



A Visual Approach to Simplifying Respiratory Drug Regimens

Stephanie Cheng, PharmD, MPH, BCGP
June 28, 2017



Adverse Effects of Inhaled Medications

Drug Category	Adverse Effects
Beta 2 agonists	Tachycardia (up to 200 beats/minute), arrhythmias, nervousness, headache, tremor, dry mouth, palpitation, nausea, dizziness, sleeplessness, hypertension or hypotension
Muscarinic antagonists	Dizziness, headache, dry mouth, dyspepsia, nausea, UTI, urinary retention, constipation
Corticosteroids	Increase risk of upper respiratory tract infections, headache, pharyngitis



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 rationale of using or not using corticosteroids in the hospice population
- Be able to list the steps to appropriately manage dyspnea in a hospice patient



Dosage Forms

- Handheld Inhaler
 - Metered dose inhaler (MDI)
 - Dry powder inhaler (DPI)
 - Aerolizers
 - HandiHaler
 - Twisthaler
 - Flexhaler
- Nebulized solution
- Oral tablet (Albuterol tablet, corticosteroid: prednisone)
- Beta 2 agonists and muscarinic antagonists
 - Short-acting and long-acting formulations

Handheld inhalers

- Require adequate inhalation force
- Require coordination to use
- Are generally more expensive compared to the nebulized solution



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

Muscarinic Antagonists

- Inhibits acetylcholine in bronchial smooth muscle
- Bronchodilation

Corticosteroids

- Inhibits the inflammatory response

Can be mixed and matched in various combinations



Respiratory Medications NOT in Combination

Corticosteroids

End in -sone or -nide

- Handheld Inhaler
 - Beclomethasone (Qvar)
 - Budesonide (Pulmicort Flexhaler)
 - Ciclesonide (Alvesco)
 - Fluticasone (Flovent HFA/Diskus)
 - Mometasone (Asmanex Twisthaler)
- Nebulized solution
 - Budesonide (Pulmicort Respules)
- Oral – Prednisone

Muscarinic Antagonists

End in -ium

- Handheld Inhaler
 - Short Acting
 - Ipratropium HFA (Atrovent HFA)
 - Long Acting
 - Acclidinium (Turdorza Pressair)
 - Tiotropium (Spiriva Handihaler/Respimat)
 - Umeclidinium (Incruse Ellipta)
- Nebulized solution - Ipratropium

Beta 2 Agonists

End in -terol

- Handheld Inhaler
 - Short Acting
 - Albuterol HFA (Ventolin HFA, Proair HFA, Proventil HFA)
 - Levalbuterol HFA (Xopenex HFA)
 - Long acting
 - Formoterol (Foradil Aerolizer)
 - Indacaterol (Arcapta Neohaler)
 - Olodaterol (Striverdi Respimat)
 - Salmeterol (Serevent Diskus)
- Nebulized solution
 - Short Acting
 - Albuterol (AccuNeb)
 - Levalbuterol (Xopenex)
 - Long Acting
 - Arformoterol (Brovana)
 - Formoterol (Perforomist)
- Oral - Albuterol



Respiratory Medications **NOT** in Combination

	Corticosteroids	Beta 2 agonists		Muscarinic antagonists	
		Short acting	Long acting	Short acting	Long acting
Handheld Inhaler (MDI or DPI)	Beclomethasone (Qvar)	Albuterol HFA (Ventolin HFA, Proair HFA, Proventil HFA)	Formoterol (Foradil Aerolizer)	Ipratropium HFA (Atrovent HFA)	Acclidinium (Turdorza Pressair)
	Budesonide (Pulmicort Flexhaler)		Indacaterol (Arcapta Neohaler)		Tiotropium (Spiriva Handihaler, Spiriva Respimat)
	Ciclesonide (Alvesco)	Levalbuterol HFA (Xopenex HFA)	Olodaterol (Striverdi Respimat)		Umeclidinium (Incruse Ellipta)
	Fluticasone (Flovent HFA, Flovent Diskus)		Salmeterol (Serevent Diskus)		
	Mometasone (Asmanex Twisthaler)				
Nebulized Solution	Budesonide (Pulmicort Respules)	Albuterol (AccuNeb)	Arformoterol (Brovana)	Ipratropium	
		Levalbuterol (Xopenex)	Formoterol (Perforomist)		
Oral	Prednisone	Albuterol			

Approach to a Patient's Inhaled Medications

- 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.

