

Original Article

Effects of Exercise and Diet in Nonobese Asthma Patients—A Randomized Controlled Trial

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What is already known about this topic? Behavioral interventions including diet and exercise have been shown to improve clinical outcomes in asthma in obese patients. However, the effects of combined exercise and diet interventions in nonobese patients with asthma remain to be investigated.

What does this article add to our knowledge? This randomized controlled trial provides the first evidence that high-intensity interval training combined with healthy diet improves asthma control and asthma-related quality of life in non-obese adults with asthma.

How does this study impact current management guidelines? The results suggest that lifestyle interventions focusing on exercise training combined and healthy diet could be considered as nonpharmacological add-on treatments in non-obese patients.

BACKGROUND: Behavioral interventions focusing on exercise and healthy diet improve asthma control in *obese* patients with asthma, but whether these interventions can lead to improvements in *nonobese* patients remains unclear. **OBJECTIVES:** In a randomized, controlled parallel-group design, we studied the effects of an 8-week intervention of either exercise (high-intensity interval training), diet (high protein/low glycemic index), or a combination of the 2, on asthma control and clinical outcomes in nonobese patients with asthma.

METHODS: Nonobese adult patients with asthma ($n = 149$) were randomized to 1 of 4 groups: an exercise group, a diet group, an exercise + diet group, or a control group. Outcomes included Asthma Control Questionnaire (ACQ) score, asthma-related quality-of-life (Asthma-Related Quality-of-Life Questionnaire [AQLQ]) score, inflammatory cell counts in induced sputum, FEV₁, fractional exhaled nitric oxide, and airway hyperresponsiveness (AHR).

RESULTS: A total of 125 patients completed the study and were included in the data analysis. Patients in the exercise + diet group improved the ACQ score from 1.9 ± 0.7 to 1.0 ± 0.7 and the AQLQ score from 5.2 ± 0.8 to 6.2 ± 0.7 , which was statistically significant when compared with changes in the control group ($P < .05$ and $< .01$, respectively). The exercise group and the diet group did not improve either the ACQ score or the AQLQ score significantly compared with the control group and there were no significant changes in sputum cell counts, FEV₁, fractional exhaled nitric oxide, or AHR within any groups following the intervention period.

CONCLUSIONS: The combination of exercise and diet improves asthma control in nonobese patients, but does not affect AHR or airway inflammation. © 2017 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2017;■:■-■)

Key words: Obstructive airway disease; Clinical trial; Diet therapy; High-intensity interval training

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Conflicts of interest: A. Astrup is coauthor of the diet/lifestyle book *Verdens Bedste Kur* (Politiken, Copenhagen 2012), subsequently published in Dutch as *Het beste dieet ter wereld* (Kosmos Uitgevers, Utrecht/Antwerpen 2013), in Spanish as *Plan DIOGENES para el control del peso. La dieta personalizada inteligente* (Editorial Evergráficas, León 2013), and in English as *World's Best Diet* (Penguin, Australia 2014). The rest of the authors declare that they have no relevant conflicts of interest.

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Abbreviations used

ACQ- Asthma Control Questionnaire
 AHR- airway hyperresponsiveness
 AQLQ- Asthma-Related Quality-of-Life Questionnaire
 FENO- fractional exhaled nitric oxide
 GI- glycemic index
 Hs-CRP- high-sensitivity C-reactive protein
 ICS- inhaled corticosteroid
 RCT- randomized controlled trial
 VO₂max- maximal oxygen uptake

unhealthy diet can improve asthma in nonobese patients with asthma.

Exercise training has been found to improve asthma control,³ airway hyperresponsiveness (AHR),⁴ and airway inflammation.⁵ However, most studies have been based on exercise interventions that consisted of low- and moderate-intensity training. *High-intensity* interval training is today widely practiced because of its superior efficacy to improve exercise capacity when compared with low- to moderate-intensity training,^{6,7} but the effects of this type of training have not yet been examined in untrained patients with asthma.

