BACK TO BASICS: ASTHMA MANAGEMENT

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• Back to Basics: Asthma Management is accredited by ACPE for pharmacists, ACPE 0154-0000-14-018-L01-P, and technicians, ACPE 0154-0000-14-018-L01-T, for 1.5 contact hours.

• Mary Klein has not disclosed any financial or conflicts of interest in relation to this program.

Objectives

• Briefly explain the pathophysiologic and pulmonary function changes that lead to a diagnosis of asthma
• List common signs and symptoms of asthma
• Describe mechanisms of action, adverse drug reactions, indications, key drug interactions, and counseling points for each class of asthma medications (Beta-2 agonists, inhaled corticosteroids, leukotriene modifiers, mast cell stabilizers, and monoclonal antibodies)
• Classify a patient’s asthma control based on symptoms and pulmonary function, and recommend a medication based on control.
• Explain appropriate monitoring parameters for asthma management

PATHOPHYSIOLOGY

Asthma Epidemiology

• 6.8 million children (9.3%) and 18.7 million adults (8%) have asthma
• Healthcare Burden:
  – 14.2 million physician visits/year
  – 1.8 million ER visits
  – 439,000 hospital admissions
  • Avg. length of stay 3.6 days
  – Albuterol: 5th most common drug mentioned at visits in 2010
  – $56 Billion in medical costs, lost school and work days, and early deaths (2007)

Asthma Epidemiology

• Disease most common in:
  — Children
  — Low socioeconomic status
  — African Americans
  — Young boys rather than girls
• Both genetic predisposition and environmental risk factors play role in disease development
Asthma Pathophysiology

- Chronic inflammatory disorder of the airways
  - Modulated by mast cells, eosinophils, lymphocytes, neutrophils, and epithelial cells
- Inflammation causes bronchial hyperresponsiveness and recurring episodes of airflow obstruction
  - Results from increased responsiveness of the trachea and bronchi to stimuli
  - Causes recurrent episodes of coughing, wheezing, breathlessness, and chest tightness (particularly at night or early in the morning)
  - Often reversible either spontaneously or with treatment

Clinical Presentation

- Shortness of breath (dyspnea)
  - Recurrent or episodic
- Nonproductive cough
- Chest tightness
- Expiratory wheezing
- Allergic rhinitis/eczema
- Use of accessory muscles to breathe
- Increased respiratory rate
- Increased heart rate
- Decreased FEV1 and PEF

Self Assessment Question #1
Which of the following is NOT consistent with the definition of asthma?

- A. Characterized by recurring episodes of airflow restriction
- B. Characterized by shortness of breath and expiratory wheezing
- C. Characterized by inflammation causing bronchial hyperresponsiveness
- D. Characterized by decreased FEV1 and PEF
Asthma Diagnosis

• Signs and symptoms present upon detailed medical history and exam
• Airflow obstruction: at least partially reversible
  – Measured by spirometry in children >5 y.o.
  – Reversibility is determined by an increase in FEV1 of >200 mL and 12 percent from baseline measure after inhalation of short-acting beta 2-agonist (SABA) – i.e. albuterol
• Other diagnoses are excluded
  – COPD, pneumonia, fibrosis, etc.

Using Spirometry for Diagnosis

• Purpose:
  – To identify and quantify abnormalities in lung function (i.e. pulmonary function tests)
• What that really means:
  – Gives practitioners the ability to determine if a lung disease is present, and if so, what kind of disease that is, and potentially a guide to its severity
  – Can also be used to assist in the management of disease after diagnosis

Key Parts of Spirometry in Asthma

• Forced Expiratory Volume in 1 Second (FEV1)
  – Volume of air expelled in one second on forceful exhalation
  – Measured in Liters
  – Gold Standard for diagnosis and monitoring of obstructive disease
• Peak Expiratory Flow (PEF)
  – Rate of air expelled in one second on forceful exhalation
  – Measured in liters/second on spirometry
    • liters/minute on peak flow meter
  – Used for diagnosis and monitoring of asthma

