How to Treat COPD:
Choosing the Right Device for Maintenance

November 15, 2012
Boston, Massachusetts

Educational Partner:
Session 1: How to Treat COPD: Choosing the Right Device for Maintenance

Learning Objectives

1. Develop appropriate chronic obstructive pulmonary disease (COPD) management strategies for patients who have physical or mental comorbidities as well as others who are difficult to manage.
2. Compare the utility and effectiveness of the different types of inhalation devices used in COPD maintenance.
3. Increase awareness, knowledge, and confidence in selecting nebulization maintenance therapy for COPD patients requiring or preferring this form of therapy.

Faculty

Amir Sharafkhaneh, MD, PhD, DABSM
Associate Professor of Medicine
Baylor College of Medicine
Houston, Texas

Dr Amir Sharafkhaneh graduated from Tehran University of Medical Sciences in Iran. He completed residency training in internal medicine at Long Island College Hospital in Brooklyn, New York, and a fellowship in pulmonary, critical care, and sleep medicine at Baylor College of Medicine (BCM) in Houston. During his fellowship, he was involved in the National Emphysema Treatment Trial, evaluating role of lung volume reduction surgery in management of patients with severe COPD.

Currently an associate professor of medicine at BCM, Dr Sharafkhaneh is a staff attending at the Michael E. DeBakey VA Medical Center, where he is in charge of the Care Coordination Program for COPD. There, he established a productive COPD clinical research operation and has led many observational, epidemiological, and clinical trials that have been reported in various peer reviewed journals. He recently coauthored COPD: A Guide to Diagnosis and Clinical Management for primary care providers. As part of his interest in improving quality of life in patients with COPD, Dr Sharafkhaneh is actively engaged in investigating sleep problems in COPD patients.

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Los Angeles, California

Dr Donald P. Tashkin is Emeritus Professor of Medicine in the Division of Pulmonary and Critical Care Medicine at the David Geffen School of Medicine at the University of California, Los Angeles (UCLA), and an attending physician at the Ronald Reagan UCLA Medical Center. His research interests include the pulmonary effects of smoked substance abuse and community air pollution; the pathophysiology, prevention, and treatment of COPD; and the pathophysiology and pharmacology of asthma. He has authored over 450 peer-reviewed journal articles as well as numerous book chapters and multimedia educational materials on topics including asthma, COPD, airway disease management, lung cancer, and the health effects of cannabis and cocaine.

Dr Tashkin serves on the editorial boards of Chest, Respiratory Research, and Respiratory Medicine. He chairs the external advisory committee of the American Lung Association (ALA) Asthma Clinical Research Centers. Dr Tashkin has received many honors, among them, the ALA Trudeau Award for outstanding and dedicated service promoting pulmonary medicine and the ALA’s 2003 California Medal for meritorious service in the campaign against lung disease.
Faculty Financial Disclosure Statements
The presenting faculty reports the following:
Dr Sharafkhaneh has served on the advisory board of Mylan Inc.
Dr Tashkin has served on the advisory boards of Mylan Inc. and Sunovion Pharmaceuticals Inc.

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Patrick J. Crowley, MBA, Managing Director; Cassie Rametta, BA, Senior Program Manager; Jeannette Fee, Director of Editorial Services; and Laurel Ranger, Medical Writer, have no financial relationships to disclose.

Suggested Reading List


Session 1  
8:00 AM - 9:15 AM 

How to Treat COPD: Choosing the Right Device for Maintenance

Speakers: 
Amir Sharafkhaneh, MD, PhD, DABSM 
Donald P. Tashkin, MD

Presenter Disclosure Information
The following relationships exist related to this presentation:

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Off-Label/Investigational Discussion
In accordance with pmICME policy, faculty have been asked to disclose discussion of unlabeled or unapproved use(s) of drugs or devices during the course of their presentations.

Drug List

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<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
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<tbody>
<tr>
<td>albuterol</td>
<td>Various</td>
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<tr>
<td>aclidinium</td>
<td>Tudorza® Pressair®</td>
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<tr>
<td>albuterol and ipratropium</td>
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<td>alfomterol</td>
<td>Brovana® Inhalation Solution</td>
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<td>beclomethasone dipropionate</td>
<td>Beconase AQ®, QNKL® Nasal Aerosol, QVAR® Inhalation Aerosol</td>
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<tr>
<td>budesonide</td>
<td>Pulmicort®, Pulmicort Redhaler®, Pulmicort Respules®, Rhinocort® Aqua®</td>
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<tr>
<td>budesonide/formoterol</td>
<td>Symbicort®</td>
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<td>ciclesonide</td>
<td>Alexess® Inhalation Aerosol, Omxaris® Nasal Spray, Zetrona® Nasal Aerosol</td>
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<tr>
<td>fluticasone propionate</td>
<td>Flonase®, Flovent®, Flovent® Diskus®, Flovent® HFA</td>
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</tbody>
</table>

Demographic Question

Relative to COPD: please indicate the approximate number of patients that you see each week with this condition.

