



The Poorly Explored Impact of Uncontrolled Asthma

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The goal of asthma management is to achieve disease control; however, despite the availability of effective and safe medications, for many patients asthma remains uncontrolled. One reason for this is the fear of long-term side effects from the regular use of inhaled corticosteroids (ICSs). Adverse effects of poorly controlled asthma (for example, obesity, pneumonia, and risks to the fetus) can be perceived as side effects of ICSs. Poorly controlled asthma adversely affects children's cardiovascular fitness, while children with well-controlled asthma perform at the same level as their peers. Children with uncontrolled asthma also have a higher frequency of obesity than children with controlled asthma. Stress can affect asthma control, and children with poorly controlled asthma are more likely to have learning disabilities compared with those with good control. In adults, focused attention and concentration are negatively affected in patients with untreated asthma, and patients with asthma are at greater risk for depression. Also, poorly controlled asthma increases the risks of severe asthma exacerbations following upper respiratory and pneumococcal pulmonary infections. ICSs used to improve asthma control have been demonstrated to improve all of these outcomes. Lastly, the risks of uncontrolled asthma during pregnancy are substantially greater than the risks of recommended asthma medications. Treatments to maintain asthma control are the best approach to optimize maternal and fetal health in the pregnancies of women with asthma. The maintenance of asthma control has significant advantages to patients and greatly outweighs the potential risks of treatment side effects.

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Abbreviations: AE = adverse event; fMRI = functional MRI; HRV = human rhinovirus; ICS = inhaled corticosteroid; LABA = long-acting β agonist; SABA = short-acting β agonist; SAE = serious adverse event; URTI = upper respiratory tract infection

Asthma treatment guidelines have identified that the primary goal of management is to achieve overall asthma control.¹⁻³ This consists of two domains: The first is current asthma control, which includes the day-to-day minimization of both daytime and nighttime symptoms, no activity limitation, minimal

rescue bronchodilator use, and no airway narrowing. The second domain includes minimizing the future risks to the patient of developing instability of their control, having severe asthma exacerbations, losing lung function over time, or experiencing side effects from their medications.

The benefits of good asthma control have been well studied and include reduced health-care resource utilization and loss of work/school days, higher probability

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of a normal quality of life, and reduced risk of exacerbations compared with poorly controlled asthma.⁴ However, poor asthma control may be associated with other less well-known impacts on the lives of patients. In addition, adverse effects of poorly controlled asthma (for example, obesity, pneumonia, and risks to the fetus) can be perceived as side effects of inhaled corticosteroids (ICSs)—the most effective medications used to achieve asthma control—because of the well-recognized association of these unwanted effects with oral corticosteroid use. The purpose of this review is to highlight some important, but less well-known, consequences of poor asthma control and the effects of maintenance treatment with ICSs on these. Specifically, information will be presented concerning the negative effects of poorly controlled asthma on physical activity and obesity, on cognitive function and educational achievement, on stress and mental health, on pneumonia risk, and on pregnancy and fetal outcomes.

ACTIVITY AND PHYSICAL FITNESS

There are significant associations between daily physical activity and cardiovascular fitness in adults as well as children,⁵ although the associations are weaker in children. In childhood and adolescence, physical activity and/or a high cardiovascular fitness reduce the risk of being overweight.⁶ Moreover, a significant dose-response relationship has been documented between physical activity/cardiovascular fitness and important risk factors for cardiovascular disease.⁷ Any increase in daily physical activity is normally considered beneficial. Also, since many patients with asthma experience exercise-induced bronchoconstriction, poorly controlled asthma could have important negative influences on the patient's daily physical activity, fitness, and risk of obesity.

Several studies have compared physical activity and/or cardiovascular fitness in children with asthma to healthy age-matched and sex-matched children. The results and conclusions vary substantially, and the findings in these studies are difficult to compare due to marked variations in methodology, populations (asthma severity), study design, power, and asthma-diagnosis criteria. The majority of these studies are of cross-sectional design and lack a thorough assessment of the level of asthma control. Thus, while some studies do not find any differences in the daily physical activity or cardiovascular fitness between groups of children with asthma and healthy children,^{8,9} several do find significantly reduced levels of physical activity or fitness in children with asthma compared with healthy children.¹⁰⁻¹² The poor characterization of level of asthma control, the treatments used, and

even the diagnostic criteria for asthma in most studies preclude an accurate analysis of the reason for this discrepancy. However, two recent studies have assessed the importance of the level of asthma control and fitness, and the amount and intensity of daily physical activity, in a population of well-characterized children with asthma.^{13,14} Children with asthma were found to be less fit, run shorter distances during exercise tests, have a higher BMI, and a higher percentage of body fat than their healthy control subjects, but no differences were found between the two groups in overall daily activity.^{13,14} However, within the asthma group, fitness and time spent in intensive daily activity depended significantly on the level of asthma control; children with poorly controlled asthma were less fit and had less intensive daily activity. Moreover, the activity of children with uncontrolled asthma was significantly less than the activity in their healthy control subjects. Similar findings have been reported in younger children.¹⁵

When the children with asthma were treated according to guideline recommendations, their asthma control improved during the year of treatment.^{13,14} The improvements in asthma control were associated with significantly greater improvements in physical activity in children with asthma than in their healthy control subjects (around 3 h per week, of which 33 min were in moderate vigorous activity) (Fig 1). Moreover, the increase in activity was associated with a significantly greater increase in cardiovascular fitness in the asthma group, indicating that the magnitude of the changes in activity was clinically important. The greatest improvements in daily activity and fitness were seen in the children with the poorest asthma control at baseline and greatest improvements in control during treatment. There are no similar studies of the effects of poor asthma control on physical activity and the benefits of improving asthma control on these parameters in adult patients with asthma. In conclusion, uncontrolled asthma adversely affects the daily activity and fitness in children, and long-term treatment both controls asthma and reverses these negative effects of the disease.

ASTHMA AND OBESITY

Studies have described a significant relationship between physical activity and body fat in healthy children,¹⁶ but they do not allow any cause-effect assessment. However, other longitudinal studies have found daily physical activity to protect against accumulation of body fat.¹⁷⁻¹⁹ The correlation between activity and obesity has generally been low to moderate, probably because many other factors are linked to obesity.

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