

Nonpharmacologic Strategies to Manage Exercise-Induced Bronchoconstriction



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KEYWORDS

• Warm-up • Face mask • Asthma • Pollution • Avoidance • Athletes • Nutrition
• Training

KEY POINTS

- There is emerging evidence that nonpharmacologic strategies can be used to supplement traditional therapy to reduce exercise-induced bronchoconstriction (EIB) severity and lessen respiratory symptoms associated with exercise.
- Most investigations into nonpharmacologic strategies have included nonathletes; extrapolating to athletes should be done with caution, and studies in athletes with EIB are encouraged.
- There is currently insufficient evidence to support the use of any nonpharmacologic EIB treatment strategy in the absence of regular pharmaceutical therapy for EIB.

INTRODUCTION

Exercise-induced bronchoconstriction (EIB) is an asthma-related condition, which occurs during or after exercise as a result of large volumes of unconditioned air entering the lower airways to meet the increased ventilatory demands of exercise.^{1,2} In susceptible individuals, EIB arises via multiple mechanisms that may involve dehydration of airway surface liquid, mucosal cooling, and epithelial damage, which induce an airway inflammatory response (involving histamine, neuropeptides, leukotrienes,

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and prostaglandins) with resultant airway smooth muscle constriction.³ Management of EIB in athletes is almost exclusively based on pharmacologic therapies (see Vibeke Backer and John Mastronarde's article, "Pharmacologic Strategies for Exercise-Induced Bronchospasm with a Focus on Athletes," in this issue), such as glucocorticoids and β_2 -agonists.^{1,2} Although clinical data on nonpharmacologic therapies have been equivocal, there is emerging evidence that nonpharmacologic strategies could be used to supplement traditional therapy to reduce EIB severity and lessen exercise respiratory symptoms (Table 1). This article reviews the evidence and provides recommendations for the use of nonpharmacologic strategies in the management of EIB.

PRE-EXERCISE WARM-UP

In approximately half of those who suffer from EIB, high-intensity pre-exercise warm-up effectively protects against subsequent bronchoconstriction.³ A recent systematic review⁵⁴ reported that intermittent high-intensity pre-exercise warm-up (repetitive sprints of approximately 30 s close to peak oxygen consumption or maximum heart rate) provides approximately 10% reduction in the fall in the forced expired volume in the first second of expiration (FEV₁) postexercise, whereas neither low-intensity nor continued high-intensity pre-exercise warm-up provides significant protection in individuals with EIB.

The refractory period or refractory effect that is induced after a first exercise bout has frequently been proposed to explain why high-intensity warm-ups protect against EIB. It has been proposed that the first exercise induces a variable period (called the refractory period) during which (2–4 h) subsequent exercise does not result in EIB. Preceding exercise may deplete constrictive mediators, induce secretion of protective mediators (particularly prostaglandins), and cause desensitization of smooth muscle to bronchoconstrictive mediators.³ Regardless of the mechanism, there is good evidence to suggest a clinical benefit of warm-ups in protecting against EIB.

Although high-intensity exercise warm-ups may attenuate EIB,^{3,54} the exercise intensity that is required for the warm-up may potentially cause perturbations in the exercising musculature and compromise subsequent exercise performance.⁴ Emerging evidence suggests, however, that isolated respiratory warm-ups can provide similar bronchoprotective effects as whole-body warm-ups.⁵⁵ Instead of using whole-body warm-up, a recent study⁵⁵ evaluated the effect of a respiratory-only warm-up on subsequent decline in FEV₁ induced by exhaustive cycling (approximately 14 minutes). In that study, subjects performed normocapnic hyperpnea at different intensities (30%–80% of maximum voluntary ventilation). All hyperpnea sessions attenuated postexercise decline in FEV₁ regardless of the intensity of the hyperpnea session conducted and without compromising cycling performance.⁵⁵ Perception of respiratory dyspnea was also reduced by preceding normocapnic hyperpnea. Consequently, both pre-exercise whole-body and respiratory warm-ups may be used to protect against EIB.

