

Pediatric Pharmacotherapy 101: Pulmonary Symptom Management

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Disclosure

- I have no relevant financial relationships with manufacturers of any commercial products and/or providers of commercial services discussed in this presentation
 - This discussion will include the use of medications for off-label indications
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Objectives

- Identify pharmacologic treatment options for secretion management in pediatric patients
 - Discuss pharmacological and non-pharmacological management of dyspnea in pediatric patients
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Secretions



Patient Case: Drooly

18 month old male with spinal muscular atrophy

- Weight: 10.5 kg
 - Spinal muscular atrophy (SMA) Type I
 - Minimal head, neck, and trunk control
 - Difficulty managing secretions
 - Experiencing respiratory decline
 - Gtube for feeds and medications
 - Parents wish to avoid aggressive therapy
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atropine 1% ophthalmic solution	Give 1 drop SL q6h prn increased secretions
glycopyrrolate (Robinul®) 1 mg/mL compounded solution	Give 1 mL g-tube TID
normal saline 0.9% solution	Inhale 3 mL (1 vial) via nebulizer daily & prn wheezing

Secretions

- Chronic issue for children with neurological impairment
- Common symptom at end of life
 - “Death rattle”
- Two components of saliva
 - Sialorrhea (thin watery secretion)
 - Thick mucus

Bavikatte G, Sit PL, Hassoon A. Management of Drooling of Saliva. *BJMP* 2012; 5(1):a507.

Causes of Secretions

- Sialorrhea can be caused by three different factors:
 - Excessive production of saliva
 - Inability to retain saliva in the mouth
 - Difficulty swallowing

Bavikatte G, Sit PL, Hassoon A. Management of Drooling of Saliva. *BJMP* 2012; 5(1):a507.

Causes of Secretions

Sialorrhea

- Neurodegenerative disorders
- Mouth, jaw or nasopharynx abnormalities
- Mouth cancer
- Dysphagia
- Psychological
- Fluid overload

Thick Secretions

- Tube feedings
- Fluid overload & edema
- Dehydration
- Infection
- Medications

Villa A, Connell CL, Abati S. Diagnosis and management of xerostomia and hyposalivation. *Ther Clin Risk Manag* 2015; 11: 45-51.

Causes of Secretions

Medication Causes

Sialorrhea

- Antipsychotics
- Antibiotics
- Benzodiazepines
- Iron
- NSAIDs
- Potassium

Thick Secretions

- Antiepileptics
- Antihypertensives
- Antispasmodics
- Cholinergics
- Opioids
- Selective Serotonin Reuptake Inhibitors (SSRIs)

Villa A, Connell CL, Abati S. Diagnosis and management of xerostomia and hyposalivation. *Ther Clin Risk Manag* 2015; 11: 45-51.

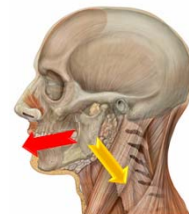
Complications of Increased Secretions

- Excessive secretions
 - Partially obstruct airway
 - Increase airway resistance
 - Increase work of breathing
-

Complications of Increased Secretions

Anterior vs. Posterior

- Anterior
 - Damp clothing
 - Irritated skin
 - Odor
- Posterior
 - Recurrent airway symptoms
 - Chronic cough
 - Choking



American Academy for Cerebral Palsy and Developmental Medicine. Sialorrhea Care Pathway 2016.

Assessment of Secretions

- Patient's ability to swallow
- Cough/gag reflex
- Characteristics of secretions
 - Color, odor, blood, signs of infection
- Oral hygiene practices
- Hydration status
- Exposure to environmental allergens
- Benefit of suctioning
- Child and family concerns

Bavikatte G, Sit PL, Hassoon A. Management of Drooling of Saliva. *BJMP* 2012; 5(1):a507.

