BODY MASS INDEX IS RELATED WITH BRONCHIAL FUNCTION AND REVERSIBILITY IN CHILDREN WITH ALLERGIC RHINITIS AND ASTHMA

CIPRANDI G¹, BRAMBILLA I², TOSCA MA³, ARRIGO T⁴, SALPIETRO A⁴, LEONARDI S⁵, LA ROSA M⁵, MARSEGLIA GL².

¹Department of Internal Medicine, IRCCS Azienda Ospedaliera Universitaria San Martino, Genoa, Italy ²Department of Pediatrics, University of Pavia - Foundation IRCCS Policlinico San Matteo, Pavia, Italy ³Department of Pediatric Pulmonology, Ospedale Gaslini, Genoa, Italy ⁴Department of Pediatrics, Unit of Pediatric Genetics and Immunology, University of Messina, Italy ⁵Department of Pediatrics, University of Catania, Italy

Several studies have outlined a possible relationship between an increased body mass index and respiratory allergic diseases, such as asthma and rhinitis. The aim of the study was to analyse the relationship between BMI and lung function, including bronchodilation test, in allergic children. The study included 153 children (103 males, mean age 12.8 years) with allergic rhinitis and mild asthma. All subjects were evaluated performing skin prick test, spirometry, and bronchodilalation test. BMI values were in the normal range as well as lung function. BMI significantly related with FEV₁, FVC values and FEV₁/FVC ratio both before and after bronchodilation. In conclusion, this study provides the first evidence that BMI is negatively related with bronchial reversibility in children with allergic rhinitis and asthma. As reversibility is related with bronchial inflammation, this finding might underline a link between overweight and allergic inflammation.

The incidence of obesity and associated co-morbidities is dramatically increasing worldwide in both children and adults (1). Several studies have also hypothesized a possible relationship between increased body mass index (BMI) and respiratory allergic diseases such as asthma and rhinitis (2-4). Moreover, a stronger association in women has been reported (4-6). Nevertheless, the mechanism for the association between respiratory allergic diseases and obesity and the reasons for the apparent difference between men and women remain yet unclear (2). Because both respiratory allergic diseases and obesity are characterized by inflammation, a common inflammatory pathway has been proposed as a plausible explanation for the association between respiratory allergic diseases and obesity (7). The current view of adipose tissue is that of an active secretory organ, sending out and responding to signals that modulate appetite, energy expenditure, insulin sensitivity, endocrine and reproductive systems, bone metabolism, inflammation and immunity (1,8). Moreover, adipose tissue produces adipokines such as leptin and adiponectin that might concur to maintaining, and/or amplifying inflammation (1,9).

Body Mass Index (BMI) is considered a universal indicator of adiposity in according to World Health Organization (WHO) criteria, it could be associated with allergic asthma and rhinitis. To this aim, a cohort of allergic children with rhinitis and mild asthma was enrolled, and we analysed the relationship among BMI and lung function, including reversibility, as there is no study that investigated this topic.

METHODS

Study design: The study included children with perennial allergic rhinitis and mild asthma. All subjects were consecutively enrolled from April to June 2011 until the previously calculated needed sample of at least150 subjects was reached. All subjects were evaluated performing skin prick test, spirometry, and bronchodilation test.

Subjects: 155 subjects were included in the study: 103 males and 52 females. The mean age was 12.8 years. The Review

Key words: body mass index, allergic rhinitis, asthma, bronchodilation.

Correspondence:
Giorgio Ciprandi, M.D.
Semeiotica e Metodologia Medica I,
Viale Benedetto XV 6, 16132 Genoa, Italy
Phone + 39 10 35338120
FAX + 39 382 527976
E-mail gio.cip@libero.it

 $0394\text{-}6320 \ (2011)$ Copyright © by BIOLIFE, s.a.s. This publication and/or article is for individual use only and may not be further reproduced without written permission from the copyright holder. Unauthorized reproduction may result in financial and other penalties

Boards approved the procedure and an informed consent was obtained from the parents of each patient.

A detailed clinical history was taken and a complete physical examination was performed. The patients were included in the study on the basis of a clinical history of: i) perennial allergic rhinitis and presence of moderate-severe nasal symptoms according to validated criteria (10) or ii) mild allergic asthma on the basis of validated diagnostic criteria (11). Exclusion criteria were: acute or chronic upper respiratory infections, anatomical nasal disorders (i.e. nasal polyps, severe septum deviation, etc.), previous or current specific immunotherapy, use of nasal and inhaled steroids in the previuos month, and use of inhaled short acting beta-agonists and antihistamines during the previous week.

All patients assumed only short acting beta agonists or oral antihistamines on demand.

Skin prick test: it was performed as stated by the European Academy of Allergy and Clinical Immunology (12). The panel of employed allergens consisted of: house dust mites (*Dermatophagoidesfarinae* and *pteronyssinus*), cat, dog, grasses mix, *Compositae* mix, *Parietariaofficinalis*, birch, hazel, olive tree, *Alternariatenuis*, *Cladosporium*, *Aspergilli* mix (Stallergenes, Milan, Italy).