Corticosteroids and long acting beta 2 agonists and muscarinic antagonists should **NOT** be used on a PRN basis.

- 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.
- See if there are any duplicate therapies
 - Discontinue any duplicate therapies
 - Are there any medications you can consolidate?



Respiratory Medications in Combination

Beta 2 Agonist + Muscarinic Antagonists

- Short Acting – PRN or Routine Use**
 - Handheld Inhaler – Albuterol/Ipratropium (Combivent Respimat)
 - Nebulized solution – Albuterol/Ipratropium (DuoNeb)
- Long acting – Routine Use Only**
 - Vilanterol/Umeclidinium (Anoro Ellipta)
 - Olodaterol/Tiotropium (Stiolto Respimat)

Corticosteroid + Beta 2 Agonist

- Long acting – Routine Use Only**
 - Budesonide/formoterol (Symbicort)
 - Fluticasone/salmeterol (Advair HFA, Advair Diskus)
 - Fluticasone/vilanterol (Breo Ellipta)
 - Mometasone/formoterol (Dulera)

All long-acting inhalers are handheld inhalers



Patient Case #1

- Terminal Diagnosis – COPD
- Medication List
 - 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) – 3mL vial via neb four times a day
 - Advair (fluticasone/salmeterol) – 1 inhalation BID
 - Duoneb (albuterol/ipratropium) – 3mL vial via neb four times a day
 - Prednisone 10mg PO daily
 - Duoneb (albuterol/ipratropium) – 3mL vial via neb q4-6 hours PRN



Respiratory Medications in Combination

	Corticosteroids	Beta 2 Agonist	Muscarinic Antagonists
Short-Acting – PRN or Routine Use			
Handheld Inhaler (MDI)		Albuterol / Ipratropium (Combivent Respimat)	
Nebulized Solution		Albuterol / Ipratropium (Duoneb)	
Long-Acting – Routine Use Only			
Handheld Device (MDI or DPI)		Vilanterol / Umeclidinium (Anoro Ellipta)	
		Olodaterol / Tiotropium (Stiolto Respimat)	
	Budesonide / Formoterol (Symbicort)		
	Fluticasone / Salmeterol (Advair HFA, Advair Diskus)		
	Fluticasone / Vilanterol (Breo Ellipta)		
	Mometasone / Formoterol (Dulera)		



Patient Case #1 – Step 1

Separate **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) – 3mL vial via neb four times a day
- Advair (fluticasone/salmeterol) – 1 inhalation BID
- Duoneb (albuterol/ipratropium) – 3mL vial via neb four times a day
- Prednisone 10mg PO daily
- Duoneb (albuterol/ipratropium) – 3mL 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 vial via neb q4-6 hours PRN

Routine orders

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



Patient Case #1 – Step 2

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
PRN	Handheld Inhaler		Albuterol HFA (Proair)	
	Nebulizer		Albuterol / Ipratropium (Combivent Respimat) Albuterol / Ipratropium (DuoNeb)	
Routine	Handheld Inhaler			
	Nebulizer			
	Oral			
Routine		Tiotropium (Spiriva) Levalbuterol (Xopenex HFA) Prednisone	Fluticasone / Salmeterol (Advair) Albuterol / Ipratropium (DuoNeb)	



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 vial via neb q4-6 hours PRN

Routine orders

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



Patient Case #1 – Step 2

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
PRN	Handheld Inhaler		Albuterol HFA (Proair)	
	Nebulizer		Albuterol / Ipratropium (Combivent Respimat) Albuterol / Ipratropium (DuoNeb)	
Routine	Handheld Inhaler		Levalbuterol (Xopenex HFA)	Tiotropium (Spiriva)
	Nebulizer		Fluticasone / Salmeterol (Advair)	Albuterol / Ipratropium (DuoNeb)
	Oral	Prednisone		

Do you see the duplicate therapies?



