Visfatin, RBP4 and STRA6 polymorphisms' in relation with childhood obesity

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INTRODUCTION

Several visfatin, retinol binding protein 4(RBP4) and high affinity receptor for RBP4, STRA6 (stimulated by retinoic acid) single nuclear polymorphisms' (SNP) have been investigated regarding their relationship with obesity with controversial results [1-3].

OBJECTIVE AND HYPOTHESIS

The aim of this study was to analyze the association of two specific SNP for visfatin, RBP4 and STRA6 with anthropometric markers of obesity in children.

METHODS

A case control study was conducted on a sample of obese children and age and sex-matched controls evaluated in the Endocrinology Department of the Mures County Hospital.

Variables analyzed:

- age, sex, environment, body mass index (BMI) standard deviation score (SDS) according to WHO reference, waist circumference SDS, bicipital skinfold SDS,
- 2 SNP for visfatin - rs4730153 and rs2302559,
- 2 for RBP 4 - rs3758539 and rs10882280,
- 2 for STRA6 - rs974456 and rs351224.

Exclusion criteria were history of severe chronic diseases, children with short stature (height ≤-2.5 SD), untreated endocrine disease, failure to obtain informed consent of the parents. Statistical analysis used SPSS v.17.0 with a level of significance of α=0.05.

RESULTS

124 obese and 81 age and sex-matched control subjects were assessed with a mean age of 11.5±2.8years for the cases and 11.7±3.3years for controls. Hardy-Weinberg equilibrium was computed to the expected genotype distribution, with the STRA6 rs974456 being deviated significantly (χ^2=4.71, p<0.05). The genotype distribution is presented in table 1.

There is no significant association between the various genotypes analyzed and anthropometric markers. The presence of allele T of the rs2302559 (OR=0.558, 95%CI 0.317-0.984, p=0.046) and allele A for the rs4730153 (OR 0.532, 95%CI 0.297-0.952, p=0.037) have a protective role against obesity defined by BMI SDS (table 2).

CONCLUSIONS

Visfatin gene SNP might be associated with childhood obesity and overweight in Romanian population, but there is the need of further larger studies in order to confirm this association.

Table 1 – Genotype distributions

SNP	Genotype	BMI>1 SD	Control	OR (95%CI, p)	Allelic distribution
NAMPT rs2302559	CC	48	43		C – 66.1%
	CT	62	27	2.057 (1.116-3.791, p=0.024)	T – 33.9%
	TT	14	11	1.14 (0.467-2.778, p=0.824)	
	CT+TT	76	28	2.432 (1.337-4.421, p=0.004)	
NAMPT rs4730153	AA	19	12	1.541 (0.654-3.627, p=0.391)	A – 39.8%
	AG	68	33	2.005 (1.079-3.725, p=0.029)	G – 40.2%
	GG	37	36		
	AA+AG	87	45	1.881 (1.05-3.371, p=0.037)	
RBP 4 rs10882280	CC	95	67		C – 88.7%
	AC	26	14	1.31 (0.636-2.694, p=0.589)	A – 11.2%
	AA	3	0	2.116 (0.215-20.794, p=0.645)	
	AA+AC	29	14	1.461 (0.718-2.973, p=0.380)	
RBP4 rs3758539	CC	85	54		C – 82.2%
	CT	33	26	0.806 (0.435-1.494, p=0.528)	T – 17.8%
	TT	6	1	3.812 (0.446-32.555, p=0.255)	
	CT+TT	39	27	0.917 (0.504-1.668, p=0.878)	
STRA6 rs974456	CC	77	51		C – 77.3%
	CT	37	24	1.021 (0.547-1.906, p=0.999)	T – 22.7%
	TT	10	6	1.104 (0.377-3.226, p=0.999)	
	CT+TT	47	30	1.038 (0.581-1.851, p=0.999)	
STRA 6 rs351224	AA	30	16	1.078 (0.487-2.387, p=0.999)	A – 45.9%
	AT	54	42	0.739 (0.385-1.420, p=0.411)	T – 54.1%
	TT	40	23		
	AT+AA	84	58	0.832 (0.451-1.537, p=0.642)	

Table 2 – Genotype-obesity association

SNP	Allele	OR	95%CI	p value
NAMPT rs2302559	C	1.366	0.591-3.127	0.522
	T	1.792	1.017-3.157	0.046
NAMPT rs4730153	A	1.881	1.05-3.37	0.037
	G	0.961	0.439-2.105	0.999
RBP 4 rs10882280	C	1.669	1.491-1.869	0.279
	A	1.461	0.718-2.973	0.381
RBP4 rs3758539	C	0.246	0.029-2.081	0.248
	T	0.918	0.505-1.668	0.879
STRA6 rs974456	C	0.912	0.318-2.615	0.999
	T	1.038	0.582-1.851	0.999
STRA 6 rs351224	A	0.833	0.451-1.536	0.643
	T	0.729	0.363-1.463	0.396

DISCUSSIONS

The escalating rate of obesity is likely to be a result of changes in lifestyle and human behavior. But, the importance of genetic factors in the development of this public health problem and its comorbidities is worth mentioned. Adipokines, biologically active factors secreted by adipose tissue, such as visfatin and RBP4 play an important role in the development of obesity-related complications not only in adults but also in children

Although there are important discrepancies in the literature it has been suggested that visfatin might have both endocrine and paracrine effects, mostly related to obesity and insulin sensitivity. The human visfatin gene is located on chromosome 7q22.3. The link between some visfatin genetic variants and obesity has been confirmed in several populations, although these are the first data on Romanian children regarding two of the most common polymorphisms of this gene.

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