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Hyperoxaluria and Calcium Oxalate Crystalluria, Development Mechanisms and Correction Possibilities

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Abstract: The article presents modern ideas of hyperoxaluria and oxalate-calcium crystaluria. Oxalic acid metabolism is investigated in normal and the main risk factors for hyperoxalaturia are considered. The clinical symptoms and diagnosis of hyperoxalaturia and oxalate-calcium crystaluria in children are described. Author presents basic principles of correction including diet therapy, drinking regime, phytotherapy, medication.

Keywords: Dysmetabolic Nephropathy in Children, Diet Therapy, Crystalluria, Oxaluria, Hyperoxalaturia, Pathogenesis, Treatment, Children

Introduction

M Crystalluria is a variant of the urinary syndrome, in which, according to the results of laboratory tests, an increased content of salt crystals is found in the urine. In the daily practice of a doctor this symptom is observed in almost every third child. The proportion of crystalluria in the structure of pediatric nephrological pathology exceeds 60% [1]. The most common is oxalate and oxalate-calcium crystalluria, which accounts for 71–75% [2,3]. Prolonged crystalluria leads to changes in the functional state of the kidneys or structural changes at the level of various parts of the nephron. The following phases of the pathological process are distinguished: preclinical (saline diathesis), clinical (dysmetabolic nephropathy, interstitial nephritis) and urolithiasis [4,5].

According to epidemiological studies, calcium oxalate nephropathies account for 14% of diseases of the urinary organs. Systems in children [6]. It has been established that intermittent calcium oxalate crystalluria, detected in childhood and adolescence, leads to the progression of tubulointerstitial disorders in adults and an increase in the frequency of a mixed variant of the urinary syndrome, characterized by severe proteinuria, hematuria, signs of membranolysis of the tubular epithelium of the kidneys, functional and structural changes in the kidneys and bladder [7].

Oxalate metabolism and mechanisms of development of hyperoxaluria, oxalate-alcium crystalluria. According to modern concepts, the homeostasis of oxalic acid in the body is maintained by two exogenous sources (food and ascorbic acid) and endogenous - the metabolism of amino acids glycine and serine. Normally, oxalates found in foods bind to calcium in the intestinal lumen and are excreted from the body mainly with feces in the form of insoluble calcium oxalate. The usual diet contains 0.1-1.0 g of oxalates, but only 2-5% of them are absorbed in the intestines.

Most of the oxalates excreted in the urine are formed in the process of metabolism from amino acids - serine, glycine, hydroxyproline, and partly from ascorbic acid [8]. Under physiological conditions, 10% of the oxalates excreted in the urine are formed from ascorbic acid and 40% from glycine.

Methodology

The study employed a descriptive and analytical approach to investigate the mechanisms of hyperoxaluria and calcium oxalate crystalluria in children, as well as current correction strategies. Data were derived from clinical observations, laboratory diagnostics, and a structured review of existing scientific literature on dysmetabolic nephropathy. Pediatric patients presenting with urinary syndrome manifestations, including crystalluria, were evaluated using microscopic urine sediment analysis, daily biochemical urine assessment for oxalate and calcium excretion, and additional indicators such as anti-crystallization capacity and lipid peroxidation activity. Ultrasound examination was used to identify structural renal changes. The methodology also incorporated analysis of etiological factors, including dietary patterns, metabolic disorders, intestinal absorption disturbances, and genetic predisposition. Particular attention was given to differentiating primary and secondary hyperoxaluria based on clinical and biochemical criteria. Therapeutic interventions were assessed through observation of dietary modifications, hydration regimens, pharmacological treatments including vitamins and magnesium supplementation, and phytotherapy. The effectiveness of treatment strategies was evaluated by monitoring changes in urinary parameters and clinical symptoms over time, allowing for a comprehensive assessment of both pathogenesis and correction possibilities.

