A Visual Approach to Simplifying Respiratory Drug Regimens

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Learning Objectives

- Be able to list at least 3 major adverse effects of inhaled medications
- Be able to visually separate the different inhaled medications into their proper classifications
- Be able to identify duplicate therapies in a patient's respiratory medication regimen
- Be able to state the risk and rational of using or not using corticosteroids in the hospice population
- Be able to list the steps to appropriately manage dyspnea in a hospice patient

Inhaled Respiratory Drugs

3 Main Categories

- Beta 2 Agonists
  - Binds to beta-2 receptors
  - Relaxation of smooth muscles in the lung
  - Dilation and opening of airways
  
  Can be mixed and matched in various combinations

- Muscarinic Antagonists
  - Inhibits acetylcholine in bronchial smooth muscle
  - Bronchodilation

- Corticosteroids
  - Inhibits the inflammatory response

Adverse Effects of Inhaled Medications

<table>
<thead>
<tr>
<th>Drug Category</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta 2 agonists</td>
<td>Tachycardia (up to 200 beats/minute), arrhythmias, nervousness, headache, tremor, dry mouth, agitation, nausea, dizziness, sleeplessness, hypertension or hypotension</td>
</tr>
<tr>
<td>Muscarinic antagonists</td>
<td>Dizziness, headache, dry mouth, dyspepsia, diarrhea, URTI, urinary retention, constipation</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Increase risk of upper respiratory tract infections, headache, pharyngitis</td>
</tr>
</tbody>
</table>

Dosage Forms

- Handheld Inhaler
  - Metered dose inhaler (MDI)
  - Aerolizer
  - HandiHaler
  - Twisthaler
  - Flexhaler

  Handheld inhalers
  - Require adequate inhalation force
  - Require coordination to use
  - Generally more expensive compared to the nebulized solution

- Nebulized solution

- Oral tablet (Albuterol tablet, corticosteroid: prednisone)

- Beta 2 agonists and muscarinic antagonists
  - Short-acting and long-acting formulations

Respiratory Medications NOT in Combination

Corticosteroids

- Handheld Inhaler
  - Budesonide (Pulmicort Flexhaler)
  - Ciclesonide (Alvesco)
  - Fluticasone (Flovent HFA/Diskus)

  Can be mixed and matched in various combinations

- Oral – Prednisone

Muscarinic Antagonists

- Handheld Inhaler
  - Ipratropium HFA (Atrovent HFA)
  - Indacaterol (Foradil Aerolizer)

- Nebulized solution
  - Ipratropium (Atrovent Respules)

Beta 2 Agonists

- Handheld Inhaler
  - Albuterol HFA (Ventolin HFA, Proair HFA, Proventil HFA)

  Can be mixed and matched in various combinations

- Oral – Albuterol

- Nebulized solution
  - Short Acting
    - Albuterol (Aerolizer)
    - Levalbuterol (Xopenex)
  - Long Acting
    - Formoterol (Foradil Aerolizer)
    - Indacaterol (Foradil Aerolizer)

- Oral – Albuterol (Aventin), Formoterol (Foradil)
Respiratory Medications NOT in Combination

<table>
<thead>
<tr>
<th>Corticosteroids</th>
<th>Beta 2 Agonists</th>
<th>Muscarinic Antagonists</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Handheld Inhaler (MDI or DPI):</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beclomethasone (Qvar)</td>
<td>Albuterol HFA (Ventolin HFA)</td>
<td>Formoterol (Foradil Aerolizer)</td>
</tr>
<tr>
<td>Budesonide (Pulmicort Flexhaler)</td>
<td>Formoterol HFA (Foradil Aerolizer)</td>
<td>Ipratropium HFA (Atrovent HFA)</td>
</tr>
<tr>
<td>Ciclesonide (Alvesco)</td>
<td>Fluticasone HFA (Flonase)</td>
<td>Indacaterol (Bystol Respimat)</td>
</tr>
<tr>
<td>Fluticasone (Flonase)</td>
<td>Olodaterol HFA (Stelatine Respimat)</td>
<td>Tiotropium (Spiriva Handihaler, Spiriva Respimat)</td>
</tr>
<tr>
<td>Mometasone (Asmanex Twisthaler)</td>
<td>Ipratropium HFA (Atrovent HFA)</td>
<td>Umeclidinium (Incruse Ellipta)</td>
</tr>
<tr>
<td>Nebulized Solution</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Budesonide (Pulmicort Respules)</td>
<td>Albuterol (Ventolin HFA)</td>
<td>Arformoterol (Bystol)</td>
</tr>
<tr>
<td></td>
<td>Leflunolide (Symbicort)</td>
<td>Formoterol (Foradil Aerolizer)</td>
</tr>
<tr>
<td>Oral</td>
<td>Prednisone</td>
<td>Albuterol</td>
</tr>
</tbody>
</table>

