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DIGESTIVE DISORDERS AND AUTISM SPECTRUM DISORDERS

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Annotation.

The study included 41 children aged 3 to 15 years with autism spectrum disorders and their parents. They answered the questions of the questionnaire concerning the presence of digestive disorders. All children were tested for celiac disease and gluten sensitivity. More than half of children with autism have digestive disorders (53.5%). The predominant symptoms are diarrhea (20.4%) and constipation (31.8%). 27% of children have selective appetite. Less common are frequent or constant burping (19.5%) and flatulence (14.5%). Among the pain syndrome, constant or recurrent pain in the lower abdomen is more common (7.5%), less often - in the upper (5%). The least common are nausea (5%) and frequent vomiting (2.5%). Celiac disease was not detected in any of the examined patients, while 41.9% of children with autism spectrum disorders have a genetic predisposition to the disease. Antibodies to gliadin Ig G are detected in 13.7% of children with ASD who do not use diet therapy.

Key words: *gastrointestinal tract, gluten intolerance, gluten-free diet, genetic markers, autism.*

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INTRODUCTION:

Autism spectrum disorders (ASD) currently attract the attention of specialists due to the high prevalence and variety of therapeutic approaches. ASD are characterized by a lack of communication, use of imagination and manifestations of stereotypical behavior, the real causes of which are not clear [1].

Observations of patients show that most children with ASD have symptoms of gastrointestinal disorders. Significant differences in the composition of the intestinal microbiota between patients of ASD and the control group were described [2]. This raises the question of the role of nutritional factors in patients with ASD. VanDeSande et al. after analyzing the available literature data for 2014, we concluded that carbohydrate digestion and absorption disorders may explain some gastrointestinal changes observed in patients with ASD, but their role in neurological and behavioral changes remains uncertain [2]. In addition, there is a relationship between improving bowel condition and reducing symptoms in some patients. Children with ASD have increased immune reactivity to gluten and associated gastrointestinal symptoms, indicating a possible pathogenetic mechanism involving impaired immunological and / or intestinal permeability in children with autism [3].

A large number of children show high selectivity to food and serious resistance to the introduction of new foods in the diet, which can subsequently lead to a deficiency of nutrients, as well as to complaints of constipation, more common among children with autism [4].

Wang LW, with co-authors (2011) children with ASD (249/589; 42%) have been shown to have significantly more problems with the gastrointestinal tract (GIT) than their healthy siblings (20/163; 12%) ($p < 0.01$). The most common problems were constipation (116/589; 20%) and chronic diarrhea (111/589; 19%). Scientists also claim that the increase in the severity of autism symptoms associated with a higher rate of gastrointestinal disorders (OR = 2.63, 95%, CI: 1.56-4.45) [5]. As a result of a double-blind randomized clinical trial involving 101 children with ASD at the age of 3 to 9 years SaadK et al. (2015) it was noted that a subgroup of patients who received digestive enzyme therapy for 3 months had a significant improvement in emotional response, overall impression and behavior, as well as reduction of symptoms from the gastrointestinal tract. According to the results of the study, the authors recommend the therapy with digestive enzymes as one of the possible options in the protocols of treatment of patients with autism in the future [6].

The existing data on the effectiveness of gluten-free diet (GFD) in the treatment of ASD are contradictory. However, the available results, which confirm the presence of positive dynamics in the inclusion of diet therapy in treatment, indirectly confirm the fact of involvement in the pathological process of gastrointestinal tract, the establishment of markers of gluten intolerance in patients with autism will clarify the etiology of this symptom [7-8].

There are three forms of gluten intolerance: celiac disease, gluten sensitivity and gluten Allergy. Celiac disease is characterized by the presence of haplotypes DQ2/DQ8 and serological markers, such as antibodies to tissue transglutaminase, endomysium, deamidated gliadin peptides. Diagnosis of gluten sensitivity is not specific. Haplotypes DQ2/DQ8 have about 50% of patients, and antigliadin antibodies are increased in 40-50% of cases, is characterized by the absence of enhancing antibodies to endomysium, tissue transglutaminase or deliberandum peptides of gliadin to the increase in the level of antibodies to gliadin. Gluten Allergy is characterized by an increase in the level of IgE to wheat protein. Therapy of all forms is to comply with a gluten-free diet (GFD). [9-11]. Purpose of research. To establish the presence of gastroenterological symptoms in children with autism spectrum disorders.

