

EXERCISE INDUCED BRONCHOCONSTRICTION

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DISCLOSURE

Grant/Research Support: Respiro (Wheezzo/Asthma)

OBJECTIVES

- Understand the definition and common symptoms associated with exercise induced bronchoconstriction (EIB)
- Understand the diagnostic methods for EIB
- Understand the approach to the management of EIB

DEFINITION

- **Airway contraction (narrowing of airways) associated with exercise**
- Initially called exercise-induced asthma but can happen without asthma

EPIDEMIOLOGY

- Approximately 5-20% of the general population
- Up to 90% of people with asthma have some degree of EIB
- Prevalence of EIB higher among **elite athletes**
 - Intense exercise on a daily basis requires large amount of ventilation
 - Exposure to respiratory stress (allergens, air pollutants, cold/dry air)
 - More commonly associated with sports that have higher endurance demands

TABLE I. Sports with different levels of risk of exercise-induced bronchoconstriction²⁰

Risk	Characteristics	Examples of sports
Low	Sports in which the athlete performs a <5- to 8-min effort	Track and field: sprint (100, 200, and 400 m), middle distance (800 and 1500 m), hurdles (100, 110, and 400 m), jumps, throws, decathlon, heptathlon, tennis, fencing, gymnastics, downhill skiing, boxing, golf, body building, weightlifting, martial arts
Medium	Sports in which the continuous effort rarely lasts more than 5-8 min	Soccer, rugby, American football, basketball, volleyball, handball, baseball, cricket, field hockey
High	Sports in which the athlete performs a >5- to 8-min effort and/or in a dry/cold air environment, and/or in a noxious air environment (chlorine exposure, ultrafine particles, traffic air pollution)	Swimming, water polo Track and field: long distance (5000 and 10,000 m), 3000-m steeplechase, pentathlon (mixed), walks (20 and 50 km), marathon Cycling, cross-country skiing, ice hockey, ice skating, biathlon, high-altitude sports

PATHOGENESIS

- Caused by heat loss, water loss or both from airways during exercise when quickly breathing in air that is drier than what is already in the body
- EIB seems to improve with inspired gas is more humidified and closer to body temperature

SYMPTOMS

- Shortness of breath, chest tightness, cough
 - 15 minutes after at least 5-8 minutes of high-intensity aerobic training
 - Resolves spontaneously within 60 minutes
- More common and more intense with inhaled cold, **DRY** air
- Other triggers:
 - Chlorine when swimming, pollution while running/cycling, air temperature during hot yoga
- Different than shortness of breath with exercise
 - typically resolves within 5 minutes

DIAGNOSIS

- Clinical symptoms (exercise-related dyspnea, cough, wheeze)
- Positive testing
 - **Exercise challenge** – most direct and preferred
 - 6-10 min of treadmill exercise to raise heart rate to 80—90% of predicted maximum
 - Spirometry is completed
 - Positive test if FEV1 decreases by 10% or more
 - **Bronchial hyperresponsiveness** (methacholine, histamine, mannitol inhalation challenge, eucapnic voluntary hyperventilation- EVH).
 - EVH is most sensitive among the indirect

EUCAPNIC VOLUNTARY HYPERVENTILATION (EVH)

- EVH protocol consisted of breathing a dry compressed gas mixture (21% O₂, 5% CO₂) at 85% maximum voluntary ventilation for 6 minutes.
- Spirometry performed
 - At baseline
 - At 1, 5, 10, 15, 20 minutes
- Positive is a fall of FEV₁ fall of 10% or more

MIMICS OF EIB

- Consider other disease entities if patient have no other asthma symptoms, normal spirometry, does not respond to pretreatment with bronchodilators
 - **Central airway obstruction** – malignancy (hemoptysis, risk factors for lung cancer)
 - **Exercise-induced laryngeal obstruction** – vocal cord dysfunction (inspiratory stridor with difficulty breathing during exercise)
 - **Exercise-induced laryngomalacia** – abnormal movement of aryepiglottic folds leading to obstruction (inspiratory stridor during exercise)
 - **Exercise-induced anaphylaxis** – (itching, hives, warmth, swelling, hypotension)
 - **Exercise-associated reflux** - (flushing, throat discomfort, chest tightness, cough)
 - **Dysfunctional breathing** – hyperventilation, mouth breathing, accessory muscle use (shortness of breath during exercise)

MANAGEMENT - NONPHARMACOLOGIC MEASURES

- **Nonpharmacologic measures**
 - Improving cardiovascular fitness to reduce minute ventilation required for a given level of exercise, decreases stimulus for bronchoconstriction
 - Inspire warmer and more humid air
 - Breathe through loosely fitting scarf or mask when exercising in cold, dry conditions
 - ?Conflicting data on pre-exercise warm-up
 - Possibly controlling environmental triggers could be helpful but not formally studied
 - Reduce chloramines in indoor pool, schedule outdoor training around low-traffic hours