Result and Discussion

Excess oxalates are excreted mainly by the kidneys. Supersaturation of urine with oxalates eventually leads to their precipitation in the form of crystals. Normally, urine is a supersaturated saline solution, which is in a state of dynamic equilibrium due to substances (inhibitors) that contribute to the dissolution or dispersion of its constituents.

A decrease in the activity of inhibitors increases the risk of hyperoxaluria (Tamma-Horsfall, osteopontin, bikunin and prothrombin fragment 1) [9]. The high affinity of oxalate for calcium and the low solubility of calcium oxalate have been proven. Urinary oxalate is the only strong chemical promoter of kidney stone formation, about 15 to 20 times more potent than excess urinary calcium. In the metabolism of oxalic acid, magnesium plays an important role, which affects the release of oxalic acid, increases the solubility of calcium phosphate, and also prevents the crystallization of oxalates [10].

There are two etiopathogenetic variants of hyperoxaluria - primary and secondary. Primary hyperoxaluria is a hereditary disease that includes three rare types of genetically determined disorders of glyoxylic acid metabolism, which are characterized by increased excretion of oxalates, recurrent calcium oxalate urolithiasis and/or nephrocalcinosis, and a progressive decrease in glomerular filtration rate with the development of chronic renal failure [11,12]. In pediatric practice, secondary or spontaneous hyperoxaluria is most common, which can be transient (with a monotonous diet, against the background of acute respiratory viral infections, intercurrent diseases) or permanent. There are several mechanisms of its development. Alimentary hyperoxaluria is associated with excessive consumption of products containing oxalic and ascorbic acids [13]. The intestinal form of hyperoxaluria is due to increased absorption of oxalates and is observed in chronic inflammatory bowel diseases, food allergies. In addition, an increase in the absorption of oxalates is noted in all conditions accompanied by impaired absorption of fats in the intestine (cystic fibrosis, pancreatic insufficiency, short bowel syndrome). Most fatty acids are absorbed in the proximal intestine. Decreased absorption of fatty acids results in calcium loss as the latter binds to them. This leaves insufficient free calcium available for oxalate binding in the distal lower intestine, resulting in a dramatic increase in oxalate resorption and urinary excretion [14]. There are a number of other factors that favor intestinal hyperoxaluria, namely: decreased diuresis associated with diarrhea; a decrease in the excretion of magnesium ions by the kidney due to a decrease in their absorption in the intestine; metabolic acidosis due to the loss of bicarbonates in the intestine. A significant role in the genesis of intestinal hyperoxaluria is played by intestinal dysbacteriosis, which results in a decrease in the number of colonies of bacteria Oxalobacter formigenes, which break down about 50% of exogenous oxalate. The absence or reduction of Oxalobacter formigenes in the intestine increases the availability of oxalate for absorption and increases its concentration in the blood and urine [15]. For the development of hyperoxaluria, a

decrease in urinary excretion of citrates (an inhibitor of oxalate crystallization), vitamin B6 deficiency (an inhibitor of oxalate formation) is also important [16].

Risk factors for secondary hyperoxaluria include hereditary predisposition, which is observed in 71% of cases in children with hyperoxaluria. This is manifested not only by the pathology of oxalate metabolism, but also by a tendency to instability of cytomembranes [17]. In the genesis of membrane destabilizing processes, an important role belongs to the processes of intensification of lipid peroxidation, activation of endogenous phospholipases and oxidative metabolism of granulocytes. With the destruction of acidic phospholipids of cell membranes, oxalate precursors are formed. Local formation of oxalates in the kidneys is possible. The causes of membrane breakdown in this case are bacterial phospholipases in pyelonephritis, exposure to membrane toxic compounds, such as sulfa drugs, environmental factors, etc., as well as seasonal climatic fluctuations, nutritional errors, emotional and physical stress.

The connection of hyperoxaluria with undifferentiated connective tissue dysplasia was noted, since oxalates are the end product of the metabolism of glycine, serine, hydroxyproline, which are included in composition of collagen [18].