Approach to a Patient’s Inhaled Medications

1) Separate the **PRN** orders from **Routine** orders
   - **For PRN therapy**, the patient should only be on a regimen that contains one beta 2 agonist and/or one muscarinic antagonist.
   - **For Routine therapy**, the patient does not have to have something from all 3 categories, but if they are on something, they should only have one of that type of medication on board.

2) See if there are any duplicate therapies
3) Discontinue any duplicate therapies
4) Are there any medications you can consolidate?

Patient Case #1

- Terminal Diagnosis – COPD
- Medication List
  - Proair HFA (albuterol) – 2 puffs q4-6 hours PRN
  - Combitvent Respimat (albuterol/ipratropium) – 1 puff q4 hours PRN
  - Spiriva Handihaler (tiotropium) – 1 cap inhaled once daily
  - Xopenex (levalbuterol) – 3 mL vial via neb four times a day
  - Advair (fluticasone/salmeterol) – 1 inhalation BID
  - Duoneb (albuterol/ipratropium) – 3 mL vial via neb four times a day
  - Prednisone 10 mg PO daily
  - Duoneb (albuterol/ipratropium) – 3 mL vial via neb q4-6 hours PRN

Patient Case #1 – Step 1

- Separated **PRN** orders from **Routine** orders
- **Proair HFA** (albuterol) – 2 puffs q4-6 hours PRN
- **Combivent Respimat** (albuterol/ipratropium) – 1 puff q4 hours PRN
- **Spiriva Handihaler** (tiotropium) – 1 cap inhaled once daily
- **Xopenex** (levalbuterol) – 3 mL vial via neb four times a day
- **Advair** (fluticasone/salmeterol) – 1 inhalation BID
- **Duoneb** (albuterol/ipratropium) – 3 mL vial via neb four times a day
- Prednisone 10 mg PO daily
- **Duoneb** (albuterol/ipratropium) – 3 mL vial via neb q4-6 hours PRN
**Patient Case #1 – Step 1**

Separate **PRN orders** from **Routine orders**

**PRN orders**
- Proair HFA (albuterol) – 2 puffs q4-6 hours PRN
- Combivent Respimat (albuterol/ipratropium) – 1 puff q4 hours PRN
- Duoneb (albuterol/ipratropium) – 3mL via neb q4-6 hours PRN

**Routine orders**
- Spiriva HandiHaler (tiotropium) – 1 cap inhaled once daily
- Xopenex HFA (levalbuterol) – 2 puffs four times a day
- Advair (fluticasone/salmeterol) – 1 inhalation BID
- Duoneb (albuterol/ipratropium) – 3mL via neb four times a day
- Prednisone 10mg PO daily

**Patient Case #1 – Step 2**

See if there are any duplicate therapies

**PRN orders**
- Proair HFA (albuterol) – 2 puffs q4-6 hours PRN
- Combivent Respimat (albuterol/ipratropium) – 1 puff q4 hours PRN
- Duoneb (albuterol/ipratropium) – 3mL via neb q4-6 hours PRN

**Routine orders**
- Spiriva HandiHaler (tiotropium) – 1 cap inhaled once daily
- Xopenex HFA (levalbuterol) – 2 puffs four times a day
- Advair (fluticasone/salmeterol) – 1 inhalation BID
- Duoneb (albuterol/ipratropium) – 3mL via neb four times a day
- Prednisone 10mg PO daily

**Patient Case #1 – Step 2**

<table>
<thead>
<tr>
<th>Dosage Form</th>
<th>Corticosteroids</th>
<th>Beta 2 Agonists</th>
<th>Muscarinic Antagonists</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRN</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Handheld Inhaler</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nebulizer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Routine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Handheld Inhaler</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nebulizer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral</td>
<td>Tiotropium (Spiriva)</td>
<td></td>
<td>Fluticasone / Salmeterol (Advair)</td>
</tr>
</tbody>
</table>

Do you see the duplicate therapies?