Spirometry: it wasperformed with a computer-assisted spirometer (Pulmolab 435-spiro 235, Morgan, England) and according to international guidelines (13,14). Briefly, 3 blows (every 5 min) were performed and the best result was considered. All subjects met the criteria for reproducibility and acceptability.

Test of bronchodilation: was performed according to international guidelines and using a salbutamol metered dose of 400 mcg. Reversibility was considered if an increase of at least 12% of FEV1 from baseline was achieved, according to international guidelines and previous study (15).

Statistical analysis and data definitions: Descriptive statistics were firstly performed and quantitative parameters were reported as with first and third quartiles [$1^{st} - 3^{rd}$ quartiles] in case of skewed distribution. Qualitative data were reported as absolute frequencies and percentages.

Correlation between quantitative variables was evaluated by means of the Pearson's correlation coefficient (r).

All tests were two sided and a *P* value less than 0.05 was considered statistically significant. The package "Statistica release 6" (StatSoft Corp., Tulsa, OK, U.S.A.) was used for all the analyses.

RESULTS

One hundred fifty-five patients, 103 males and 52 females, were included in the study.

Median BMI was 18.58 and thus in the normal range as well as the quartiles as reported in Table 1.

Lung functions parameters were in the normal ranges and 43 children showed reversibility (Table 1).

A clear relationship has been observed between BMI and some functional parameters as reported in Table 2. In particular, BMI significantly and positively related with

 ${\rm FEV}_1$ (p=0.026), FVC (p=0.004) and negatively with the ratio between ${\rm FEV}_1$ and FVC (p=0.002) at baseline. In addition, BMI significantly and positively related with ${\rm FEV}_1$ (p=0.044), FVC (p=0.007) and negatively with the ratio between ${\rm FEV}_1$ and FVC (p=0.008) after bronchodilation test.

DISCUSSION

There is evidence that the prevalence of allergic disorders, such as rhinitis and asthma, has world-widely increased in developed countries (16). Even though several environmental factors have been hypothesized to be involved in the development of allergic diseases, none could fully explain the rapid increase of the prevalence. However, some lifestyle factors, including dietary factors, alcohol consumption, physical inactivity, and obesity, have recently obtained distinctive regard. Indeed, the increase in affluence, typical of western society, may result in increased availability of foods and decreased physical activities, both of them may contribute to promote the prevalence of obesity and overweight. In addition, there is evidence that obesity and overweight are linked with allergic diseases probably because of the immunogical effects of adipose tissue on the development of allergies. Obesity has been associated with an increased risk of asthma both in children and adults (17,18). However, the real association between obesity and allergic disorders is unclear. Many cross-sectional surveys pointed out that obesity is a risk factor for asthma. Moreover, a genderdependant influence was observed and a significant association between body fat and asthma in women but not in men was found (2).

A recent meta-analysis of prospective epidemiological studies concerning the relationship between obesity and asthma has been recently published (19). Most of them evidenced that obesity was a risk factor for the development of asthma (OR ranging between 1.1 and 3.0) and that obesity preceded the development of asthma (3). However, the studies including lung function assessment showed conflicting results. One study evidenced an increased risk of bronchial hyperreactivity in obese patients (20). In contrast, another study provided evidence of lower risk of BHR (21) and another survey reported less airflow obstruction in obese patients (22), even though obese patients reported more respiratory complaints and used more bronchodilator drugs than normal-weight patients.

On the basis of these data, the present study was designed to analyse the possible relationship between BMI and lung function, including bronchial reversibilityin children with allergic rhinitis and mild asthma.

This study confirms that BMI is related with lung

Table I. Clinical and functional parameters of the study subjects

	Median	25°th-75°th percentile
BMI	18.58	15.63-21.19
FVC at baseline	99.27	88.67-108.71
FEV ₁ at baseline	97.79	88.66-110.63
FEF ₂₅₋₇₅ at baseline	94.34	73.79-111.83
FEV ₁ /FVC ratio at baseline	88.2	81.9-93.38
FVC after bronchodilation	101.23	93.09-110.01
FEV ₁ after bronchodilation	105.72	97.58-115.2
FEF ₂₅₋₇₅ after bronchodilation	113.43	95.4-127.89
FEV,/FVC ratio after bronchodilation	91.75	87.4-95.3

Table II. Relationships between BMI and lung function parameters

	p-value	r
BMI vs % FEV1 (at baseline)	0.0266	0.179
BMI vs % FVC (at baseline)	0.0004	0.288
BMI vs % FEF25-75 (at baseline)	0.8776	0.0124
BMI vs % Index of Tiffenau (at baseline)	0.0022	-0.246
BMI vs % CHG (after bronchodilation)	0.1683	-0.113
BMI vs % FEV1(after bronchodilation)	0.0445	0.165
BMI vs % FVC (after bronchodilation)	0.0071	0.220
BMI vs % FEF25-75 (after bronchodilation)	0.735	0.0277
BMI vs % Index of Tiffenau (after bronchodilation)	0.0086	-0.215

function and in addition provides a new information about the link between BMI and reversibility. This finding underlines the fact that the possible mechanisms of association between obesity and respiratory allergy could depend on mechanical consequences linked with fat build up. However, the most relevant outcome was the negative relationship between reversibility and BMI. As reversibility may be associated with bronchial inflammation (15), this finding might underline a link between overweight and allergic inflammation.