1. None
2. 1 to 10
3. 11 to 20
4. 21 to 30
5. 31 to 40
6. 41 to 50
7. 51 to 60
8. > 60

Drug List (cont)

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
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<tr>
<td>fluticasone propionate</td>
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<td>formoterol</td>
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<td>indacaterol</td>
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<td>ipratropium</td>
<td>Atrovent®, Atrovent® HFA</td>
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<td>levodulor</td>
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<td>levodolopex</td>
<td>Percora®, Sinecles®, Staleve®</td>
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<td>momotasefuroate</td>
<td>Asmanex Twister®</td>
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<tr>
<td>pirbuterol</td>
<td>Maxair® Autohaler®</td>
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<td>rufullinolast</td>
<td>Dalires® Tablets</td>
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<td>salmeterol</td>
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<td>theophylline</td>
<td>Various</td>
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<tr>
<td>tiotropium</td>
<td>Spiriva® Handihaler®</td>
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</table>

Learning Objectives

• Develop appropriate chronic obstructive pulmonary disease (COPD) management strategies for patients who have physical or mental comorbidities as well as others who are difficult to manage
• Compare the utility and effectiveness of the different types of inhalation devices used in COPD maintenance
• Increase awareness, knowledge, and confidence in selecting nebulization maintenance therapy for COPD patients requiring or preferring this form of therapy
### Polling Question (Pre-Test)

**Among your patients receiving maintenance therapy, how would you describe their level of adherence?**

1. Excellent—almost all of my patients adhere to their prescribed regimen
2. Good—most of my patients adhere to their prescribed regimen
3. Fair—at least half of my patients adhere to their prescribed regimen
4. Poor—less than half of my patients adhere to their prescribed regimen

### Polling Question (Pre-Test)

**How often do you prescribe long-acting beta₂-agonists (LABAs) for maintenance therapy for your COPD patients?**

1. Always
2. Usually
3. Sometimes
4. Never

### Polling Question (Pre-Test)

**How confident do you feel about selecting an appropriate LABA and delivery device for maintenance therapy for your patients based on their individual characteristics?**

1. Very confident
2. Somewhat confident
3. Not very confident
4. Not confident at all

### Polling Question (Pre-Test)

**How confident do you feel about your ability to instruct patients in the use of a dry powder inhaler (DPI) for maintenance therapy?**

1. Very confident
2. Somewhat confident
3. Not very confident
4. Not confident at all

### Case Study 1

- George W., a 75-year-old retired office worker with a 10-year history of COPD recently has been experiencing more shortness of breath and difficulty helping his wife around the house. He also has required frequent SABA refills.
- George smoked a pack of cigarettes a day for 50 years, but quit at diagnosis of COPD. He has osteoarthritis, particularly in the hands, and also suffers from type 2 diabetes mellitus (DM). He has had several transient ischemic strokes over the last few years.
- **Medications:**
  - LABA using a dry powder inhaler as COPD maintenance therapy, as well as a SABA for rescue therapy and an oral glucocorticoid for treatment of acute exacerbations
  - A sulfonylurea for glucose control
  - An antiplatelet agent to reduce the risk of stroke
  - A nonsteroidal anti-inflammatory drug for osteoarthritis
Case Study 1—Poor Disease Control

• Signs of possible nonadherence
  – Frequent exacerbations
  – Patient is going through rescue medication too quickly
  – Forced expiratory volume in 1 second (FEV$_1$)% predicted has declined more than expected

Case Study 1—Course of Action

• George is asked about his use of LABA and SABA therapy, and he admits to inconsistent use of LABA maintenance therapy and difficulty in using his inhaler
• An office demonstration of how he is using the LABA inhaler shows that his technique is poor, and, as a result, it is unlikely that much of the medication is reaching the lungs
• George is prescribed a LABA using a nebulizer
• He is educated on the need to use the maintenance therapy and to reserve rescue medication only for breakthrough episodes

Case Study 1—Follow-up

• At the next visit 3 months later, George expresses satisfaction with the nebulizer and its ease of use
• He reports needing less rescue medication and having fewer symptoms. He is able to help around the house and has even begun taking a short walk every morning

COPD

COPD—Overview

Epidemiology of COPD

• ~14 million American adults have been diagnosed with COPD
  – The true prevalence is probably higher because many individuals with mild grade COPD remain asymptomatic
  • 63% of adults with expiratory airflow obstruction are not aware of their problem
• Chronic and unspecified bronchitis accounts for 11.7 million visits to physicians’ offices, hospital outpatient clinics, and emergency departments (ED) annually
  – Other COPD accounts for 6.1 million visits
• COPD is the third leading cause of death in the U.S.