**Patient Case #1 - Step 3**

**Discontinue any duplicate therapies**

- Determine the severity of the patient’s COPD or lung condition.
- If they are taking nebulized inhaled medications, they most likely do not have enough positive inhalation force to use handheld inhalers.
- Consider keeping the nebulized solutions and D/C the handheld inhalers.

Hospice patients with a terminal diagnosis of COPD or lung cancer generally do not have enough positive inhalation force to use handheld devices and should be on nebulized therapy.
### Step 3 Discontinue any duplicate therapies

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</thead>
<tbody>
<tr>
<td>PRN Handheld Inhaler</td>
<td>Albuterol HFA (Proair)</td>
<td>Albuterol / Ipratropium (Combivent Respimat)</td>
<td></td>
</tr>
<tr>
<td>Nebulizer</td>
<td>Albuterol / Ipratropium (Combivent Respimat)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Routine Handheld Inhaler</td>
<td>Tiotropium (Spiriva)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nebulizer</td>
<td>Fluticasone / Salmeterol (Advair)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nebulizer</td>
<td>Albuterol / Ipratropium (Combivent Respimat)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral</td>
<td>Prednisone</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Which medications would you discontinue?

### Patient Case #2

#### Terminal diagnosis – CHF and COPD

- **Medications**
  - Ventolin HFA (albuterol) – 2 puffs q4-6 hours PRN
  - Lasix (furosemide) – 20mg tab BID
  - Potassium chloride – 20mEq tab BID
  - Advair (fluticasone/salmeterol) – 1 inhalation BID
  - Levothyroxine – 75mcg tab daily
  - Ipratropium neb – 1 vial via neb four times a day
  - Lisinopril – 10mg tab daily
  - Lorazepam – 1mg q4 hours PRN
  - Duoneb (albuterol/ipratropium) – 3mL vial via neb q4-6 hours PRN
  - Haloperidol – 1mg BID

### Step 4 Consolidating Medications

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<thead>
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</tr>
</thead>
<tbody>
<tr>
<td>PRN Nebulizer</td>
<td>Albuterol / Ipratropium (Combivent Respimat)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nebulizer</td>
<td>Albuterol / Ipratropium (Combivent Respimat)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Routine Oral</td>
<td>Albuterol / Ipratropium (Combivent Respimat)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Are there any medications you can consolidate?

### Patient Case #2 – Step 1

Separate **PRN** orders from **Routine** orders

- Ventolin HFA (albuterol) – 2 puffs q4-6 hours PRN
- Advair (fluticasone/salmeterol) – 1 inhalation BID
- Ipratropium neb – 1 vial via neb four times a day
- Duoneb (albuterol/ipratropium) – 3mL vial via neb q4-6 hours PRN

### Patient Case #2 – Step 1

Separate **PRN** orders from **Routine** orders

- **PRN**
  - Ventolin HFA (albuterol) – 2 puffs q4-6 hours PRN
  - Duoneb (albuterol/ipratropium) – 3mL vial via neb q4-6 hours PRN

- **Routine**
  - Ipratropium neb – 1 vial via neb four times a day
  - Advair (fluticasone/salmeterol) – 1 inhalation BID
Patient Case #2 – Step 2

See if there are any duplicate therapies

- **PRN**
  - Ventolin HFA (albuterol) – 2 puffs q4-6 hours PRN
  - Duoneb (albuterol/ipratropium) – 3mL via neb q4-6 hours PRN

- **Routine**
  - Ipratropium neb – 1 vial via neb four times a day
  - Advair (fluticasone/salmeterol) – 1 inhalation BID

Do you see the duplicate therapies?