On the other hand, the possible limits of this study may be: the mild severity of asthma, the restricted number of patients, and the relative disproportion between genders. However, this cohort assures the statistical significance of the findings.

In conclusion, this study provides the first evidence of a significant relationship between BMI and bronchial reversibility in allergic children. Further studies should be addressed to investigate the role of the adipokines in the pathogenesis of these relationships.

REFERENCES

- 1. Fantuzzi G. Adipose tissue, adipokines, and inflammation. J Allergy ClinImmunol 2005;115:911-9.
- McLachlan CR, Poulton R, Car G, Cowan J, Filsell S, Greene J, et al. Adiposity, asthma, and airway inflammation. J AllergyClinImmunol. 2007;119:634-9.
- Ford ES. The epidemiology of obesity and asthma. J Allergy ClinImmunol2005;115:897-909.
- Bråbäck L, Hjern A, Rasmussen F. Body mass index, asthma and allergic rhinoconjunctivitis in Swedish conscripts-a national cohort study over three decades. Respir Med. 2005;99:1010-4.
- Beckett WS, Jacobs DR Jr, Yu X, Iribarren C, Williams
 OD. Asthma is associated with weight gain in females
 but not males, independent of physical activity. Am J

- RespirCrit Care Med 2001;164:2045-50.
- Chen Y, Rennie D, Cormier Y, Dosman J. Sex specificity of asthma associated with objectively measured body mass index and waist circumference. Chest 2005;128:3048-54.
- 7. Weiss S. Obesity: insight into the origins of asthma. NatImmunol 2005; 6:537-9.
- Weisberg SP, McCann D, Desai M, Rosenbaum M, Leibel RL, Ferrante AW Jr. Obesity is associated with macrophage accumulation in adipose tissue. J Clin Invest 2003;112: 1796-808.
- Cottam DR, Mattar SG, Barinas-Mitchell E, Eid G, Kuller L, Kelley DE, et al. The chronic inflammatory hypothesis for the morbidity associated with morbid obesity: implications and effects of weight loss. ObesSurg2004;14: 589-600.
- Bousquet J, Van Cauwenberge P, Khaltaev N Allergic rhinitis and its impact on asthma. J Allergy ClinImmunol 2001;108(5 Suppl):S147-S334
- Global Initiative for Asthma. Pocket Guide for Asthma Management and Prevention. National Hearth, Lung and Blood Institute, National Institute of Health, Bethesda, MD, 1997, NIH Publication no. 96-3659B.
- Dreborg S (Ed.). EAACI Subcommittee on Skin Tests.
 Skin tests used in type I allergy testing. Position Paper.
 Allergy 1989; 44 (Suppl.10):22-31
- Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, et al. Interpretative strategies for lung function tests. EurRespir J 2005;26:948-68

- Miller MR, Hankinson J, Brusasco V, Burgos R, Casaburi R, Coates R, et al. Standardisation of spirometry. EurRespir J 2005; 26:319-38
- Ciprandi G, Quaglini S, Giunta V, Cirillo I. VAS assessment of bronchodilation test might select rhinitis patients for a screening spirometry. Inv J Allergy ClinImmunol 2010;20: 419-24
- Asher I. ISAAC International Study of Asthma and Allergies in Childhood. PediatrPulmonol. 2007;42:100-6.
- 17. Hersoug LG, Linneberg A. The link between the epidemics of obesity and allergic diseases: does obesity induce decreased immune tolerance? Allergy 2007;62:1205-13
- 18. Matricardi PM, Gruber C, Wahna U, Lau S. The asthmaobesity link in childhood: open questions, complex evidence, a few answers only. ClinExpAllergy 2007;37:476-84
- 19. Beuther DA, Weiss ST, Sutherland ER. Obesity and asthma. Am J RespCrit Care Med 2006;174:112-9
- Chinn S, Jarvis D, Burney P. Relation of bronchial responsiveness to body mass index in the ECRHS. European Community Respiratory Health Survey. Thorax 2002;57:1028-33
- 21. Schachter LM, Salome CM, Peat JK, Woolcock AJ. Obesity is a risk for asthma and wheeze but not for airway hyperresponsiveness. Thorax 2001;56:4-8
- 22. Sin D, Jones RL, Man SF. Obesity is a risk factor for dyspnea but not for airflow obstruction. Arch Intern Med 2002;162:1477-81