Initial Classification of Asthma

Severity Classification Varies By Age

Key Components of Diagnosis and Monitoring

Initial Classification of Asthma

Components of Questions

Initial Classification of Asthma

Components of Questions

Initial Classification of Asthma
Self Assessment Question #2:  
A Case Example
• A 14 year old Hispanic female with the following signs, symptoms, and lab results:
  – Daytime symptoms twice a week
  – Nighttime symptoms once a week
  – FEV1 of 87%
• How would you initially classify this patient’s asthma based on her symptoms?
  – A. Intermittent
  – B. Mild Persistent
  – C. Moderate Persistent
  – D. Severe Persistent

Initial Classification of Asthma

Key Points to the Steps
• Intensity of therapy increases with each increasing step
• Step up when needed and down when possible
• Limits on initiation/diagnosis:
  – For age 12 and older: Step 4 or 5
  – For age 5-11: Step 3 or 4
  – For age 4 and under: Step 3
• Consider short term systemic steroids for severities above these steps initially

What Are The Steps?

THE DRUGS!
**Short Acting Beta Agonists (SABA)**

- **MOA:**
  - Relaxes bronchial smooth muscle by action on β₂-receptors
- **Place in Therapy:**
  - A part of every patient’s regimen!
  - NOT for daily management
  - Treatment of choice for exercise-induced bronchoconstriction

<table>
<thead>
<tr>
<th>Medication</th>
<th>Recommended Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albuterol (MDI)</td>
<td>2 puffs 1 minute before exercise</td>
</tr>
<tr>
<td>Albuterol (DPI)</td>
<td>2 puffs q 4-6 hours</td>
</tr>
<tr>
<td>Levalbuterol (MDI)</td>
<td>0.63 mg/puff 2 puffs q 6 hours</td>
</tr>
<tr>
<td>Levalbuterol (DPI)</td>
<td>0.63 mg/puff 5 puffs q 6 hours</td>
</tr>
<tr>
<td>Ipratropium</td>
<td>4-8 puffs 1-2 times 2 times before exercise</td>
</tr>
</tbody>
</table>

- **Dosage Forms:**
  - MDI or nebulizer
- **Adverse Reactions:**
  - Tachycardia, headache, diziness, nervousness, nausea, hypokalemia

- **Counseling Points:**
  - Shake MDI well before use
  - Use holding chamber/spacer for MDI
  - Nebulizer can be mixed with budenoside or ipratropium

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**Inhaled Corticosteroids (ICS)**

- **MOA:**
  - Potent vasoconstrictor with anti-inflammatory activity.
  - Effectiveness due to its direct local effect
- **Place in Therapy:**
  - Key treatment in long-term management of asthma
  - NOT for acute symptoms

**Dosage and Administration of ICS**

<table>
<thead>
<tr>
<th>Age</th>
<th>Dosage</th>
<th>Time of Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5-2 yrs</td>
<td>1.25 mg</td>
<td>q 4h</td>
</tr>
<tr>
<td>2-3 yrs</td>
<td>2.5 mg</td>
<td>q 4h</td>
</tr>
<tr>
<td>3-4 yrs</td>
<td>3.75 mg</td>
<td>q 4h</td>
</tr>
<tr>
<td>4-5 yrs</td>
<td>5 mg</td>
<td>q 4h</td>
</tr>
</tbody>
</table>

- **Dosage Forms:**
  - MDI, DPI, and nebulizer
- **Adverse Reactions:**
  - Thrush, cough, throat irritation, growth suppression?
- **Counseling Points:**
  - Effect seen in a few weeks
  - Should not discontinue suddenly
  - Rinse out mouth with water
Long Acting Beta Agonists (LABA)

- Salmeterol and Formoterol
- MOA:
  - Relaxes bronchial smooth muscle by selective action on beta2-receptors
- Place in Therapy:
  - In combination ONLY for moderate and severe persistent asthma
  - NOT for acute symptoms

