РОЗДІЛ 3

ЛІКУВАННЯ ТА ПРОФІЛАКТИКА ЗАХВОРЮВАНЬ ДИТЯЧОГО ВІКУ

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EATING DISORDERS ASSOCIATED WITH SNV *TAS2R38* IN CHILDREN WITH OBESITY

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Aim: to determine the contribution of SNV *TAS2R38* to the development of eating disorders in metabolically unhealthy obesity in children.

Materials and methods: 210 obese children aged 6–18 years were examined. The main group (n=128) according to the IDEFICS 2014 recommendations was represented by children with MUO. The control group (n=82) consolidated of children with metabolically healthy obesity (MHO). Whole genome sequencing (NGS, CeGat, Germany) was performed in 31 children of the main and 21 children of the control group. Statistical analysis included variational analysis with calculation of Student's test (t); Spearman's correlation analysis by calculating the Spearman's rank correlation coefficient (ρ) and bioinformatic analysis. The critical value of the level of statistical significance (p) for all types of analysis was accepted at the level of $p<0.05$ (5%).

Results. External (3.4±0.2 points; 52.5±5.1%) and emotiogenic (2.9±0.2 points; 34.2±5.9%) types of eating disorders were equally often diagnosed in children suffering from metabolically unhealthy obesity with an «average» degree of deviation above normal, $p>0.05$. The restrictive type of eating behavior was observed in the phenotype of metabolically healthy obesity (2.5±0.2 points, with a «very low» degree of deviation above the norm of 9.4±2.9%). The probability of detecting a heterozygous C/G variant of the rs713598 *TAS2R38* genotype in the main group was 1.75 times higher compared to the control group and was associated with the external type of eating disorder, $p<0.05$.

Conclusions. The C/G-genotype of SNV *TAS2R38* rs713598 is strongly associated with metabolically unhealthy childhood obesity and externalizing eating disorder.

Key words: *taste 2 receptor member 38, eating behavior, obesity phenotypes, metabolically unhealthy obesity, children.*

Introduction

The high prevalence of obesity in the world is associated with a violation of the type of eating behavior that is formed in childhood and is due to molecular genetic mechanisms. Eating disorders (ED) of external, emotional, restrictive types), physical inactivity and obesity are among the most acute public health problems faced by children and adults [4; 6].

Emotional ED is characterized by eating in response to emotions, both negative and positive, when food can be used as a coping mechanism for stress, sadness and anxiety or

can serve as a reward. External ED is a food response in response to exposome stimuli (the presence of food, the pleasant smell of food, or the presence of other people). Restrictive eating disorder focuses on a restrictive diet to regulate body weight.

Eating disorders in childhood are associated with elevated BMI during adolescence and are strongly associated with morbidity and mortality in adulthood. Dyslipidemia, metabolically associated fatty liver disease, adult-type lactase deficiency, type 2 diabetes mellitus, obstructive sleep apnea, arterial hypertension are associated with a metabolically unhealthy obesity (MUO) phenotype in children [1; 2].

Obesity was 1.13 times more likely to be registered in children who had more conflict situations in middle school age (95% CI 1.05–1.22) and restrictive eating disorders [7].

At present, there are works that have demonstrated the relationship between an emotional eating disorder and increase in the risk of obesity in children with SNV in the *dopamine D2 receptor* gene (*DRD2*) [10] and the *serotonin (5-HTT) transporter gene* (*SLC6A4*) [3; 5].

Genetically determined emotional, external or restrictive eating disorders associated with genetic markers – single nucleotide variants (SNV) of the *gene taste 2 receptor member 38 (TAS2R38)*, associated with the perception of bitterness, are formed in early childhood and lead to a high prevalence of obesity, including a phenotype with a complicated course – MUO.

Aim: to determine the contribution of SNV *TAS2R38* to the development of eating disorders in metabolically unhealthy obesity in children.

Materials and methods

The work is a fragment of the research work of the Department of Pediatrics 1 and Medical Genetics of the Dnipro State Medical University «Prediction of the development of childhood diseases associated with civilization» (state registration number 0120U101324).

Clinical examination of patients during inpatient treatment on the basis of the children's endocrinology department of the Communal non-commercial enterprise «Dniprovsk City Clinical Hospital No. 9» of the Dnipro City Council» was carried out in accordance with the Declaration of Helsinki. The list of additional paraclinical examination methods was compiled in accordance with the Order of the Ministry of Health of Ukraine dated September 24, 2022 No. 1732 «On approval of the Standards of medical care «Obesity in children». To verify comorbid conditions associated with obesity in children, we used the recommendations of the European Society of Endocrinologists and the Pediatric Endocrinological Society [8].

