COPD Exacerbations: Prevention, Treatment & Avoiding Admission/Readmission

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DISCLOSURES
No financial relationship with any pharmaceutical manufacturer or medical device company

OBJECTIVES
- Analyze the current modalities that prevent exacerbations of COPD.
- Formulate a pharmacologic plan that will decrease exacerbations in your patients with COPD.
- Evaluate the pharmacologic and non-pharmacologic therapies that help to avoid hospitalization or readmission.

COPD STATISTICS
- Third leading cause of death in the U.S.
- More than 120,000 deaths per year
- More than 12 million people are diagnosed with COPD
- An additional 12 million are likely to have COPD & are undiagnosed

COPD STATISTICS
- Responsible for ~ 700,000 hospitalizations annually
- ~ 20% of patients hospitalized with COPD exacerbations are rehospitalized within 30 days of discharge & COPD only accounted for 27.6% of these rehospitalizations
- Half occur within 2 weeks of discharge
**COPD READMISSIONS**
- Hospital Readmissions Reduction Program (HRRP) – penalize hospitals for 30 day readmissions
- Include COPD in October 2014

**OUTDATED TERMINOLOGY**
- Chronic airflow obstruction due to chronic bronchitis and emphysema
- Chronic bronchitis: productive cough for 3 consecutive months in 2 consecutive years
- Emphysema: abnormal enlargement of airspaces distal to terminal bronchioles with destruction of their walls

**DIAGNOSIS**
- Clinical suspicion with symptoms, history & exposures
- Spirometry is required to make the diagnosis!
- Post-bronchodilator values
- FEV₁/FVC ratio of < 70%

**CLASSIFICATION OF SEVERITY**

<table>
<thead>
<tr>
<th></th>
<th>GOLD (2014)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage</td>
<td>Description of Breathing</td>
</tr>
<tr>
<td>I</td>
<td>Mild COPD (FEV₁ &gt; 80% predicted)</td>
</tr>
<tr>
<td>II</td>
<td>Moderate COPD (50 – 80% predicted)</td>
</tr>
<tr>
<td>III</td>
<td>Severe COPD (30 – 50% predicted)</td>
</tr>
<tr>
<td>IV</td>
<td>Very severe COPD (FEV₁ &lt; 30% predicted)</td>
</tr>
</tbody>
</table>

A defining characteristic of COPD at all levels of severity is an FEV₁/FVC ratio of less than 70%.

**ASSESSMENT**
- Current level of patient’s symptoms
- Severity of the spirometric abnormality
- Exacerbation risk
- Presence of comorbidities

**MMRC DYSPNEA SCALE**

<table>
<thead>
<tr>
<th>GRADE</th>
<th>DESCRIPTION OF BREATHLESSNESS</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>I only get breathless with strenuous exercise.</td>
</tr>
<tr>
<td>1</td>
<td>I get short of breath when hurrying on level ground or walking up a slight hill.</td>
</tr>
<tr>
<td>2</td>
<td>On level ground, I walk slower than people of the same age because of breathlessness or have to stop for breath when walking at my own pace.</td>
</tr>
<tr>
<td>3</td>
<td>I stop for breath after walking about 100 yards or after a few minutes on the level ground.</td>
</tr>
<tr>
<td>4</td>
<td>I am too breathless to leave the house or I am breathless when dressing or undressing.</td>
</tr>
</tbody>
</table>
COPD ASSESSMENT TEST (CAT)
- Validated questionnaire (8 questions) that the patient completes
- Suitable for routine use – 3-6 months
- Measure health status
- Scoring ranges from 0 – 40
- Available in multiple languages
- Online or print version at: www.CATestonline.org

GOLD GROUPINGS
- GROUP A: Low risk, less symptoms
  - GOLD 1-Mild or 2-Moderate airflow limitation
  - 0-1 exacerbations/year
  - mMRC grade 0-1
  - CAT score < 10
- GROUP B: Low risk, more symptoms
  - GOLD 1-Mild or 2-Moderate airflow limitation
  - 0-1 exacerbations/year
  - mMRC grade ≥ 2
  - CAT score ≥ 10

GOLD GROUPINGS
- GROUP C: High risk, less symptoms
  - GOLD 3-Severe or 4-Very Severe airflow limitation
  - ≥ 2 exacerbations/year
  - mMRC grade 0-1
  - CAT score < 10
- GROUP D: High risk, more symptoms
  - GOLD 3-Severe or 4-Very Severe airflow limitation
  - ≥ 2 exacerbations/year
  - mMRC grade ≥ 2
  - CAT score ≥ 10