Leukotriene Inhibitors (LTRA)

- Montelukast, Zafirlukast, and Zileuton
- MOA:
  - Leukotriene receptor inhibition has been connected to reduced airway edema, smooth muscle relaxation, and decreased inflammation
- Place in Therapy:
  - Alternative/adjunctive therapy in mild, moderate, and severe persistent asthma
  - Beneficial in those with seasonal allergy triggers
  - NOT for acute symptoms

Mast Cell Stabilizers (Cromolyn)

- MOA:
  - Prevents release of histamine and leukotrienes by inhibiting degranulation
- Place in Therapy:
  - Alternative therapy in mild persistent asthma
  - May be used in those with seasonal allergies prior to exposure

Long Acting Beta Agonists (LABA)

- Dosage Forms:
  - MDI, DPI
- Adverse Reactions:
  - Headache, dizziness, increased heart rate (?)
- Counseling Points:
  - Twice daily
  - If a single drug inhaler is used, must be taken with ICS
    - May be easier to use fixed dose combination with fluticasone (Advair), mometasone (Dulera), or budesonide (Symbicort)

Leukotriene Inhibitors (LTRA)

- Dosage Forms:
  - Montelukast: tablet with chewable
  - Zafirlukast and zileuton: tablet only
- Adverse Reactions:
  - Suicidal ideation in children
  - Monitor hepatic function with zafirlukast and zileuton
- Counseling Points:
  - Chews contain phenylalanine
  - Zafirlukast: BID on empty stomach

Mast Cell Stabilizers (Cromolyn)

- Dosage Forms:
  - MDI and nebulizer
- Adverse Reactions:
  - Metallic taste in mouth, cough, throat irritation
- Counseling Points:
  - Not for acute attacks
  - May take up to 4 weeks to work
Methylxanthines (Theophylline)

- **MOA:**
  - Blocks PDE, increasing smooth muscle cAMP and causing bronchodilation
- **Place in Therapy:**
  - Alternative therapy, salvage therapy
- **Dosage Forms:**
  - Extended release tablets, capsules, and solution

Monoclonal Antibody (Omalizumab)

- **MOA:**
  - IgG antibody that inhibits IgE binding on mast cells and basophils, decreasing allergic response
- **Place in Therapy:**
  - In severe persistent asthma ONLY, with concomitant allergies
- **Dosage Forms:**
  - SC injection (stored refrigerated) q4 weeks

Anticholinergics (Ipratropium)

- **MOA:**
  - Blocks acetylcholine causing smooth muscle relaxation
- **Place in Therapy:**
  - NOT for long term treatment
  - Safety not established in <12 y.o.
  - Hospital/emergency room treatment
  - Provides additive benefit to SABA
  - Drug of choice for bronchospasm related to beta-blockers
  - Alternative if patient cannot tolerate SABA

Methylxanthines (Theophylline)

- **Adverse Reactions:**
  - Toxicity concern!
  - GI upset, hyperactivity, insomnia, tachycardia
  - CYP interactions
- **Counseling Points:**
  - Report signs/symptoms of theophylline toxicity
  - Requires regular blood work
  - Minimize caffeine intake; extremes in protein and carb intake
  - Extended release: take 1 hour before or 2 hours after meal to avoid dose dumping

Monoclonal Antibody (Omalizumab)

- **Adverse Reactions:**
  - Injection site reactions, pain
  - Anaphylaxis concern
  - Dizziness, headache, myalgia
- **Counseling Points:**
  - Dosing based on weight and baseline IgE levels
  - Monitor for signs of anaphylaxis within 2-4 days of injection

Anticholinergics (Ipratropium)

- **Dosage Forms:**
  - MDI or nebulizer
- **Adverse Effects**
  - Dry mouth, dizziness, upset stomach, vision changes
- **Patient Counseling**
  - Close eyes when inhaling medication (glaucoma effect)
Self Assessment Question #3

Which of the following is TRUE regarding medications for the management of asthma?