MATERIALS AND METHODS:

The study involved 41 children aged 3 to 15 years (Median – 6 years, 25 percentile – 5 years, 75 percentile – 8 years), including preschoolers – 27 children, younger students – 11 children, adolescents – 3 people. Boys were 37 people and girls - 4 patients. All children diagnosed with autism spectrum disorder living in the Voronezh region. Also, their parents, who were asked to pass a questionnaire on a specially designed questionnaire, the questions of which were devoted to the state of the gastrointestinal tract in their child.

To diagnose gluten intolerance used the definition of the content in the serum of IgG antibodies to gliadin and IgA to deliberandum peptides of gliadin by ELISA. For technical reasons – (blood sampling is difficult due to the peculiarities of the course of the underlying disease) serological diagnosis was carried out in 33 children from 41 participants of the study. To exclude the selective deficiency of immunoglobulin A, its determination was carried out in the blood serum.

The presence of haplotypes of HLA-system DQ2/DQ8 by polymerase chain reaction was also investigated. Genetic typing was performed on 31 children with ASD. The material for the study was the venous blood of patients taken from the ulnar vein.

Statistical analysis was carried out using Statistica 6.0 statistical program. Methods of descriptive statistics (relative values expressed as a percentage, determination of median and interquartile range – 25-75%) were used.
All stages of the research correspond to the legislation of the Russian Federation, international ethical standards and normative documents of research organizations. Conducted the study was approved by ethical Committee in of the "Voronezh state medical University named after N. N. Burdenko" Ministry Of Health Of Russia. Parents gave written informed consent to participate in the study.
The results of the study and their discussion.

RESULTS AND DISCUSSION:

The survey showed that every second child with ASD had significant gastroenterological complaints characterized by recurrent or persistent nature of the course. We found such symptoms in 53.5% of patients (22 out of 41). Along with this it should be noted that patients of ASD met and complaints of violations of the gastrointestinal tract, which in the survey parents described as rare, brief, episodic, does not violate the condition of the child, and noted they have more children.

Most often, children with autism had stool disorders. The presence of recurrent diarrheal syndrome was indicated by 14.6% (n=6), and constant 10.0% (n=4 people). Complaints of frequent constipation were 29.3% (n=12), permanent constipation was 2.5% (n=1). As rare violations of a chair in the form of the liquefied and / or frequent parents noted at each second child (53,6%, 22 people), and in the form of constipation at each third (31,7%, 13 people). The data we obtained on Russian children with ASD are consistent with the data of the Wang LW study with co-authors [5] on 589 children in the United States, whose stool disorder was also the most common problem.

Burp and flatulence are the next most frequent, more than half of the children (56.1%, n=23) had each of these conditions. 14.6% (n=6) complained of frequent burps, 4.9% (n=2) had constant burps, and 36.6% (n=15) had rare burps. Flatulence as a whole disturbed 56,1% (n=23). Occasionally it was observed in 41.5% (n=17) of children, often-9.5 % (n=4), 5% of children (n=2) constantly had bloating, and 2.5% of parents (n=1) found it difficult to answer the question.

Complaints of pain in the lower abdomen disturbed 41.6% (n=17) of children. Their episodic occurrence was indicated by 34% (n=14) of respondents, recurrent pain was noted in 2.5% (n=1) of the studied, and constant in 5% of children (n=2), 5% (n=2) of parents noted that children can not report their anxiety from the abdomen. Pain in the upper abdomen also disturbed children (34%, n=14): periodically - 29% of children (n=12), often (n=1) and constantly (n=1) complained of 2.5% of the subjects. In 5% of children (n=2) parents can not verify / identify pain due to age and characteristics of the underlying disease.

Only one child (2.5%) was often concerned about vomiting, the remaining 34% (n=14) children rarely vomited. 27% of children (n=11) had a complaint of nausea, while only 5% of the examined (n=2) noted it as a frequent phenomenon. 10% (n=4) of parents could not answer this question. Most rarely in children with ASD we found a complaint of rare heartburn - 7.5% (n=3) children, and 12% (n=5) respondents found it difficult to answer.

A significant number of parents (27%, n=11) indicated selective appetite in children, which is consistent with the results of the LiuX study. et al., which indicate selectivity in the diet of patients with autism [4].

Genetic markers of susceptibility to celiac disease were found in 41.9% of children (n=13 of 31), with a predominance of haplotype DQ2 (n=8, 61.5%), compared with DQ8 (n=4, 30.7%) and their combination DQ2/DQ8 (n=1, 7.8%). The structure of markers of genetic predisposition to celiac disease in children with autism corresponds to the data on the prevalence of haplotype DQ2, both in the population as a whole and among patients with celiac disease, including in the Voronezh region [12-13].

