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

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EVIDENCE-BASED ANSWER

Inhaled short-acting beta-agonists (SABAs) are most effective in preventing exercise-induced bronchoconstriction, followed by inhaled mast cell stabilizers and anti-cholinergic agents (strength of recommendation [SOR]: **A**, multiple randomized control trials [RCTs]). Less evidence supports the use of leukotriene antagonists and inhaled corticosteroids, either individually or in combination (SOR: **B**). Underlying asthma, which commonly contributes to exercise-induced bronchoconstriction, should be diagnosed and controlled first (SOR: **C**).

CLINICAL COMMENTARY

Control the asthma and the need for pre-treatment often becomes unnecessary

Because truly isolated exercise-induced bronchoconstriction is uncommon in a nonasthmatic child, and because bronchospasm in a child during exercise more commonly indicates undiagnosed asthma, search for treatable asthma when a child wheezes with exercise. These children have sputum eosinophilia reflecting inflammation, and they are best served by addressing the underlying asthma with inhaled corticosteroids. Once the asthma is under control, their need for "the best pre-treatment" (a SABA) often becomes irrelevant. Ask the child whether he or she is having more shortness of breath and difficulty breathing after exercise than during exercise; this reveals those most likely to benefit from treatment.

Evidence summary

It is difficult to interpret studies on exercise-induced bronchoconstriction (the rather uncommon presence of exercise-induced bronchospasm in a nonasthmatic) and exercise-induced asthma (the more common situation of asthma worsened by exercise). Many studies include both types of patients.

A systematic review of 24 RCTs (of which 13 evaluated children) showed that SABAs, mast cell stabilizers, and anti-cholinergics provide a significant protective effect against exercise-induced bronchoconstriction with few adverse effects (the child subgroup analyses did not differ significantly from pooled results). Mast cell stabilizers were found less effective at attenuating bronchoconstriction than SABAs, with an average maximum decrease in the forced expiratory volume in 1 second (FEV_1) of 11.9% compared with 4.6% for beta-agonists (child subgroup: weighted mean difference=7.3%; 95%

FAST TRACK

Bronchoconstriction after exercise is best prevented by controlling the underlying asthma, avoiding allergens, and choosing appropriate sports activities

confidence interval [CI], 3.9–10.7). Complete protection (defined in this study as maximum % decrease in FEV_1 <15% post-exercise) and clinical protection (50% improvement over placebo) measures were included. Fewer children had complete protection (pooled: 66% vs 85%, odds ratio [OR]=0.3; 95% CI, 0.2–0.5) or clinical protection (pooled: 55% vs 77%, OR=0.4; 95% CI, 0.2–0.8).

Mast cell stabilizers were more effective than anticholinergic agents, with average maximum FEV_1 decrease of 9.4% compared with 16.0% on anticholinergics (child subgroup: weighted mean difference=6.6%; 95% CI, 1.0–12.2). They also provided more individuals with complete protection (pooled: 73% vs 56%, OR=2.2; 95% CI, 1.3–3.7) and clinical protection (pooled: 73% vs 52%, OR=2.7; 95% CI, 1.1–6.4). Combining mast cell stabilizers with SABAs did not produce significant advantages in pulmonary function over SABAs alone. No significant subgroup differences were seen based on age, severity, or study quality.[1]

Another systematic review of 20 RCTs (15 studying children and 5 studying adults) with patients aged >6 years showed that 4 mg of nedocromil (Tilade) inhaled 15 to 60 minutes before exercise significantly reduced the severity and duration of exercise-induced bronchoconstriction compared with placebo. It had a greater effect on patients with severe exercise-induced bronchoconstriction (defined as an exercise-induced fall in lung function >30% from baseline).[2]

Eight RCTs (5 studying children) were included in a systematic review of patients aged >6 years that found no significant difference between nedocromil and cromoglycate with regards to decrease in FEV_1, complete protection, clinical protection, or side effects.[3]

Leukotriene antagonists have been recommended on a trial basis with follow-up to evaluate the treatment response.[4] Although there are several long-term studies of leukotriene antagonists for adults, few have studied children. A recent study assessed the effects of montelukast (Singulair) on 64 children with exercise-induced bronchoconstriction. After 8 weeks of treatment, the montelukast group showed significant improvements (compared with placebo) in asthma symptom scores (24.3 ± 8.2 before vs 17.8 ± 6.8 after 8 weeks of montelukast treatment, $P<.05$; vs 17.7 ± 6.7 8 weeks after stopping treatment, $P<.05$), maximum percent fall in FEV_1 after exercise (36.5 ± 10.2% before vs 27.6 ± 14.4% after 8 wks of treatment, $P<.01$; vs 26.7 ± 19.4% 8 weeks after stopping treatment, $P<.01$), and time to recovery (41.8 ± 8.1 min before vs 25.3 ± 23.3 min after 8 weeks of treatment, $P<.01$; vs 27.7 ± 26.5 min 8 weeks after stopping, $P<.05$).[5]

Therapies awaiting further study include a combination of budesonide (Pulmicort) and formoterol (Foradil), which is similar to the currently available preparation of fluticasone and salmeterol (Advair Diskus) but contains a long-acting beta-agonist with quicker onset. The phosphodiesterase-4 inhibitors roflumilast (Daxas) and cilomilast (Ariflo)—neither of which have been FDA-approved—and inhaled low-molecular-weight heparin have potential efficacy.[6] Other options suggested for this problem—including inhaled furosemide, vitamin C, antihistamines, calcium channel blockers, and reduced dietary salt intake—need further study.[7]

Recommendations from others

Review articles on this topic suggest the following to prevent exercise-induced bronchoconstriction: controlling baseline asthma, avoiding known allergens, choosing appropriate sports with short bursts of activity, and selecting warm, humid environments for the activities.[6–8] Some authorities recommend warm-up before athletic events to take advantage of a 30- to 90-minute refractory period. This can help prevent exercise-induced bronchoconstriction; however, effects vary considerably from person to person.[7,8]

The National Asthma Education and Prevention Program recommends prevention of exercise-induced bronchoconstriction by optimally controlling underlying asthma. If a patient remains symptomatic during exercise, you should review medication usage, understanding of dosage instructions, and administration technique before any changes in the treatment regimen.[9]

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