MANAGEMENT - PHARMACOLOGIC THERAPY

- **Pharmacologic therapy**
 - Treat both EIB and underlying asthma
 - Rapid-acting bronchodilator or SABA (**albuterol**)
 - Prophylaxis: take 5-20 minutes before exercise
 - Rapid-onset long-acting bronchodilator or LABA (**formoterol**) in combination with inhaled glucocorticoid (**budesonide**)
 - Leukotriene-receptor antagonists or LTRA (**montelukast**) can be helpful
 - Inhaled muscarinic antagonist (**ipratropium**) for those intolerant of SABA

SABA USE

- **Short acting beta agonists (SABA) – albuterol, levalbuterol**
 - Most effective quick relief of EIB
 - All patients should have access to SABA and be instructed on use
 - Generally two puffs is sufficient
 - Prophylaxis treatment 5- 20 minutes before exercise
- **Quick onset long acting beta agonist (LABA)/inhaled corticosteroid**
 - Budesonide-formoterol – may also be effective
- Frequent use of inhaled beta-agonists can lead to decreased efficacy
 - **Those who exercise regularly and require frequent SABA use, it is important for them to have sufficient control of their asthma**

INTOLERANCE TO ALBUTEROL

- **Alternate SABA – levalbuterol**
 - Use 1 puff instead of 2
- **Leukotriene receptor antagonists (LTRAs)**
 - American Thoracic society guideline reviewed 11 randomized trials and found that LTRAs reduce EIB in most patients.
- **Inhaled muscarinic antagonist (ipratropium)**
 - Partial protection, less effective compared to SABA

REFRACTORY TO SABA

- Consider **poor asthma control** as the cause
- May need to step-up therapies including use of inhaled glucocorticoids (ICS)
 - ICS **does not have immediate protective effect**
 - Improves airway hyperresponsiveness over weeks to months

RECURRENT EXERCISE

- More than 3 hours of daily of exercise requiring daily SABA use presents a challenge
- Try **LABA/ICS** preventative
- Try **LTRAs**
 - Can be taken at least 2 hours prior to exercise to have max protective effect
 - Montelukast has longer protective effect (24hours)

Management of exercise-induced bronchoconstriction (EIB)

Clinical problem	Intervention	Comments
All patients with EIB	Educate about features of exercise that are likely to provoke EIB (eg, effect of temperature, dry air, intensity of exertion, allergens, pollution) and measures for mitigation	
	Educate about use of SABA to treat EIB symptoms (eg, albuterol two puffs)	
	Educate about use of SABA or other agent to prevent EIB	
	Advise caution about vigorous exercise when asthma is poorly-controlled	
Patients intolerant of SABA	Try one puff of albuterol instead of two	May not provide adequate prevention of EIB symptoms.
	Review inhaler technique and consider use of spacer/chamber	
	Improve general control of asthma (eg, with inhaled glucocorticoid) to reduce need for prophylaxis	If asthma not well-controlled (based on frequency/severity of symptoms or need for rescue inhaler, low peak flow or FEV ₁), add inhaled glucocorticoid. If asthma is otherwise well-controlled, try alternate preventive agents.
	Try alternate SABA (eg, levalbuterol)*	Try levalbuterol if above interventions are unsuccessful and levalbuterol is available. Levalbuterol can also be used for breakthrough symptoms. May not completely eliminate adverse effects of SABA.
	Try regular use of LTRA*†Δ	LTRA may be more effective in children than adults.
	Try ipratropium two puffs, 20 to 30 minutes prior to exercise*Δ	
	Substitute cromolyn or nedocromil (where available) for SABA for prophylaxis*Δ	
EIB refractory to SABA	Add regular use of LTRA	
	Improve general control of asthma (eg, with inhaled glucocorticoid)	
	Use cromoglycate with SABA as prophylaxis (where available)	
	Reassess diagnosis	
Patients who exercise for more than three hours or more than once per day	Avoid LABA monotherapy or daily use of SABA	Tachyphylaxis may occur with daily SABA or LABA.
	Try LTRA	May be more effective for prevention of EIB in children than adults.
	Improve general control of asthma (eg, with inhaled glucocorticoid)	
Patients who exercise in extreme conditions (eg, high intensity or in dry cold air)	Try methods for mitigation (eg, warm-up, scarf or face mask), depending on setting	
	Empiric trial of combination albuterol-ipratropium 20 to 30 minutes prior to exercise	

