Medications in Pediatric Asthma

Seventh Pediatric Asthma Education Conference
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Objectives

• Apply the NHLBI guidelines stepwise approach to asthma treatment to a pediatric patient with asthma
• Discuss the classes of medications used in pediatric asthma
• Review correct inhaler technique
• Discuss ways to increase adherence

Fast Facts

• Leading chronic disease in children
• Third leading cause of hospitalizations in children
  • Note: African Americans 3x more likely to be hospitalized
• Ten people die from asthma every day
  • Note: African Americans 3x more likely to die from asthma
• Annual cost of asthma $81.9 billion
  • Includes medical costs, loss of work and loss of school days

Asthma Capitals 2015

*Memphis ranked #1 (from #2 last year) due to poor air quality, poor public smoking bans, high medication use and ER visits
Asthma

• Risk Factors for Asthma
  • Atopic disease
  • Exposure to smoke/secondhand smoke
  • Parental history of asthma

Asthma

• Risk Factors for Asthma-related Death
  • Previous severe exacerbation (ICU admit)
  • 2 or more hospitalizations in past year
  • 3 or more ED visits in the past year
  • Hospitalization or ED visit in past month
  • More than 2 canisters of SABA/month
  • Low socioeconomic status
  • Psychosocial problems

Pathophysiology

• Three components
  • Airflow obstruction
  • Airway hyper-responsiveness
  • Inflammation (variety of mediators)
  • Airway remodeling can occur

Airways in Asthma
**Goals of Treatment**

- Reduce Impairment
  - Prevent chronic symptoms
  - Minimize SABA use
  - Maintain normal activity and lung function
- Reduce Risk
  - Prevent exacerbations
  - Minimize hospitalizations/ED visits
  - Prevent reduced lung growth
  - Minimize adverse effects

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**‘READ’ the Triggers**

<table>
<thead>
<tr>
<th>Common Triggers</th>
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**Treatment: 0 to 4 Years of Age**

<table>
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</tr>
<tr>
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**Treatment: 5 to 11 Years of Age**

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**Treatment: ≥ 12 Years of Age**

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**Drug Treatment**

- **“Rescuers”** — commonly used in asthma exacerbations
  - Short-acting β₂ agonists [SABA]
  - Systemic steroids
- **“Controllers”** — long-term, maintenance therapy
  - Inhaled corticosteroids [ICS]
  - Long-acting β₂ agonists [LABA]
  - Leukotriene Receptor antagonists [LTRA]
  - Biologics
Rescue Therapies

Short Acting $\beta_2$ - Agonists

- Albuterol (Ventolin®, ProAir®, Proventil®)
  - MDI (HFA)/nebs
  - Ventolin®, ProAir® have dose counters
- Levalbuterol (Xopenex®)
  - MDI (HFA)/nebs

Mechanism of action
- Acts at $\beta_2$ receptors to relax smooth muscle via activation of adenylate cyclase and increasing cAMP

When to take
- At the first sign/symptom of an asthma exacerbation
- Prior to exercise for exercise-induced bronchospasm

Adverse effects
- Increased heart rate
- Tremor
- Headache
- Hyperactivity

Drug interactions
- MAO inhibitors, other adrenergic meds (hypertensive crisis)
- Beta blockers (potentially block effects of medicine)
Inhaler Overview

Corticosteroids for Exacerbation
- Dexamethasone versus prednisone
  - Longer half-life
  - One dose equals ~5 day course
    - Can give 2nd dose given 48 hours prn
  - Increases adherence and decreases ED returns
  - Reduces length of stay in hospitalizations

Rescue Therapy Clinical Pearls
- Increasing albuterol use indicates inadequate control
- Oral Albuterol should NOT be prescribed
- Patients need more than one SABA inhaler
- Ipratropium (an anti-cholinergic) use reserved for emergency department only

Controller Medications
Inhaled Corticosteroids (ICS)