Clinical manifestations

The first manifestations of hyperoxaluria in children can be already in the first year of life. Most often, hyperoxaluria is recorded during periods of intensive growth of a child 7-8 and 10-14 years old. In most cases, oxalate crystalluria is detected by chance, sometimes against the background of acute respiratory viral infections, intercurrent diseases. Often, parents notice in a child a decrease in the volume of urine during the day, the precipitation of a large amount of salts. When questioned in children, recurrent abdominal pain is detected. Sometimes inflammation of the genitals develops due to constant irritation of the skin and mucous membranes, while urinating, there may be a burning sensation or other dysuric disorders. Against the background of crystalluria, an infection of the urinary system is often formed.

A visual assessment of urine indicates its saturated character, spontaneous sedimentation is possible. Hyperstenuria (urine relative gravity greater than 1030) in the absence of glucosuria should alert for hyperoxaluria.

In the future, against the background of crystalluria, slight microhematuria and / or proteinuria, abacterial leukocyturia appear, which indicates damage to the kidneys and is referred to as "dysmetabolic nephropathy".

Diagnostics

Microscopic examination of the urinary sediment can reveal oxalate colorless crystals in the form of postal envelopes, which is not the basis for the diagnosis of hyperoxaluria. Biochemical study of daily urine (transport of salts) allows you to clarify the presence of hyperoxaluria and hypercalciuria. The normal level of oxalates is less than 0.57 mg/kg/day, calcium is less than 4 mg/kg/day. [19]. In children with hyperoxaluria in nephrological hospitals, an analysis is carried out for the anti-crystal-forming ability of urine to calcium oxalate, which is reduced. The test for peroxide in the urine allows you to evaluate the activity of the processes of lipid peroxidation of cytomembranes.

An ultrasound examination of the kidneys in some children reveals echopositive inclusions in the pelvis and calyces.

Treatment

Basic therapy for hyperoxaluria and calcium oxalate crystalluria includes therapeutic nutrition and sufficient drinking regimen [21]. The main dietary recommendations are the creation of a rational balanced diet, taking into account the age needs of the child and the characteristics of impaired metabolism. With hyperoxaluria, foods with a high content of oxalic acid (1.0-10.0 g / kg of product weight) are excluded - chocolate, cocoa, tea, sorrel, spinach, parsley, beets, rhubarb, beans, nuts, buckwheat. Foods containing a moderate amount of oxalates (0.3-1.0 g / kg of product weight) are limited - black currants, sour varieties of apples and berries, beans, carrots, tomatoes, citrus fruits, as well as rich in vitamin C - rose hips, peppers sweet, sea buckthorn, cauliflower.

With hypercalciuria, the appointment of a diet low in sodium is indicated. To do this, it is enough to exclude salted crackers, chips, pasta, processed cheese, sausage, canned vegetable juices, tomato sauce, pickles. The use of calcium with food and drinks should correspond to the age requirement:

for children 1-3 years old - 500 mg / day, 4-8 years old - 800 mg / day, 9 years and older - 1300 mg / day. The average calcium content in foods is as follows: milk (240 ml) - calcium 300 mg, cottage cheese (113 g) - 110 mg, yogurt (170 g) - 250 mg, cheese (28 g) - 195-335 mg, ice cream (113 d) - 100 mg. Sufficient drinking regimen is a universal way to treat any crystalluria, as it helps to reduce the degree of saturation of salts in the urine.

The daily fluid requirement is at least 50 ml/kg. It is recommended to take weakly alkaline and low-mineralized mineral waters in the amount of 3-5 ml/kg/day. in three doses, a course of one month, 2-3 times a year. The basis of drug treatment is antioxidant and membrane stabilizing therapy, since one of the links in the pathogenesis of hyperoxaluria in most cases is membranopathy [22]. Within 3-4 weeks, vitamin A should be prescribed quarterly (1000 IU / year of the child's life per day), vitamin E (1-1.5 mg / kg of body weight per day, not more than 15 mg / day).

