Medications for Managing COPD in Hospice Patients

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Director of Clinical Operations
Outcome Resources
Goal of medications in COPD

- Decrease symptoms and/or complications
- Reduce frequency & severity of exacerbations
- Medications do not modify the long-term decline in lung function seen with COPD
Drug Treatment Principles

- COPD is a progressive disease
- More medications are required as COPD worsens
- Maintain regular treatment as long as possible
- Regimens should be patient-specific & influenced by:
  - severity of symptoms
  - frequency and severity of exacerbations
  - patient’s ability to effectively use available drug delivery devices
Problems Managing Palliative Care in COPD

- High degree of uncertainty with prognosis for COPD
- Illness trajectory of COPD does not fit hospice model
- Gradual slow decline interspersed with unpredictable exacerbations – often followed by *improvement*
- Frequent duplications in the medication regimen (unnecessary high costs)
COPD: Acute Exacerbations

- **Acute event** in the natural course of COPD
- A worsening from baseline symptoms:
  - Increased dyspnea, cough, sputum volume (sputum may also change in color)
- More significant change than typical day to day variation
- Patients and caregivers need to know how to recognize this
- Usually warrants a change in meds (often temporary)
- Common causes: respiratory infection, air pollution
Types of Medication for COPD

Primary drugs:

- **Inhaled bronchodilators** *(mainstay of treatment)*
  - Beta-2 agonist
    - Example: albuterol (Proventil)
  - Anticholinergic
    - Example: tiotropium (Spiriva)

- **Inhaled corticosteroids**
  - Example: fluticasone (Flovent)

Secondary drugs:

- Antitussives
- Antibiotics
- Mucolytics
- Roflumilast (Daliresp)
- Theophylline
- Prednisone
An Abundance of Inhaled Medications

There are 29 different inhaled respiratory drug products available today....*

Short-acting beta agonist bronchodilators
Long-acting beta agonist bronchodilators
Short-acting anticholinergic (muscarinic antagonist) bronchodilators
Long-acting anticholinergic bronchodilators
Combinations of short-acting beta agonist & short-acting anticholinergic bronchodilators
Inhaled steroids
Combinations of long-acting beta agonist bronchodilators & inhaled steroids
Combinations of long-acting beta agonist bronchodilators & long-acting anticholinergic bronchodilators
Many available in both nebulizer and MDI dosage forms

*Real potential for therapeutic duplication/overlap
Bronchodilators: Beta-2 agonist & Anticholinergic

- Both types administered as inhalants
- Different mechanisms of action to achieve same end result:
  - relaxation of bronchial smooth muscle leading to dilation of bronchial airways
- May be given via MDI or Nebulizer
- Can be used together for enhanced effectiveness
- Beta agonist has the quicker onset of action
- Both available in short-acting and long-acting forms
Inhaled Beta-2 agonists

❖ Short acting: (4 – 6 hour duration of effect):
  - Albuterol (Proventil MDI & nebulizer)
  - Levalbuterol (Xopenex MDI & nebulizer)

❖ Long acting:
  - Salmeterol (Serevent MDI only) - 12 hour duration
  - Formoterol (Foradil MDI, Perforomist nebulizer) - 12 hour duration
  - Aformoterol (Brovana nebulizer only) – 12 hour duration
  - Indacaterol (Arcapta MDI only) - 24 hour duration

❖ Primary side effects: tremor, tachycardia, nervousness, nausea
Role of the Beta-2 agonists

**Short-acting:** albuterol (Proventil), levalbuterol (Xopenex)
- routine QID therapy or PRN for acute SOB
- appropriate for acute exacerbations or maintenance use
- available in MDI or nebulizer solution
- mainstay of treatment

**Long-acting:** (Serevent, Foradil, Perforomist, Brovana, Arcapta):
- for routine maintenance therapy only
- more effective & convenient for chronic management of COPD
- not indicated for PRN use or “rescue use”
- available in MDI or nebulizer solution
- always have an additional order for PRN short-acting beta-2
Xopenex (levalbuterol) vs Albuterol

- Albuterol efficacy - No clinical difference from Xopenex
- Albuterol side effects:
  - No significant difference from Xopenex in adults:
    - Tremor
    - Increased BP
    - Increased heart rate
- Cost/Day

<table>
<thead>
<tr>
<th></th>
<th>Dose</th>
<th>Albuterol</th>
<th>Xopenex</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDI</td>
<td>2 puffs QID</td>
<td>$2.00</td>
<td>$5.00</td>
</tr>
<tr>
<td>Nebulizer</td>
<td>1 inh. QID</td>
<td>$3.00</td>
<td>$31.00</td>
</tr>
</tbody>
</table>

