Asthma: When Albuterol Fails
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Special Thanks to Dr. Elaine Pomeranz, MD

DISCLOSURES

• There are no conflicts of interest to disclose
OBJECTIVES

• Discuss potential reasons albuterol may fail
• Review appropriate adjunctive therapies
• Outline step-wise escalation of asthma management
• Review evidence for various forms of respiratory support

STEP 1 - IDENTIFY WHAT YOU’RE TREATING

<table>
<thead>
<tr>
<th>Asthma</th>
<th>Bronchiolitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;2 years of age</td>
<td>&lt;2 years of age</td>
</tr>
<tr>
<td>+ Family History</td>
<td>+ Fever</td>
</tr>
<tr>
<td>+ Personal history of atopy</td>
<td>Preceded by URI sx</td>
</tr>
<tr>
<td>+ Wheezing, prolonged expiratory, poor aeration</td>
<td>+ Tachypnea, rales, wheezing, work of breathing</td>
</tr>
</tbody>
</table>
DIFFICULTIES WITH PEDIATRIC ALBUTEROL

• Low tidal volumes
• Smaller airways result in higher resistance
• Shorter I:E ratio increases drug loss with exhalation
• Behavioral

DRUG DEPOSITION IN YOUNG CHILD

pMDI/Spacer and Nebulizer with loose fitting face mask
DRUG DEPOSITION IN YOUNG CHILD

Tightly fitted masks - Screaming

pMDI/Spacer, tightly fitted - Inhaling quietly
**STEP 2 - TROUBLESHOOTING ALBUTEROL**

- Be flexible
- Enlist the family
- pMDI/spacer vs nebulizer decreases stay in ED
- Blow-by is negligible - not recommended
STEP 2 - TROUBLESHOOTING ALBUTEROL

**Medication Dosing**

*Recommended starting doses, may choose different dosing based on clinical judgement*

<table>
<thead>
<tr>
<th>Albuterol Weight based starting dosing</th>
<th>Nebulizer</th>
<th>MDI</th>
<th>Continuous (*titrate to effect)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-10 kg</td>
<td>2.5 mg (0.5 mL)</td>
<td>2-4 puffs</td>
<td>7.5 mg/hr</td>
</tr>
<tr>
<td>10-20 kg</td>
<td>2.5 mg (0.5 mL)</td>
<td>4 puffs</td>
<td>10 mg/hr</td>
</tr>
<tr>
<td>&gt;20 kg</td>
<td>5 mg (1 mL)</td>
<td>8 puffs</td>
<td>15 mg/hr</td>
</tr>
</tbody>
</table>

DIVISION OF PEDIATRIC EMERGENCY MEDICINE

STEP 3 - MAXIMIZE ADJUNCTIVES

- **Systemic Corticosteroids**
  - Prednisone based regimens - PO for mild/moderate, IV for severe
  - Dexamethasone based regimens - IV, IM, or PO
- **Anticholinergics (e.g. ipratropium)**
  - Parasympathetic blockage, increase beta-agonist
  - For moderate-severe exacerbations, or poor response to short-acting beta agonists (SABAs)
STEROIDS: DEX Vs. PRED

• Dexamethasone associated with:
  ○ Shorter length of stay
  ○ Lower hospital costs
  ○ Improved compliance
  ○ Improved tolerance

• Similar rates of symptom relapse, readmission

• No difference in ICU transfer rates

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**Dosing For Asthma Medications**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosing Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methylprednisolone</td>
<td>1 mg/kg Q6H</td>
</tr>
<tr>
<td>Prednisone/Prednisolone</td>
<td>60 mg Q6H</td>
</tr>
<tr>
<td>0-30 kg</td>
<td>2 mg/kg/day</td>
</tr>
<tr>
<td>&gt;30 kg</td>
<td>60 mg/day</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>0.6 mg/kg (max 16 mg) once daily, 1-2 days total</td>
</tr>
</tbody>
</table>
**STEP 4 - IV MAGNESIUM**

- Blocks calcium → smooth muscle relaxant
- May result in hypotension
- For severe exacerbations failing initial therapies
- Given as bolus
  - Currently investigating infusion vs inhaled

<table>
<thead>
<tr>
<th>Dosing For Asthma Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Magnesium Sulfate</strong></td>
</tr>
<tr>
<td>0-40 kg</td>
</tr>
<tr>
<td>40-50 kg</td>
</tr>
<tr>
<td>&gt;50 kg</td>
</tr>
</tbody>
</table>