An obligatory component of the therapy of hyperoxaluria and calcium oxalate crystalluria is the use of phytopreparations. Despite the large selection of medicinal plants and their preparations, it is important to use only those whose effectiveness and safety have been proven by scientific research. Such a phytopreparation is Uralesan, standardized according to the content of biologically active substances of medicinal plants: active substances in 100 ml: fir oil - 0.419 g, peppermint oil - 0.105 g, liquid extract of wild carrot fruits - 1.204 g, liquid extract of hop cones - 1.726 g, oregano herb liquid extract - 1.195 mg. those. high-quality natural remedy with fully studied and proven properties of plants, strict observance of the principles of selection and careful selection of seed material, cultivation of raw materials on plantations in an ecologically safe area, standardization of each stage of production, litholytic, membrane-stabilizing and antioxidant effects. The drug "Uralesan" also helps to maintain the pH of urine in the range of 6.2-6.8, binds calcium into chelate complexes [23]. In an experimental and clinical study, the ability of the components of the phytopreparation Uralesan to suppress the processes of pathological crystallization of urine in urolithiasis in 86% of cases after 20 days of its administration was proved.

Metabolic therapy includes the use of magnesium preparations, vitamin B6. The preferred form of magnesium in this case is magnesium citrate, as this substance is an inhibitor of the crystallization of oxalates in the urine. The drug, which includes magnesium citrate (100 mg Mg ++) and vitamin B6 (10.0 mg), is called "Magne-B6 Antistress" (children over 6 years old 10-30 mg / kg / day). expedient it the appointment of a course for two months three times a year. Children with hypercalciuria are contraindicated in calcium and vitamin D preparations, with hyperoxaluria - ascorbic acid preparations.

Another such effective phytopreparation is Canephron N (Bionorica SE, Germany), standardized by the content of biologically active substances of medicinal plants: centaury herb (Centaurii herba), lovage root (Levistici radix), rosemary leaves (Rosmarini folia). This is a phytoneering preparation, i.e. high-quality natural remedy with fully studied and proven properties of plants, strict adherence to the principles of selection and careful selection of seed material, growing raw materials on plantations in an ecologically safe area, standardization of each stage of production Pharmacological properties of the drug "Canephron N", except for anti-inflammatory, antibacterial, antispasmodic - have diuretic, litholytic, membrane-stabilizing and antioxidant effects. The drug "Canephron N" also helps to maintain the pH of urine in the range of 6.2-6.8, binds calcium into chelate complexes [23].

V.V. Length et al. [26] studied the clinical efficacy of Canephron N for 3 months in children with sporadic dysmetabolic nephropathy with calcium oxalate crystalluria. It was shown that treatment with Canephron N compared with therapy with a complex of vitamins (A, E, B6-2 courses for 3 weeks with a break of 6 weeks) is more effective and leads to a faster and more significant decrease in the frequency and severity of hematuria, hyperoxaluria, calciuria and lipiduria . The results also showed that the most

the effectiveness of therapy is achieved only by three months of treatment with Canephron N. In many articles it is written that the use preparations "Uralesan" and "Kanefron N" for six months (14 days a month) against the background of complex treatment of children with impaired oxalate metabolism provided a significant decrease in the level of daily excretion of oxalates [27].

Membrane stabilizing properties of the drug "Canephron N" are shown in the study by K.E. Kazakova et al. [28]. The use of the drug for one month as monotherapy or in combination with vitamins A, E, Essentiale in children with dysmetabolic nephropathy (oxalaturia - in 75%) led to the elimination of hyperoxaluria, the normalization of lipid peroxidation processes in the cell and, consequently, to the stabilization of cell membranes. Thus, the preparations "Uralesan" and "Canephron" can be used both in a medical complex and separately for a long course in children with hyperoxaluria and calcium oxalate crystalluria. With intestinal hyperoxaluria, depending on its causative factor, therapy is expanded by the inclusion of probiotics, enzymes, and calcium preparations.

Conclusion

In conclusion, it should be emphasized that early detection of oxalic acid metabolism disorders and their timely correction can prevent the development of metabolic (oxalate or calcium oxalate) nephropathy in children.

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