use separate agents Spiriva + Serevent

Stiolto Respimat* (tiotropium/olodaterol) LAMA/LABA
- Not covered
- Preferred LABA is Serevent Diskus
-Preferred LABA is Arcapta Neohaler

Tier 1, QL
*As of 1/9/2017
REFERENCES