CORRESPONDENCE

Retinol, beta-carotene, oxidative stress, and metabolic syndrome components in obese asthmatic children

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To the Editor,

The relationship between obesity and asthma has been subject of study by several authors. Multiple mechanisms have been proposed to explain this association. The produced mediators in adipose tissue, leptin, and low adiponectin, seem to regulate the proliferation of T cells and play an important role in the pathophysiology of lung disease (1). They can also worsen systemic inflammation and the uncontrolled production of free radicals (1). The reduction in antioxidant defenses may lead to oxidative stress and consequently to airway and systemic compromise (2).

Retinol and carotenoids participate in adipocyte metabolism, immune regulation, integrity of respiratory epithelium, and lipid and glucose metabolism (3). Decreased retinol plasma concentrations have been reported in asthmatic (4, 5) and obese (6, 7) children. High serum beta-carotene concentrations result in increased serum all-trans retinoic acid (ATRA) concentrations. ATRA induces an increased Th2 immune response and leads to atopy development (8). However, studies have yet to evaluate those vitamins with regard to obese children with asthma.

The present study aimed to evaluate the plasma concentrations of retinol, beta-carotene, malondialdehyde (MDA), high-sensitivity C-reactive protein (hsCRP), and the components of metabolic syndrome in obese children and adolescents with or without asthma as well as to assess retinol and beta-carotene concentrations according to their asthma severity.

We evaluated two groups: 30 obese atopic asthmatic children (GOA) and 26 obese non-asthmatic children (GO). Both groups were paired by gender, age, and body mass index (BMI) *z*-scores (zBMI ± 0.5 standard deviations). Exclusion criteria considered other chronic diseases, a height-to-age z-score (zH) lower than or equal to −1 standard deviation, presence of infectious or inflammatory diseases, intake of vitamin supplements in the previous six months or oral corticosteroids at least three months before data collection. Weight and height were assessed in all patients and further zBMI and zH scores were calculated by World Health Organization AnthroPlus® software. Patients with zBMI higher than +2 was defined as obese and those with higher than +3, as severe obese. GOA were classified according to severity of asthma (IA: intermittent asthma, MIPA: mild persistent asthma, MOPA: moderate persistent asthma, and SPA: severe persistent asthma) (9).

After 12 hours of fasting, peripheral blood was collected in a low-light room to measure retinol and beta-carotene (high-performance liquid chromatography), total cholesterol and its fractions (colorimetric enzymatic method), hsCRP (chemiluminescence), MDA (spectrophotometry) and oral glucose tolerance test (1.75g/kg body weight/day up to a maximum of 75 g of a maltodextrin, fasting and 120 minutes serum glucose). The study was approved by the Research Ethics Committee of the Federal University of Sao Paulo.

Statistical analysis was performed with SPSS (Statistical Package for Social Sciences Inc., Chicago, IL, USA – Windows version 20.0). Analyse of data normality was made using the Shapiro-Wilk normality test. For qualitative variables Chi-square or Fisher test was used. Association between continuous

Table 1 Demographic, clinical, and laboratorial data of the groups: obese asthmatic (GOA) and obese non-asthmatic (GO)

Variable	GOA (n = 30)	GO (n = 26)	p-value
Age			
Years	11.2 ± 2.7	10.6 ± 2.7	0.352*
Gender			
Male	21 (70%)	17 (65.3%)	0.779†
Race			
Caucasian	15 (50%)	13 (50%)	0.605†
Per capita income			
US dollars	175.00 (67.0,375.0)	150.00 (50.0,500.0)	0.630‡
Pubertal stage			
3 or more	6 (20%)	10 (38.4%)	0.163†
Obesity			
Severe	14 (46.7%)	16 (61.5%)	0.295†
Systolic blood pressure			
High	6 (20%)	9 (34.6%)	0.243†
Diastolic blood pressure			
High	8 (26.7%)	4 (15.4%)	0.347†
LDL-c			
High	6 (20%)	3 (11.5%)	0.481†
HDL-c			
Low	4 (13.3%)	7 (26.9%)	0.313†
Triglycerides			
Increased	14 (46.7%)	12 (46.1%)	0.591†
Fasting glycemia			
>100 mg/dl	4 (13.3%)	9 (34.6%)	0.111†
120 min glycemia			
>140 mg/dl	4 (13.3%)	1 (3.8%)	0.358†
Retinol			
<1.05 umol/L	2 (6.7%)	5 (19.2%)	0.226†

Cholesterol fractions: LDL-c and HDL-c.

*Student's t. Mean ± s.d.

†Chi-square. Number (%).

‡Mann–Whitney *U*-test. Median (minimum;maximum).

