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ORIGINAL ARTICLE

Visceral adiposity is associated with cytokines and decrease in lung function in women with persistent asthma

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Abstract Abdominal obesity is associated with a risk of cardiovascular diseases, metabolic syndrome and decreased lung function. However, it is not known whether asthma control is influenced by the accumulation of adipose tissue in the various abdominal compartments.
Objective: To determine associations among abdominal adiposity distribution, asthma control, lung function and cytokines in women.
Methods and design: In this cross-sectional study of asthmatic women, data on demographic variables, comorbid conditions, disease history, anthropometric and spirometric measurements were collected. Subcutaneous (SAT) and visceral (VAT) adipose tissues were measured by ultrasound, and the steatosis level was obtained. Asthma control was assessed according to Global Initiative for Asthma (GINA) criteria. Atopy was defined on the basis of allergen-specific Immunoglobulin E and/or skin prick testing. Cytokine levels were determined using enzyme-linked immunosorbant assays (ELISAs).
Results: Eighty-three asthmatic women were included, 37% of whom had uncontrolled asthma. After controlling for variables, a negative association between asthma control and VAT and the VAT/SAT ratio was observed. VAT was negatively associated with respiratory parameters after controlling for explanatory variables. In an adjusted model, body mass index (BMI) and SAT were inversely associated with the adiponectin serum level and VAT was associated with the

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interleukin 6 level. In conclusion, visceral obesity was negatively associated with asthma control and lung function; and positively associated with increased levels of interleukin 6 in women. We hypothesize that women should be studied as a separate group, and we suggest further studies with a control group to know if the uncontrolled asthmatic group is directly affected by visceral adipose inflammatory markers.

Introduction

It was recently reported that abdominal obesity is increasing faster than overall obesity.[1] Abdominal obesity is associated with cardiovascular risk, metabolic syndrome[2,3] and decreased lung function.[4] However to date, there is a lack of correlation between obesity related inflammatory markers and asthma.[5] The precise mechanism and the significance of the association between adipokines, asthma and visceral obesity, considered to be the most inflammatory are unknown. Most studies investigating the association between asthma and obesity have considered only body mass index.[6,7] However, the use of this parameter has limitations because it does not distinguish between fat mass and muscle or identify the distribution of body fat.[8] We hypothesized that the accumulation of abdominal fat in the visceral compartment, which is particularly associated with increased inflammatory markers,[9,10] could adversely affect lung function and worsen asthma control in women. It is possible that the greater risk and morbidity of asthma in women[11,12] is in part due to the hormonal changes that occur throughout life,[13] and these changes may be associated with different forms of fat accumulation, which may interfere with asthma immunoregulation and control. Therefore, we aimed to evaluate the associations among ultrasound measurements of abdominal fat, serum concentrations of inflammatory cytokines, asthma control and lung function in women.

Materials and methods

This cross-sectional study was conducted in asthmatic women diagnosed with persistent asthma, as defined by Global Initiative for Asthma (GINA)[14] criteria, using clinical data and lung function testing in an outpatient asthma clinic at the University Hospital Gaffrée and Guinle (HUGG) from August 2014 to January 2015. The subjects were older than 17 years and were routinely followed up for more than one year. Treatment with fixed doses based on GINA guidelines[14] were initiated at least three months prior to the study by the same physician. All the patients under 65 years old had BMI values between 18.5 and 39.9 kg/m^2 (weight in kilograms divided by the square of the height in meters), whereas the BMI for those older than 65 was between 22.0 and 41.9 kg/m^2 and 22.0 and 41.9 kg/m^2.[15] Subjects were excluded if they were current smokers or had smoked within the past 5 years, were pregnant or nursing, had a history of psychiatric diseases, active pulmonary disease, malignancy, immunodeficiency, autoimmune diseases, congestive heart failure, cardiovascular disease, thyroid dysfunction, were chronic users of systemic corticosteroids or immunosuppressive drugs, had previous use of immunotherapy or had experienced an airway infection or exacerbation during the four weeks preceding the study.

Data collection

Demographic data [age and education (less than or more than five years)], number of parities, duration of disease (less or more than 15 years), onset of disease (before or after the age of 12 years), onset after menopause, rhinitis symptoms, use of drugs for diabetes, hypertension or gastro-oesophageal reflux disease (GERD), use of systemic corticosteroids and emergency room visits during the year prior to the study, assessment of asthma severity and control, anthropometric measurements (weight, height, waist circumference), and pulmonary function parameters including pre-bronchodilator percent-predicted FEV_1 (forced expiratory volume in one second), FVC (forced vital capacity) and the FEV_1/FVC ratio were obtained.

Assessment of asthma control and severity

Asthma control was defined as fully, partly controlled or not controlled according to the GINA guidelines 2012.[14] In addition, asthma severity was defined based on the GINA 2002 guidelines, which divide patients into 4 categories, mild intermittent, mild, moderate and severe persistent, based on the frequency of symptoms, spirometry results and pharmacological treatment.[16] Peak expiratory flow (PEF), expressed as the percentage of the predicted value based on age, sex, and height, was used to assess asthma control and severity.[17]

Anthropometric measures

Weight and height were measured to the nearest 0.1 kg and 0.1 cm, respectively, according to standard protocols.[15] Waist circumference (WC) was measured to the nearest 0.1 cm using a nonelastic tape measure, at the midpoint between the lower costal margin and iliac crest at the end of a normal expiration in supine position, with no clothes over the site of the measurement and with the arms extended laterally and the feet together. All measurements were performed by the same physician. BMI, waist-to-height ratio (WHtR) and waist-to-hip ratio (WHR) were calculated. The BMI value was categorized as normal, overweight or obese