- **Mechanism of Action**
  - Anti-inflammatory agents
  - Decrease protein synthesis
  - Migration of leukocytes and fibroblasts
  - Block late reaction to allergens
  - Decrease hyper-responsiveness of airway

- **Adverse effects**
  - Throat:
    - Reduced by rinsing and spitting with water after each puff AND using spacer
  - Coughing:
    - Reduced by using spacer with MDI
  - Growth issues:
    - Uncontrolled asthma poses greater risk than ICS

**Inhaled Corticosteroid Products**

- **Beclomethasone (QVAR®)**
  - MDI

- **Budesonide (Pulmicort®)**
  - Nebulizer
  - Turbuhaler™ (DPI)

- **Ciclesonide (Alvesco®)**
  - MDI

- **Flunisolide (Aerospan®)**
  - MDI

- **Fluticasone (Flovent®)**
  - MDI
  - Diskus (DPI)

- **Mometasone (Asmanex®)**
  - Twisthaler™ DPI

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**Assthma Care Quick Summary EPR-3, revised 9/12**

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Long-Acting β2-Agonists (LABAs)

- FDA warnings:
  - Reviewed 4 trials w/combination therapy vs ICS alone
  - No increase in asthma-related deaths in combination therapy vs ICS
  - Combination therapy beneficial in decreasing asthma exacerbations
  - Removed boxed warning about asthma-related deaths for combination products
  - Boxed warning on LABAs alone will remain for asthma-related death
  - Pediatric and adolescents requiring a LABA should use a combination product (LABA and corticosteroid) to ensure medication compliance

Table 1. Adjusted Mean Adult Height among 54 Study Participants.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline (N=168)</th>
<th>Matched (N=180)</th>
<th>Matched vs Baseline (95% CI)</th>
<th>P Value</th>
<th>Cramer's V Value</th>
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<tbody>
<tr>
<td>All</td>
<td>174.2 (175.7)</td>
<td>174.3 (175.7)</td>
<td>-0.1 (0.5 to 0.3)</td>
<td>0.001</td>
<td>0.06</td>
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<tr>
<td>Sex</td>
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<tr>
<td>Male</td>
<td>174.1 (175.7)</td>
<td>174.3 (175.7)</td>
<td>-0.2 (0.5 to 0.1)</td>
<td>0.001</td>
<td>0.06</td>
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<tr>
<td>Female</td>
<td>174.3 (175.7)</td>
<td>174.4 (175.7)</td>
<td>-0.1 (0.5 to 0.3)</td>
<td>0.001</td>
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<tr>
<td>Age at entry</td>
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<tr>
<td>≤12 yr</td>
<td>174.1 (175.7)</td>
<td>174.3 (175.7)</td>
<td>-0.2 (0.5 to 0.1)</td>
<td>0.001</td>
<td>0.06</td>
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<tr>
<td>&gt;12 yr</td>
<td>174.3 (175.7)</td>
<td>174.4 (175.7)</td>
<td>-0.1 (0.5 to 0.3)</td>
<td>0.001</td>
<td>0.06</td>
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<tr>
<td>Pediatric interaction</td>
<td>0.02</td>
<td>0.00</td>
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</table>

Mean values for adult height have been adjusted for age, sex, and BMI.
**Long-Acting β₂-Agonists**

- Clinical pearl for patients/caregivers
  - Emphasize this is for long term control
  - Not for acute episodes
- Combination products
  - Watch increasing the dose... must increase the strength of the product

**Combination Products**

- Fluticasone and salmeterol (Advair®)
  - HFA MDI 45/21, 115/21, 230/21 mcg/puff (≥12 years old)
  - Diskus down to 4 years of age
- Budesonide and formoterol (Symbicort®)
  - MDI 80/4.5, 160/4.5 mcg/puff (≥5 years old)
- Mometasone + formoterol (Dulera®)
  - MDI: 100/5, 200/5 mcg/puff (≥12 years old)