GOALS FOR TREATMENT FOR STABLE COPD
- Reduce symptoms
  - Relieve symptoms
  - Improve exercise tolerance
  - Improve health status
- Reduce risk
  - Prevent disease progression
  - Prevent & treat exacerbations
  - Reduce mortality

EXACERBATIONS
- Acute events
- Worsening of the patient’s respiratory symptoms that are beyond normal day-to-day variation
- Leads to a change in medication

SYSTEMIC BIOMARKERS
- No single biomarker for exacerbations
- Assessment relies on clinical presentation
- Evaluating several in large studies
  - C-reactive protein
  - Procalcitonin
**CARDINAL SYMPTOMS**
- Cough increases in frequency & severity
- Sputum production increases in volume &/or changes character
- Dyspnea increases

**ADDITIONAL SIGNS & SYMPTOMS**
- Decreased pulmonary function
- Tachypnea
- Chest x-ray unchanged

**EFFECTS OF EXACERBATIONS**
- Negatively impacts patient’s quality of life
- Symptoms & lung function take several weeks to recover
- Accelerate the rate of decline of lung function
- Associated with significant mortality – especially those needing hospitalization
- High socioeconomic costs

**EXACERBATION CHARACTERISTICS**
- More frequent in the winter months – November – February
- More severe in the winter
- Increased morbidity during the winter season

**ETIOLOGY**
- Viral or bacterial infections – 70 – 80 %
- Environmental pollution 20 – 30 %
- Unknown

**VIRAL INFECTIONS**
- 1/3 to 2/3 of exacerbations
- Rhinoviruses – most common
- Influenza
- Parainfluenza
- Coronavirus
- Adenovirus
- Respiratory syncytial virus
- Human metapneumovirus
**Bacterial Infections**
- 1/3 to 1/2 of exacerbations
- Haemophilus influenzae
- Moraxella catarrhalis
- Streptococcus pneumoniae
- Pseudomonas aeruginosa*
- Enterobacteriaceae*

* Severe to very severe disease

**Differential Diagnosis**
- Pneumonia
- Pulmonary embolism
- Congestive heart failure
- Cardiac arrhythmia
- Pneumothorax
- Pleural effusion

**Prevention**
- Tobacco cessation
- Influenza & pneumococcal vaccines
- Knowledge of current therapy & inhaler technique
- Use of long-acting bronchodilators – with or without inhaled corticosteroids
- Phosphodiesterase-4 inhibitors

**Tobacco Cessation**
- Most important intervention for all COPD patients!

**Natural History of COPD**

**Vaccines**
- Influenza – annually every fall – will decrease number of exacerbations
- Pneumococcal – once – with a booster in 5 years if patient is < 65 years old with first vaccination – reduces pneumococcal pneumonia & pneumococcal bacteremia
- Prevnar 13 – adults are now using
**PNEUMOCOCCAL**

- Prevnar 13 – works better than Pneumovax 23 to induce an immune response in older adults
- Medicare only pays for both vaccinations at this time!

- Prevnar 13 covers 11 serotypes that aren’t in Pneumovax 23
- Prevnar 13 have one serotype that isn’t in Pneumovax 23

**NEW CHANGES:**

- All those 65 and older
- Need BOTH Pneumovax 23 and Prevnar 13

<table>
<thead>
<tr>
<th>Pneumococcal vaccine status</th>
<th>FIRST give</th>
<th>THEN give</th>
</tr>
</thead>
<tbody>
<tr>
<td>None/unknown</td>
<td>Prevnar 13</td>
<td>Pneumovax 23 12 months later</td>
</tr>
<tr>
<td>Pneumovax 23 given after 65</td>
<td>Prevnar 13</td>
<td>N/A</td>
</tr>
<tr>
<td>Pneumovax 23 before 65</td>
<td>Prevnar 13 &amp; 5 years after pneumatic 23</td>
<td>Pneumovax 23 - 12 months after</td>
</tr>
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**INHALERS & TECHNIQUE**

- Important for deposition of medication
- Patient compliance & understanding of the use of multiple inhalers
- Reassess use and knowledge at each office visit

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**LONG ACTING ANTICHOLINERGICS**

- Long acting anticholinergic - muscarinic antagonist:
  - tiotropium (Spiriva)
  - aclidinium (Tudorza)
  - umeclidinium (Incruse) or in combination with a LABA - umeclidinium & vilanterol (Anoro)

**LONG ACTING BETAL-2 AGONISTS**

- LABAs:
  - formoterol (Foradil)
  - salmeterol (Serevent)
  - indacaterol (Arcapta)

