

Randomised controlled trial

Aerobic exercise training reduces bronchial hyper-responsiveness and serum pro-inflammatory cytokines in patients with asthma

10.1136/ebmed-2015-110260

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Commentary on: França-Pinto A, Mendes FAR, de Carvalho-Pinto RM, *et al.* Aerobic training decreases bronchial hyper-responsiveness and systemic inflammation in patients with moderate or severe asthma: a randomised controlled trial. *Thorax* 2015;70:732–9.

Context

Exercise is a well-known trigger for asthma symptoms. In patients with asthma, strenuous physical activity increases the risk of an asthma attack, with a 'U'-shaped curve showing that moderate exercise training carries a lower risk of asthma compared to high-intensity exercise training. Lack of physical activity appears to be independently associated with increased bronchial hyper-responsiveness (BHR).¹ These observations are confirmed by a growing number of murine studies, but reviews examining the epidemiological evidence for such associations in humans show that the overall evidence on exercise and asthma is, at best, very low.^{2–3} França-Pinto *et al* carried out a randomised controlled trial (RCT) investigating the effect of exercise on asthma-related outcomes in patients with asthma.

Methods

Four hundred and sixty-four adults were assessed for eligibility and 58 (clinically stable patients with asthma) were randomised to either a control (CG) or intervention/training group (TG) for 12 weeks. The intervention consisted of aerobic training (indoor treadmill for 35 min), yoga (breathing exercises) and an educational programme. The CG consisted of an educational programme and breathing exercises only. The study's primary outcome was BHR, defined with a histamine provocation test performed according to the American Thoracic Society guidelines.⁴ The study was powered at 80% to detect a clinical improvement through an increment in PC₂₀ of one doubling dose (dd). Other outcomes included markers of inflammation (cytokines, exhaled nitric oxide (FeNO)), total IgE, atopy, asthma symptoms, asthma quality of life (Asthma Quality of Life Questionnaire (AQLQ)), induced sputum and a cardiopulmonary exercise test.

Findings

At 12-week follow-up, 22 participants in the TG and 21 in the CG had complete data. The TG improved in BHR compared to the CG (PC₂₀ of 1 dd; 95% CI 0.3 to 1.7 dd). The TG group also had a statistically significant reduction in serum levels of some cytokines (interleukin (IL) 6;

p=0.042) and MCP-1 (Monocyte Chemo-attractant Protein); p=0.045) and fewer asthma exacerbations than the TG (p<0.05). No differences were observed between groups in other markers (IL-5, IL-8 and IL-10, IgE, asthma symptoms, FeNO and induced sputum). IL-4, tumour necrosis factor (TNF) α and RANTES were outside the limits of assay and were not analysed. Overall AQLQ improved in TG (p<0.05).

Commentary

The authors show that an adequately planned aerobic training programme in patients with asthma can improve disease. The main contribution of this RCT lies in the well-designed exercise programme, the strict follow-up, the inclusion of patients under proper medical treatment and the use of a gold-standard to measure changes in BHR. The study was further strengthened by the low attrition bias at follow-up. It is therefore plausible that the changes observed in BHR and asthma exacerbations are due to the introduction of aerobic exercise, while the possibility of a synergic effect of aerobic and yoga exercises cannot be completely excluded.

Experimental evidence shows that low-to-moderate intensity aerobic exercise reduces inflammation and remodelling.⁵ The authors correctly state that serum cytokine levels may not necessarily reflect airway inflammation; however, exercise training effects are more detectable in the systemic immune response.⁶ This paper partially supports these findings, showing a reduction in IL-6 and MCP-1. No changes in IL-5, IL-8 and IL-10 are in partial disagreement with animal studies. Finally, because of the lack of measurement of IL-4, TNF α and RANTES, it was not possible to reinforce recent data showing a reduction of IL-4 after regular exercise.⁷

Implications for practice

This study shows that a programme of regular aerobic exercise can lead to a reduction in BHR and asthma exacerbations, and to an improved quality of life, in patients with asthma. These results suggest that exercise should be included as a part of a comprehensive care plan for the patient with asthma.

Competing interests None declared.

Ethics approval Ethics Review Board of the Clinical Hospital (protocol 0121/10).

Provenance and peer review Commissioned; internally peer reviewed.

References

- Brasholt M, Baty F, Bisgaard H. Physical activity in young children is reduced with increasing bronchial responsiveness. *J Allergy Clin Immunol* 2010;125:1007–12.
- Eichenberger PA, Diener SN, Kofmehl R, *et al.* Effects of exercise training on airway hyperreactivity in asthma: a systematic review and meta-analysis. *Sports Med* 2013;43:1157–70.
- Pakhale S, Luks V, Burkett A, *et al.* Effect of physical training on airway inflammation in bronchial asthma: a systematic review. *BMC Pulm Med* 2013;13:38.
- Reddel HK, Taylor DR, Bateman ED, *et al.* An official American Thoracic Society/European Respiratory Society statement: asthma control and exacerbations: standardizing endpoints for clinical asthma trials and clinical practice. *Am J Respir Crit Care Med* 2009;180:59–99.
- Del Giacco SR, Firinu D, Bjermer L, *et al.* Exercise and asthma: an overview. *Eur Clin Res J* 2015;2:27984.
- Gleeson M, Bishop NC, Stensel DJ, *et al.* The anti-inflammatory effects of exercise: mechanisms and implications for the prevention and treatment of disease. *Nat Rev Immunol* 2011;11:607–15.
- Del Giacco SR, Scorcu M, Argiolas F, *et al.* Exercise training, lymphocyte subsets and their cytokines production: experience of an Italian professional football team and their impact on allergy. *Biomed Res Int* 2014;2014:429248.