Diet-Induced Weight Loss in Obese Children With Asthma: A Randomized Controlled Trial

PURPOSE OF THE STUDY. The goal of this study was to assess if dietary intervention (DI) can achieve weight loss in obese asthmatic children and if diet-induced weight loss leads to changes in asthma outcomes.

STUDY POPULATION. The study evaluated 32 obese (BMI z score ≥1.64 SD score) children aged 8 to 17 years, with a physician diagnosis of asthma. Exclusion criteria included unexplained weight change during the past 3 months, inflammatory or endocrine disorders, and respiratory disorders other than asthma.

METHODS. In this 10-week, randomized controlled trial, 32 obese asthmatic children were randomized to a wait-list control (WLC) group (n = 16) or a DI group (n = 16). DI participants had a targeted 500-kcal/d reduction from individually calculated age- and gender-appropriate energy requirements and either attended dietitian counseling sessions or were contacted by telephone weekly. Asthma status, quality of life, tobacco exposure, dynamic and static lung function, and plethysmography were assessed at baseline and postintervention.

RESULTS. BMI z score was significantly reduced in the DI group versus the WLC group. Expiratory reserve volume (ERV) increased significantly within the DI group compared with baseline; however, the ERV difference between the 2 groups was not statistically significant. The Asthma Control Questionnaire score improved significantly within the DI group compared with the WLC group. There was no change in the number or proportion of eosinophils or neutrophils within or between groups. There was a nonsignificant trend toward reduction in percentage of neutrophils in the DI group. C-reactive protein (CRP) increased significantly in the WLC group compared with the DI group. No change was observed in IL-6, leptin, or adiponectin levels within or between groups. Change in BMI z score correlated with change in CRP and change in exhaled nitric oxide. Change in the Asthma Control Questionnaire was associated with change in CRP.

CONCLUSIONS. DI can induce acute weight loss in obese asthmatic children, with improvements in static lung function, asthma control, and self-reported quality of life. DI was effective in reducing BMI z score by a statistically significant 0.2 BMI SD score, which is comparable to previous studies. Systemic and airway inflammation did not change after weight loss.

REVIEWER COMMENTS. This is a novel pilot study. Previous studies of weight-loss interventions in asthmatic patients have primarily been in adults, and the majority have investigated surgically induced weight loss. Limitations to the present study include small sample size, uneven randomization, and self-report of several measures. Despite these acknowledged limitations, the findings suggest that DI can improve multiple asthma outcomes. Given the high prevalence of obesity in the asthmatic pediatric population, additional and larger trials are warranted. Areas for future study include additional outcome measures such as use of rescue medications, asthma-related hospitalizations, and potential adverse effects.

Normocaloric Diet Improves Asthma-Related Quality of Life in Obese Pubertal Adolescents

PURPOSE OF THE STUDY. The goal of this study was to determine if a supervised normocaloric diet would help improve asthma-related quality of life (AR-QoL) in obese prepubertal adolescents with asthma.

STUDY POPULATION. Fifty-one children between 12 and 16 years of age diagnosed with stable allergy-induced asthma and obesity (BMI >95th percentile of the Centers for Disease Control and Prevention BMI-for-age growth charts) were recruited from an allergy clinic in Guadalajara, Mexico.

METHODS. Children were randomized to undergo a 28-week dietary program consisting of a monitored normocaloric diet (n = 26) and matched to a control group who had no dietary restrictions (n = 25). AR-QoL questionnaires and pulmonary function test results were recorded before and after the intervention period.

RESULTS. Energy and macronutrient intake were significantly different in the test group compared with control subjects (2231 ± 231 vs 3243 ± 278 kcal/d; P = .001) with increased consumption of carbohydrates, fat, and saturated fat among the control subjects’ diet. Although the mean BMI z score significantly declined in the test group, the mean BMI z score remained unchanged in the control group. There was significant improvement in AR-QoL scores in the dietary intervention group compared with control subjects (P < .001). They also reported fewer episodes of asthma rescue inhaler use (17 vs 39; P = .02), as well as fewer nighttime awakenings (11 vs 2; P < .001). There seemed to be more improvement in forced expiratory volume in 1 second values among the study group, but the results were not statistically significant.

CONCLUSIONS. The normocaloric dietary intervention was associated with improved AR-QoL and some asthma control. Dietary programs may serve as a complementary approach to asthma management.
nonpharmacologic therapeutic strategy in obese adolescents who have asthma.