**TIOTROPIUM**

- Reduce exacerbations by 24% compared to ipratropium over a 1-year period
- Reduce exacerbation frequency
- Reduce hospitalizations
MEDICATION ABBREVIATIONS
- SABA = Short-acting beta-2 agonist
- LABA = Long-acting beta-2 agonist
- SAMA = Short-acting muscarinic antagonist (anticholinergic)
- LAMA = Long-acting muscarinic antagonist (anticholinergic)
- ICS = Inhaled corticosteroid
- PDE-4 inh = Phosphodiesterase-4 inhibitor

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>SABA pm or SAMA pm</td>
<td>LAMA or LABA, or SABA &amp; SAMA</td>
<td>Theophylline</td>
</tr>
<tr>
<td>B</td>
<td>LAMA or LABA</td>
<td>SABA &amp;/or SAMA, Theophylline</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>ICS/LABA or LAMA</td>
<td>LAMA &amp; LABA</td>
<td>PDE-4 inh or SABA &amp;/or SAMA, Theophylline</td>
</tr>
<tr>
<td>D</td>
<td>ICS/LABA or LAMA</td>
<td>ICS &amp; LAMA or ICS/LABA &amp; LAMA or ICS/LABA &amp; PDE-4 inh or LAMA &amp; LABA &amp; LAMA or ICS/LABA &amp; PDE-4 inh</td>
<td>Carbocysteine, SABA &amp;/or SAMA</td>
</tr>
</tbody>
</table>

INHALED CORTICOSTEROIDS
- Studies in COPD complex
- Benefits:
  - Improved lung function & 6-min walk
  - Improved QOL scores
  - Fewer AECOPD
- Adverse effects:
  - Higher risk of death
  - Greater frequency of pneumonia
  - No change in long-term lung function

INHALED CORTICOSTEROIDS
Conclusion:
- If patient has GOLD Stage III-IV and repeated exacerbations (Groups C or D), add ICS
- If ICS are utilized, it appears prudent to combine with a LABA

PHOSPHODIESTERASE-4 INHIBITORS
- Only one on U.S. market – roflumilast (Daliresp)
- Useful to reduce exacerbations in:
  - Patients with FEV₁ of < 50 % predicted
  - Chronic bronchitis
  - Frequent exacerbations

HAND HYGIENE
- Hand washing
  - Application of plain or antiseptic soap
  - Mechanical friction by rubbing for a minute
  - Rinsing with water
  - Drying with disposable towel
- Alcohol Hand-rub
  - Vigorous friction, rubbing and drying are unnecessary
  - Rub alcohol on both hands until it dries, ~ 15-30 seconds
**Medical History Assessment**
- Severity of COPD
- Duration of exacerbation
- Number of previous episodes & if hospitalized
- Comorbidities
- Present treatment regimen
- Prior mechanical ventilation

**Signs of Severity**
- Accessory muscle use
- Paradoxical chest wall movements
- Central cyanosis
- Peripheral edema
- Hemodynamic instability
- Change in mental status

**Evaluation Tools**
- Pulse oximetry
- Arterial blood gas – if hospitalized
- Chest x-ray
- EKG, BNP
- CBC
- BMP
- NO spirometry at this time

**Pharmacologic Therapy**
- Short acting beta-2 agonists are preferred – use routinely throughout exacerbation
- Add short acting anticholinergic if not already taking an anticholinergic
- MDI with spacer works well
- Nebulizer therapy best for severe to very severe COPD patients

**Pharmacologic Therapy**
- Oral corticosteroids:
  - Shorten recovery time
  - Improve lung function & hypoxemia
  - Reduce risk of early relapse
  - Diminish treatment failure
  - Lessen hospital stay
- 40 mg of prednisone per day for 5 days

Mucolytic agents:
- Examples: guaifenesin, n-acetylcysteine
- Variable effect in patients with COPD
- Ineffective at shortening the course or improving outcomes of patients with AECOPD

ANTIBIOTICS

- Look for sputum purulence
- Assess for cardinal symptoms – at least 2 of 3 present OR requiring hospitalization
- Check local bacterial resistance patterns
- No need for sputum cultures unless recurrent exacerbations occur or with more severe disease

CURRENT RECOMMENDATIONS

- Use antibiotics wisely:
  - Use the right antibiotic for the correct length of time
  - Try to narrow the antibiotic spectrum as much as possible, and as quickly as possible
  - Stop the antibiotics as early as safety allows

ANTIBIOTICS FOR OUT-PATIENTS

- Risk stratification:
- Mild disease:
- No antibiotics
- Increase bronchodilators
- Symptomatic therapy
- Instruct patient about cardinal symptoms and when to contact the office