Epidemiology of COPD (cont.)

• COPD death rate increased 102.8% between 1970 and 2002
  – Among the 6 leading causes of death, only COPD and DM had an increase in the death rate
  • Death rate in DM increased 3.2% during that time period
  – Death rates decreased in heart disease (-52.1%), cancer (-2.7%), accidents (-41%), and stroke (-63.1%) between 1970 and 2002

COPD—Disease Course

- The natural course of COPD is variable
- COPD is a progressive disease
- COPD is a chronic, incurable disease, but treatment can reduce symptoms, increase exercise tolerance, improve quality of life (QOL), reduce exacerbations, and perhaps decrease mortality

COPD—Assessment

- Spirometric assessment
  - However, the correlation between FEV₁, symptoms, and impairment of a patient’s health-related QOL is weak

<table>
<thead>
<tr>
<th>GOLD spirometric level</th>
<th>Exacerbations (per year)</th>
<th>Hospitalizations (per year)</th>
<th>3-year Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOLD 1: Mild (FEV₁ ≥ 80% predicted)</td>
<td>0.7-0.9</td>
<td>0.11-0.2</td>
<td>11%</td>
</tr>
<tr>
<td>GOLD 2: Moderate (50% ≤ FEV₁ &lt; 80% predicted)</td>
<td>1.1-1.3</td>
<td>0.25-0.3</td>
<td>15%</td>
</tr>
<tr>
<td>GOLD 3: Severe (30% ≤ FEV₁ &lt; 50% predicted)</td>
<td>1.2-2.0</td>
<td>0.4-0.54</td>
<td>24%</td>
</tr>
<tr>
<td>GOLD 4: Very severe (FEV₁ &lt; 30% predicted)</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

COPD—Classification

- Revised 2011 GOLD Guidelines published in December presented a new system for classifying COPD
  - Change from stages I-IV to grades A-D
  - New system takes into account airflow limitation, exacerbations, and symptoms based on either mMRC or CAT score

COPD—Impact of Treatment

Nonpharmacologic Interventions

- Smoking Cessation
  - Most important intervention
  - Slows disease progression and decline in FEV₁
  - Decreases morbidity and reduces mortality

### COPD—Impact of Treatment (cont.)

#### Nonpharmacologic Interventions

- **Pulmonary Rehabilitation**
  - Includes
    - Respiratory muscle training
    - Exercise training
    - Strength and endurance training
    - Educational and nutritional components
  - Improves exercise capacity
  - Reduces perceived intensity of dyspnea
  - Reduces anxiety and depression associated with COPD
  - Increases strength
  - Improves survival
  - Improves recovery after hospitalization for exacerbation
  - Enhances effects of long-acting bronchodilators

#### Immunization

- Influenza and antipneumococcal vaccines may reduce hospitalization due to influenza and pneumonia

#### Continuous low-flow supplemental oxygen

- For patients with significant hypoxemia (PaO2 ≤ 55 mm Hg or SaO2 < 88%) or PaO2 between 55 mmHg and 60 mmHg or SaO2 of 88%
  - If there is evidence of
    - Pulmonary hypertension
    - Peripheral edema or
    - Polycythemia
  - Has been shown to increase survival

#### Bronchodilators

- Central to treatment
- Include
  - beta2-agonists, anticholinergics, and methylxanthines
- Short-acting agents used for rescue, have faster onset of action
- Long-acting agents used for maintenance therapy in patients with moderate to severe COPD
  - More effective in improving lung function, symptom control, and health-related QOL

#### Phosphodiesterase-4 (PDE-4) inhibitors

- Limited bronchodilator activity
- Improves FEV1 in patients treated with a bronchodilator
- Reduces moderate and severe exacerbations in patients treated with corticosteroids
- Patient-related outcomes and effects on exacerbations remain controversial
COPD—Impact of Treatment (cont.)