Patient Case #1 – Step 2

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
PRN	Handheld Inhaler			
	Nebulizer			

PRN	Albuterol HFA (Proair)	Albuterol / Ipratropium (Combivent Respimat)
		Albuterol / Ipratropium (DuoNeb)



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

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
PRN	Handheld Inhaler		Albuterol HFA (Proair)	
	Nebulizer		Albuterol / Ipratropium (Combivent Respimat)	
Routine	Handheld Inhaler		Levalbuterol (Xopenex HFA)	Tiotropium (Spiriva)
			Fluticasone / Salmeterol (Advair)	
	Nebulizer		Albuterol / Ipratropium (DuoNeb)	
	Oral	Prednisone		

Which medications would you discontinue?



Step 3 Discontinue any duplicate therapies

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
PRN	Handheld Inhaler		Albuterol HFA (Proair)	
	Nebulizer		Albuterol / Ipratropium (DuoNeb)	
Routine	Handheld Inhaler		Levalbuterol (Xopenex HFA)	Tiotropium (Spiriva)
			Fluticasone / Salmeterol (Advair)	
	Nebulizer		Albuterol / Ipratropium (DuoNeb)	
	Oral	Prednisone		

The combination therapy of using 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.



Step 4 Consolidating Medications

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
PRN	Nebulizer		Albuterol / Ipratropium (DuoNeb)	
Routine	Nebulizer		Albuterol / Ipratropium (DuoNeb)	
	Oral	Prednisone		

Are there any medications you can consolidate?



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

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 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

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
PRN	Handheld Inhaler		Albuterol HFA (Proair)	
	Nebulizer		Albuterol / Ipratropium (DuoNeb)	
Routine	Handheld Inhaler	Fluticasone / Salmeterol (Advair)		
	Nebulizer			Ipratropium neb

Do you see the duplicate therapies?



Patient Case #2 – Step 2

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
PRN	Handheld Inhaler			
	Nebulizer			

PRN Albuterol HFA (Ventolin) Albuterol / Ipratropium (Duoneb)



Patient Case #2 – Step 3

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
PRN	Handheld Inhaler		Albuterol HFA (Proair)	
	Nebulizer		Albuterol / Ipratropium (DuoNeb)	
Routine	Handheld Inhaler	Fluticasone / Salmeterol (Advair)		
	Nebulizer			Ipratropium neb

Discontinue any duplicate therapies



Patient Case #2 – Step 2

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
PRN	Handheld Inhaler		Albuterol HFA (Ventolin)	
	Nebulizer		Albuterol / Ipratropium (DuoNeb)	
Routine	Handheld Inhaler			
	Nebulizer			
	Oral			

Routine Ipratropium neb Fluticasone / Salmeterol (Advair)



Patient Case #2 – Step 4

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
PRN	Nebulizer		Albuterol / Ipratropium (DuoNeb)	
Routine	Handheld Inhaler	Fluticasone / Salmeterol (Advair)		
	Nebulizer			Ipratropium neb

Is there any medications you can consolidate?



Patient Case #2 – Step 4

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
PRN	Nebulizer		Albuterol / Ipratropium (DuoNeb)	
Routine	Handheld Inhaler	Fluticasone / Salmeterol (Advair)		
	Nebulizer			Ipratropium neb

- 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 **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.

Leuppi JD, Schuetz P, Bingisser R, et al. Short-term vs conventional glucocorticoid therapy in acute exacerbations of chronic obstructive pulmonary disease: the REDUCE randomized clinical trial. JAMA. 2013;309:2223-2231.



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.**

Nannini, Laserson, Poole. Combined corticosteroid and long-acting beta-2 agonists for chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2012;(9):CD006829.



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



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.**

Magnussen, Disse, Rodriguea-Roisin, et al. Withdrawal of inhaled glucocorticoids and exacerbations of COPD. N. Engl. J. Med. 2014;371:1285-4.



Management of Dyspnea

Step 2: Optimize current inhaled therapy

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



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



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

Management of Dyspnea

Step 4: Addition of a benzodiazepine to reduce anxiety

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



Questions?

Stephanie Cheng, PharmD, MPH, BCGP

Clinical Pharmacist
Hospice Pharmacy Solutions
scheng@hospicepharmacysolutions.com



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