Discontinue any duplicate therapies

Is there any medications you can consolidate?
**Patient Case #2 – Step 4**

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>PRN</td>
<td>Nebulize</td>
<td>Albuterol / Ipratropium (DuoNeb)</td>
<td>Ipratropium neb.</td>
</tr>
<tr>
<td>Routine</td>
<td>Nebulize</td>
<td>Fluticasone / Salmeterol (Advair)</td>
<td>Ipratropium neb.</td>
</tr>
</tbody>
</table>

- Patients with end stage COPD generally do not have enough positive inhalation force to use handheld inhalers.
- The patient is already on nebulized solutions.
- Plan
  - D/C Advair and Ipratropium neb
  - Use Duoneb routinely and PRN
  - Add oral Prednisone, if a steroid is necessary

**Note regarding inhaled corticosteroids use in COPD**

- The use of inhaled corticosteroids (ICS) in COPD is controversial.
- Routine use of ICS has been associated with an increased risk of pneumonia, thrush, dysphonia and reduction in bone density.
- ICS are also expensive medications that has been shown to have a minimal impact on COPD exacerbations.
- In a Cochrane Database Systematic Review, the risk of COPD exacerbations have only been reduced by one exacerbation per patient every four years for patients who were taking an ICS compared to salmeterol alone.


**Management of Dyspnea**

**Step 1: Non-pharmacological interventions**

- Elevate the head of the bed
- Use a fan to move cool air over the patient
  - Open a window if possible
- Eliminate environmental irritants
- Give reassurance during acute distress
- If feasible, teach the patient breathing exercises and relaxation techniques
- Mouth breathing and supplemental oxygen will dry out the mouth. Maintain adequate humidity in the room and provide good oral hygiene

**Step 2: Optimize current inhaled therapy**

- Optimize Oxygen treatment
- Optimize nebulized inhalated medications
  - Discontinue duplicate therapies
  - Replace handheld inhalers with nebulized treatment

**Note regarding inhaled corticosteroids use in COPD**

- In the WISDOM (Withdrawal of Inhaled Glucocorticoids and Exacerbations of COPD) trial, published in the NEJM 2014, ICS were withdrawn from patients who were receiving both a long-acting beta agonists and a long-acting muscarinic antagonists over a period of 12 weeks.

- These patients did not experience an increase in exacerbation or worsening of their condition over the 52 week study period with the withdrawal of ICS.

The study authors recommended discontinuation of ICS for patients with severe or very severe COPD.


**Management of Dyspnea**

**Step 1: Non-pharmacological interventions**

- Elevate the head of the bed
- Use a fan to move cool air over the patient
  - Open a window if possible
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**Step 2: Optimize current inhaled therapy**

- Optimize Oxygen treatment
- Optimize nebulized inhalated medications
  - Discontinue duplicate therapies
  - Replace handheld inhalers with nebulized treatment

**Note regarding inhaled corticosteroids use in COPD**

- The REDUCE study, published in JAMA 2013, demonstrated that a short 5-day course of oral prednisone 40mg to manage acute COPD exacerbations was noninferior to a 14 day course.

- Time to next COPD exacerbation in patients with very severe COPD (GOLD stage IV disease)
  - 5 day steroid group = 43.5 days
  - 14 day steroid group = 29 days

Therefore, a short 5-day course with taper of oral prednisone 40mg/day would be appropriate for acute COPD exacerbations compared to a 14 day course.

Management of Dyspnea

Step 3: Addition of an opioid to reduce respiratory rate

**Morphine (MSIR, Roxanol)**
5 – 10mg PO/SL q1 hour PRN

**OR**

**Oxycodone (OxyIR, OxyFast)**
2.5 – 7.5mg PO/SL q1 hour PRN

**Titrate to effect and monitor respiratory rate**

Management of Dyspnea

Step 4: Addition of a benzodiazepine to reduce anxiety

**Lorazepam**
0.5 – 2mg PO/SL/IV q4 hours PRN

Conclusion

• By identifying and discontinuing duplicate inhaled respiratory therapies, patients would be able to avoid potential toxicity and adverse effects.

• This also helps hospices reduce costs towards more cost-effective medications

Questions?

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Summary

• Approach to a patient’s inhaled medications
  1) Separate PRN orders from Routine orders
  2) See if there are any duplicate therapies
  3) Discontinue any duplicate therapies

• Duoneb (routinely and prn), plus Prednisone (if a steroid medication is needed) is the most cost-effective therapy for hospice patients with a terminal diagnosis of COPD or lung cancer.

• Inhaled corticosteroids should be discontinued in patients with severe or very severe COPD.

• A short 5-day course with a taper of oral Prednisone 40mg/day would be appropriate for acute COPD exacerbations.

• Management of dyspnea
  1) Non-pharmacological interventions
  2) Optimize current inhaled therapy
  3) Addition of an opioid to reduce respiratory rate
  4) Addition of a benzodiazepine to reduce anxiety