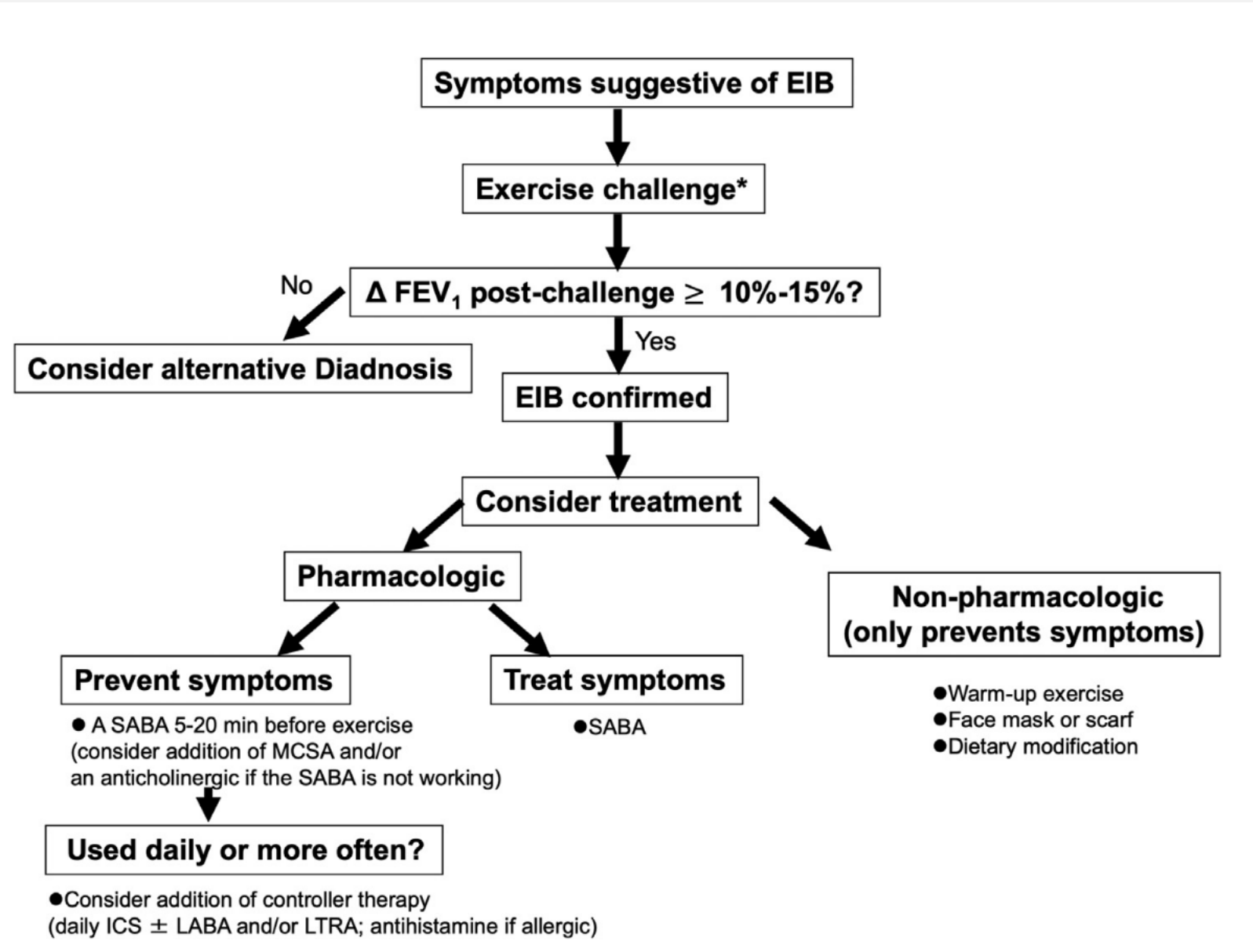
SABA: short-acting beta-agonist; FEV₁: forced expiratory volume in one second; LTRA: leukotriene-receptor antagonist; LABA: long-acting beta-agonist.

* Choice between levalbuterol, LTRA, ipratropium, and cromoglycate is based on drug availability and patient/clinician preference.

† LTRA must be taken at least two hours prior to exercise if used episodically.

Δ Patient will still need to have a SABA inhaler available for treatment of breakthrough symptoms.

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WORLD ANTI-DOPING AGENCY

- **World anti-doping agency (WADA)** published guidelines for diagnosis and management of asthma in athletes
 - Included list of medications that require a therapeutic use exemption (TUE)
 - Beta-agonists are on its prohibited medication (concerns about performance enhancement)
 - However does allow maximum dose before requiring TUE
 - Inhaled corticosteroids and LTRAs are allowed without TUE
 - Systemic corticosteroids are prohibited



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