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The beneficial effects of physical exercise on antioxidant status in asthmatic children

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Abstract
Background: The pathogenesis of asthma involves both airway inflammation and an oxidant/antioxidant imbalance. It is demonstrated in asthmatic adults that exercise programmes improve lung function, a mechanism yet to be elucidated. The purpose of this study was to investigate the possible beneficial effects of physical exercise on antioxidant status in asthmatic children which may lead to ameliorated lung function.
Methods: The study enrolled thirteen control and thirty asthmatic children. The asthmatic group was subdivided into two: the first group receiving only pharmacological treatment (n = 15) and the second receiving pharmacological treatment with exercise programme (n = 15) for 8 weeks. Blood samples were drawn from the subjects before and after treatment periods. As oxidant stress markers blood levels of malondialdehyde (MDA) and total nitric oxide (NO), and as antioxidant status, glutathione peroxidase (GSH-Px) and superoxide dismutase (SOD) enzyme activities were assessed.
Results: Before any treatment was initiated, MDA and NO levels in the asthmatic group were significantly higher than the controls (3.40 ± 0.96 nmol/ml vs 2.46 ± 0.58 nmol/ml, and 12.53 ± 2.10 vs 9.40 ± 1.39 micromol/L, respectively). Both SOD ($p = 0.0001$) and GSH-Px ($p = 0.023$) activities were significantly lower in the asthmatic group. Pharmacological treatment and exercise programme together significantly improved lung performance and decreased the levels of oxidant stress markers, in concordance with a significantly increase in antioxidant enzyme activity measures when compared to the pharmacological treatment.
Conclusion: Structured exercise programme in asthmatic children resulted in better lung function, which may be attributed to its effect on antioxidant status.

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Introduction

The pathogenesis of chronic obstructive lung diseases such as asthma is complex. It involves both airway inflammation and an oxidant/antioxidant imbalance.[1] The link between chronic inflammation and oxidative stress is activated inflammatory cells, including neutrophils and eosinophils, which generate reactive oxygen species (ROS).[2] Pro-inflammatory cytokines released from activated cells stimulate the production of reactive oxygen species, which act as signalling mediators for a variety of signal transduction pathways and gene expression.[3,4] Elevated levels of ROS such as hydroxyl radicals, superoxides, and peroxides in inflammatory conditions have been reported in various inflammatory diseases.[5] These molecules exert a number of toxic effects that have been demonstrated in many different biological systems.[6] The ROS are likely to play a vital role in the pathogenesis of asthma because they have been shown to be associated with many pathophysiological changes that are relevant in asthma, such as increased lipid peroxidation, increased airway reactivity and secretions, increased production of chemoattractants, and increased vascular permeability.[7]

Multiple defence systems, collectively called antioxidants, are present in the human body to prevent the damage caused by the ROS.[8] These defence systems include enzymatic antioxidants such as superoxide dismutase (SOD), which degrades superoxide anion (O^{2-}), and glutathione peroxidase (GSH-Px), which detoxifies hydrogen peroxide (H_2O_2)[9] and non-enzymatic antioxidants such as the GSH (glutathione) redox system[1,10] However, when the production of harmful ROS exceeds the capacity of the body's antioxidant defences to detoxify them, a condition known as oxidative stress occurs. Oxidative stress leads to changes such as modification of receptor activity and signalling as well as the release of endogenous mediators of inflammation.

Children and adults with asthma may avoid exercise because of their respiratory symptoms and they may have reduced exercise tolerance due to the increased sensation of dyspnoea.[11,12] The results of previous studies on the influence of exercise on spirometry are contradictory, some reporting improvement.[13] The basic pathogenetic mechanisms underlying these changes in asthmatic patients taking exercise are unclear.

The current study was designed to investigate the possible beneficial effect of physical exercise on antioxidant status in asthmatic children which may lead to ameliorated lung function.

Materials and methods

Subjects

Thirty children aged 8-13 years diagnosed with asthma (Group 1) in the Pediatric Allergy and Pulmonology Department of the Medical Faculty of Celal Bayar University were enrolled in the study. During the selection process, potential candidates for inclusion in the asthmatic group of the study were asked about their general sporting habits. Those children who stated that they regularly participated in exercise and/or were part of a sports team were excluded from the study. The diagnosis of asthma was based on history of recurrent cough and wheezing with prolonged expiration time which demonstrated clinical reversibility with a short acting beta-2 agonist bronchodilator therapy. Immunocompromised patients, patients with a history of chronic inflammation/rheumatological disorder, and patients with autoimmune diseases were excluded. Asthma patients had not been receiving any medication and had not had any symptoms of lower or upper respiratory tract infection or asthma exacerbation during the period four weeks prior to the study.

The control group (Group 2) consisted of 13 age-matched healthy children. They were chosen from those referred to the paediatric outpatient clinic in the University Hospital, where all children periodically undergo check-ups for their growth and development. Control patients were evaluated with regard to chronic and/or severe infections, rheumatological and autoimmune disorders, familial and personal history of atopy and also by laboratory tests. Children were included in the control group if they had no personal and familial history of atopy and no signs of atopic disorder.

All patients were examined physically and their forced vital capacity (FVC) and forced expiratory volume 1 (FEV1) was measured. The study was approved by the Institutional Ethical Review Board and informed consent was taken from the parents or guardians of all children taking part in the study.

Study design

All thirty asthmatic patients started to receive the standard pharmacological treatment (fluticazone 250 μg/day). The patient group was randomly divided into two equal groups. One group (Group 1a) received only the pharmacological treatment for eight weeks. The other group (Group 1b) received the pharmacological treatment and was assigned to an exercise programme carried out by the Physiotherapy and Rehabilitation Department. Group 1b children exercised twice a week for an hour on a bicycle for eight weeks. The rate of exercise was determined according to the resting heart rate of the children. Their submaximal heart rate was determined as 50% higher than their resting heart rate. Their target heart rate during exercise was determined as 80% of the submaximal heart rate. The pedalling rate required to reach the target heart rate was determined using a pulse oximeter during exercise. During the eight week exercise programme, 15 minutes of warm-up exercise was followed by 45 minutes of cycling at the target heart rate.

Blood sampling

For baseline values, venous blood samples were drawn from Group 1 and 2 at the beginning of the eight week period. At the end of eight weeks of pharmacological treatment or pharmacological treatment in addition with an exercise programme, post treatment samples were obtained from the subjects in Groups 1a and 1b.

After an overnight fast, blood samples were collected into evacuated plain and K_3EDTA containing tubes. Samples were centrifuged at 4,000 rpm for 10 minutes within 2 hours