Effect of Sex on Lung Function Following Inhaled Corticosteroid Therapy in Obese Children with Asthma: Postprint

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Abstract

Objective: To investigate the effect of gender on lung function in obese asthmatic children before and after inhaled corticosteroid (ICS) therapy.

Methods: A total of 190 asthmatic children were stratified by gender into a male group (102 cases, normal-weight/obese 57/45) and a female group (88 cases, normal-weight/obese 46/42). Lung function was measured in all children before treatment and after one year of standardized ICS therapy, including forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), forced expiratory flow at 50% of vital capacity (MEF50), and forced expiratory flow at 25% of vital capacity (MEF25).

Results: Before treatment, there were no statistically significant differences in lung function between males and females in any group (all $P>0.05$). After one year of ICS therapy, FVC% and FEV1% in both normal-weight male and female groups were significantly increased compared with before treatment ($P<0.05$). In the obese male group, FVC% and FEV1% were significantly increased compared with before treatment ($P<0.05$), while in the obese female group, only FVC% was increased compared with before treatment ($P<0.05$).

Conclusion: ICS therapy can improve large airway ventilation function in asthma. The effect of gender on the improvement of large airway ventilation function in asthma with ICS therapy depends on body mass index, manifested as a minimal influence of gender on ICS therapy in normal-weight asthmatic children, while the degree of improvement in lung function in obese female asthmatic children was significantly lower than that in obese male asthmatic children.

Full Text

Abstract

Objective: To investigate the effect of gender on lung function in obese asthmatic children before and after inhaled corticosteroid (ICS) therapy. **Methods:** A total of 190 asthmatic children were divided by gender into a male group (102 cases, with 57 normal-weight and 45 obese) and a female group (88 cases, with 46 normal-weight and 42 obese). Lung function parameters including forced expiratory volume in one second (FEV1), forced vital capacity (FVC), maximal expiratory flow at 50% of FVC (MEF50), and maximal expiratory flow at 25% of FVC (MEF25) were measured before treatment and after one year of standardized ICS therapy. **Results:** No statistically significant gender differences in lung function were observed in any group at baseline (all $P>0.05$). After one year of ICS treatment, both normal-weight males and females showed significant increases in FVC% and FEV1% compared to baseline ($P<0.05$). Obese males demonstrated significant improvements in FVC% and FEV1% ($P<0.05$), whereas obese females showed improvement only in FVC% ($P<0.05$). **Conclusion:** ICS therapy improves large airway ventilation function in asthmatic children, and the influence of gender on this improvement is dependent on body mass index. Gender appears to have minimal impact on ICS treatment response in normal-weight children, but female obese asthmatic children exhibit significantly less improvement in lung function compared to their male obese counterparts.

Key words: asthma; gender; pulmonary function; children; obesity

Introduction

Bronchial asthma is a chronic inflammatory airway disease involving multiple cells and cellular components, including eosinophils, mast cells, T lymphocytes, neutrophils, and airway epithelial cells. In recent years, the relationship between obesity and asthma has garnered increasing attention, with global rates of obesity and asthma rising in parallel [1-2]. According to World Health Organization data, obesity is increasing dramatically worldwide, with the combined overweight/obesity rate reaching 29.9% in China [3]. The incidence of asthma is also significantly higher in obese individuals [4]. Obesity adversely affects asthma by increasing disease prevalence, severity, and refractoriness while reducing treatment responsiveness [5-6], leading to its classification as a distinct clinical phenotype [7].

Inhaled corticosteroids (ICS) represent the most effective anti-inflammatory agents and constitute first-line therapy for asthma control. However, treatment response to ICS diminishes with increasing body mass index (BMI) [8], contributing to the growing burden of refractory asthma. Research from the European Asthma Consortium indicates that adult refractory asthma predominantly affects obese women, with a male-to-female ratio of 1:4 [9-10], though findings in

pediatric asthma remain inconsistent. Our previous studies demonstrated that ICS significantly improves large airway ventilation function in normal-weight asthmatic children, while obesity attenuates this beneficial effect on lung function [11]. The current study investigates whether this inhibitory effect of obesity exhibits gender differences, specifically examining how gender influences ICS treatment outcomes in obese asthmatic children.

Methods

Study Population and Grouping

We enrolled 190 children with newly diagnosed asthma from our hospital' s asthma clinic between March 2014 and September 2015, with follow-up exceeding one year. All participants met the following inclusion criteria: (1) aged 5-12 years; (2) first-time asthma diagnosis according to the Guidelines for the Diagnosis and Prevention of Bronchial Asthma in Children (2016 edition) [12]; (3) stable mild asthma with forced expiratory volume in one second (FEV1) 80% of predicted value. Exclusion criteria included: (1) acute asthma exacerbation; (2) concurrent active or chronic pulmonary diseases, severe immune disorders, malignancies, coronary heart disease, or hypertension; and (3) irregular ICS use for less than one year following diagnosis.

Participants were stratified by gender into a male group (n=102) and female group (n=88). Each gender group was further divided by weight status: normal-weight (BMI between the 15th and 95th percentile for age and gender) and obese (BMI exceeding the 95th percentile for age and gender). No statistically significant differences were observed between male and female groups in age, BMI, or the normal-weight/obese distribution ratio ($P>0.05$, Table 1).

