The Management of Asthma in Special Populations

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Objectives

- Describe the mechanism of action and therapeutic rationale for the medications used to treat asthma in special populations.
- Outline the goals for treating asthma in special populations.
- Given patient information, select an optimal treatment regimen for patients with exercise induced bronchoconstriction (EIB), childhood or adolescent asthma, or asthma in pregnancy and justify your choices based on the information presented.
- Compare the preferred treatment regimens used to manage childhood and adolescent asthma and asthma in pregnancy with those used to manage asthma in adult patients.
Exercise Induced Bronchoconstriction (EIB)
Background

- Airway narrowing 5-10 minutes after cessation of vigorous exercise
- Usually resolves in another 20-30 minutes
- Prevalence – 40-80% in patients with asthma
- Bronchoconstriction only, no chronic inflammatory response
  - Related to fluxes in heat and water that develop in tracheobronchial tree during exercise
  - Not known exactly how bronchial narrowing is produced, may be related to fluid osmolality
- Not prolonged or dangerous, hospitalization not required
The main difficulty with EIB is resulting limitation on activity.
Diagnosis of EIB

- **History**
  - Cough, SOB, chest tightness, wheezing, endurance problems during and after vigorous activity

- **Objective evidence to confirm**
  - 15% decrease in peak flow between measurements taken before and after vigorous activity
Symptoms of EIB

During Exercise
- Rapid breathing
- Irregular breathing
- Decreased endurance

Following exercise
- Cough
- Wheezing
- Shortness of breath
- Chest tightness
Influencing factors

- Type of exercise
  - Intensity
  - Duration
- Environment
  - Warm vs. cold air
  - Humid vs. dry air
Goals of EIB therapy

- Allow patients to live a normal, active lifestyle
- Prevention of exercise-induced symptoms

Patients with EIB should be able to participate in any activity they choose without experiencing symptoms.
Prevention of EIB

- **Warm-up**
  - 6-10 minute warm-up period with slow, mild, graduated exercise intensity to start

- **Cool-down**
  - End with a graduated warm down
Drug Treatment of EIB

First-line treatment
- Inhaled rapid acting β-2 agonist

Second-line treatments
- Cromolyn/Nedocromyl
- Leukotriene modifiers
- Inhaled long acting β-2 agonists
Use of β-2 Agonist in EIB

- 2 puffs, 10-15 minutes before exercise – relieves EIB in 80% of patients
- Duration of protection – 2 to 2.5 hours
- May also be used after exercise for symptoms slow to resolve
Use of Inhaled Long-Acting β-2 Agonists in EIB

- Salmeterol – 2 puffs 30 minutes before exercise
- Formoterol – 1 inhalation 15 minutes before exercise
- Duration of protection – 10 to 12 hours
- When to use:
  - If exercise is planned for more than 3 hours
  - In children or adolescents to avoid inhaler use in front of peers
Cromolyn/Nedocromil in EIB

- 2 puffs, 10-15 minutes before exercise
- Duration of protection – 1.5 to 2 hours
- Somewhat less effective than β-2 agonists
Leukotriene Modifiers in EIB

- Why do they work?
- Advantages
  - Oral administration
  - Long duration of action
Oral Montelukast Compared with Inhaled Salmeterol to Prevent Exercise-Induced Bronchoconstriction

191 adults randomized to montelukast 10 mg/day or salmeterol 2 puffs bid

After 8 weeks, both groups had less EIB – montelukast showed greater improvement

26% of montelukast, 40% of salmeterol required rescue β-agonist use after exercise
Medication Use in Competition

**USOC**
- Allowed without prior approval – cromolyn, nedocromil, ipratropium, theophylline, leukotriene modifiers
- Require prior approval – inhaled beta agonists, inhaled corticosteroids

**NCAA**
- Permits most medications except oral beta agonists
Asthma in Children and Adolescents
Prevalence

- 7% of persons under 18 years of age
- 50-80% of children with asthma develop symptoms before 5 yo
- 50-70% of children with asthma have a permanent or temporary symptom-free remission by adulthood.
- Usually, symptoms return to some degree later in life
- 1999, 74/1000 among blacks, 50 among whites, 44 among Latinos
Asthma in Children

- Prevalence increased 160% in children less than 4 yo from 1980 to 1994
- Increased 72% in children 5 to 16 yo
- Rates have remained stable from 1997-2000
- 3,028,000 MD visits for children < 15 yo
- 570,000 ER visits for wheezing
- 164,000 hospitalizations
- Over 8.7 million prescriptions for children <17 yo
Factors Associated with ONSET of Asthma Symptoms in Children

- Allergy
- Family history of asthma/allergy
- Perinatal exposure to tobacco smoke
- Viral respiratory infections
- Smaller airways at birth and early life
- Male gender
- Low birth weight
Factors Associated with CONTINUING Asthma

- Allergy
- Family history of asthma/allergy
- Perinatal exposure to passive smoke and aeroallergens
Asthma Symptoms in Young Children

- Cough may be the only symptom
- Tachypnea with accessory muscle use
- Decreased activity level and alertness
- Recurrent sinusitis, rhinitis, or upper respiratory tract infections
Symptom Considerations

Assessment of severity based entirely on symptoms for children less than 5 years old because most are unable to use peak flow meters optimally.
Pharmacotherapy

Follows the same basic principles as those for adults with special consideration for growth, school, and social development.
Pharmacotherapy