**STEP 5 - SYSTEMIC BETA AGONIST**

- Epinephrine vs Terbutaline
- Effective even with poor ventilation
- Prefer the more readily available option (often epi)
- Terbutaline more common in ICU

<table>
<thead>
<tr>
<th>Systemic (injected) beta₂-agonists</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Epinephrine 1:1,000</strong> (1 mg/ml)</td>
</tr>
<tr>
<td>0.01 mg/kg up to 0.3-0.5 mg every 20 min for 3 doses sq.</td>
</tr>
<tr>
<td><strong>Terbutaline (1 mg/ml)</strong></td>
</tr>
<tr>
<td>0.01 mg/kg every 20 min for 3 doses then every 2-6 h as needed sq.</td>
</tr>
</tbody>
</table>
STEP 6 - HELIOX

- Converts turbulent to laminar flow
- Improves delivery of SABAs to distal airways
- Limits FiO2
- Recent studies suggest no improvement in clinical outcomes

STEP 7 - KETAMINE

- Bronchodilatory and sedative effects
- Can avoid intubation vs use as RSI med
- Similar efficacy to theophylline with improved safety
- Can aggravate bronchorrhea
- Initial bolus of 0.5-1 mg/kg over 2-4 minutes, followed by infusion of 0.5-2 mg/kg/hr
HIGH FLOW NASAL CANNULA

• Limited evidence
• Often better tolerated than CPAP/BIPAP
• Potentially delays non-invasive ventilation
• Does not appear to decrease intubations

NON-INVASIVE VENTILATION

• Limited evidence
• Increasingly being used to avoid intubation
• Reasonable to use in short trials
MECHANICAL VENTILATION

- Do not delay once deemed necessary
  - Apnea or Coma
  - PCO2 ≥42 mmHg
  - Inability to speak or AMS
  - Worsening fatigue/intercostal retractions

- Anticipate rapid desaturation and laryngospasm with RSI

- Increased risk for cardiovascular collapse and barotrauma

FINAL STEP - EDUCATION

- Review the Discharge Plan
- Review triggers and Asthma Action Plan
- Discuss signs, symptoms, home management
- Encourage appropriate follow-up
- Consider referrals and home peak flow meters
NOT RECOMMENDED

• Methylxanthines
• Antibiotics except as needed for comorbid conditions
• Aggressive hydration
• Chest PT
• Mucolytics
• Sedation (except as part of RSI)

KEY POINTS

• Know what you’re treating
• Be flexible and work with families
• Consider reasons albuterol may fail
• Reasonable to attempt alternatives to intubation, but only for short trial
REFERENCES

- Kirkland SW, Cross E, Campbell S, et. al. Intramuscular versus oral corticosteroids to reduce relapses following discharge from the emergency department for acute asthma. *Cochrane Database Systematic Review*. 2018; 6.
METHYLXANTHINES (E.G. THEOPHYLLINE)

• Phosphodiesterase inhibitor resulting in bronchodilation
• Narrow therapeutic window and numerous drug interactions
• Not recommended by National Asthma Education and Prevention Program
• Recent evidence shows similar clinical improvement at subtherapeutic levels

<table>
<thead>
<tr>
<th>Aerosol Device and Interface</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small-volume nebulizer with mask or hood</td>
<td>Infant</td>
</tr>
<tr>
<td>Small-volume nebulizer with mask</td>
<td>≤ 3 y</td>
</tr>
<tr>
<td>Small-volume nebulizer with mouthpiece</td>
<td>≥ 3 y</td>
</tr>
<tr>
<td>pMDI with valved holding chamber/spacer and mask</td>
<td>&lt; 4 y</td>
</tr>
<tr>
<td>pMDI with valved holding chamber/spacer</td>
<td>≥ 4 y</td>
</tr>
<tr>
<td>DPI</td>
<td>≥ 4 y</td>
</tr>
<tr>
<td>MDI</td>
<td>≥ 5 y</td>
</tr>
<tr>
<td>Breath-actuated MDI (eg. Autohaler)</td>
<td>≥ 5 y</td>
</tr>
<tr>
<td>Breath-actuated nebulizer</td>
<td>≥ 5 y</td>
</tr>
</tbody>
</table>

From Reference 17.
pMDI = pressurized metered-dose inhaler
DPI = dry powder inhaler