Non-Pharmacological Options for Secretions

- Oropharyngeal suctioning
- Positioning
- Mobilization
- Encourage mouth care
 - Moistened oral swabs
- Ice chips, flavored popsicles
- Decrease fluid intake

Bavikatte G, Sit PL, Hassoon A. Management of Drooling of Saliva. *BJMP* 2012; 5(1):a507.

Secretion Management

Focus of Management

- Able to expectorate: thin secretions
 - Nebulized saline
 - guaiFENesin (Robitussin[®], Mucinex[®])
 - dornase alfa (Pulmozyme[®])
 - For use in cystic fibrosis (CF) patients only

- Unable to expectorate: dry secretions
 - Anticholinergics
 - atropine
 - glycopyrrolate (Cuvposa[®], Robinul[®])
 - hyoscyamine (Levsin[®])
 - scopolamine (Transderm Scop[®])

Bavikatte G, Sit PL, Hassoon A. Management of Drooling of Saliva. *BJMP* 2012; 5(1):a507.

Agents to Thin Secretions

Agents to Thin Secretions

Nebulized Saline

- No age restrictions
- Side effects
 - Rare
 - Can induce bronchospasm
 - Slight risk of hemoptysis due to irritation
- Typical starting dose
 - Inhale 3 mL (1 vial) with nebulizer q4h scheduled or prn
- Routes
 - Inhaled
 - 0.9% & 3% nebulized solution

Rogers DF. Mucoactive Agents for Airway Mucus Hypersecretory Diseases. *Respir Care* 2007;52 (9):1176-1193.

17

Agents to Thin Secretions

guaifENesin (Robitussin®, Mucinex®)

- Age restrictions
 - 2 years of age
 - SR: >12 years of age
- Side effects
 - Drowsiness, headache, rash, nausea
- Typical starting dose

Age	Dose	Max
<2 years	2 mg/kg PO	q4h
2-5 years	50-100 mg PO	q4h 600 mg/day
6-11 years	100-200 mg PO	q4h 1200 mg/day
>12 years	200-400 mg PO	q4h 2400 mg/day

- Routes
 - PO

• Liquid, granules, tablet, SR tablet

Rubin BK. Mucolytics, Expectorants, and Mucokinetic Medications. *Respir Care* 2007;52(7):859-865.

18

Agents to Thin Secretions

dornase alfa (Pulmozyme®)

- Age restrictions
 - >5 years of age
- Side effects
 - Cough, headache, fever, rash, urticarial, voice changes
- Typical starting dose
 - Inhale 2.5 mg (1 vial) with selected nebulizer once daily
- Routes
 - Inhalation
 - Solution for nebulization
- Once opened, refrigerate & use within 24 hours

Rogers DF. Mucoactive Agents for Airway Mucus Hypersecretory Diseases. *Respir Care* 2007;52 (9):1176-1193.

19

Anticholinergic Agents

Focus on drying secretions

Agents to Dry Secretions

atropine (Isopto Atropine®)

- No age restrictions
- Side effects
 - Skin flushing, rapid or irregular heartbeat, fever, hallucinations, constipation
- Typical starting dose

Weight	Solution	Dose
<10 kg	0.25%	1 drop SL q6h prn
11-24 kg	0.5%	1 drop SL q6h prn
>25 kg	1%	1 drop SL q6h prn

- Routes
 - Ophthalmic solution administer sublingually
- 1 drop atropine 1% ophthalmic solution delivers ~ 0.5 mg atropine
- 0.25% & 0.5% solutions must be compounded from the 1% solution

Rapoport A. Sublingual Atropine Drops for the Treatment of Pediatric Sialorrhea. *J Pain Symptom Manage* 2010;40:783-788.

