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Polymorphism of *PPARG* (*P12A*), *APOA1* (*G75A*) and *APOE* (*C112A* and *A158C*) Genes in Children With Obesity and Arterial Hypertension: A Case-Control Study

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Article received: Nov 8, 2017; **submitted to publication:** Aug 26, 2018

Background. *The genetic nature of a comorbid development of obesity and arterial hypertension (AH) in children is poorly studied. In this regard, it is important to study genes, the polymorphism of which is associated with disturbances in both metabolic processes and control of arterial pressure.* ***Objective.*** *Our aim was to study the association of polymorphisms P12A (rs1801282) of the PPARG gene, G75A (rs670) of the apolipoprotein A1 gene (APOA1), C112A (rs429358) and A158C (rs7412) of the apolipoprotein E gene (APOE) with the development of obesity and AH in children.* ***Methods.*** *The study included children with obesity and AH (case) and healthy children (control) aged from 10 to 17 years. Gene polymorphism was studied by polymerase chain reaction in real time. We determined blood concentrations of cholesterol and its fractions, triglycerides, apoA1, apoB, fasting glucose and glucose tolerance test for all children.* ***Results.*** *Groups of patients with obesity and AH (n =69) and healthy children (n =49) were comparable by age and sex. In the case group, there were more carriers of the A allele (25 versus 9% in the healthy group; p =0.002) and the AA genotype (13% and 2%, respectively; df =2, p =0.031) of APOE C112A polymorphism. PPARG and APOA1 polymorphisms as well as APOE A158C polymorphism were not associated with the development of obesity and AH in children. The carriers of the APOE e2 allele had lower concentrations of low density lipoproteins and apoB in the blood; the carriers of the PPARG G allele had lower glycemia values, and the carriers of the A allele of APOA1 G75A polymorphism had higher glycemia values.* ***Conclusion.*** *The APOE C112A polymorphism is associated with a comorbid development of obesity and AH in children. The pathogenetic significance of PPARG and APOA1 polymorphisms warrants further investigation.*

Key words: *children, obesity, arterial hypertension, cholesterol, apolipoprotein, polymorphism, genes, PPARG, APOA1, APOE.*

(***For citation:*** Kovtun Olga P., Ustyuzhanina Margarita A. Polymorphism of *PPARG (P12A), APOA1 (G75A)* and *APOE* (*C112A* and *A158C*) Genes in Children With Obesity and Arterial Hypertension: A Case-Control Study. *Voprosy sovremennoi pediatrii — Current Pediatrics*. 2018; 17 (4): 307–315. doi: 10.15690/vsp.v17i4.1924)

RESULTS

Table 1. Percentile distribution of lipid metabolism values in healthy children (*n* = 49)

Parameters	Optimal Values*	Acceptable Values*	High / Low Values*
Total cholesterol, mmol / L	<4.2	4.2−4.55	>4.55
Triglycerides, mmol / L	<0.93	0.93−1.23	>1.23
LDL, mmol / L	<2.1	2.1−2.46	>2.46
Apolipoprotein B, g / L	<0.85	0.85−0.97	>0.97
HDL, mmol / L	>1.09	1.09−0.97	<0.97
Apolipoprotein A1, g / L	>1.66	1.66−1.55	<1.55

Note. LDL / HDL — low / high density lipoproteins. * — optimal, acceptable and high concentrations of total cholesterol, triglycerides, LDL cholesterol and apoB corresponded to the percentile values < 75, 75-95, and > 95; optimal, acceptable and low values of HDL and apoA1 — > 25, 25-10, and < 10.

Table 2. Comparative characteristics of children with obesity and arterial hypertension (case) and healthy children (control)