- A. Albuterol is a first line choice for the chronic, long term management of severe persistent asthma
- B. Anticholinergics such as ipratropium can be used interchangeably with albuterol for quick relief
- C. Inhaled corticosteroids are the treatment of choice in mild persistent asthma
- D. The side effect profile of theophylline has no effect on its use in practice.

Goals of Asthma Treatment

- Prevent chronic symptoms
- Prevent exacerbations
- Maintain normal activity levels
- Maintain normal pulmonary function
- Optimize drug therapy
- Satisfy patient’s and families’ goals for asthma care

Interviewing an Asthma Patient

- How long have you had asthma?
- Does anyone else in your family have asthma?
- Have you ever been hospitalized with an asthma attack?
- Have you ever had a tube inserted in your throat to help you breathe? (intubation)
- Describe the symptoms that you have when you are having trouble with your asthma?
- Can you tell me what triggers your asthma?
Interviewing an Asthma Patient

- Please demonstrate how you use your inhaler.
  - If patient is using incorrectly, counsel them at this point on correct technique
  - You should also discuss priming and cleaning of inhaler
  - Use package inserts as an aid in teaching when available
- How are you taking your inhalers? (What time of day?)

Back to the Guidelines

Steps, Revisited

<table>
<thead>
<tr>
<th>Step</th>
<th>Preferential Advice</th>
<th>Patient's Advice: Early Week</th>
<th>Step</th>
<th>Preferential Advice</th>
<th>Patient's Advice: Late Week</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pretest</td>
<td>Low dose ICS Medium dose ICS</td>
<td>5</td>
<td>Posttest</td>
<td>High dose ICS Medium dose ICS</td>
</tr>
<tr>
<td>2</td>
<td>Pretest</td>
<td>Low dose ICS Medium dose ICS</td>
<td>6</td>
<td>Posttest</td>
<td>High dose ICS Medium dose ICS</td>
</tr>
<tr>
<td>3</td>
<td>Pretest</td>
<td>Low dose ICS Medium dose ICS</td>
<td>7</td>
<td>Posttest</td>
<td>High dose ICS Medium dose ICS</td>
</tr>
<tr>
<td>4</td>
<td>Pretest</td>
<td>Low dose ICS Medium dose ICS</td>
<td>8</td>
<td>Posttest</td>
<td>High dose ICS Medium dose ICS</td>
</tr>
</tbody>
</table>

Self Assessment Question #4: Case Example, Part 2

- A 14 year old Hispanic female with mild persistent asthma presents with:
  - FEV1 of 76%
  - Nighttime symptoms once a month
  - Albuterol use 4 times a week due to symptoms that somewhat limit her outdoor activity
- She currently takes fluticasone 44mcg 2 puffs bid in addition to her albuterol
Self Assessment Question #4: Case Example, Part 2

- What do you recommend for her treatment?
  - A. Continue the same dose medication – her asthma is well controlled.
  - B. Start omalizumab SC q4weeks
  - C. Step up to Advair 250/50 1 puff BID
  - D. Step up to fluticasone 110mcg MDI to 2 puffs BID

How is Her Control?

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Baseline</th>
<th>6 months</th>
<th>12 months</th>
<th>18 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shortness of breath</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chest tightness</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nighttime symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Activity limitation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medication use</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Use the Steps as a Guide!

<table>
<thead>
<tr>
<th>Step</th>
<th>Preferred Action</th>
<th>Alternate Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ICS Low</td>
<td>ICS Medium</td>
</tr>
<tr>
<td>2</td>
<td>ICS Medium</td>
<td>ICS High</td>
</tr>
<tr>
<td>3</td>
<td>ICS High</td>
<td>LABA High</td>
</tr>
<tr>
<td>4</td>
<td>LABA High</td>
<td>LABA Medium</td>
</tr>
<tr>
<td>5</td>
<td>LABA Medium</td>
<td>LABA Low</td>
</tr>
</tbody>
</table>