21

Agents to Dry Secretions

atropine (Isopto Atropine®)



take note

- Drop of atropine 1% = 0.5 mg atropine
 - Drop of atropine 0.5% = 0.25 mg atropine
 - Drop of atropine 0.25% = 0.125 mg atropine
- 1% solution commercially available
 - 0.25% or 0.5% solutions must be compounded
 - To prepare 0.25% solution, combine 2.5 mL atropine 1% with 7.5 mL water
 - To prepare 0.5% solution, combine equal parts atropine 1% and water

Agents to Dry Secretions

glycopyrrolate (Cuvposa[®], Robinul[®])

- No Age Restrictions
 - Infants may be hypersensitive to effects
- Side Effects
 - Paradoxical excitation may occur in infants
 - Constipation, sedation, confusion, visual disturbances
- Dose
 - PO (Cuvposa[®]): 40-100 mcg/kg q6-8h
 - IV (Robinul[®]): 4-10 mcg/kg q3-4h
- Routes
 - PO, IM, IV, SQ
 - Solution, tablets, injection
 - Solution may contain propylene glycol
 - Injection contains benzyl alcohol

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23

Agents to Dry Secretions

glycopyrrolate (Cuvposa[®], Robinul[®])



take note

- Does not cross the blood-brain barrier
 - Least likely to cause CNS side effects
 - Confusion
 - Visual disturbances
-

Agents to Dry Secretions

hyoscyamine (Levsin[®], Hyomax-SL[®])

- Age Restrictions
 - PO: None
 - IV: > 18 years
- Side Effects
 - Constipation, sedation, confusion, visual disturbances

- Dose

- < 2 years of age:

Weight (kg)	Dose (drops)	Max Daily Dose (drops)
3.4	4	24
5	5	30
7	6	36
10	8	48

- 2-12 years of age: 0.0625-0.125 mg q4h prn, NTE 0.75 mg/day

- >12 years of age: 0.125-0.25 mg q4h prn, NTE 1.5 mg/day

- Routes

- Solution, tablets, ODT

Hugel H, Ellershaw J, Gambles M. Respiratory Tract Secretions in the Dying Patient: A Comparison between Glycopyrronium and Hyoscine Hydrobromide. . *J Palliat Med* 2006; 9(2):279-284.

Agents to Dry Secretions

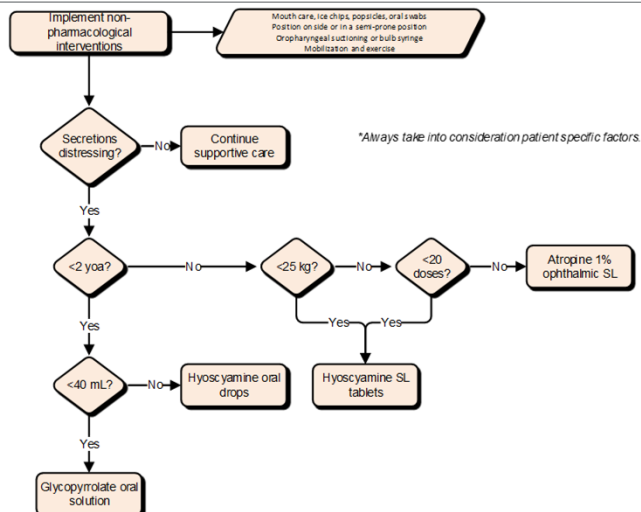
scopolamine (Transderm Scop[®])

- Age Restrictions
 - > 12 years
- Side Effects
 - Drowsiness, confusion, visual changes
- Typical Starting Dose
 - >12 years: 1 patch applied topically q3days
 - Difficult to dose in children <12 years
 - Approximately 12 hours to peak effect
- Routes
 - Transdermal patch
 - Apply patch to hairless area behind one ear
 - Do not cut patches

Mato A, Limeres J, Tomas I, Munoz M, Abuin C, Feijoo JF, Diz P. Management of drooling in disables patients with scopolamine patches. *Br J Clin Pharmacol* 2010;69(6):684-688.

26

Anticholinergic Selection



Hunt MO, Jenkins LS. Secretions. In: Hunt MO, Protus BM, Winters JP, Parker DC. Pediatric Palliative Care Consultant. Dublin: HospiScript, c2014. p. 249-254.