210 obese children aged 6–18 years were examined. The main group (n=128) according to the IDEFICS 2014 recommendations was represented by children with MUO. The control group (n=82) consolidated of children with metabolically healthy obesity (MHO).

Whole genome sequencing (NGS, CeGat, Germany) was performed in 31 children of the main and 21 children of the control group.

All children underwent a general clinical, immunobiochemical examination with electrochemiluminescence detection, enzymatic colorimetric method in the certified laboratory «Synevo» (Dnipro, Ukraine), sonographic and bioimpedance examination.

The Dutch Eating Behavior Questionnaire (DEBQ) was used to assess the type of eating behavior. The emotional type of eating behavior was determined when evaluated on the corresponding DEBQ scale more than 1.8 points, the external type _– when assessed on the corresponding DEBQ scale more than 2.7 points and the restrictive type–- when assessed on the corresponding DEBQ scale more than 2.4 points. The degree of eating disorder was expressed as follows: «very low» (0% – 19%); «low» (20% – 39%); «average» (40% – 59%); «increased» (60% – 79%); «high» (80% – 100%) [9].

Statistical analysis included variational analysis with calculation of Student's test (t); Spearman's correlation analysis by calculating the Spearman's rank correlation coefficient (ρ) and bioinformatic analysis. The critical value of the level of statistical significance (p) for all types of analysis was accepted at the level of $p<0.05$ (5%).

Results

In total, 210 children were included (mean age: 12,2 years; 49.8% female). In the comparison groups, children did not differ in age and sex, $p>0.05$. However, the proportion of children with MUO (61.4%) was 1.5 times higher than the proportion of children with MHO (40.2%) in the total cohort of obese children.

External (3.4±0.2 points; 52.5±5.1%) and emotiogenic (2.9±0.2 points; 34.2±5.9%) types of eating disorders were equally often diagnosed in children suffering from metabolically unhealthy obesity with an “average” degree of deviation above normal, $p>0.05$. The restrictive type of eating behavior was observed in the phenotype of metabolically healthy obesity (2.5±0.2 points, with a «very low» degree of deviation above the norm of 9.4±2.9%).

Three SNVs of the *TAS2R38* genes were identified among obese patients by NGS: rs10246939, rs1726866, rs713598 with CADD – 9.46; 12.15; 13.24 respectively.

The probability of detecting a heterozygous C/G variant of the rs713598 *TAS2R38* genotype in the main group was 1.75 times (OR 1.75; 95% CI 1.1–6.35) higher compared to the control group and was associated with the external type of eating disorder (ρ=0.32), Figure 1, $p<0.05$.

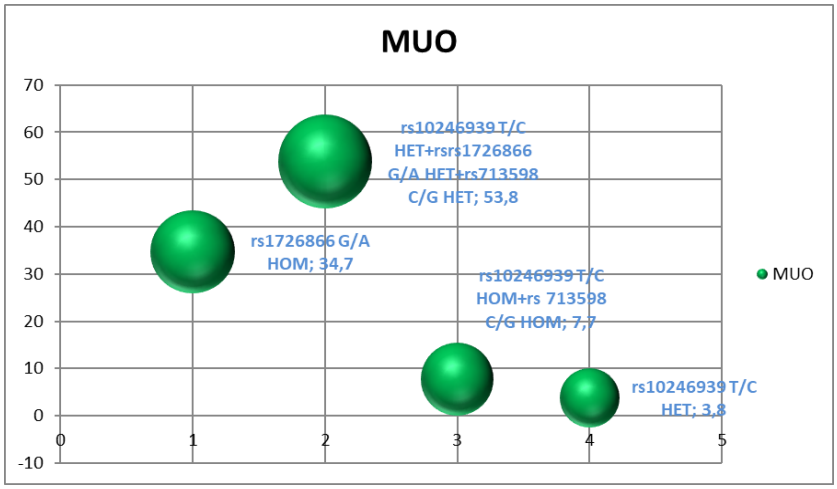

Fig. 1. Genetic variants of SNV *TAS2R38* in metabolically unhealthy obesity in children.

The following three SNVs of the *TAS2R38* genes were identified among obese patients by NGS: rs10246939, rs1726866, rs713598 with CADD – 9.46; 12.15; 13.24 respectively.

In this work, for the first time, we have demonstrated an association between eating disorders and a genetically determined disturbance in the perception of bitterness.

Conclusions

Types of eating behavior in children suffering from metabolically unhealthy obesity are associated with *TAS2R38* gene genotypes and require personalized nutritional modification.

Correlation with the formation of MUO has an external type of ED, significantly more often diagnosed with the highest degree of deviation in eating behavior in the C/G - genotype of SNV *TAS2R38* rs713598.

Conflict of interest: the authors report the existence of a conflict of interest.

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