AVOIDANCE OF TRIGGERS

Heat and Moisture Exchanger Face Masks

Exercise in dry and cold environments can be a significant trigger of bronchoconstriction. The bronchoconstriction is thought to be caused by dehydration of the airway surface liquid, which causes cell shrinkage and release of inflammatory mediators, precipitating airway smooth muscle constriction.⁵⁶ Repeated exposure of the airways to cold dry air may also lead to airway epithelial cell damage, microvascular leakage,

Table 1
Nonpharmacologic strategies to manage exercise-induced bronchoconstriction

Strategy	Intervention	Potential Effect	Evidence Level	Pitfalls	References
Pre-exercise warm-up	Repetitive 30-s bouts close to Vo_{2max}/HR_{max}	Reduces postexercise fall in FEV_1	Good	May accumulate peripheral fatigue prior to exertion	3–4
Face masks	HME face masks	Reduces postexercise fall in FEV_1	Insufficient	May affect ventilation and be associated with discomfort	5–8
Omega-3 fatty acid supplementation	3 g/d EPA and 2 g/d DHA	Reduces systemic inflammation Reduces airway inflammation Reduces postexercise fall in FEV_1	Medium Insufficient Insufficient	Side effects: acid reflux, bloating, diarrhea, and nausea	9–13
Caffeine	5–10 mg/kg bw	Induces bronchodilation Reduces postexercise fall in FEV_1 Improves respiratory muscle fatigue resilience Counteracts exercise-induced hypoxemia	Good Medium Medium Insufficient	Slow absorption Side effects: muscle tremors, tachycardia	14–21
Vitamins and antioxidants	1500 mg/d vitamin C 64 mg/d β -carotene	Reduces systemic inflammation Scavenge ROS Reduces postexercise fall in FEV_1	Medium Medium Insufficient	Side effects: diarrhea, vomiting, headache, insomnia, nausea, kidney stones	22–33
Breathing control	See Table 2	Reduces perception of respiratory symptoms	Insufficient		34–37
Respiratory muscle training	30 breaths $\times$ 2/d at 50% of MIP	Improves respiratory muscle fatigue resilience Reduces asthma severity	Good Insufficient	Time-consuming	38–53

Abbreviations: HR_{max} , maximum heart rate; MIP, maximum inspiratory pressure; ROS, reactive oxygen species; Vo_{2max} , maximum oxygen consumption.

and airway remodeling, which may worsen asthma severity.⁵⁷ Given the increased risk of bronchoconstriction in dry and cold environments, individuals with asthma may be advised to avoid exercise outside. This places obvious constraints on athletes with asthma-related conditions who have to train and compete in dry and cold environments and also the proportion of individuals with asthma who engage in physical activity as part of their daily routines during the winter months.

Face masks that incorporate a heat and moisture exchanger (HME) are a novel non-pharmacologic tool to counteract EIB in dry and cold environments. Although few studies have investigated the efficacy of HME face masks in counteracting EIB, some studies have demonstrated a protective effect as measured by an attenuation in postexercise decline in FEV₁.⁵⁻⁸ This suggests that individuals with asthma may use HME face masks to protect against EIB when they engage in moderate to vigorous exercise in cold dry environments. Currently, it is unknown whether the HME face masks reduce airway inflammation over acute and multiple bouts of exercise. Nor is it known whether HME face masks reduce respiratory symptoms and β_2 -agonists usage over several weeks of engaging in exercise in dry cold environments. If HME face masks are considered as part of a nonpharmaceutical therapy plan, the design of the masks needs to be considered, because individuals with asthma-related conditions are unlikely to wear the masks if they find the masks large and cumbersome. Athletes may not see HME face masks as a viable strategy to prevent EIB because the masks may not be practical wear to achieve optimal sporting performance or permitted by the rules of the sport.

