Relationship between RBP4 level and two of its genes' polymorphisms with body composition and metabolic profile in obese children

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INTRODUCTION

The role of retinol binding protein 4 (RBP4) in the insulin resistance associated with obesity is still unclear and various studies have analyzed the role of its gene's polymorphisms as a potential key to understanding the mechanisms involved [1-3].

OBJECTIVE AND HYPOTHESIS

The current study aimed to analyze the relationship between RBP4 levels, the distribution of two SNP (rs3758539 and rs10882280) and the metabolic, anthropometric parameters and body composition in obese vs. normal weight children.

METHODS

A retrospective observational study was conducted on a sample of 213 children, age 5-18 years, divided in two groups according to body mass index (BMI) standard deviation scores (SDS): a group with overweight/obesity (BMI >1SDS) and a normal weight group (-1<BMI<1SDS) who were evaluated in the Endocrinology Department of the Mures County Hospital. Demographic data, body composition (bioimpedance analysis), metabolic profile (glucose, insulin, lipids, uric acids), and RBP4 level were evaluated in every subject. Additionally, the genetic analysis of 2 SNP of the RBP4 gene were analyzed (rs3758539 and rs10882280). The study was approved by the local ethics committee and all subjects and legal representatives signed an informed consent. Statistical analysis used SPSS v. 25 with a level of significance α=0.05.

RESULTS

130 overweight and obese and 83 age and sex matched normal weight children were included. Levels of RBP4 negatively correlate with glucose levels (r= -0.178, p=0.022), but not after adjusting for age and sex. Body composition, metabolic profile and anthropometric parameters differ significantly between study groups, but RBP 4 levels are similar albeit higher in the obese group (13.1 vs 11.8 µg/ml, p=0.194) (Table 1). None of the SNP are associated with obesity, even after adjusting for sex.

DISCUSSIONS

Our study found significant higher levels of both insulin and HOMA IR in the obese group, results concordant to the study of 173 obese and multi-ethnic adolescents which concluded that gender, pubertal stage, BMI, WC, and body fat percentage had significant, positive correlations with fasting insulin and HOMA index [4]. The majority of studies regarding RBP4 gene's polymorphism were conducted on adults, yielding inconclusive results, without consistency all throughout. We observed that the variant A allele of the RBP4 rs10882280 is significantly associated with hypercholesterolemia.

CONCLUSIONS

RBP4 gene polymorphisms rs3758539 and rs10882280 are not associated with obesity in Romanian children. RBP 4 level is higher in obese children and correlates only with glucose levels.

Table 1 – General characteristics of the study groups

Parameter	Control (BMI< 1SD)	Case (BMI≥ 1SD)	p value
AGE (years)	11.64 ± 3.3	11.47 ± 2.8	0.635
HEIGHT (cm)	-0.01 ± 1.23	0.80 ± 5.77	0.038
BMI SDS	-0.10 ± 0.56	2.48 ± 3.64	<0.0001
WAIST SDS	0.75 ± 0.85	2.54 ± 0.67	< 0.0001
SKINFOLD SDS	-0.49 ± 1.54	2.97 ± 3.00	<0.0001
FAT MASS (kg)	7.56 ± 3.72	22.44 ± 21.03	<0.0001
MUSCLE MASS (kg)	32.01 ±9.95	37.64 ± 12.15	<0.0001
GLUCOSE (mg/dl)	81.16 ± 7.99	82.67 ± 8.63	0.18
CHOLESTEROL (mg/dl)	156.98 ± 28.02	167 ± 36.02	0.04
TRIGLICERIDES (mg/dl)	71.24 ± 57.91	89.87 ± 44.25	<0.0001
HDL-CHOLESTEROL (mg/dl)	55.46 ± 11.23	51.09 ± 14.85	0.001
URIC ACID (mg/dl)	4.23 ± 1.08	4.91 ± 1.15	<0.0001
RBP4 (ng/ml)	13035 ± 8303.92	15477 ± 12957.67	0.19
INSULIN (mIU/L)	23.47 ± 11.47	37.01 ± 19.75	<0.0001
HOMA INDEX	4.66 ± 2.29	7.58 ± 4.18	<0.0001

Table 2 – Genotype-obesity association

SNP	Allele	OR	95% CI	p value
RBP4 rs3758539	C- wild-type allele	0.750	0.1822-3.087	0.958
	T variant allele	0.929	0.513-1684	0.929
RBP4 rs10882280	C- wild-type allele	1.012	0.165-6.192	0.989
	A variant allele	1.473	0.725-2.992	0.368
STRA6 rs974456	C- reference allele	1.237	0.467-3.277	0.859
	T variant allele	1.087	0.612-1.930	0.889
STRA6 rs351224	T- wild-type allele	0.886	0.456-1.720	0.850
	A variant allele	0.926	0.508-1.689	0.923

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References

1. Kotnik P, Fischer-Posovszky P, Wabitsch M.. RBP4: a controversial adipokine., Eur J Endocrinol. 2011 Nov;165(5):703-11. doi: 10.1530/EJE-11-0431
2. Shajarian M et al., Association of RBP4 gene variants with adverse lipid profile and obesity, Gene. 2015 Apr 25;561(1):1-5. doi: 10.1016/j.gene.2014.12.071.
3. Codoñer-Franch P et al, Association of RBP4 genetic variants with childhood obesity and cardiovascular risk factors, Pediatr Diabetes. 2016 Dec;17(8):576-583. doi: 10.1111/pedi.12339
4. 19. Ling JC, Mohamed MN, Jalaludin MY, Rampal S, Zaharan NL, Mohamed Z. Determinants of High Fasting Insulin and Insulin Resistance Among Overweight/Obese Adolescents. Sci Rep 2016; 8; 6:36270