Pharmacologic Interventions
• Combination therapy
  – Combining bronchodilators with different mechanisms and durations of action may improve bronchodilation
  – Beta₂-agonists used with an anticholinergic or theophylline may improve lung function and health status
  – Combining an ICS with a LABA may improve lung function and health status and reduce exacerbations
  – May reduce mortality (unproven)

GOLD Guidelines on Management of Stable COPD

GOLD Guidelines on the Management of Stable COPD, December 2011
• Overall approach to managing stable COPD should be individualized to address symptoms and improve QOL
• Bronchodilator medications central to the symptomatic management of COPD (Evidence A)
  – Given on as needed basis or on regular basis to prevent or reduce symptoms and exacerbations
• Principal bronchodilator treatments (Evidence A)
  – Beta₂-agonists
  – Anticholinergics
  – Methylxanthines, used singly or in combination
  – Theophylline is not recommended as first-line therapy

GOLD Guidelines on Management of Stable COPD (cont.)

Most Recent Gold Guidelines—December 2011

Initial Pharmacologic Management of COPD

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>First Choice</th>
<th>Second Choice</th>
<th>Alternative Choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>SAMA pm or SAMA pm</td>
<td>LAMA or LABA or SABA + SAMA</td>
<td>Theophylline</td>
</tr>
<tr>
<td>B</td>
<td>LAMA or LABA</td>
<td>LAMA + LABA</td>
<td>SABA and/or SAMA Theophylline</td>
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<tr>
<td>C</td>
<td>ICS + LABA or LAMA</td>
<td>LAMA + LABA</td>
<td>PDE-4 inhibitor SABA and/or SAMA Theophylline</td>
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<tr>
<td>D</td>
<td>ICS + LABA or LAMA</td>
<td>ICS + LABA + LAMA or ICS + LABA + PDE-4 inhibitor or LABA + PDE-4 inhibitor</td>
<td>SABA and/or SAMA Theophylline</td>
</tr>
</tbody>
</table>

SAMA = short-acting muscarinic antagonist, LABA = long-acting muscarinic antagonist.

GOLD Guidelines on Management of Stable COPD, December 2011
• Regular treatment with long-acting inhaled bronchodilators is more effective and convenient than treatment with short-acting bronchodilators (Evidence A)
• Regular treatment with long-acting inhaled bronchodilators is more effective and convenient than treatment with short-acting bronchodilators (Evidence A)
• Chronic treatment with systemic glucocorticosteroids should be avoided because of an unfavorable benefit-to-risk ratio (Evidence A)

COPD—Difficult-to-Treat Patients
• Subpopulations of difficult-to-treat COPD patients make disease management a challenge
  – Elderly
    • Have more comorbidities
    • Disorders such as those of the cardiovascular and musculoskeletal systems (cachexia, muscle dysfunction, osteoporosis) and psychological disorders (depression and/or anxiety) are common in COPD patients, and can complicate treatment
  – Twenty-five percent of those over age 65 years suffer from 2 of the 5 most common chronic diseases (including COPD) and 10% have 3 or more; in those 75 years and older, those figures rise to 40% and 25%, respectively

COPD—Difficult-to-Treat Patients (cont.)

- Disabilities may be a barrier to adherence and disease control1
  - Elderly patients may have cognitive deficits that make adhering to medication regimens more difficult1
  - They may have physical disabilities, such as poor vision or osteoarthritis, that may make opening medication packages, reading directions, or effectively operating medication delivery devices difficult1
  - The presence of comorbidities may increase cognitive effects and physical difficulties as well as require multiple medications that may decrease adherence1
  - COPD itself may affect cognition negatively, particularly in the elderly2,3


COPD Medication Delivery Devices (cont.)

- Number of different types of devices available
  - Advantages include multiple dosing (>100 doses/canister), shorter administration time, compactness and portability of the device
  - An important disadvantage is the requirement of a specific inhalation technique, which requires adequate patient coordination
  - Multiple steps involved
    - Most common error is the failure to synchronize inhalation with pMDI actuation
    - 26% of patients demonstrate inadequate breath holding
    - 19% have overly rapid inspiration leading to oropharyngeal deposition instead of pulmonary delivery
  - Even with proper technique, pMDIs deposit only 10%-20% of labeled dose to the lungs, while much of the medication remains in the mouth and oropharynx
    - This can lead to adverse events
  - Use of spacer devices eliminates need to coordinate inhalation with actuation, but spacers are bulky and increase time for medication delivery