- Inhaled ipratropium bromide should be added to each inhalation of beta-2 agonist for exacerbation treatment (esp. more severe)
- Oral CS’s should be administered within 45 minutes of the onset of an acute asthma exacerbation
- Inhaled corticosteroids are a standard part of the maintenance therapy.
  - More effective than long-acting beta agonists, inhaled nedocromil, and leukotriene modifiers
  - Growth velocity decreased, final adult height not affected
- Cromolyn, nedocromil, or leukotriene modifiers often first line in mild or moderate persistent asthma
Pharmacotherapy

Other pharmacotherapy issues in children:

- Oral medications – possible better adherence
- MDI’s with holding chambers vs, nebulizers
  - MDI plus holding chamber/spacer – shorter stays in the ED and lower HR than nebulizer pts.
- Omalizumab – prevents binding of IgE and limits release of allergic mediators
  - Use reserved for moderate to severe asthma – reduces rate of serious exacerbations, reduces ED visits and hospitalizations
  - $10,000/patient/year – limited use
Medication Adherence Problems in Children

- Unpalatable
- Difficulty swallowing
- Medication regimen conflicts with parent’s schedule or school
  - When possible, avoid medication outside of school
- Child not actively involved with medication regimen

One study found a 40% adherence rate
Asthma During Pregnancy
Background

- One of the most common potentially serious problems to complicate pregnancy
- 3.7-8.4% of pregnancies complicated with asthma
- 33% of patient’s symptoms worsen during pregnancy
- Severe patients at highest risk
Issues of Concern

- Small changes in maternal lung function dramatically affect fetal oxygenation
- Uncontrolled asthma in pregnancy can lead to:
  - Preeclampsia
  - Preterm birth
  - Fetal death
  - Low birth weight
  - Complications during pregnancy
- Adequately controlled asthma patients have similar outcomes to non-asthmatic populations
Treatment Goals

- Minimal or no chronic symptoms day or night
- Minimal or no exacerbations
- Maintain normal pulmonary function
- No limitations on activity
- Minimal use of short-acting beta$_2$-agonist
- Avoid adverse drug reactions
Four Components of Management

- Assessment and monitoring, including objective measures of pulmonary function
  - Initially – spirometry
  - Routinely – PEF
- Trigger identification and avoidance
- Patient education
- Stepped pharmacologic therapy
Manage Co-Existing Conditions

Rhinitis, sinusitis, GERD may exacerbate co-existing asthma

- Intranasal CSs for allergic rhinitis
- Antihistamines of choice are loratadine or cetirizine
- If decongestant is required, external nasal dilator (topical metazoline) or intranasal CS
- Focus on nonpharmacologic methods to manage GERD
Pharmacotherapy

General Principles
- Individualized treatment plan for each patient
- Stepped care approach based on severity
- Inhaled medications preferred over oral
- Medications with documented use in pregnancy are preferred

Risks associated with uncontrolled asthma far outweigh possible side effects associated with drug therapy
Updated in 2004

Published in J Allergy Clin Immunol 2005; 115: 34-46.

http://www2.us.elsevierhealth.com/scripts/om.dll/serve?action=searchDB&searchDBfor=art&artType=fullfree&id=as009167490402679x
Recommendations

- **Mild Intermittent**
  - Inhaled beta agonist prn
  - Albuterol preferred

- **Mild persistent**
  - Daily, low-dose, inhaled CS
  - Budesonide preferred – Pregnancy Cat. B
  - Other agents may be continued if used with success prior
  - Alternatives – cromolyn, LTM’s, theophylline
Recommendations

Moderate Persistent
- Preferred:
  - Low-dose inhaled CS + long acting, inhaled $\beta_2$ agonist
  - Medium dose, inhaled CS

Severe Persistent
- First, assess inhaler technique and adherence
- Then, increase to high-dose, inhaled CS
- If this is insufficient, add systemic CS
Asthma Medications and Pregnancy

- Rapid-acting beta agonists
  - Reassuring safety data
  - May be used
- Long-acting beta agonists
  - Animal studies have not been reassuring
  - Limited data on use during pregnancy
- Ipratropium
  - Little human data on use during pregnancy
  - Considered if little improvement after first inhaled beta agonist dose
Asthma Medications and Pregnancy

- **Cromolyn**
  - Safe for use
  - Utility is for mild persistent patients
  - Less effective than inhaled CS’s

- **Nedocromil**
  - No human data on use during pregnancy
Asthma Medications and Pregnancy

**Inhaled corticosteroids**
- Reduce risk of asthma exacerbations, improve FEV₁
- No studies have related use to adverse perinatal outcomes
- Budesonide – EBM, Preg. Cat. B

**Systemic corticosteroids**
- Use during the first trimester associated with increased risk for cleft lip (w or w/o cleft palate)
  - Risk is 3x that of the general population
- Increased risk of preeclampsia, preterm, LBW infants
Asthma Medications and Pregnancy

Theophylline

- Safe at recommended doses (serum conc. - 5-12 mcg/mL)
- Animal studies show association between high-dose theophylline and adverse pregnancy outcomes
- May be used as an alternative add-on in addition to inhaled CS’s
Asthma Medications and Pregnancy

- Montelukast or zafirlukast
  - Minimal human data on use during pregnancy
  - Reassuring animal studies

- Zileuton
  - Minimal human data on use during pregnancy
  - No reassuring animal studies
Questions