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Patient Case: Drooly

18 month old male with spinal muscular atrophy

- Possible causes of increased secretions in Drooly:

Possible Causes	Examples	Treatment Options
Sialorrhea	Neurodegenerative disorders	atropine glycopyrrolate (Cuvposa®) hyoscyamine (Levsin®)
Thick secretions	Fluid status Infection Medications	nebulized saline

Patient Case: Drooly

18 month old male with spinal muscular atrophy

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glycopyrrolate (Robinul®) 1 mg/mL compounded solution	Give 1 mL G-tube TID
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- Medication concerns:
 - Multiple anticholinergic agents
 - Receiving atropine 1% ophthalmic solution without dilution
 - Glycopyrrolate solution being compounded
 - Glycopyrrolate scheduled

Patient Case: Drooly

18 month old male with spinal muscular atrophy

- Medication recommendations:
 - Utilize either glycopyrrolate or atropine
 - glycopyrrolate (Cuvposa®) (1 mg/5 mL) 1 mg G-tube q6h prn secretions
 - atropine 0.5% solution 1 drop SL q6h prn secretions
 - Compound using 5 mL water and 5 mL atropine 1% solution
 - Continue nebulized saline as needed
- New medication regimen:

Medications	Directions
glycopyrrolate (Cuvposa®) 1 mg/5 mL	Give 1 mg (5 mL) Gtube q6h prn secretions
normal saline 0.9% solution	Inhale 3 mL (1 vial) via nebulizer daily & prn wheezing

Summary

- Determine cause of secretions
 - Focus of management
 - Able to expectorate: thin secretions
 - Nebulized saline
 - guaiFENesin (Robitussin[®], Mucinex[®])
 - dornase alfa (Pulmozyme[®])
 - For use in cystic fibrosis (CF) patients only
 - Unable to expectorate: dry secretions
 - Anticholinergics
 - atropine
 - glycopyrrolate (Cuvposa[®], Robinul[®])
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Dyspnea

Patient Case: Oliver

11 year old male with congenital hydrocephalus

- Weight: 36 kg
- Lives at home with parents
- Bedfast
- PEG tube
- PMH:
 - Spastic quadriplegic
 - Renal & hepatic dysfunction
 - Seizures

Patient Case: Oliver

11 year old male with congenital hydrocephalus

Medication	Directions
calcium carbonate	1,000 mg (4 mL) PEG bid
clonidine (Catapres®)	0.1 mg PEG qhs
diazepam (Diastat®)	15 mg PR prn seizure >5 min
magnesium oxide (Mag-Ox®)	400 mg PEG qday
polyethylene glycol (Miralax®)	17 g PEG qday
morphine	2.5 mg SL/PEG q4h prn pain
potassium & sodium phosphate (Neutra-Phos®)	2 packets PEG qm & 1 packet qhs
valproic acid (Depakene®)	900 mg PEG q6h

Dyspnea

- Prevalence
 - 30-80% of pediatric palliative care patients
- Uncomfortable awareness of breathing
- Shortness of breath, difficulty breathing, or painful breathing

Moody K, Siegel L, Scharbach K, et al. Pediatric Palliative Care. *Prim Care Clin Office Pract* 2011;38:327-61.

Dyspnea Causes

Reversible Causes of Dyspnea

Mechanism	Causes	Treatment Options
Anxiety	Fear of suffocation/difficulty breathing	Benzodiazepine
Blood disorders	Anemia, metabolic acidosis	Transfusion
Bronchospasm	Asthma	Bronchodilator
Cough	Secretions, infection, tumor	Nebulized saline
Fluid	Secretions, edema, infection	Decrease fluids, diuretic
Pain	Inflammation, metastasis	Opioid, corticosteroid
Pulmonary embolism	Clotting disorder	Anticoagulants
Pneumothorax	Malignancy, interstitial lung disease	Thoracentesis
Secretions	Dehydration, Medications	Anticholinergic

Hunt MO, Jenkins LS. Dyspnea. In: Hunt MO, Protus BM, Winters JP, Parker DC. Pediatric Palliative Care Consultant. Dublin: HospiScript, c2014. p. 109-115.