Air Pollution

Air pollution has been shown to increase asthma severity and may have significant effects on athletes due to the high ventilation rates they achieve and sustain during intense exercise.⁵⁸ Air quality is inversely correlated with exercise-induced respiratory symptoms.⁵⁹ The risk is also greater in those athletes who train on a regular basis in environments with poor air quality.⁶⁰ Small particles, in particular ultrafine ones (<100-nm diameter) like those from combustion engines, have high lung deposition and may cause epithelial damage. These particles include ozone, sulfur dioxide, nitrogen oxides, and particulate matter (PM) (PM smaller than 2.5- μ m diameter). Ice skaters are particularly exposed to combination of cold dry air as well as PM less than 1- μ m diameter in confined spaces of indoor ice arenas and from multiple ice-resurfacings by gas-powered or propane-powered machines. Particle inhalations have been shown to induce oxidative stress, airway inflammation, and airway remodeling. All these result in higher prevalence of asthma symptoms and great degree of small airway dysfunction.⁶¹⁻⁶⁴

With regard to management, mechanical barriers, such as face masks, may help reduce the effects of polluted particles.⁵ Avoidance of training in low humidity conditions or during times of high levels of atmospheric pollutants is advisable, yet its practical usage and scientific benefit is still questionable. Similarly, whenever possible, it may be recommended to avoid training close to busy major roadways or during rush hours or other times of elevated vehicular congestion.⁶⁵

Swimming

The pathogenic mechanisms of EIB classically involve both osmolar and vascular changes in the airways in addition to cooling of the airways.^{2,56} Increased minute ventilation during exercise requires significant warming and humidification of the inspired air. The resulting respiratory heat and water loss from the airway mucosa into the inspired air may release bronchoconstrictive mediators. In that respect, sports

in warm humid environments, such as indoor pools, are encouraged. Swimming has often been recommended as a less asthmogenic trigger compared with other sports, because of the humid environment. Yet, a recent Cochrane review concluded that there is insufficient evidence to suggest that aquatic-based exercise is superior to comparative nonaquatic exercise in asthmatics.⁶⁶

Chlorination is the most commonly used method for ensuring water hygiene in swimming pools. Chlorine gas and its aerosol byproducts (eg, trichloramine, hypochlorous acid, and monochloramine and dichloramine), which float just above the water surface, may affect the nose, pharynx, larynx, trachea, and bronchi, with chronic exposure leading to structural epithelial changes. During exercise, nasal breathing at rest shifts to oronasal breathing, thereby significantly reducing the filtering effect of the nose. Aerosol particles travel and deposit further into the lung. Trichloramine gas formed in chlorinated pools was suggested as a cause for EIB in competitive swimmers and increased airway hyperreactivity (as measured by methacholine or eucapnic voluntary hyperventilation [EVH] challenge) has been demonstrated in swimmers.^{67–69} Increasing evidence supports the notion that chronic repetitive swimming in indoor pools may induce airway epithelial damage, inflammation, and remodeling^{68–70} and increase the risk for atopy and asthma.^{71–73} A recent study found increased levels of 8-isoprostane (as a marker of airway oxidative stress) in the exhaled breath condensate of competitive swimmers after a swimming session.⁷² Whenever possible, swimmers should train in pools cleaned with nonchlorine water disinfection methods (such as copper/silver and ozone) as well as in well-ventilated pool environments. Yet, apart from some case reports,⁷⁴ the scientific evidence to support or refute many of these recommendations is lacking.

DIETARY STRATEGIES

Omega-3 Fatty Acid Supplementation

Populations who consume large quantities of oily fish have a lower prevalence of asthma.⁷⁵ Oily fish are rich in omega-3 fatty acids: eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). EPA and DHA are precursors to powerful agents involved in the resolution of inflammation. Two mechanisms of action underpinning the anti-inflammatory bioactions include the ability of EPA to compete with arachidonic acid as a substrate for cyclooxygenase-2 and 5-lipoxygenase enzymes and be converted to less inflammatory leukotrienes and prostanoids^{76,77} and to generate the potent anti-inflammatory E-series resolvins.⁷⁶ DHA may also alter gene transcription and translation via direct or indirect actions on intracellular signaling pathways.⁷⁸