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Table 2 Median values of clinical and laboratorial data of the groups: obese asthmatic (GOA) and obese non-asthmatic (GO)

Variable	GOA (n = 30)	GO (n = 26)	p-value*
BMI (z-score)	3.0 (2.0,6.9)	3.3 (2.4,6.1)	0.153
hsCRP (mg/dl)	3.8 (0.4,20.0)	0.9 (0.9,4.0)	0.027
Retinol (umol/L)	1.55 (0.9;3.1)	1.60 (0.9,4.0)	0.678
Beta-carotene (umol/L)	0.30 (0.1;1.0)	0.15 (0.1,0.6)	0.005
MDA (umol/L)	2.8 (1.5,9.0)	3.0 (2.5,9.0)	0.846

hsCRP, High-sensitivity C-reactive protein; MDA, malondialdehyde. *Mann–Whitney *U*-test. Median (minimum;maximum).

variables was determined with Student's *t* test or Mann-Whitney U test. A two-sided p-value of less than 0.05 was considered statistically significant.

There were no significant differences between groups regarding to demographic, clinical and laboratorial data (Table 1), except for hsCRP and beta-carotene levels (Table 2). Retinol levels were significantly lower among patients with moderate or severe persistent asthma in comparison with those with intermittent asthma; for beta-carotene we did not observe significant difference (Figure 1).

Higher prevalence of retinol lower concentration has been described in asthmatic children (4, 5). Some limitations in the published studies have to be considered: not evaluating nutritional status and inflammatory biomarkers, and using anthropometric indices that are not appropriate to identify obesity.

The serum levels of retinol in GOA and GO were similar, maybe because 55.9% of our patients had controlled asthma, fewer exacerbations and less epithelial damage. However, on analyzing patients according to asthma severity, the mean serum levels of retinol were significantly lower in children with moderate or severe persistent asthma in comparison with those with intermittent asthma, similar to Indian asthmatic children younger than our patients (4).

Patients from GOA presented higher serum levels of beta-carotene in contradiction to what had been described in another study (5). A higher intake of beta-carotene observed in GOA in comparison with GO (data not shown) may be the possible explanation for this discrepancy. High beta-carotene concentrations can be suggested as a potential risk factor for asthma. The mechanism is not yet been established and further studies are needed (8).

Asthma and obesity are diseases that can occur with inflammation (1). Although they remain controversial, studies have indicated an association between obesity and the increased incidence of asthma, poor disease control, and increased exacerbations. The inflammatory process present in obesity and potentiated by asthma is also associated with decreased endothelial function, increasing cardiovascular risk (2, 10).

GOA showed higher hsCRP concentrations. Obesity *per se* and asthma may be associated with increased hsCRP serum levels by different mechanisms including increased production of IL-6 (2, 10).

Our study has several limitations: we did not assess airways inflammation and oxidative stress and we did not assess other nutrients related to antioxidant defence.

In conclusion there were no differences between obese asthmatic children and obese non-asthmatic children regarding serum levels of retinol, components of metabolic syndrome and oxidative stress marker. Lower serum levels of retinol were associated with asthma severity. Higher beta-carotene concentrations in GOA suggest its participation as a potential risk factor for asthma in obese children.

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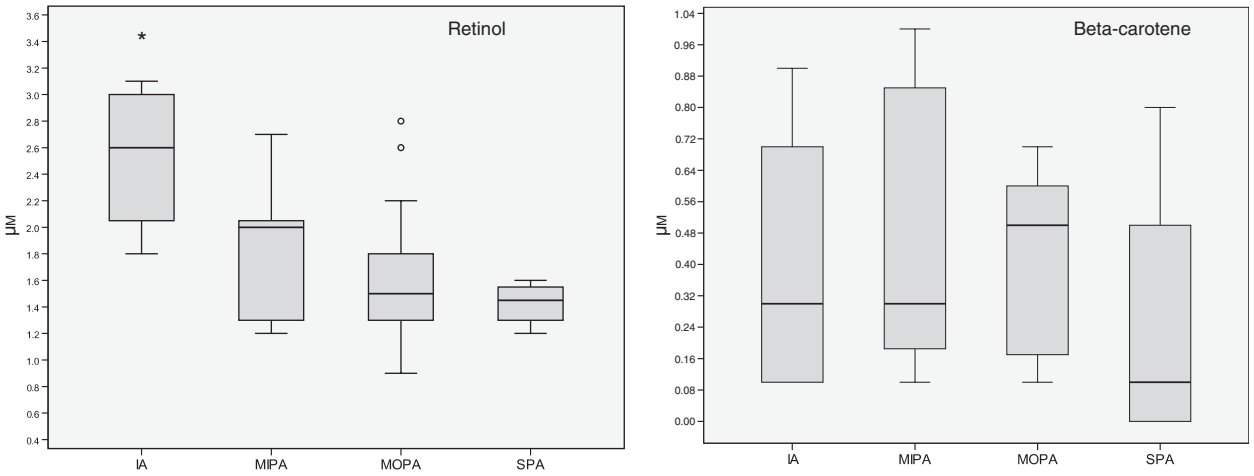


Figure 1 Retinol and beta-carotene concentrations in the obese asthmatic (GOA) according to asthma severity. * Mann–Whitney *U*-test: significant comparisons IA > MOPA and SPA. IA: intermittent asthma (n=4), MIPA: mild persistent asthma (n=7), MOPA: moderate persistent asthma (n=15), and SPA: severe persistent asthma (n=4).

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