- Reserve Xopenex for pediatrics or adult patients intolerant to Albuterol because of above side effects
Inhaled Anticholinergics

✧ Short-acting: ipratropium (Atrovent)
  - routine QID therapy or PRN for acute SOB
  - appropriate for acute exacerbations or maintenance use
  - available in MDI or nebulizer solution

✧ Long-acting:
  - for routine maintenance therapy only (not PRN)
    - Spiriva (tiotropium): ................once a day
    - Incruse Ellipta (umeclidinium):....once a day
    - Tudorza (aclidinium): .................twice a day
  - only available in MDI form (no long-acting nebulizer solution)
  - Atrovent MDI is slightly cheaper but not significant
Bronchodilator Combination Products

- Beta agonist + Anticholinergic: more effective than either drug alone
- Combination may result in fewer side effects (use less of each drug)
- Available as short or long-acting products -
  - Duration of effect: 4 to 6 hours -
    - Combivent MDI: albuterol + ipratropium
    - Duoneb solution: albuterol + ipratropium
  - Duration of effect: 24 hours -
    - Anoro Ellipta MDI: vilanterol + umeclidinium
Optimization of COPD Therapy with Combination Bronchodilator Products

- Combination Beta-Agonist and Anticholinergic Bronchodilator
- Most effective method of addressing dyspnea in COPD

<table>
<thead>
<tr>
<th>Products</th>
<th>Dosing</th>
<th>Admin method</th>
<th>Cost/day (AWP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DuoNeb*</td>
<td>q.i.d.</td>
<td>Nebulizer</td>
<td>$8</td>
</tr>
<tr>
<td>Combivent*</td>
<td>q.i.d.</td>
<td>MDI</td>
<td>$11</td>
</tr>
<tr>
<td>Anoro-Ellipta**</td>
<td>q.d.</td>
<td>MDI (DPI)</td>
<td>$11</td>
</tr>
</tbody>
</table>

* Albuterol - Ipratropium (may also use PRN)
** Vilanterol - Umeclidinium (not for PRN use)
Inhaled Corticosteroids

Add to the regimen in patients with **severe** COPD if:
- They are already receiving routine bronchodilators & still symptomatic
- And are having repeated exacerbations

Effects:
- Reduces inflammation in lungs (use routinely, not PRN)
- **May** reduce *frequency* of exacerbations in severe COPD ?
- Benefits are *much less* dramatic in COPD than in Asthma
- Will **increase** the possibility of pneumonia
- Will not decrease overall mortality
Withdrawal of Inhaled Steroids during Optimized Bronchodilator Management

- 2400 COPD patients receiving triple therapy:
  Serevent b.i.d., Tiotropium q.d., & Fluticasone 500mcg b.i.d. x 6 weeks

- Step-down Steroid withdrawal started in 1200 of above patients

- Step-down done in 3 stages over 12 weeks.

- Results: the two groups had no difference in dyspnea
Conclusions from WISDOM Trial

• Withdrawing inhaled steroids may be an option for many COPD patients

• Withdrawal of inhaled steroids will reduce side effects and save considerable amounts of money

• Most patients w/ COPD don’t show beneficial response to inhaled steroids

• A trial of inhaled steroid withdrawal will NOT increase the risk of exacerbation even in patients w/ severe COPD
# Inhaled Corticosteroid Products

<table>
<thead>
<tr>
<th>Metered Dose Inhalers</th>
<th>Cost per day (AWP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmicort (budesonide) BID</td>
<td>$4.00</td>
</tr>
<tr>
<td>Qvar (beclomethasone) BID</td>
<td>$4.00</td>
</tr>
<tr>
<td>Flovent (Fluticasone) BID</td>
<td>$6.00</td>
</tr>
<tr>
<td>Asmanex (mometasone) BID</td>
<td>$7.00</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nebulizer Solution</th>
<th>Cost per day (AWP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmicort (budesonide) BID</td>
<td>$26.00</td>
</tr>
</tbody>
</table>

**Oral steroid:**
Prednisone 10mg daily
20 cents per day
Combination L.A. Bronchodilator / Steroids

- Advair: salmeterol & fluticasone (twice daily)
- Symbicort: formoterol & budesonide (twice daily)
- Dulera: formoterol & mometasone (twice daily)
- Breo Ellipta: vilantererol & fluticasone (once daily)

- Only available in metered dose inhaler dosage-form
- For routine use only, not for PRN use
L.A. Beta Agonist - Steroid Combinations