The anti-inflammatory properties of EPA and DHA make a diet high in oily fish an attractive addition to the therapy for individuals with EIB. Initial investigations demonstrated 10 weeks' dietary supplementation of EPA, 3.2 g/d, and DHA, 2.2 g/d, reduced leukotriene production by 50% but not reduction in postexercise decline in FEV₁ in asthmatics.⁹ Using the same EPA and DHA dietary supplementation over a 3-week period, however, Mickleborough and coworkers^{10,11} reported significant reductions in airway inflammation, which was accompanied by 64% to 80% reductions in FEV₁ fall postexercise in individuals with EIB. Postexercise decline in FEV₁, while on EPA and DHA supplementation, was similar to that in the non-EIB control group. In addition, EPA, 3.2 g/d, and DHA, 2 g/d, were observed as favorably as montelukast, 10 mg/d, in reducing airway inflammation and hyperpnea-induced bronchoconstriction in participants with mild to moderate persistent asthma.¹² There seems, however, no additional benefit of combining EPA and DHA supplementation with montelukast, 10 mg.¹² Furthermore, a recent pilot study found no beneficial effect of vitamin D and

fish oil supplementation for 3 weeks on reduction in FEV₁ induced by EVH in recreational athletes with EIB.⁷⁹

Recently, the marine lipid fraction of the New Zealand green-lipped mussel (*Perna canaliculus*), PCSO-524, which is rich in omega-3 fatty acids, has been shown to produce similar reductions in inflammation and bronchoconstriction (57% reduction of FEV₁ fall) after an EVH challenge.⁸⁰ In this investigation, the attenuation of airway inflammation and bronchoconstriction cannot be explained entirely by the EPA and DHA content of PCSO-524, because the amounts of EPA and DHA consumed daily were only 72 mg and 48 mg, respectively. Therefore, it may be that the additional constituents of PCSO-524 act synergistically with EPA and DHA to bring about the anti-inflammatory effect and reduction in bronchoconstriction.

Although a low intake of EPA and DHA does not seem a safety issue, a few side effects can occur, such as a fishy aftertaste, flatulence, acid reflux, bloating, diarrhea, nausea, and possibly an increased risk of bleeding and immunosuppression with a high intake of omega-3 fatty acids.¹³ The initial investigations provide promise for EPA and DHA dietary supplementation to protect against EIB and associated airway inflammation. Large-scale clinical studies in individuals with EIB are required, however, to determine the minimum effective dose and duration required to observe the beneficial effect and to compare the effect of combining omega-3 fatty acid supplementation with prevention inhaler therapy (eg, inhaled glucocorticoids).

Caffeine

Caffeine (1,3,7-trimethylxanthine) is among the most commonly used supplements by athletes.⁸¹ Although formerly subjected to antidoping regulations, the restrictions on caffeine were lifted by the World Anti-Doping Agency in 2004 and it can as such be used freely in and out of competition. Caffeine works as a nonselective competitive adenosine receptor antagonist for all subtypes of the adenosine receptor^{82,83} but may also act as a phosphodiesterase inhibitor.⁸⁴ Accordingly, caffeine induces intracellular cyclic adenosine monophosphate-dependent/protein kinase A signaling, which like β_2 -agonists, causes smooth muscle relaxation.⁸⁵ Studies have shown dose-related bronchodilator effects of caffeine on basal airway function.⁸⁶ The interest in caffeine as a bronchoprotective agent started approximately 30 years ago when Becker and coworkers¹⁴ observed that 10 mg/kilogram of body weight (kg bw) of orally ingested caffeine had a similar bronchodilating effect as oral theophylline, 5 mg/kg bw, in children with asthma.¹⁴ Comparable bronchodilating effect was later shown in adult asthma patients after ingestion of caffeine,¹⁵ 5 mg/kg bw, or 3 cups of coffee.¹⁶