**Dosing:** 2 puffs twice daily for MDI products

**Adverse effects similar to individual agents**

**Leukotriene Receptor Antagonists**

- Mechanism of Action
  - Blocks leukotriene receptors which have been associated with asthma inflammatory processes as well as allergic response in nasal passages
- Adverse Effects
  - Sedation
  - Psychiatric events (abnormal dreams, anxiety, depression, insomnia)
- Available Products
  - Montelukast (daily dosing)
    - 6 mos-5 yrs: 4 mg
    - 6-14 yrs: 5 mg
    - 15 yrs+: 10 mg
  - Zafirlukast (twice daily)
    - 5-11 yrs: 10 mg/dose
    - 12 yrs+: 20 mg/dose

**Watch Drug Interactions!**
Biologics

- **Omalizumab**
  - Anti-immunoglobulin E (IgE) monoclonal antibody
  - ≥ 6 years of age
  - Persistent asthma not well controlled with ICS
  - Positive allergic skin test
  - Dose determined by weight and IgE level prior to treatment

- **Mepolizumab**
  - Interleukin-5 receptor antibody
  - ≥ 12 years of age
  - Severe asthma with eosinophilic phenotype
  - Dose: 100 mg subQ every 4 weeks

Benefits of Biologics

- **Omalizumab**
  - Decreases asthma exacerbations
  - More symptom-free days
  - Less hospitalizations and urgent care visits
  - Reduces missed school days
  - Decreases daily rescue medication use

- **Mepolizumab**
  - Decreases asthma exacerbations
  - Improves FEV1
  - Better asthma control scores
  - Decreases daily oral corticosteroid dose

Omalizumab

- Adverse effects
  - Anaphylaxis, ‘serum sickness’ type reaction
  - Hypersensitivity reactions (Black Box Warning)
  - Warrant administration under direct supervision
  - Usually occur within 2 hrs of admin
  - Can occur up to 24 hrs post and anytime during therapy
  - Prescribe EpiPen®
Choosing a Step-Up Therapy

- **BADGER Study**
  - Best Add-on Therapy Giving Effective Responses
  - Mild to moderate persistent asthma
  - 100 mcg inhaled fluticasone twice daily baseline
    - Inhaled fluticasone 250 mcg twice daily
    - Inhaled fluticasone 100 mcg + 50 mcg salmeterol bid
    - Inhaled fluticasone 100 mcg bid + montelukast
  - Triple-crossover design

- **BADGER Study**
  - Post hoc analysis
  - No Eczema = LABA step up therapy
  - Eczema broken down further
    - African American: ICS step-up
    - White Hispanics: LTRA step-up
    - White Non-Hispanics: LABA or LTRA

- **BADGER Study**
  - Percent of Patients

- **BADGER Study**
  - Favier Comparisons
  - LABA vs. ICS
  - LABA better
  - ICS better
  - LABA vs. LTRA
  - LABA better
  - ICS better
  - LTRA better
  - ICS vs. LTRA
  - ICS better
  - LTRA better

- **BADGER Study**
  - Percent of Patients

- **BADGER Study**
  - Take Home Points
  - Consider patient and safety profile of medication
  - Needs further analysis before using BADGER as basis for choice of therapy
  - BARD (Best African-American Response to Asthma Drug)
    - Role of step-up therapy comparing increased ICS dose versus LABA
    - Study completed July 2017; no published results yet
Metered Dose Inhalers (MDI)

- Assess appropriate technique at each visit
- Able to be used in young ages
- Always use with spacer
- Products with counters preferred
- Flotation in water does not work!

Why Use A Spacer?