**Advantages - Disadvantages**

- **Bronchodilator & Steroid Combinations**
  - **Advantage**: convenience of once or twice daily dosing
  - **Disadvantage**: high cost, questionable benefit of inhaled steroid, no anticholinergic bronchodilator (may need to add w/ additional cost)
  - Patient must be capable of using an MDI effectively

### Table: Bronchodilator & Steroid Combinations

<table>
<thead>
<tr>
<th>Category/Drug</th>
<th>Dosage</th>
<th>Dosage form</th>
<th>Cost/day (AWP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advair</td>
<td>250/50 BID</td>
<td>MDI</td>
<td>$12.00</td>
</tr>
<tr>
<td>Symbicort</td>
<td>80/4.5 BID</td>
<td>MDI</td>
<td>$11.00</td>
</tr>
<tr>
<td>Dulera</td>
<td>100/5 BID</td>
<td>MDI</td>
<td>$10.00</td>
</tr>
<tr>
<td>Breo Ellipta</td>
<td>100/25 QD</td>
<td>MDI</td>
<td>$10.00</td>
</tr>
</tbody>
</table>
Role of Oral Corticosteroids (Prednisone)

- Indicated for short-term management of COPD exacerbations
- Dose: Prednisone 40mg once daily x 5 days
- Long term (maintenance) use is not recommended due to SE
- Side effects with long term therapy:
  - next slide
  - SE not associated with inhaled steroids
Prednisone Side Effects

- **Short-term (< 10 days)**
  - Hyperglycemia, fluid retention, insomnia, psychosis

- **Mid-term (2 – 8 weeks)**
  - Cushingoid appearance, thin skin, thrush, GI bleeding, muscle wasting, myopathy, increased susceptibility to infection, adrenal suppression

- **Long-term (months – years)**
  - Osteoporosis, cataracts, glaucoma
<table>
<thead>
<tr>
<th>Comparison</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDI</td>
<td>- Lower cost</td>
<td>- Requires some skill to use</td>
</tr>
<tr>
<td></td>
<td>- No equipment needed</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Portable</td>
<td></td>
</tr>
<tr>
<td>Nebulizer</td>
<td>- No skill required</td>
<td>- Higher cost for drug (2-3X or more)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Extra equipment &amp; expense</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- More side effects (more drug needed)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Not all are portable</td>
</tr>
</tbody>
</table>
Methods of Administration

**MDI**
- Active inhalation
- Preferred method
- Requires training & practice to coordinate inhalation with actuation of the container

**Nebulizer**
- Passive inhalation
- Drug is vaporized into a mist for gradual inhalation over 10 to 20 minutes
- Used in elderly, infants, and cognitively impaired
- Preferred management of acute exacerbation of COPD
Three Types of MDI’s

✿ **Moist dose inhaler** (HFA propellant type MDI) – provides suspension mist
  - Examples: Proventil HFA (albuterol)

✿ **Dry powder inhaler** (DPI) provides fine powder
  - Examples: Serevent diskus, Advair, diskus, Spiriva handihaler, Breo Ellipta, Anoro Ellipta

✿ **Soft Mist inhaler** (SMI) - provides very fine mist, propellant-free
  - Examples: Combivent respimat
Procedure for Use of the MDI’s

- Patient preference varies for DPI, HFA propellant based, or Soft Mist MDI
- All require some degree of coordination between inhalation and actuation of device
- Soft Mist inhaler may be easiest to use and may provide more drug to the lungs than other MDI devices
- Important to understand & follow specific directions supplied with each type of MDI device
- Different procedures are required for each type
Role of Antibiotics in COPD

- Short courses (7 – 10 days) appropriate for COPD exacerbation (Doxycycline, Levofloxacin, Amoxicillin, Azithromycin)

- Controversy: continuous use of prophylactic antibiotics to prevent infection in COPD?
  - not recommended by Global Initiative for Chronic Obstructive Lung Disease (GOLD)

- Recent report: Azithromycin (Zithromax) 250mg PO qd for 1yr
  - Reduced frequency of exacerbations & improved QoL.
  - Very minimal side effects noted.
  - Cost: $220/month approx.
Role of Mucolytics

Definition
- an expectorant that helps dissolve thick mucus

Drugs
- Guaifenesin (Mucinex, Robitussin, Organidin)
- Potassium iodide (SSKI)

Overall benefits may be small
- Exacerbations may be reduced in patients not being treated with inhaled steroids
Role of Antitussives

- Cough has a significant *protective* role in COPD
- Use antitussives only when cough is keeping the patient from sleeping or excessively troublesome

Drugs:
- Codeine* & derivatives (Robitussin AC, Hycodan)
- Dextromethorphan or D.M., (Robitussin DM)
- Benzonatate (Tessalon)

- All opioids have cough suppressant effects
Theophylline?