Although caffeine shows promise as a bronchodilator, only a few studies have investigated its potential to counteract EIB, none of which has been performed in athletes. In nonathletes, ingestion of caffeine was shown to have a postexercise bronchoprotective effect compared with placebo in individuals with EIB.¹⁷ Although postexercise decline in FEV₁ was 24% for placebo, it was less than 1% after ingestion of caffeine, 7 mg/kg bw, and 8% after caffeine, 3 mg/kg bw. In accordance with this observation, Duffy and Phillips¹⁸ observed that ingestion of caffeine, 10 mg/kg bw, reduced bronchoconstrictor response to EVH-provocation compared with placebo in EVH-positive individuals. When compared with inhalation of β_2 -agonist salbutamol (albuterol, 180 mg), ingestion of caffeine, 9 mg/kg bw, was shown as effective as salbutamol in attenuating postexercise reduction in FEV₁ in asthmatics with EIB.¹⁹

Aside from its bronchoprotective effect, caffeine has a variety of other effects of relevance for airway function during exercise. During submaximal exercise, as little

oral caffeine as 3 mg/kg bw has been shown to modulate ventilatory dynamics by reducing the physiologic dead space ventilation/tidal volume ratio and breathing frequency while concurrently increasing tidal volume.^{87,88} In addition, caffeine may counteract exercise-induced hypoxemia (desaturation) in elite athletes at submaximal intensities²⁰ and improve respiratory muscle fatigue resilience.²¹

Despite the small number of studies undertaken, there is some evidence to suggest that caffeine has the potential to reduce EIB severity and improve ventilatory dynamics and respiratory muscle fatigue resilience during exercise. The amount of orally ingested caffeine needed for bronchoprotection is approximately 5 mg/kg bw to 10 mg/kg bw, equivalent to 2 cups to 4 cups of coffee. It seems, however, that the bronchoprotective effect of caffeine is highly individual. A limitation of caffeine is the slow absorption rate when ingested, giving rise to a bronchodilator response 2 hours after ingestion. Future studies should investigate more thoroughly the therapeutic efficacy of caffeine as a bronchoprotective substance during exercise in athletes with EIB.

Vitamins and Antioxidants

Supplementation with various vitamins and antioxidants has attracted some attention as a means to counteract EIB because of their ability to suppress proinflammatory signaling,²² to lower levels of histamine^{23,24} and prostaglandin F₂ α ,²⁵ and to scavenge reactive oxygen species.^{26,27} In practical terms, however, interpretation of the therapeutic efficacy of each individual vitamin and antioxidant as bronchoprotective substances in EIB is limited by the small number of studies that have been undertaken in individuals with EIB, especially in athletes. Most convincing is the bronchoprotective effect of acute and chronic supplementation with vitamin C on postexercise decline in FEV₁ in individuals with EIB.^{25,28–30} In addition, 1 week supplementation with β -carotene (64 mg), a provitamin A carotenoid, has been shown to reduce postexercise reduction in FEV₁.³¹ Conflicting results have been observed after 1-week supplementation with the carotenoid lycopene (30 mg), in which a postexercise bronchoprotective effect was found in asthmatic individuals with EIB, whereas adolescent athletes with EIB had no effect.^{32,33}

STRATEGIES TO REDUCE PERCEPTION OF EXERTIONAL DYSPNEA

Strategies that may help control EIB are discussed previously. In addition, there may be a role for using breathing control and inspiratory muscle training (IMT) to enable athletes with EIB to reduce perceptions of exertional dyspnea.

Breathing Control

A significant symptom of EIB is dyspnea during and after exercise. There are a variety of breathing exercises that may benefit individuals who experience asthma/EIB exacerbations that include yogic breathing^{34–36} and physiotherapist-supervised breathing training.³⁷ Although these forms of breathing control exercises may not be able to reduce asthma severity, they may be able to reduce the perception of respiratory symptoms and increase perception of asthma control.³⁴ Moreover, breathing exercises have been shown to improve quality of life,³⁵ reduce use of relief medication,³⁵ and reduce the levels of anxiety and depression³⁷ and airway hyperresponsiveness.³⁶ Future research is required to understand the mechanisms behind these observations in asthmatic individuals.