Within the research field of nutrition, there is an increasing interest in the efficacy of diets with a *high protein content* and a *low glycemic index* (GI)—an index calculated by ranking foods on the basis of their effect on blood sugar levels.⁸ A Pan-European study found that an *ad libitum* diet with an overall low GI combined with a high protein content was effective in maintaining weight loss in obese patients.⁹ In addition, following the dietary principles of low GI had a favorable effect on levels of low-grade systemic inflammation, which has been suggested to act as a potential link between airway inflammation and dietary pattern in asthma.¹⁰

The aim of the present study was to test whether an 8-week behavioral intervention consisting of either (1) exercise (high-intensity interval training), (2) diet (ad libitum diet with a high protein content [25%-28% of energy intake] and a low GI), or (3) a combination of the 2 interventions would improve clinical outcomes including asthma control and quality of life, airway inflammation, AHR, blood eosinophil counts, and markers of low-grade systemic inflammation compared with usual care in *nonobese* patients with asthma.

Some of the results of this study have been previously reported in the form of an abstract.¹¹

METHODS

The study was approved by the Ethic Committee of Copenhagen, Denmark (H-4-2013-116) and registered at ClinicalTrials.gov (ID: NCT02355964).

Patients

We included patients aged 18 to 65 years with a body mass index of more than 20 and less than 30 kg/m,² an Asthma Control Questionnaire (ACQ) score¹² of 1.0 or more, and at least 1 positive diagnostic test demonstrating variable airflow obstruction: a mannitol test, methacholine test, or reversibility test. Patients should *either* have been on a stable prophylactic treatment regime with inhaled corticosteroids (ICSs), ICS + long-acting beta₂-agonist, and/or leukotriene antagonist *or* have had no prophylactic treatment at least 3 months before enrollment. Patients' self-reported adherence

to their prophylactic ICS treatment (in case patients were using ICS) was assessed preintervention and postintervention by asking the following questions: (1) "How many puffs a day of your inhaler have your doctor prescribed?" and (2) "During an average week over the last 2 months, how many puffs have you taken during one week?" as described and validated by Foster et al.¹³ Adherence scores ranged from 0% to more than 100%, the latter in case the patients used more puffs than prescribed by their doctor.

STUDY DESIGN

The study was a single-center randomized controlled parallel-group study with 4 randomization groups: (1) exercise group, (2) diet group, (3) exercise + diet group, and (4) control group (usual care).

The randomization was done using opaque sealed envelopes with a computer-generated block randomization method with a block size of 12, to ensure equal distribution of patients in treatment groups throughout the shifting seasons. The investigators who carried out postintervention spirometry, mannitol tests, and handing out of questionnaires and all laboratory technicians were blinded to the randomization. Because the interventions were nonpharmacological add-on treatments and the study aimed to be a real-life set-up, patients were informed to seek medical assistance from someone other than the study staff member, that is, their family doctor or regular pulmonary specialist, if they felt in need for adjustments in their asthma medicine during the course of the study. In case changes were made in patients' asthma medicine, it was recorded at follow-up.

Intervention groups

Exercise group. The training intervention consisted of 8 weeks of high-intensity interval training using the "10-20-30" concept⁶ on indoor spinning bikes 3 times a week, supervised by a trained spinning instructor with a bachelor degree in Sports Science. Each session included 10-minute warm-up at a low intensity followed by either two, three, or four 5-minute intervals (during weeks 1-2, 3-5, and 6-8, respectively). Each 5-minute interval consisted of 5 consecutive 1-minute intervals divided into 30, 20, and 10 seconds at an intensity corresponding to less than 30%, less than 60%, and more than 90% of maximal intensity. A total of 8 spinning instructors took turns to conduct the training sessions, and all were given careful instructions to maintain strict consistency with the 10-20-30 concept as described above. Patients were instructed to take 2 puffs of their regular short-acting beta-2 agonist 10 to 15 minutes before the training and during the training sessions if necessary to prevent bronchoconstriction. All training sessions were carried out in a hospital setting and the instructors were given careful instructions on how to call for immediate emergency assistance and initiate treatment with oxygen if a patient experienced dyspnea that did not pass after immediate rest and additional inhalation of short-acting beta-2 agonist.

Diet group. The 8-week diet intervention included 5 group counseling sessions (2-6 patients/group) and 1 individual counseling session with a trained study dietician. Patients bought and prepared their own food on the basis of principles of an overall high protein content (25%-28% of energy) and a low GI (≤ 55).⁹ Furthermore, in compliance with the energy distribution, the diet was designed to be anti-inflammatory and therefore contained higher amounts of vegetables, fruits, nuts, lean meat, fish, and seafood in accordance with the anti-inflammatory index of foods developed by Shivappa

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