COPD Medication Delivery Devices

- DPI
  - Breath-actuated device designed to reduce difficulty encountered with pMDIs; convenient, compact, portable device providing rapid medication delivery; has dose counter, indicating amount of medication remaining; some DPIs emit inspiratory-flow signals to prompt proper technique and adherence
  - Single- and multi-dose devices
  - Requires the patient to generate sufficient inspiratory force in order to deaggregate the powdered medication formulation
  - The rate of ineffective inhalation due to inadequate peak inspiratory flow (PIF) correlates with patient age and severity of airflow obstruction
    - Elderly patients with severe COPD may not be able to achieve adequate inspiratory flow against the resistance of the device
  - Requires PIF rate >30 L/min through the device
  - Humidity or inappropriately blowing into the device may cause clumping of powdered medication, resulting in ineffective delivery of medication
  - Advantages
    - Requires slow deep breath; a 10-second breath hold is recommended3
    - High fine particle fraction2
    - High lung deposition (reduced oropharyngeal deposition)2
  - Disadvantages
    - Requires some coordination between actuation and inhalation3
    - Requires slow deep breath; a 10-second breath hold is recommended3


COPD Medication Delivery Devices (cont.)

- Soft Mist Inhaler
  - Advantages
    - Compact,1 portable,1 multiple dosing2
    - Propellant-free2
    - Does not require high generation of inspiratory flow3
    - High fine particle fraction2
    - High lung deposition (reduced oropharyngeal deposition)2
  - Disadvantages
    - Requires some coordination between actuation and inhalation3
    - Requires slow deep breath; a 10-second breath hold is recommended3

COPD Medication Delivery Devices (cont.)

- Nebulizers
  - Easiest for patients to use, requires minimal cognitive ability and no hand-breath coordination, manual dexterity, or hand strength; visible mist may give patients confidence in medication delivery
  - Three types—compressor-driven jet nebulizer, conventional ultrasonic nebulizer, and high efficiency vibrating mesh nebulizer (quieter and allows for faster medication delivery)
  - However, conventional ultrasonic nebulizers do not readily aeroseize drug suspensions
  - Relatively long duration of medication delivery, poor portability, need for daily cleaning, and trouble and cost associated with proper maintenance and replacement of nebulizers
  - Cleaning requires disassembling nebulizer and soaking all components in warm soapy water, rinsing, and air drying before next use
  - Device can last 6 months with proper care, while disposable units last 2 weeks


COPD Medication Delivery Devices (cont.)

- Vibrating mesh or vibrating plate nebulizers
  - Higher lung deposition
  - Negligible residual volumes
  - Faster rate of nebulization
  - Battery operated
  - More portable than ultrasonic or jet nebulizers
  - Cost is comparable to ultrasonic nebulizers but much higher than conventional jet nebulizers
  - Must be cleaned regularly to prevent build-up of deposit and blockage of apertures, can be challenging to disassemble and re-assemble for cleaning
  - Risk of overdosing using doses approved for use with jet nebulizers (due to more efficient delivery of medication to the lung)

COPD Medication Delivery Devices
ACCP/ACAAI Guidelines

• Summary of Randomized Controlled Trial Results
  – Outpatient management of COPD with bronchodilators shows no difference in pulmonary function response between delivery devices
  – Increases in heart rate greater after administration of albuterol by nebulizer than after administration by MDI

• Recommendations
  – MDI (with or without spacer/holding chamber), nebulizer, and DPI are all appropriate for delivery of inhaled bronchodilators. Quality of evidence: good; net benefit: substantial; strength of recommendation: A
  – Selection of an appropriate aerosol delivery device for inhaled bronchodilators includes the patient’s ability to use the device correctly, patient preference, the availability of the drug/device combination, compatibility between the drug and the delivery device, the lack of time or skills to properly instruct the patient in the use of the device or to monitor its appropriate use, the cost of therapy, and the potential for reimbursement. Quality of evidence: good; net benefit: substantial; strength of recommendation: B


Case Study 2

Case Study 2—Course of Action

• Gayle H., a 63-year-old receptionist for a pediatrician has been controlled on her SABA rescue medication since being diagnosed with Grade B* COPD 3 years ago. She smoked half a pack of cigarettes for 35 years and quit at diagnosis. She also suffers from early stage Parkinson’s disease (PD) and hypertension.
  – Medications:
    – Levodopa for Parkinson’s Disease
    – Angiotensin-converting enzyme (ACE) inhibitor
    – SABA
  – The patient is having to use her SABA rescue medication more and more frequently. Recently, she has been unable to work in her garden, even for a short while, and says she sometimes gets breathless at work and has to take a break and use rescue medication.

Polling Question

In elderly patients with cognitive problems and/or physical disabilities, what device would you typically prescribe for maintenance therapy?