Antibodies of class A to deamidized gliadin peptides in all patients did not exceed the standard parameters (0 - 10 U/ml), which excludes the presence of celiac disease in the examined children. Note that the study established the fact of deficiency of IgA in one child in the presence of haplotype DQ2, indicating the potential for celiac disease in him. From further examination parents refused. Note also that the study involved 4 children who observe strict GFD, which means that serological tests in these patients will be negative, in this case, the results of the tests can only

be judged on the severity of diet. Of these, two had haplotypes DQ2/ DQ8, DQ8 and, respectively, the possibility of celiac disease.

Diagnostically significant increase of class G antibodies to gliadin were present in 12.1% of patients in General among the patients (4 of the 33 children) and 13.7 percent among the non-compliant GFD, indicating the existence of sensitivity to gluten. 4 children on HDB, in our opinion, also had the same form of gluten intolerance, as evidenced, according to parents, the effectiveness of diet therapy.

CONCLUSION:

1. More than half of children with autism have digestive disorders (53.5%). The predominant symptoms are diarrhea (20.4%) and constipation (31.8%). 27% of children have selective appetite. Less common are frequent or constant burping (19.5%) and flatulence (14.5%). Among the pain syndrome, constant or recurrent pain in the lower abdomen is more common (7.5%), less often - in the upper (5%). The least common are nausea (5%) and frequent vomiting (2.5%).

2. Celiac disease was not detected in any of the examined patients, with a genetic predisposition to the disease have 41.9% of children with ASD. Antibodies to gliadin Ig G are detected in 13.7% of children with ASD, not obeyed

Competing interests

The authors declare that they have no competing interests.

REFERENCES:

1. Vinogradova K.N. Etiology of autism spectrum disorders. Modern foreign psychology. 2014; 3(4):112-131.
2. Van De Sande, M., Van Buul, V., & Brouns, F. (2014). Autism and nutrition: The role of the gut–brain axis. Nutrition ResearchReviews, 2014; 27(2), 199-214.
3. LauNM, GreenPH, TaylorAK, HellbergD, AjamianM, TanCZ, KosofskyBE, HigginsJJ, RajadhyakshaAM, AlaediniA. Markers of Celiac Disease and Gluten Sensitivity in Children with Autism.PLoSOne. 2013;8(6):e66155.
4. Liu X, Liu J, Xiong X, Yang T, Hou N, Liang X, Chen J, Cheng Q, Li T. Correlation between Nutrition and Symptoms: Nutritional Survey of Children with Autism Spectrum Disorder in Chongqing, China. Nutrients. 2016;8(5): E294.
5. Wang LW, Tancredi DJ, Thomas DW. The prevalence of gastrointestinal problems in children across the United States with autism spectrum disorders from families with multiple affected members.J Dev Behav Pediatr. 2011;32(5):351-60.
6. Saad K, Eltayeb AA, Mohamad IL, Al-Atram AA, Elserogy Y, Bjørklund G, El-Houfey AA, Nicholson B A Randomized, Placebo-controlled Trial of Digestive Enzymes in Children with Autism Spectrum Disorders.ClinPsychopharmacolNeurosci. 2015;13(2):188-93.
7. Bavykina I.A., Zvyagin A.A., Nastausheva T.L., Bavykin D.V. Serologic and genetic markers of gluten intolerance in autism spectrum disorders. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 2018; 9 (2): 38-42.
8. Zvyagin A. A., Bavykina I. A., Bavykin, D. V. Gastroenterological symptoms in children with autism spectrum disorders. Voprosy detskoy diyetologii. 2018; 16. (2): 52-55.
9. Belmer S.V. Modern principles of diet therapy of celiac disease. Rossiyskiy vestnik perinatologii i pediatrii. 2012; 57(6): 97-100.
10. Bavykina I.A., Zvyagin A.A. Prevalence of haplotypes of HLA - system in children with gluten intolerance in the Voronezh region. Prikladnyye informatsionnyye aspekty meditsiny. 2015;18(3):59-62.
11. Yankina G.N.. Kondratyeva E.I.. Loshkova E.V. Terentyeva A.A. Features of diagnosis and treatment of various forms of wheat protein intolerance. Voprosy detskoy diyetologii. 2017; 5(1):13-24.
12. Zvyagin A.A., Bavykina I.A. The effectiveness of gluten-free diet in the treatment of autism spectrum disorders in children. Pediatrics. Magazine them. G. N. Speransky. 2017; 96(6):197-200.
13. Kondratyeva E.I.. Yankina G.N.. Dolbneva O.V. Prevalence of polymorphic variants of HLA DQA1 and DQB1 genes in patients with celiac disease in Tomsk and Krasnodar. Voprosy detskoy diyetologii. 2012; 2:11.