EXERCISE INDUCED ASTHMA

Background

1. Definition: Exercise induced symptoms of asthma in patients who have asthma.
    - Exercise induced bronchoconstriction is airway obstruction with exercise without presence of chronic asthma.

Pathophysiology

1. Pathology of dz
    - Hyperosmolarity theory
        - Hyperventilation during exercise causes evaporative water loss
        - Water loss causes hypertonicity/hyperosmolarity of cells
        - Change in cell composition causes release of bronchoconstricting mediators
            - Histamine
            - Prostaglandins
            - Leukotrienes
    - Airway rewarming theory
        - Large volume of cold air overwhelms ability of airways to warm air
        - Cold air reaches distal airways causing airway narrowing and edema
    - Inflammatory mediator theory
        - People that exercise frequently, especially in cold air, develop chronic inflammatory changes
        - Increased levels of IL-8, LTC4, LTD4, and histamine
        - TH-2 lymphocytes increased
            - Increased IgE
            - Increased activation of eosinophils
2. Incidence/ prevalence
    - About 10% of pts w/o dx of asthma will have bronchospasm w/exercise
    - Approx. 20.5 million Americans have asthma.[i]
    - Between 60-90% of people with asthma experience Exercise-Induced Bronchospasm (EIB)/EIA and consider it a major trigger of asthma symptoms. [i]
3. Risk factors[i]
    - High ventilation sports
        - Football
        - Basketball
    - Endurance sports
        - Cross country skiing
        - Swimming
        - Long-distance running
    - Winter sports
    - Participation in a location w/environmental pollutants (ex: automobile exhaust, sulfur dioxide, nitrogen dioxide, smoke, ozone, chlorine)
    - Cold temperatures
    - Dry air
    - Allergens, molds, dust, irritants

- Respiratory tract infections
- Sinusitis
- Rhinitis
- Concurrent medications ex: salicylates, NSAIDs, beta-blockers
- Pre-exercise food: peanuts, celery, shrimp, grain, carrots, bananas

4. Morbidity/ mortality
    - Unrecognized and inadequately treated cases increase risk of sudden death in a given athlete
    - All individuals involved in physical activity should be aware of exercise-induced asthma risks
    - morbidity associated w/this disease decreased by specifically training coaches/trainers to recognize and treat exercise-induced asthma

Diagnostics

1. History
    - Personal or family hx of asthma
    - Symptoms
        - Cough
        - Wheeze
        - Chest tightness
        - Dyspnea
        - Peak at 5 to 10 min into exercise
        - May last up to 60 min
        - Refractory period
            - Period during which repeated exertion causes less bronchoconstriction
2. Physical Examination
    - Generally negative when pt is evaluated
    - Careful ENT exam
        - Rule out nasal allergies, sinusitis, or otitis
    - Careful cardiac exam
        - Rule out cardiac arrhythmias and murmurs
    - During exacerbation, will resemble that of an asthmatic
        - Wheeze/ rhonchi
        - Prolonged expiratory phase
        - Poor inspiratory effort
        - Increased work of breathing
            - Nasal flaring
            - Substernal/subcostal retractions
3. Diagnostic Testing[i]
    - Measure change in FEV_1 before and after a standardized exercise challenge test (ECT) on treadmill or bicycle ergometer
        - Gold Standard
        - Minute ventilation must reach the target level in first 4 minutes of the challenge.

        - Exercise-induced bronchoconstriction defined by plotting FEV_1 as percentage of pre-exercise baseline FEV_1 at each post-exercise interval.
            - 10% decrease in baseline FEV_1 (i.e., <90% of baseline) generally accepted as abnormal response.
            - Some authors suggest a decrease of 15% (i.e., <85% of baseline FEV_1) more diagnostic of EIB/EIA, particularly if exercise performed in the field[v]
    - In elite athletes: sport specific challenges, free running asthma screening tests (FRAST), measures of direct bronchial responsiveness to methacholine (MCH), and indirect responsiveness to eucapnic voluntary hyperpnea (EVH) or mannitol.
    - EIB/EIA quantified using maximum percent fall index, which is maximum reduction in lung function post-exercise, expressed as a percent of the pre-exercise value.
        - Calculated using formula:

$$\frac{FEV_1/PEF_{pre-exercise} - \text{minimum } FEV_1/PEF_{post-exercise}}{FEV_1/PEF_{pre-exercise}} \times 100$$

        - A result of 50% or more clinically significant

Differential Diagnosis

1. Key Differential Diagnoses
    - Vocal cord dysfunction
    - Central airway obstruction
    - Cystic Fibrosis
    - Laryngomalacia
    - Cardiac arrhythmias
    - Congestive Heart Failure (CHF)
    - Pulmonary or cardiac shunt
    - Gastroesophageal reflux dz
    - Normal physiologic exercise limitation