1. MDI
2. DPI
3. Nebulizer

*Grade B, typically GOLD 1 or GOLD 2 and/or 0-1 exacerbation per year and mMRC grade ≥ 2 or CAT score ≥ 10.

Case Study 2—Follow-up

• Gayle has hand control issues due to the PD, and, therefore, an LABA using a nebulizer is prescribed
  – Due to PD, she experienced specific problems with activation, coordinating activation with inhalation, and positioning her SABA inhaler
  – Nebulizers require minimal patient cooperation and coordination
  – She is educated on the need to use the LABA regularly, as prescribed, and to reserve the SABA as rescue medication for acute symptoms

• At a follow-up visit 3 months later, Gayle reports fewer symptoms of COPD and less use of rescue medication

COPD—Cost Savings of Adherence

- Maintenance therapy in COPD decreases hospitalizations and expenditures

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Cost Savings</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAMA + LABA</td>
<td>$5889</td>
</tr>
<tr>
<td>LABA + ICS</td>
<td>$3330</td>
</tr>
<tr>
<td>LAMA + LABA/ICS</td>
<td>$10,317</td>
</tr>
</tbody>
</table>

*Adherent versus nonadherent: LAMA + LABA, n=25 and n=39, respectively; LABA + ICS, n=74 and n=180, respectively; LAMA + LABA/ICS, n=21 and n=25, respectively.


COPD—Maintenance Therapy Is Underused

- Retrospective medical record review of over 50,000 COPD patients
  - Found that 66.3% of managed care patients are not prescribed any maintenance therapy for COPD
  - 59.1% receive no therapy
  - 7.2% are prescribed an inhaled SABA only
  - In the Medicare population, 70.9% of COPD patients are not prescribed maintenance therapy
  - 66% receive no therapy
  - 4.9% are prescribed a SABA only


COPD—Maintenance Therapy Is Underused (cont.)

| Baseline Respiratory Pharmacotherapy Use Among US Veterans Affairs Population |
|------------------------------|-----------------|-----------------|
| n % of total 59,906 % of treated 36,285 |
| Treated                      | 36,285          | 100.0           |
| ICS + LABA combination        | 449             | 0.7             |
| ICS + LABA combination 250/50| 261             | 0.4             |
| ICS                          | 11,177          | 18.6            |
| SABA                         | 32,629          | 54.5            |
| LABA                         | 2176            | 3.6             |
| Short- or long-acting anticholinergic | 13,493 | 22.5  |
| Untreated                    | 23,621          | 39.4            |


COPD—Adherence to Maintenance

- Adherence to maintenance regimens is also poor
  - Among patients prescribed long-term therapy with LAMA, LABA, or fixed-dose combinations of ICS and LABA, a substantial proportion switch therapy
  - Persistence, even including those who switch, is low
  - Persistence rates with any long-acting drug at 1, 2, and 3 years has been found to be 36%, 23%, and 17%, respectively, in an analysis of a large pharmaceutical database


LABAs and LAMAs

- Should be used regularly in moderate COPD (Grade B) if symptoms are not well controlled with as needed SABA, and for severe to very severe COPD (Grades C & D)²³
- Yet, one study found only 54% of patients were using long-acting bronchodilators when FEV₁ was < 80% predicted³
- Poor familiarity with recommendations, low self-efficacy, and time constraints identified as barriers to adherence to COPD guidelines³


LABAs and LAMAs (cont.)

- Another study found that SABAs were used without concomitant long-acting bronchodilators for 20% of moderate, 14% of severe, and 8% of very severe COPD patients
  - Long-acting bronchodilators + ICS used in 12% of patients with moderate COPD, 19% with severe COPD, and 2% with very severe COPD


LABAs and LAMAs (cont.)

- Fear of complications may prevent greater use of long-acting bronchodilators
  - There was a small but significant increase in asthma-related deaths with salmeterol in asthma patients, raising concerns about LABA monotherapy in asthma patients.
  - This increase was not noted in children and adolescents using formoterol along with concomitant ICS or other LABA/ICS combinations.
- However, COPD is a different disease, occurring in a different population.
  - Safety of LABAs is well-established in the COPD population.
  - Some increased risk is associated with beta-agonists in patients with COPD and concomitant congestive heart failure.