ANTIBIOTICS FOR OUT-PATIENTS

- Risk stratification – Uncomplicated versus complicated:
  - Complicated COPD =
    - > 65 years of age
    - Comorbid conditions (especially cardiac)
    - Severe COPD
    - Frequent exacerbations (≥ 3 or per year)
    - Antimicrobial therapy within last 3 months

ANTIBIOTICS FOR OUT-PATIENTS

- Moderate-to-severe COPD Uncomplicated:
  - Advanced Macrolide (azithromycin, clarithromycin)
  - Cephalosporin (cefuroxime, cefpodoxime, cefdinir)
  - Doxycycline
  - Trimethoprim/sulfamethoxazole

ANTIBIOTICS FOR OUT-PATIENTS

- Moderate-to-severe COPD Complicated:
  - Fluoroquinolone (moxifloxacin, gemifloxacin, levofloxacin)
  - Amoxicillin/clavulanate
  - If at risk for Pseudomonas – use ciprofloxacin & obtain a sputum culture
INDICATIONS FOR HOSPITALIZATION
- Marked increase in symptoms
- Severe underlying COPD
- New physical signs – i.e. cyanosis, peripheral edema
- Failure to respond to therapy
- Serious comorbidities
- Frequent exacerbations
- Older age
- Insufficient support at home

TREATMENT GOALS FOR THE HOSPITAL
- Identify & ameliorate cause of exacerbation if possible
- Optimize lung function with bronchodilators & other agents
- Avert need for intubation if possible
- Prevent complications of immobility, thromboemboli & deconditioning
- Address nutritional needs

OXYGEN THERAPY
- Target of an arterial oxygen tension (PaO₂) of 60-70 mmHg
- Oxyhemoglobin saturation of 90-94%
- Nasal cannula
- Venturi mask
- Non-rebreather mask
- CPAP or BiPap therapy
- Endotracheal intubation

NONINVASIVE VENTILATION (NIV)
- Mechanical ventilation delivered through noninvasive interface
  – Face mask
  – Nasal mask
  – Nasal prongs

Began in early 1990s
- Non-invasive positive pressure ventilation (NIPPV)
- More effective and more cost effective than endotracheal intubation & mechanical ventilation
- Decreased mortality in respiratory failure patients with acute exacerbations

Mortality high with small subset of patients (~ 5%) needing to be transitioned from NIV to invasive ventilation – especially older patients
**Discharge Issues**
- Inhaler technique
- Reinstate proper inhalers for maintenance therapy
- Oxygen therapy
- Deconditioning
  - Physical therapy at home
  - Pulmonary Rehabilitation
- Tobacco cessation

**Discharge Issues**
- Dual-insured patients (i.e. Medicaid) more likely to be readmitted – social issues need to be addressed
- Comorbidities account for ~70% of readmissions
- Seeing a patient within 2 weeks of discharge is presumed to be best

**Preventing Readmission**
- No clear data on what actually prevents rehospitalizations!
- No studies targeting 30-day readmissions

**Discharge Office Visit**
- Need early re-assessment of the patient
- Spirometry performance - diagnosis
- Oxygen therapy
- Testing for co-morbidities – sleep study for OSA, bone density, etc.
- Review of medications
- Pulmonary rehabilitation
- Tobacco cessation
- Advanced directives

**Education of the Patient**
- Recognition of the symptoms of exacerbations
- When to call the office
- Self-management plan

**COPD Action Plans**
- 2/3 patients know when an exacerbation is imminent
- Earlier initiation of antibiotics & steroids
- No significant effect on healthcare utilization, quality of life, lung function, functional capacity, symptom scores or mortality – meta-analysis
**COMPREHENSIVE CARE MANAGEMENT PROGRAM**

- Randomized, controlled trial of 20 VA outpatient clinics
- Intervention:
  - 4 individual teaching sessions
  - 1 group teaching session
  - Action plan (with RX for prednisone & antibiotic)
  - Proactive telephone calls
- Purpose – reduce risk of COPD hospitalizations
- Primary outcome – time to first COPD hospitalization

**COMPREHENSIVE CARE MANAGEMENT PROGRAM - continued**

- 209 patients intervention group & 217 in usual care group
- Monitoring committee STOP intervention due to safety concerns
- 28 (all cause) deaths in intervention group
- 10 deaths (all cause) in usual care group
- 10 versus 3 deaths due to COPD
- Unanticipated excess mortality – why???

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**REFERENCES**

- UpToDate