- Improved coordination of MDI and breathing
- Improved deposition of medication in lungs
- Decreases thrush and cough
- Clean weekly with warm, soapy water

MDI Technique

- Directions for use
  - Shake inhaler and remove cap
  - Place inhaler in backside of spacer
  - Place mouthpiece in mouth and insures tongue does not block (or mask over mouth and nose)
  - Spray 1 puff, take deep breath and hold for 10 seconds (or watch 5-6 breaths if using spacer/mask)
  - Wait 1-2 minutes before repeating if additional puffs needed.

Why Use A Spacer?

- Improved coordination of MDI and breathing
- Improved deposition of medication in lungs
- Decreases thrush and cough
- Clean weekly with warm, soapy water
Dry Powder Inhalers

- Clinical Pearls
- Patients > 6 years of age
- Keep dry!
- Keep upright or on its side
- Do not require shaking
- Do require "priming" of inhaler
- No spacer necessary
- Rinse and spit after each puff

DPI Technique

- Prime device
- Inhale fast, deep breath
- Hold breath for 10 seconds
- Repeat as needed for each puff
  - Try to wait 1 minute between puffs
  - No spacer needed
  - Remember to keep device level and do not blow into device

Asthma Action Plan

- Personalized, written care plan for managing asthma
- Include triggers for the patient
- Provides symptom management for parents and school
- Recommended for all patients

<table>
<thead>
<tr>
<th>Level</th>
<th>Signs &amp; Symptoms</th>
<th>FEV1</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>Mild Exacerbation</td>
<td>Dyspnea or Tachypnea w/activity Can lie down Increased respiratory rate End expiratory wheeze</td>
<td>&gt;70%</td>
<td>Treat at home w/SABA Consider course or oral steroids</td>
</tr>
<tr>
<td>Moderate Exacerbation</td>
<td>Dyspnea or tachypnea interferes w/activity Prefers sitting Shorter cry/Talks in phrases Difficulty feeding Increased respiratory rate Uses accessory muscles Loud wheezing Elevated heart rate</td>
<td>40-69%</td>
<td>Office or ED visit Use SABA Oral Corticosteroids</td>
</tr>
<tr>
<td>Severe Exacerbation</td>
<td>Dyspnea/tachypnea at rest Sits upright Increased respiratory rate Use of accessory muscles Loud wheezing in inhalation and ex Elevated heart rate</td>
<td>&lt;40%</td>
<td>ED visit and possibly hospitalization</td>
</tr>
<tr>
<td>Life Threatening</td>
<td>Too dyspnic to speak; perspiring</td>
<td>&lt;25%</td>
<td>ED visit/ICU</td>
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</table>
**Asthma Action Plan**

- Rule of Twos
  - >2 days/week symptoms or SABA use
  - >2 times/month nighttime awakenings
  - >2 times/year exacerbations

**Assessing Control Hints**

- Rule of Twos
  - >2 days/week symptoms or SABA use
  - >2 times/month nighttime awakenings
  - >2 times/year exacerbations

**Reasons for Poor Control**

- Adherence
- Unresponsive to therapies
- Improper inhaler techniques
- Poor comorbid conditions control
- Psychosocial stressors
- Misdiagnosis

**Medication Adherence**

- Rs Prescribed: 100%
- Rs Filled: 88%
- Rs Taken: 76%
- Rs Continued: 47%
**Patterns of Non-Adherence**

- Unwittingly
  - Poor instructions on use of the medication
  - Lack of understanding rationale for treatment
- Intentional
- Unplanned
  - Child-raising issues
  - Lack of routine (not used to taking daily meds)
  - Lack of motivation


**What Can We Do?**

- Doctor-Centred model
  - Physician is the leader of treatment
  - Physician dominates the conversation
  - Patient is passive
  - Physician is blame-oriented
  - Physician does most of the taking
  - Physician may not adhere to treatment plan
- Patient-Centred model
  - Patient is the leader of treatment
  - Patient is involved
  - Patient is empowered
  - Patient is positive
  - Physician follows patient’s lead


**Other Clinical Pearls**

- Flu shots!!
- Like devices
References

- Lexi-Comp online.