Parameter	Case *n* = 62	Control *n* = 49	*p*
Age, years	14 (12; 15)	14 (12; 16)	0.443
Sex (girls), abs. (%)	19 (31)	16 (32)	1.000
BMI, kg / m^2	31.3 (29.0; 34.5)	18.9 (18.2; 20.3)	0.001
BMI SDS	2.82 (2.34; 3.17)	0.06 (-0.50; 0.25)	0.001
SBP_{off}, mmHg	130 (124; 136)	108 (104; 110)	0.001
DBP_{off}, mmHg	74 (68; 81)	66 (62; 70)	0.001
Hereditary history, abs. (%)*			
• Cardiovascular diseases	62 (100)	34 (69)	0.001
• Metabolism disorders	61 (98)	18 (37)	0.001
Social characteristics, abs. (%)			
• Single-parent family	27 (44)	7 (14)	0.003
• Higher education (mother)	29 (47)	34 (69)	0.017
• Higher education (father)	18 (29)	27 (55)	0.006
Regular physical activity**, abs. (%)			
• Child	5 (8)	36 (73)	0.001
• Mother	11 (18)	17 (35)	0.042
• Father	7 (11)	19 (39)	0.001
Features of eating behaviour, abs. (%)			
• Breakfast (child)	41 (66)	47 (96)	0.001
• Breakfast (parents)	24 (38)	42 (86)	0.001
• Tradition of family meals	24 (39)	41 (84)	0.001
• Eating at night	35 (56)	10 (20)	0.001
• Snacks during the day	51 (82)	37 (76)	0.314

Note. * — cases of diseases in relatives of the first and second degree of kinship (for more details, see Methods); ** — physical activity not less than 60 min / day. BMI — body mass index, SDS — standard deviation score, SBP_{off} / DBP_{off} — systolic / diastolic blood pressure (office measurement results).

Table 3. Distribution of alleles and genotypes of *PPARG*, *APOA1* and *APOE* genes in children in the compared groups

Groups	**Allele Frequencies, abs. (%)**		***p* (*df* = 1)**	**Genotype frequencies, abs. (%)**			***p* (*df* = 2)**
PPARG, P12A	*C*	*G*		*CC*	*CG*	*GG*	0.291
Case	50.5 (81.5)	11.5 (18.5)	0.120	41 (66)	19 (31)	2 (3)	
Control	43.5 (88)	5.5 (12)		39 (79)	9 (18)	1 (2)	
APOA1 G75A	*G*	*A*		*GG*	*GA*	*AA*	0.170
Case	47 (75.5)	15 (24.5)	0.071	35 (56)	24 (39)	3 (5)	
Control	42 (86)	7 (14)		36 (74)	12 (24)	1 (2)	
APOE C112A	*C*	*A*		*CC*	*CA*	*AA*	**0.031**
Case	46.5 (75)	15.5 (25)	**0.002**	39 (63)	15 (24)	8 (13)	
Control	44.5 (91)	4.5 (9)		41 (84)	7 (14)	1 (2)	
APOE A158C	*A*	*C*		*AA*	*AC*	*CC*	0.201
Case	57 (92)	5 (8)	0.500	54 (87)	6 (10)	2 (3)	
Control	44.5 (91)	4.5 (9)		40 (82)	9 (18)	-	

Table 4. Distribution of *APOE* alleles in children in the compared groups

Groups	**Allele Frequencies, abs. (%)**			***p* (*df* = 2)**
	e2	***e3***	***e4***	
Case	7 (11)	33 (53)	22 (36)*	0.041
Control	8 (16)	34 (69)	7 (14)	

Note. * **—** $p = 0.012$ when comparing the distribution of the corresponding allele with the value in the control group.

Table 5. Lipid metabolism values in children with obesity and arterial hypertension depending on the allelic variants of the *APOE* gene

Parameter	**Carriers of allelic variants of the *APOE* gene**			***p***
	***e2*, *n* = 7**	***e3*, *n* = 33**	***e4*, *n* = 22**	
Total cholesterol, mmol / L	3.7 (2.9; 4.1)	4.3 (3.6; 4.8)	4.2 (3.8; 4.9)	0.244
Triglycerides, mmol / L	1.25 (0.78; 2.06)	1.19 (0.86; 1.55)	1.16 (0.85; 1.99)	0.995
LDL, mmol / L	1.68 (1.41; 2.05)	2.39 (1.89; 2.58)	2.49 (2.07; 2.86)	**0.017**
Apolipoprotein B, g / L	0.75 (0.61; 0.8)	0.83 (0.75; 0.94)	0.89 (0.83; 1.08)	**0.026**
HDL, mmol / L	1.15 (0.84; 1.20)	0.93 (0.83; 1.08)	0.89 (0.76; 1.01)	0.101
Apolipoprotein A1, g / L	0.75 (0.61; 0.80)	1.6 (1.55; 1.69)	1.53 (1.47; 1.68)	0.180

Note. LDL / HDL **—** cholesterol of low / high density lipoproteins.

FINANCING SOURCE
Not specified.

CONFLICT OF INTERESTS
Not declared.