**REVIEWER COMMENTS.** Asthma and obesity are 2 chronic conditions that are becoming more prevalent in children today. Moreover, there is often a direct relationship between the 2 factors; increased BMI is associated with dose-dependent increases in asthma incidence and severity. The authors were able to limit their study subjects to obese prepubertal children, providing a clearer picture of how emphasizing a normocaloric diet not only can contribute to a decreased BMI but also to improved AR-QoL. Although many allergy practices have incorporated asthma educational strategies at diagnosis and follow-up, perhaps it is time to also include standardized nutritional recommendations. Encouraging our youngest patients with asthma to maintain a normal BMI may not only help reduce exacerbations and potential for steroid adverse effects but also contribute to optimal lung development during this critical growth period.

**METHODS.** DNA was extracted from saliva- and blood-derived samples. CpG sites were selected from the ADRB2 CpG island promoter region. DNA methylation assays were performed by staff blinded to the study. Methylation profiles for each locus represent a combination of saliva and blood sources. Caregivers completed questionnaires about asthma symptoms and rescue medication use within the past 4 weeks, as well as unscheduled health care visits and school absences related to asthma in the past 12 months. Subjects underwent prebronchodilator and postbronchodilator spirometry.

**RESULTS.** After adjusting for age, race, gender, preterm birth, family history of asthma, diagnosis of eczema, and sample source, percent methylation of the ADRB2 promoter showed a strong inverse association with dyspnea (odds ratio: 0.2; \( P = .002 \)). There was no evidence of allele-specific differences in methylation.

**CONCLUSIONS.** This study is the first showing increased methylation at the ADRB2 gene being inversely associated with dyspnea, contributing to an improved asthma phenotype.

**REVIEWER COMMENTS.** Typically, DNA CpG hypermethylation leads to decreased expression of the gene product. Data are inconsistent regarding the relationship between B2AR density in the airways and severity of asthma. This study showed that methylation can play a role in asthma phenotypes. More polymorphisms will need to be studied before concluding that methylation is independent of genotype.

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**β-2 Adrenergic Receptor Gene Methylation Is Associated With Decreased Asthma Severity in Inner-City Schoolchildren: Asthma and Rhinitis**


**PURPOSE OF THE STUDY.** The \( \beta_2 \)-adrenergic receptor (B2AR) is the major target of \( \beta \)-agonist bronchodilators. The gene encoding the B2AR (ADRB2) has been mapped to chromosome 5q31-33, a region identified as a susceptibility locus for asthma or atopy. Epigenetic changes are heritable changes in gene expression, not encoded by DNA sequence changes (eg, methylation of cytosine-phosphate guanine [CpG] islands within regulatory regions of DNA). A variably methylated CpG island overlaps ADRB2. The purpose of this study was to determine the effects of methylation on asthma symptoms, morbidity, and lung function.

**STUDY POPULATION.** This study was nested within the SICAS (School Inner-City Asthma Study) and involved children who had a physician’s diagnosis of asthma within the past 12 months.

**METHODS.** DNA was extracted from saliva- and blood-derived samples. CpG sites were selected from the ADRB2 CpG island promoter region. DNA methylation assays were performed by staff blinded to the study. Methylation profiles for each locus represent a combination of saliva and blood sources. Caregivers completed questionnaires about asthma symptoms and rescue medication use within the past 4 weeks, as well as unscheduled health care visits and school absences related to asthma in the past 12 months. Subjects underwent prebronchodilator and postbronchodilator spirometry.

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**Decreased Levels of Lipoxin A4 and Annexin A1 in Wheezy Infants**


**PURPOSE OF THE STUDY.** The authors measured levels of lipoxin A4 (LXA4) and annexin A1 (ANXA1) in children with a history of infantile wheezing. Lipoxins and annexins are classes of mediators involved in the resolution of inflammation.

**STUDY POPULATION.** Fifty-nine children with a history of wheezing with no underlying disease and 28 healthy control subjects were recruited in this Turkish study. Ages ranged from 6 to 36 months, and all children had a history of ≥3 wheezing attacks with no previous corticosteroid treatment during the preceding month.

**METHODS.** Blood samples were taken to measure LXA4 and ANXA1 levels by using enzyme-linked immunosorbent assay. Total IgE levels and eosinophil counts were also measured.

**RESULTS.** No significant differences in total IgE levels were detected between children with wheezing and control children. LXA4 (66 ± 35 vs 120 ± 11 pg/mL; \( P < .05 \)) and ANXA1 (14.45 ± 3.26 vs 16.40 ± 1.94 ng/mL; \( P < .05 \)) levels were significantly lower in the wheezing group than in the control group. In the wheezing group, a significant correlation was found between the serum total IgE level and the percentage and absolute number of eosinophils (\( r = -0.223, P = .02 \)). No correlation was
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