Therapeutics

1. Acute Treatment
    - Pharmacological pre-treatment
    - Short acting beta-agonist (SABA)
        - Example: albuterol
        - First-line tx, most effective in preventing exercise-induced bronchoconstriction (SOR:A)[i]
        - Use: 2-4 puffs given 15 min before exercise as prophylaxis
        - Quick onset of action
        - Provides relief for up to 4 hrs
        - Is rescue medication and can be repeated if prophylaxis ineffective
        - Caution: overuse can lead to tachyphylaxis within 1 wk of regular use; however, medication should not be discontinued if still effective[i]
        - Should be used w/spacer to ensure more efficient medication delivery

- Long acting beta-agonist (LABA)[iii]
  - Example: Salmeterol
    - 50 mcg x 1, 30-60 min before exercise
  - Caution: can lead to tachyphylaxis within 4 weeks of use; increased risk of sudden death without use of concomitant inhaled corticosteroid
  - Provides protection for 6-12 hrs in first 30 days, then drops to 6 hrs (not applicable if used less than 3 days per week)
- Mast cell stabilizers (MCS)[i]
  - Example: Nedocromil sodium (not available in US)
    - 4 mg, 15-60 min before exercise
  - Example: Cromolyn
    - 20 mg NEB x 1, 10-60 min before exercise
  - Not as effective as SABA
  - Can be used in combination
- Leukotrine receptor antagonists (LTRA)
  - Example: Singular
    - 10 mg adults, 5 mg children
    - More than 2 hrs before exercise
    - Expect effect from 8-24 hrs
    - Use with caution in patients with history of psychiatric conditions due to possible behavioral side-effects.[iii]
- Short-acting anticholinergics (SAAC)
  - Example: Atrovent
    - 2 puffs, 30 min before exercise
    - Decreases mucus
    - Blocks muscarinic cholinergic receptors in bronchial smooth muscle.[iii]
- Nonpharmacologic therapy[iii]
  - Physical conditioning
  - Warm up and cool down
  - Nasal breathing
  - Avoidance of cold weather
  - Avoid environmental allergens
  - Face mask or other aid to warm and humidify inhaled air

2. Long-Term Care
   - Underlying asthma, which commonly contributes to exercise-induced bronchoconstriction, should be diagnosed and controlled first (SOR:C)[i]
   - Control allergy and asthma
   - Antihistamines
   - Intra-nasal steroids
   - Inhaled corticosteroids (ICS)
   - Dietary salt restriction may improve lung function after exercise and possibly base line lung function. [iv]
     - Very difficult to maintain due to severe sodium restriction (less than 165mmol/day)

Follow-Up

1. Return to play
    - Monitor closely after an acute attack
    - An athlete's peak flow should be >85% of baseline
        - Should be free of wheezing before returning to field of play
    - Incomplete response to "rescue" medications on sideline
        - Restrict from play
        - Refer for further medical evaluation
2. Return to office
    - Routine follow-up yearly; appropriate if symptoms under control
    - Reassess treatment strategies with any exacerbation
3. Refer to specialist
    - For uncontrolled symptoms despite maximal therapy
    - May be utilized earlier in more competitive athletes
4. Admit to hospital
    - For respiratory compromise requiring intubation
    - For exacerbations requiring continuous bronchodilator therapy or continuous oxygen admin

Prognosis

1. Excellent prognosis with proper therapy
2. Should not pose a health risk or limit athletic achievement.

Prevention[ii]

1. Control baseline asthma
2. Avoid known allergens
3. Choose appropriate sports with short bursts of activity
4. Choose warm, humid environments for activities
5. Warm-up before athletic events (take advantage of a 30-90 minute refractory period)

Patient Education

1. Handout from Family Doctor

Evidence Based Inquiries

1. What best prevents exercise-induced bronchoconstriction for a child with asthma?

References

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[ii]Preston J, Cucuzzella M, Jamieson B. What best prevents exercise-induced bronchoconstriction for a child with asthma? *Journal of Family Practice.* 2006; 55(7):631-633.

[iii] Millward DT, Tanner LG, Brown MA. Treatment options for the management of exercise-induced asthma and bronchoconstriction. *The Physician and Sports Medicine.* 2010 Dec;38(4):74-80.

[iv] Pogson Z, McKeever T. Dietary sodium manipulation and asthma. Cochrane Database of Systematic Reviews 2011, Issue 3. Art. No.: CD000436. DOI: 10.1002/14651858.CD000436.pub3.

[v] Guidelines for Methacholine and Exercise Challenge Testing—1999. Am. J. Respir. Crit. Care Med.January 1, 2000 vol. 161no. 1 309-329. Available at: http://ajrccm.atsjournals.org/content/161/1/309.full

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