Complications From Poor Maintenance Therapy

- Failure to adhere to GOLD Guidelines results in
  - More frequent exacerbations
  - More frequent hospitalizations

Rescue Therapy—SABAs and SAMAs

- Appropriate use of SABAs and SAMAs
  - These agents act more quickly than the LABA salmeterol and LAMAs, and, therefore, are appropriate as symptom-driven rescue therapy.
- Inappropriate use
  - Frequent use of SABAs or SAMAs is a sign of poorly controlled disease.
  - SABAs and SAMAS do not provide long-acting relief of symptoms; in patients with moderate to severe COPD, they should be used solely as rescue medication in conjunction with maintenance therapy with long-acting bronchodilators.

Adverse Effects of COPD Medication

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Serious Adverse Effects</th>
<th>Common Adverse Effects</th>
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</thead>
<tbody>
<tr>
<td>Anticholinergics</td>
<td>• Mephylaxis</td>
<td>• Cough</td>
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Adverse Effects of COPD Medication (cont.)

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References:

**ICSs for COPD**

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<tr>
<td>Beclomethasone dipropionate</td>
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<td>DPI</td>
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* Use of ICSs can improve lung function and symptoms and decrease acute exacerbation and frequency of exacerbations.
* Long-term use in the elderly increases risk of cataract formation and glaucoma, decreases bone mineral density, and increases fracture rate.

**Safety of Long-Term Use of LABAs in COPD**

- Nebulized formoterol, 12-month open-label trial
  - 569 subjects with COPD received twice daily 20 μg formoterol inhalation solution for nebulization or 2 μg formoterol fumarate DPI for 52 weeks
  - Adverse effects (AEs) and safety profile similar between treatment groups
  - Majority of AEs were mild to moderate in severity and unrelated to treatment
  - Exacerbation experienced by 15.8% of nebulizer group and 17.9% of DPI group
  - No clinically important changes in vital signs and no treatment-related increases in cardiac arrhythmia, heart rate, or QTc prolongation
  - Death occurred in 1.3% and more than 1 serious AE occurred in 16.2% of nebulizer group, compared with 1.9% and 17.9% of DPI group, respectively

**Efficacy and Safety of Maintenance Therapy**

- Nebulized formoterol vs placebo as add-on therapy to tiotropium bromide in COPD patients
  - At 6 weeks, FEV₁, AUC significantly greater in formoterol group than placebo (1.57 vs 1.38 L [P<0.001])
  - Other lung function measures also improved—FEV₁,
  - Forced vital capacity (FVC), and post-dose IC at day 1; these were maintained through week 6
  - Dyspnea also improved after 6 weeks to both a statistically and clinically significant extent
  - AE occurred in 37% of formoterol group vs 51% of placebo group; the most common AEs in the formoterol group were acute bronchitis (3.8%), COPD exacerbation (2.6%), and dyspnea (2.6%)
Poor Control or Nonadherence (cont.)

• Biomarkers
  - Identifying Patients Exhibiting Signs of


Delivery Device Problems in Select Populations

• Physical issues (eg, arthritis, visual problems), the presence of multiple comorbidities, and cognitive issues may compromise a patient’s ability to use a delivery device effectively.

• Deficiencies in inhaler device technique and adherence to treatment regimen may lead to suboptimal health outcomes in COPD patients:
  - User technique, particle size, and type of delivery device affect the efficacy of inhaled medications.
  - Evidence indicates that only 36% of elderly patients use an MDI properly.
  - Technique is affected by cognitive impairment and physical disability.
  - Can be difficult to coordinate actuation and inhalation.
  - Use of a large volume spacer (US) can improve the patient’s ability to use this device.

• Nebulizers may be preferable in certain subgroups of patients:
  - Elderly
  - Those with severe disease and frequent exacerbations
  - Those with physical and/or cognitive limitations
  - Those who fail to respond satisfactorily to treatment with hand-held inhalers despite adequate instruction
  - Financial issues and patient preferences that enhance adherence may favor nebulized therapy over other inhaler devices
  - Nebulized medications are a good option for sicker, frailer elderly patients, and those with cognitive problems.

• DPIs require less coordination, but the patient must be able to generate a certain minimum PIF rate (> 30 L/min) through the resistance of the device that some older patients may not be able to achieve.
  - PIF rates decline with age.
  - Evidence also suggests that up to 40% of patients aged > 65 years do not use DPIs correctly.
  - Effects of incorrect use of DPIs
    - Chronic cough, wheezing, and poorer health-related QOL associated with incorrect inhalation technique in patients with asthma.

Delivery Device Problems in Select Populations (cont.)

• Biomarkers
  - The only accepted biomarker in COPD is FEV₁; however, this proves less than optimal in many cases for monitoring response to treatment.