Pulmonary Function Testing

Baseline pulmonary function was measured using a MasterScope spirometer (Jaeger, Germany) by a dedicated pulmonary function technician. Lung function parameters were assessed before treatment and after one year of ICS therapy. Primary outcome measures included forced expiratory volume in one second (FEV1), forced vital capacity (FVC), maximal expiratory flow at 25% of FVC (MEF25), and maximal expiratory flow at 50% of FVC (MEF50), all expressed as percentages of predicted values. Large airway function was represented by FEV1 and FVC, while small airway function was represented by MEF50 and MEF25.

Statistical Analysis

Data were analyzed using SPSS 17.0 software. Continuous variables were expressed as mean ± standard deviation. Comparisons between two groups were performed using t-tests, while comparisons among multiple groups employed one-way ANOVA with LSD-t tests for post-hoc pairwise comparisons. Cate-

gorical data were presented as frequencies and compared using chi-square tests. Statistical significance was defined as $P<0.05$.

Results

Gender Effects on Baseline Lung Function in Newly Diagnosed Asthmatic Children

At initial diagnosis, no statistically significant gender differences were observed in large airway function (FVC%, FEV1%) or small airway function (MEF50%, MEF25%) between normal-weight and obese groups (all $P>0.05$, Table 2).

Body Weight Effects on Lung Function Changes Following ICS Therapy

After one year of ICS treatment, normal-weight children (both males and females) demonstrated significant improvements in FVC%, FEV1%, and MEF50% compared to baseline (all $P<0.05$). In contrast, obese children showed significant improvements only in FVC% and FEV1% (both $P<0.05$, Table 3).

Gender Effects on Lung Function Changes Following ICS Therapy

Following one year of ICS therapy, normal-weight males exhibited significant improvements in FVC%, FEV1%, and MEF50% (all $P<0.05$), whereas normal-weight females showed significant improvements only in FVC% and FEV1% (both $P<0.05$). Among obese children, males demonstrated significant increases in both FVC% and FEV1% (both $P<0.05$), while females showed improvement solely in FVC% ($P<0.05$, Figure 1 [Figure 1: see original paper]).

Discussion

The impact of obesity on asthma has received considerable attention, with numerous studies investigating gender-specific effects, though findings remain inconsistent. The association between BMI and asthma appears more pronounced in adult women than men [9,14], but pediatric studies yield conflicting results. Lu et al. [15] found increased asthma incidence among overweight and obese girls but not boys in a cohort of 4,828 children, whereas Gilliland et al. [16] reported higher asthma rates in obese boys. Krystofová et al. [17] demonstrated BMI-asthma correlations in both sexes, while a Japanese nationwide cross-sectional study found no gender differences in the association between obesity and current asthma from school age through adolescence [18]. These discrepancies may arise because BMI serves only as a screening tool for obesity, failing to account for body composition, fat distribution, and ethnic variations in adiposity at equivalent BMI values.

Our study of newly diagnosed asthmatic children revealed no significant baseline lung function differences between obese and normal-weight groups [13], with gen-

der playing an even more limited role. We hypothesize that obesity duration may critically influence pulmonary function changes [19], a notion supported by our previous animal studies showing that adult-onset obesity induced airway hyperresponsiveness whereas early-life weight changes did not significantly affect lung function [20]. Through one-year follow-up, we observed that ICS therapy improved large airway function (FVC, FEV1) in normal-weight asthmatic children, while obese females showed improvement only in FVC. This pattern aligns with European Asthma Consortium findings in adults and may relate to sex hormone physiology. Female hormones play important roles in asthma pathogenesis [21], and their secretion is affected by obesity [22]. Progesterone upregulates airway 2-receptor function, promoting bronchial smooth muscle relaxation and reducing airway hyperresponsiveness, but its levels are decreased in obese women [23]. Conversely, estrogen modulates airway inflammatory cells such as mast cells and eosinophils, and its levels are elevated in obese females [24]. Consequently, obese female asthmatic children exhibit reduced progesterone (which inhibits airway hyperresponsiveness) and increased estrogen (which promotes inflammation), resulting in attenuated lung function improvement compared to obese males. Additionally, serum adiponectin levels correlate with long-term asthma risk in female patients, suggesting that increasing adiponectin may reduce this risk [25].

Furthermore, gender-specific fat distribution patterns may influence asthma-related lung function [26], as males predominantly accumulate muscle mass while females accumulate adipose tissue, potentially explaining the pronounced gender differences in obese asthma. Comprehensive analysis reveals that one year of ICS therapy significantly improved both large (FVC%, FEV1%) and small (MEF50%) airway function in normal-weight asthmatic children, whereas obese children showed improvements only in large airway parameters (FVC%, FEV1%). This partially contradicts our previous findings [11], possibly due to different gender distributions across study groups.

In conclusion, gender influences the improvement in lung function following ICS therapy in asthmatic children, with obese females demonstrating significantly less improvement than both normal-weight children and obese males. These differences likely relate to sex hormone secretion and adipose tissue distribution patterns. Clinically, this raises the question of whether obese female asthmatic children require higher ICS doses or longer treatment duration to achieve comparable improvements in lung ventilation, warranting further investigation. Limitations of this study include the relatively small sample size and short follow-up duration, which should be addressed in future research with larger cohorts and more detailed efficacy assessments.

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Note: Figure translations are in progress. See original paper for figures.