Inhaled Corticosteroids (ICS)

<table>
<thead>
<tr>
<th>ICS Dose</th>
<th>0-1 years of age</th>
<th>2 years of age</th>
<th>≥3 years of age</th>
</tr>
</thead>
<tbody>
<tr>
<td>50mcg</td>
<td>Low Dose</td>
<td>Low Dose</td>
<td>Low Dose</td>
</tr>
<tr>
<td>110mcg</td>
<td>Low Dose</td>
<td>Low Dose</td>
<td>Low Dose</td>
</tr>
<tr>
<td>220mcg</td>
<td>Low Dose</td>
<td>Low Dose</td>
<td>Low Dose</td>
</tr>
</tbody>
</table>

Self Assessment Question #4: Case Example, Part 2

- What do you recommend for her treatment?
  - A. Continue the same dose medication – her asthma is well controlled.
  - B. Start omalizumab SC q4weeks
  - C. Step up to Advair 250/50 1 puff BID
  - D. Step up to fluticasone 110mcg MDI to 2 puffs BID
Asthma Control Test

- Two versions
  - Childhood: <12 years old
  - Adult: ≥ 12 years old
- Used as a screening tool to assess control over past 4 weeks
  - Not diagnostic
  - Helpful method to start conversations between patients and providers

Asthma Control Test

- In the past 4 weeks, how much of the time did your asthma keep you from getting as much done at work, school, or at home?
- During the past 4 weeks, how often have you had shortness of breath?
- During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?
- During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication (such as albuterol)?
- How would you rate your asthma control during the past 4 weeks?

Peak Flow Testing

- For self monitoring, measured using a peak flow meter
  - Not meant to be a diagnostic tool
  - Maximum rate of exhaled air in L/min upon forced exhalation
  - PEF is a function of the amount of effort by patient
  - Patients should establish their personal best PEF
    - Should be the best PEF achieved on a good day when their asthma is under control
    - PEF varies by age and weight – use tables to estimate normal

Jones RM. Patient Assessment in Pharmacy Practice. 2nd Ed. 2008.
Using a Peak Flow Meter

- Make sure device and your hands are clean
- Properly place the mouthpiece on the peak flow meter
- Ensure that the indicator is at zero before giving to patient
- Instruct the patient to stand with feet together and with good posture
- Could consider sitting down if the patient is not able to stand
- Instruct patient to exhale as hard and fast as he/she is able.
- Repeat 1-2 times to determine personal best.

Using Peak Flow to Calculate Control Zones

<table>
<thead>
<tr>
<th>Zone</th>
<th>% of PEF</th>
<th>Action Needed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Green</td>
<td>80-100%</td>
<td>Follow regular medication schedule and proceed with normal activities</td>
</tr>
<tr>
<td>Yellow</td>
<td>50-80%</td>
<td>Asthma may be worsening. Use asthma action plan to get back to green zone.</td>
</tr>
<tr>
<td>Red</td>
<td>&lt;50%</td>
<td>Seek medical attention immediately.</td>
</tr>
</tbody>
</table>

Asthma Action Plans: Home Exacerbation Management

- **Green zone**: PEF ≥ 80% predicted or personal best
  - If no symptoms, no change required

- **Yellow zone**: PEF ≥ 50% to 79% predicted or personal best
  - Symptoms: Persistent wheezing, coughing, chest tightness, shortness of breath, decrease in activity
    - Children: also runny nose, less activity
    - Contact healthcare professional
    - Treatment:
      - Increase albuterol frequency
      - Maintenance therapy may be increased (i.e. doubling ICS temporarily)
      - PO corticosteroid if authorized to do so

- **Red zone**: PEF < 50% predicted or personal best
  - Symptoms: sustained difficulty breathing, increased work of breathing, unable to sleep or minimal activities
  - Contact your physician and visit ER
  - Treatment:
    - SABA + PO corticosteroid + change in maintenance therapy + additional therapy

QUESTIONS?

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References