Non-Reversible Causes of Dyspnea

Mechanism	Causes	Treatment
Airway obstruction	Tumor, airway abnormalities	Supportive
Cardiac	Heart failure, pulmonary hypertension	
Muscle weakness	Cachexia, neuromuscular degenerative conditions	
Parenchymal failure	Cystic fibrosis (CF), pneumonia, interstitial disease	

Hunt MO, Jenkins LS. Dyspnea. In: Hunt MO, Protus BM, Winters JP, Parker DC. Pediatric Palliative Care Consultant. Dublin: HospiScript, c2014. p. 109-115.

Dyspnea Assessment

Dyspnea Assessment

- Possible etiologies of dyspnea
 - Disease progression
 - History
 - Onset, duration
 - Precipitating and relieving factors
 - Physical exam
 - Quality and depth of respirations
 - Character of lung sounds
 - Presence of stridor and/or obstructive noises
 - Presence of upper airway congestion
 - Respiratory effort (use of accessory muscles)
 - Severity
-

Dyspnea Assessment

Pediatric Dyspnea Scale

1	2	3	4	5	6	7
No trouble at all	A tiny bit	A little	Some	Quite a bit	A lot	Very much trouble

Khan FI, Reddy RC, Baptist AP. Pediatric Dyspnea Scale for use in hospitalized patient with asthma. *J Allergy Clin Immunol* 2009;123(3): 660-4.

Non-Pharmacological Options

Non-Pharmacological Options for Dyspnea

- Deep, slow breathing
 - Improve air circulation/quality
 - Provide a draft, using fans or open windows
 - Minimize dyspnea triggers
 - Avoid strong odors, perfumes or smoke
 - Reposition to comfort
 - Usually upright position
-

Dyspnea Management

Dyspnea Management

- Decrease perception of dyspnea
 - Opioids
 - Typically $\frac{1}{4}$ - $\frac{1}{2}$ of normal pain doses
 - Benzodiazepines
 - If significant anxiety
 - Oxygen
 - Nebulized agents
 - Saline
 - Albuterol
 - Opioids
 - Controversial
-

Dyspnea Management

Opioids

- Potential mechanisms
 - Suppress respiratory awareness
 - Decrease response to hypoxia and hypercapnia
 - Sedative properties
 - Vasodilation in the lungs
 - Improve the ventilation/perfusion ratio
 - Typically $\frac{1}{4}$ - $\frac{1}{2}$ of normal pain doses
 - Anticipate side effects
 - Implement strategies to prevent constipation
-

Dyspnea Management

Opioids for Dyspnea



take note

- Utilize short-acting opioids
 - Methadone is not safe or beneficial in treating dyspnea
- Typically $\frac{1}{4}$ - $\frac{1}{2}$ normal pain doses

Patient Case

Patient Case: Oliver

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Patient Case: Oliver

11 year old male with congenital hydrocephalus

What recommendations would you make for Oliver?

Patient Case: Oliver

11 year old male with congenital hydrocephalus

Possible causes of dyspnea in Oliver:

Mechanism	Causes	Treatment Options
Anxiety	Fear of suffocation/ difficulty breathing	Benzodiazepine
Cough	Secretions, infection, tumor	Nebulized saline
Fluid	Secretions, edema, infection	Decrease fluids, Diuretic
Secretions	Dehydration, Medications	Anticholinergic

Patient Case: Oliver

11 year old male with congenital hydrocephalus

Management of possible dyspnea symptoms in Oliver:

- Initiate non-pharmacological interventions
 - Improve air circulation
 - Reposition upright
 - Ensure contributing causes are addressed
 - Anxiety
 - Secretions
 - Utilize current morphine prn order
-

Summary

- Dyspnea is a common distressing symptom seen at end of life
 - Focus on reversible causes if present
 - Implement non-pharmacological interventions
 - Decrease perception of dyspnea
 - Opioids
 - Benzodiazepines
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Questions?

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