SCIENCE AND INNOVATION
INTERNATIONAL SCIENTIFIC JOURNAL VOLUME 3 ISSUE 5 MAY 2024
ISSN: 2181-3337 | SCIENTISTS.UZ

WHAT IS OROTACIDURIA

[1]Sharipov S.A., [2]Kasimov U.K., [3]Mukhamedova S.N.
[1,2]The student of Tashkent Pediatric Medical Institute, Department of Biochemistry
[3]Research advisor, The assistant of Tashkent Pediatric Medical Institute, Department of Biochemistry
https://doi.org/10.5281/zenodo.11176050

Abstract. *Orotic aciduria is a hereditary disease of pyrimidine synthesis, which is manifested by increased urinary excretion of orotic acid (orotate), T-lymphocyte deficiency, megaloblastic anemia, and delayed mental and physical development. With this disease, the activity of the enzymes orotidyl pyrophosphorylase and orotidyl decarboxylase, which convert orotic acid into the nucleotide orotidine monophosphate necessary for the synthesis of nucleic acids, is reduced.*

Keywords: *orotaciduria, ornithine cycle, pyrimidine, enzyme, uridine, dihydrouracil, dihydrothymine, pantothenic acid, dihydroorotic acid.*

Relevance.

There are 2 types of hereditary primary oratociduria. Type 1: The function of 2 enzymes is lost:

a) orotate phosphotidyl transferase and

b) orotidylate monophosphate decarboxylase.

In childhood, it is typical: developmental delay, megaloblastic anemia and orotaciduria. Patients are prone to infections. Pathology is largely determined by the lack of synthesized uridine, so introducing it into the body prevents the development of a number of symptoms.

Type 2: Associated only with OMP decarboxylase deficiency. In such patients, the urine excretes mainly orotidine and a small amount of orotic acid. When treating gout with allopurinol, excretion of orotic acid may be observed, which is due to the phosphoribosylation of allopurinol and, consequently, a decrease in the phosphoribosylation activity of orotic acid and, as a consequence, its accumulation. However, with long-term use of the drug, orotaciduria stops, since the body adapts to work in these conditions.

Orotaciduria	Hyperorotaciduria. Sharp lag mental and physical development. Megaloblastic anemia	1. Enzyme deficiency orotate phosphoribosyl transferase and orotidine monophosphate decarboxylase 2. Reduced inhibition carbamoyl phosphate synthetase UTP mechanism feedback 3. Pyrimidine nucleotide deficiency

The main pathway of pyrimidine catabolism in humans and mammals involves the reduction of uracil or thymine to form fully hydrogenated heterocycle, respectively, dihydrouracil or dihydrothymine. Cytosine cleavage occurs by the same mechanism as the other two nucleotides,

after it deamination at the first stage under the action of the enzyme cytosine deaminase and formation of uracil. Ring opening in dihydrouracil leads to the formation of β-ureidopropionic acid, which is further hydrolyzed to CO[2], NH[3] and β-alanine. With a similar mechanism transformation of thymine from it produces CO[2], NH[3] and β-aminoisobutyric acid. The products of pyrimidine catabolism are either excreted from the body or reused are utilized in other metabolic processes. Thus, ammonia is included in ornithine urea formation cycle. β-alanine is used in the biosynthesis of vitamin B3(pantothenic acid), which, in turn, is necessary for the synthesis of coenzyme A and acyl transfer protein - a component involved in the synthesis of fatty acids. The synthesis of pyrimidine nucleotides also occurs in stages, first carbamoyl phosphate is formed from NH[3], CO[2], ATP. Then with the participation of aspartic acid dihydroorotic acid is formed, then orotic acid. Orotic acid further reacts with 5'-phosphoribosyl-1-pyrophosphate, with this synthesizes orotidine 5-phosphate, which is then decarboxylated with formation of uridine monophosphate, which is the common precursor of all pyrimidine nucleotides.

The purpose of this study.

Orotaciduria is a genetic disease caused by the deficiency of enzymes that convert orotic acid to cytidylic acid and is inherited in an autosomal recessive manner, to carry out early diagnosis and prevention. Indeed, all patients with orotaciduria have noticeable, although very low, UMP synthase activity. It has been established that the content of orotic acid in the urine of patients (1 g/day or more) significantly exceeds the amount of orotate that is synthesized daily normally (about 600 mg/day). The decrease in the synthesis of pyrimidine nucleotides, observed in this pathology, disrupts the regulation of the KAD. Clinically, the most characteristic consequence of orotaciduria is megaloblastic anemia, caused by the body’s inability to ensure the normal rate of division of erythrocyte cells. It is diagnosed in children on the basis that it is not treatable with folic acid supplements. Insufficient synthesis of pyrimidine nucleotides affects intellectual development, motor ability and is accompanied by disturbances in the functioning of the heart and gastrointestinal tract. The formation of the immune system is disrupted, and increased sensitivity to various infections is observed zyme through the retroinhibition mechanism, which results in overproduction of orotate.

Materials and methods of research.

Urine from 1,358 mentally retarded subjects was screened for the presence of elevated concentrations of orotic acid and orotidine. This survey was conducted in search of occult variants of hereditary orotic aciduria which might be associated with mental retardation. Although no homozygous variants weredetected, 9 subjects with persistently abnormal urinary screening tests were discovered. Assays of erythrocyte orotidylate decarboxylase and phosphoribosyltransferase enzymes showed deficient activities for 2 of these subjects typically found in red cells of persons heterozygous for hereditary orotic aciduria. The same studies were conducted on urine and blood samples from the families of the affected subjects, and additional family members were also found to be affected. Detection of two unrelated heterozygotes among so small a screened population suggests, as previously noted, a higher frequency of the abnormal gene than that indicated by the extreme rarity of the homozygous condition. This study demonstrates the usefulness of the urinary screening test mass surveys and indicates the need for further study of the prevalence of the mutant gene.

Researchs and discussion.

According to the conducted studies and views, this pathological process can be associated with anomalies of the musculoskeletal system, strabismus and congenital heart diseases. Some statistics show that patients have increased susceptibility to lymphopenia and infections, including candidiasis, fatal varicella, and meningitis. Immune findings are variable and include decreased T cell numbers, impaired delayed-type hypersensitivity reactions, decreased T cell-mediated killing, and decreased IgG and IgA. The disease is caused by mutations in the UMPS gene, which encodes a protein with orotate phosphoribosyltransferase and orotidyl decarboxylase activity.

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