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Osteoprotegerin and insulin resistance in childhood obesity: a new interplay?

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Introduction

Childhood obesity constitutes a phenomenon with epidemic prevalence in a worldwide context, leading to significant increase in the prevalence of metabolic co-morbidities.
Osteoprotegerin (OPG) is α tumor necrosis factor receptor superfamily glucoprotein that is acting as a decoy receptor for receptor activator of nuclear factor kappa B ligand (RANKL) with an anti-resoptive bone effect. Lately, it has been reported a positive association between OPG levels and cardiovascular morbidity and mortality[1-2]. Additionally, there is evidence that OPG in obese adults participates in the pathogenesis of atherosclerosis and cardiovascular diseases by promoting inflammation, which is known to be linked to insulin resistance (IR)[3-4]. Data regarding the relationship among obesity, insulin resistance and OPG in children and adolescents are sparse[5].
The aim of the study was to assess serum OPG levels in obese children and adolescents and explore any possible associations with insulin resistance.

Methods

A total of 160 individuals aged 10.7 years (age range: 2.6-17.8 years) were enrolled. Participants were grouped according to their body mass index into obese and controls, after applying the International Obesity Task Force criteria for childhood and adolescent obesity.
All obese participants underwent an Oral Glucose Tolerance Test (OGTT) in order to evaluate their glucose metabolism status. Homeostasis Model Assessment for Insulin Resistance Index (HOMA-IR) was calculated appropriately in order to assess insulin resistance status. Values of HOMA-IR>2.5 for pre-pubertal individuals and >4 for pubertal participants, defined as insulin resistance. Anthropometrical measures were recorded. Serum OPG levels were measured by a commercially available ELISA kit.

Results

Serum osteoprotegerin levels were found increased in obese participants compared to controls, but this increase did not reach statistical significance (p:0.133). When grouping total sample according to pubertal status into children and adolescents, OPG levels were found augmented in the obese in both subgroups but statistical significance was reached only in the adolescents subgroup.
During correlation analysis, OPG levels were positively correlated to BMI-SD values (r:0.24, p:0.028), to fasting insulin levels (r:0.293, p:0.007), to area under the curve for insulin during OGTT (r:0.224, p:0.046) and to HOMA-IR (r:0.289, p:0.009).

Negative association was found between OPG and age (r:-0.22, p:0.043) among obese individuals.

Table 1. Clinical characteristics and osteoprotegerin levels, in relation to the weight status.

Table 1	Obese (n=85)		Controls (n=75)	
	Children (n=40)	Adolescents (n=45)	Children (n=43)	Adolescents (n=32)
Age (years)	11.84 (2.6-16.5)		10.8 (3.3-17.8)	
	9.4 (2.6-12.1)	13.1 (11.5-16.5)	8.2 (3.3-11.9)	13 (11.2-17.8)
BMI-SD	2.19 (2-3.96)		0.39 (-2.57-1)	
	2.29 (2-3.96)	2.13 (2-2.98)	0.29 (-2.6-0.98)	0.6 (-1.94-1)
HOMA-IR	2.9 (0.8-14.7)		1.7 (0.5-2.5)	
	3.2 (0.8-7.6)	2.8 (1.2-14.7)	1.6 (0.6-2.4)	1.8 (0.5-2.5)
OPG (pmol/lt)	6.09 (4.68-229.9)*		4.81 (4.6-28.98)*	
	9.13 (4.69-40.9)#	4.68 (4.68-229.9)^	8.93 (4.69-28.61)#	4.6 (4.6-28.98)^

Data: median (min-max).p *:0.133, #:0.477, ^:0.019

During subgroup analysis, obese participants were divided according to the level of insulin resistance into obese-IR and obese-NIR individuals. Interestingly, only obese-IR individuals exhibited significantly higher serum OPG levels compared to either controls or to obese-non IR individuals (p<0.001). Inversely, obese-NIR participants did not present elevated serum OPG levels compared to controls. After adjustment for both BMI-SD and age, serum OPG levels were still significantly higher in obese-IR participants compared to controls/obese-NIR (p=0.001).

Table 2	Obese (n=85)		Controls (n=75)
	IR (n=41)	NIR (n=44)	
OPG (pmol/lt)	12.3 (4.7-229.9)∞¥	4.68 (4.68-34.57)∞#	4.81 (4.6-28.98)∞ ¥ #

Data: median (min-max).p: ∞<0.001, ¥<0.001, #:0.148

Serum OPG levels did not differ among obese participants, when they were grouped according to their glucose metabolism status. Impaired glucose tolerance or impaired fasting glucose did not correlate to serum OPG levels.

Conclusions

Insulin resistance may influence OPG levels in childhood and adolescent obesity, indicating a new interplay between them.

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