- Effective oral bronchodilator for routine maintenance
- Not for PRN usage
- Rarely used b/c potential side effects & drug intxns
- Theo-24, Uniphyll, Theo-Dur (all sustained release)
- Dosage: 200mg to 400mg BID
- Lab monitoring of theophylline blood levels recommended
- Inhaled bronchodilators are preferred in COPD
- Side effects:
  - nausea/vomiting, insomnia, restlessness, tremors, cardiac arrhythmia, seizures
Drug Regimen Options & Costs: (MDI)

<table>
<thead>
<tr>
<th>Common Combinations</th>
<th>Cost-Effective Alternatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Albuterol 2 puffs Q4h prn Serevent 1 puff Q12h</td>
<td>Albuterol 2 puffs QID and Q4h prn</td>
</tr>
<tr>
<td>AWP cost /day: $10.00</td>
<td>AWP Cost/day: $2.00</td>
</tr>
<tr>
<td>2) Albuterol 2 puffs Q4h prn Serevent 1 puff Q12h Spiriva 1 puff q24h</td>
<td>Combivent Respimat 1 puff QID and prn</td>
</tr>
<tr>
<td>AWP cost/day: $21.00</td>
<td>AWP Cost/day: $11.00</td>
</tr>
<tr>
<td>3) Albuterol 2 puffs Q4h prn Spiriva 1 puff Q24h Advair diskus 1 puff Q12h</td>
<td>Combivent 2 puffs QID and prn Qvar 80mcg BID</td>
</tr>
<tr>
<td>AWP cost/day: $25.00</td>
<td>AWP cost/day: $17.00</td>
</tr>
</tbody>
</table>
# Drug Regimen Options & Costs: (Nebulizer)

<table>
<thead>
<tr>
<th>Common Combinations</th>
<th>Cost-Effective Alternatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Albuterol solution Q4h prn Perforomist or Brovana soln Q12h</td>
<td>Albuterol solution QID &amp; prn</td>
</tr>
<tr>
<td></td>
<td>AWP cost /day: $28.00</td>
</tr>
<tr>
<td></td>
<td>AWP Cost/day: $7.00</td>
</tr>
<tr>
<td>2) Albuterol/Ipratropium soln (Duoneb) QID and prn</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>AWP cost/day: $8.00</td>
</tr>
<tr>
<td>3) Albuterol solution Q4h prn Perforomist or Brovana Q12h Budesonide solution Q12h</td>
<td>Albuterol solution QID &amp; prn</td>
</tr>
<tr>
<td></td>
<td>AWP cost/day: $54.00</td>
</tr>
<tr>
<td></td>
<td>AWP cost/day: $31.00</td>
</tr>
</tbody>
</table>
Daliresp (roflumilast)

- Oral drug for **severe** COPD
- **Only for**: COPD w/ chronic bronchitis & **history of exacerbations**
- **Not for**: COPD characterized by emphysema
- **Dose**: 500mcg PO once daily routinely – to reduce exacerbations
- **Mech. of action**: phosphodiesterase inhibitor (antiinflammatory)
- **Concern**: High potential for side effects
- (14% stopped drug in clinical trials):
  - nausea/vomiting
  - Diarrhea
  - wt. loss
  - adverse psychiatric events, increased suicide risk
COPD Medication Summary Points

- All patients should have a short-acting B-2 agonist bronchodilator (for prn or rescue)
- Combine Beta-2 agonists and Anticholinergics = increased bronchodilator effectiveness
- Avoid therapeutic duplications; such as:
  - 2 or more anticholinergic bronchodilators
  - 2 or more LA beta agonist bronchodilators
  - 2 or more inhaled steroids
  (pay particular attention to combination products)
…More Summary Points

- MDI method preferred, IF patient can demonstrate good technique
- Nebulizer therapy is more costly and inconvenient but more effective for weak, frail, or confused patients
- LA Beta-2 agonist bronchodilators offer more convenience; but at a cost
- LA bronchodilators and inhaled steroids are NOT for PRN use
- Inhaled steroids may not be very beneficial for COPD
- Manage acute exacerbations with Prednisone and antibiotics
G.O.L.D.

- Global initiative for chronic
- Obstructive
- Lung
- Disease

For more information on COPD:
www.goldcopd.org

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Helping You Help Your Patients

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