It is currently unknown how these forms of breathing control exercises may be beneficial for athletes with EIB, whose main symptoms are experienced during

exercise. The use of breathing training, however, incorporating IMT and breathing technique training (Table 2), has been shown helpful in reducing the perception of breathing in an athlete with nonasthmatic exercise respiratory conditions.³⁸ Future research is required to investigate how athletes with EIB respond to using breathing exercises. Furthermore, the current breathing control methods may need to be adapted to replicate respiratory control during exercise rather than focusing on breathing control at rest.

Respiratory Muscle Training

Respiratory muscle training is an easy and cheap way to enhance both inspiratory and expiratory muscle strength³⁹ and also has been associated with improvements in exercise performance during various exercise protocols in healthy individuals.^{40,41} Despite decades of research into the applications of respiratory muscle training, the area is still controversial and subject to scientific debate.^{42–44} Respiratory muscle training has shown some promise in the management of chronic obstructive pulmonary disease,⁴⁵ inspiratory stridor,³⁸ and exercise-induced vocal cord dysfunction.^{46,47} Although studies also have shown that respiratory muscle training may have beneficial effects on asthma severity and β_2 -agonist usage,^{48–50} a recent Cochrane review, based on 113 asthmatics, concluded that there is no conclusive evidence to support or refute the therapeutic efficacy of IMT in asthma.⁵¹ Nevertheless, given individuals with EIB may experience airway obstruction and airflow limitation during intense exercise,⁵² which potentially puts a larger work load on respiratory muscles,^{3,53} it could be speculated that respiratory muscle training may be beneficial for athletes with EIB. To the authors' knowledge, however, no studies have investigated the effectiveness of respiratory muscle training on EIB severity.⁸⁹

SUMMARY AND FUTURE CONSIDERATIONS

There are numerous nonpharmacologic strategies that can be used to support the treatment of EIB; however, the evidence is inconclusive and future studies are encouraged before any recommendations are implemented. There is currently insufficient

Table 2 Summary of breathing training for athletes	
Breathing Control Methods	Overview
Breathing technique	Encourage initiation of inspiration from the lower rib cage. Inspiratory maneuver should be smooth with little tension through the shoulders and neck. Aids, such as elastic strap or hands placed on sides of torso over lower ribs, can be used to help athletes. Athlete can begin to attempt to practice this technique in functional sport specific positions.
IMT	Ensure breathing technique is addressed before initiating IMT. Athletes with poor breathing technique, who proceed directly to IMT, may experience exacerbation of their symptoms. IMT should incorporate forceful inspiratory maneuvers through a handheld device providing resistance to the inspired airflow. Focus during the IMT should be on good breathing technique (as described previously). An IMT session should comprise 30 continuous forced inspiratory efforts at the equivalent of 30 breath repetitions maximum, with relaxed expiration.

Data from Dickinson J, McConnell A, Ross E, et al. The BASES expert statement on assessment and management of non-asthma related breathing problems in athletes. The Sport and Exercise Scientist, Issue 45, Autumn 2015, British Association of Sport and Exercise Sciences, www.bases.org.uk.

evidence to support the use of any nonpharmacologic EIB treatment strategy in the absence of regular pharmaceutical therapy for EIB. Although there are some encouraging findings with regard to nutritional supplementation and respiratory muscle training, future studies are encouraged, especially in athletes. Most studies have included nonathletes and extrapolation to athletes should, therefore, be done with caution. Furthermore, data on other commonly used supplements by athletes, such as β -alanine and creatine, are lacking in relation to EIB. For instance, β -alanine supplementation increases intracellular content of carnosine, which, among other factors,⁹⁰ may affect nitric oxide production and modulate inflammation,^{91,92} both of which could affect EIB severity. In addition, creatine supplementation has been shown to exacerbate airway inflammation, increase airway hyperresponsiveness, and induce smooth muscle thickening in mice.⁹³ No studies, however, have, to the authors' knowledge, investigated the effect of creatine supplementation on EIB severity in athletes. Consequently, there are numerous nonpharmacologic strategies yet to be studied in athletes with EIB.

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