• Deficiencies in inhaler device technique and adherence to treatment regimen may lead to suboptimal health outcomes in COPD patients:
  - User technique, particle size, and type of delivery device affect the efficacy of inhaled medications.
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Use of Nebulizers in Subgroups of Patients

• Clinical symptoms and signs
  - Frequent exacerbations
  - Increased use of rescue medications
  - Declining lung function (FEV₁)
  - Increased disability (greater difficulty with performing activities of daily living [ADLs])
  - Reduced ability to exercise


Identifying Patients Exhibiting Signs of Poor Control or Nonadherence

• Clinical symptoms and signs
  - Frequent exacerbations
  - Increased use of rescue medications
  - Declining lung function (FEV₁)
  - Increased disability (greater difficulty with performing activities of daily living [ADLs])
  - Reduced ability to exercise


Identifying Patients Exhibiting Signs of Poor Control or Nonadherence (cont.)

• Biomarkers
  - The only accepted biomarker in COPD is FEV₁; however, this proves less than optimal in many cases for monitoring response to treatment.


Identifying Patients Exhibiting Signs of Poor Control or Nonadherence (cont.)

• Evaluating the frequency, severity, and duration of exacerbations
  - Exacerbations begin to occur in more severe disease (Grades C & D)
    - Consider re-evaluation of current treatment in patients with frequent exacerbations (i.e. 2 or more per year)
    - COPD Assessment Test—8 items, scored from 0 to 5
      - Covers the domains of cough, phlegm, chest tightness, exercise limitations, limitations of ADLs, sense of confidence, sleep disturbances, level of energy
    - Score of 10 or more indicates a level of symptoms warranting more aggressive management
  - Markers of exacerbation severity
    - Arterial carbon dioxide tension and breathing rate associated with the severity of COPD exacerbations

Strategies for Improving Adherence and Disease Control

- Use of the appropriate device tailored to the needs of the individual patient
  - Improves patient adherence and ability of patient to use the inhaler correctly, thereby increasing the likelihood of achieving optimal outcomes
  - Cost considerations may play a role as well
- Medications administered using pMDI or DPI devices require Medicare Part D
- Medicare Part B covers 80% of the cost of nebulizer equipment and medication, which may make it the more affordable option
- Patient preference should be considered as well
- Survey of 82 patients using nebulizers found that adherence was high, and reported adverse effects minor and infrequent; patients felt the benefits of the nebulizer outweighed the disadvantages


Patient and Caregiver Training and Education

- Critical factor in appropriate use of inhalers
  - Evidence indicates that teaching interventions substantially increase the likelihood of proper inhaler use
  - Physicians should review patients’ inhaler technique regularly to ensure that adequate amounts of medication are being received
  - Education of caregivers is important as well, as many patients rely on caregivers
  - Self-management education has been associated with a reduction in hospital admission, with no indication of adverse effects
    - Odds ratio, 0.64; 95% confidence interval, 0.47 to 0.89
  - Training of the patient in the use of inhaler devices often is poorly addressed


Conclusions

- COPD is a chronic, progressive disease
- Proper management of the disease can reduce acute exacerbations, hospitalizations, and symptoms, and improve QOL for patients
- Maintenance therapy is underutilized overall
- Some populations of patients, such as the elderly, cognitively impaired, or physically disabled, may have difficulty using maintenance medication delivery devices, even when maintenance therapy is prescribed, and thus may receive less than optimal amounts of medication
- Failure to use maintenance therapy appropriately may result in increased acute exacerbations, hospitalizations, and costs
- Careful consideration of patient factors in selecting medication and delivery devices can improve patient outcomes

Polling Question (Post-Test)

In the future, how often will you prescribe LABAs for maintenance therapy for your COPD patients?
1. Always
2. Usually
3. Sometimes
4. Never

Polling Question (Post-Test)

How confident do you feel about your ability to instruct patients in the use of a dry powder inhaler (DPI) for maintenance therapy?
1. Very confident
2. Somewhat confident
3. Not very confident
4. Not confident at all
Polling Question (Post-Test)

In the future, in elderly patients with cognitive problems and/or physical disabilities, what will you prescribe for maintenance therapy?

1. I will not prescribe therapy for these patients
2. I will have them use a SABA for rescue therapy as needed rather than a LABA for maintenance
3. I will prescribe a LABA using a breath-activated inhaler for these patients and a SABA for rescue therapy as needed
4. I will prescribe a LABA / ICS fixed dose combination
5. I will prescribe a LABA using a nebulizer for these patients and a SABA for rescue therapy as needed

Questions & Answers