Exercise-Induced Bronchoconstriction in Asthmatic Children
A Comparative Systematic Review of the Available Treatment Options

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Abstract

The aim of this article is to critically review the efficacy and safety data from randomized controlled trials (RCTs) using inhaled corticosteroids (ICSs), long- or short-acting \(\beta_2\)-adrenoceptor agonists (LABAs, SABAs), parasympatholytics...
and oral leukotriene receptor antagonists in the management of exercise-induced bronchoconstriction (EIB) in children with persistent asthma (EIA).

The studies with sufficient information on patient characteristics and outcomes were chosen using a MEDLINE search. Results from the individual searches were combined and repeated. Studies were also found by reviewing the reference lists of the articles not included in this review. Studies focusing solely on individuals with asthma and other allergic co-morbidities (i.e. a degree of bronchial reversibility) were considered in this review. To make the paper evidence-based, the design and the quality of different studies were assessed employing the Sign criteria (evidence level [EL] and grades of recommendation [GR]). No additional statistical analyses were performed. Most of studies included paediatric patients with underlying EIA.

We need to distinguish children with recurrent asthma symptoms in whom EIB is also present (patients with EIA) from asthmatic subjects whose symptoms appear only as a result of exercise (patients with EIB). Further controller treatment is indicated in patients with EIA and further reliever treatment in patients with EIB. ICSs are the first-choice controller drugs for EIA in children with persistent asthma (Sign grade of recommendation [GR]:A). In children with EIA without complete control with ICSs, SABAs (GR:A), leukotriene receptor antagonists (LTRAs) [GR:A] or LABAs (GR:A) may be added to gain control. Treatment with relievers such as SABAs (GR:A), parasympatholytics (GR:B) or, eventually, LABAs (GR:A), administered 10–15 minutes before exercise is the most preferable method of preventing EIB symptoms in children; however, not as monotherapy in children with EIA.

The disadvantages and controversy relating to inhaled β₂-adrenoceptor agonist use lie in the development of tolerance to their effect when they are used on a regular basis, and the possibility of a resulting underuse of ICSs in patients with EIA. Researchers and guidelines recommend that if any patient requires treatment with a β₂-adrenoceptor agonist more than twice weekly, a low dose of ICSs should be administered. Inhaled parasympatholytics may be effective as preventive relievers in some children with EIB or EIA, especially among those with increased vagal activity. LTRAs have a well balanced efficacy-safety profile in preventing the occurrence of EIB symptoms in children. Compared with LABAs, LTRAs produce persistent attenuation of EIB and possess an additional effect with rescue SABA therapy in persistent asthmatic patients with EIA. A disadvantage of LTRAs is a non-response phenomenon. There are still insufficient data on the efficacy-safety profiles of ICS/LABA combination drugs in the treatment of EIA in children to recommend this treatment without caution. Safety profiles of inhaled SABAs, anticholinergics and montelukast in approved dosages seem sufficient enough to recommend use of these drugs in the prevention of EIB symptoms in children. Many researchers agree that treatment of EIA in children should always be individualized.

### 1. Exercise-Induced Bronchoconstriction (EIB) in Asthmatic Children

Physical activity is an important trigger of asthma symptoms for most patients, including children. Exercise-induced bronchoconstriction (EIB) can also be a unique asthma phenotype. Exercise-induced asthma (EIA) and EIB are terms used to describe a transient narrowing of the airways that follows vigorous exercise.