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## Risk Factors, Clinical and Laboratory Features and Prevention of Oxalate Nephropatia in Children

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### ABSTRACT

*In recent years, the frequency has been increasing kidney diseases in children, including dysmetabolic nephropathy, which is associated, on the one hand, with worsening environmental situation, and on the other, with improved quality diagnostics. In this regard, the problem of early diagnosis, prescribing adequate dietary and drug therapy acquires special relevance. The article considers some aspects of etiology, pathogenesis, and criteria diagnosis of dysmetabolic nephropathy in children. Allocated attention to the clinical manifestations of this pathology and the main principles of treatment and prevention.*

One of the urgent problems of pediatrics at the present stage are diseases of the urinary system (US). Epidemiological studies conducted at the turn of the XX-XXI centuries, showed that the prevalence of US pathology depending on environmental conditions in the area of the child's residence varies from 60: 1000 up to 187: 1000 children [1,7,8]. In the structure of the pathology of US prevail diseases of congenital and hereditary genesis having hidden the beginning and torpid current, among which a large proportion falls on exchange, dysmetabolic nephropathies (DN).

Dysmetabolic nephropathies are understood to be large group nephropathies with different etiology and pathogenesis, but combined themes, that their development is related to exchange violations. Exchange pathology leads changes in the functional state of the kidneys or structural shifts. At the level of various elements of nephron. Dysmetabolic nephropathy in diseases associated with severe water-salt metabolism disorders that develop in ventricular - intestinal diseases with toxic syndrome and disorders haemodynamics. These may include kidney lesions occurring on the background of phosphorus-calcium metabolism disorders in hyperparathyroidism, hypervitaminose D and other diseases. Term "dysmetabolic nephropathy," is used in the narrow sense, denotes polygenically inherited (multifactor) nephropathy, which is associated with a disorder of oxalic acid metabolism and manifests itself in conditions family instability cytomembrane.

Healthy children release single small salt crystals with urine (most commonly oxalates and tripelphosphates) of 0.03-0.055 mkm; which do not cause damage to renal tissue. Believe that damaging effect on the urinary system organs is possible if crystals in urine sediment more than 10 in the field of view and at their size more than 12mkm. In

the process of crystal formation three principal factors: supersaturation of channel fluid beyond its limits stability, reduced activity of supersaturation inhibitors, presence of precipitation activators.

Crystalluria -is a variant of urinary syndrome, in which by results of laboratory studies in urine are found high content of salt crystals. In the daily practice of the doctor this symptom is observed in almost one in three children. Specific gravity of crystalloids in the structure of children's nephrological pathology exceeds 60% [1]. The most common is oxalate and oxalate-calcium crystallium, which accounts for 75.0-80.0% [1,2,14].

To form a crystal, it is necessary to have an ionic pair – anion and a cation (e.g. calcium ion and oxalate ion). Urine supersaturation the different kinds of ions eventually lead to their precipitation in crystals and their subsequent growth. A huge role plays in this regard dehydration of urine, which leads to an increase in ion concentration in urine even with their normal production. Except for saturation degree, ion solubility is influenced by ionic strength, ability to complex formation, urine current rate, urine pH [13,17,19].

The problem of sporadic dysmetabolic nephropathies is highly relevant in pediatrics and childhood nephrology. It is due to the high incidence of disease in the population, as well as possibility of its progression up to the development of urolithiasis disease and/or interstitial nephritis.

Established intermixing oxalate-calcium has been found to be crystalluria, identified in childhood and adolescence, leads to progression of tubulointerstitial disorders in adults; increasing the frequency of the mixed version of urinary syndrome; characterized by pronounced proteinuria, hematuria, features renal canal epithelium membrane lysis, functional and structural changes from kidney and bladder [5]. Among DN associated with water-salt, carbohydrate, phosphorus-calcium and other types of exchange, special attention in connection with the greatest prevalence found in 20% of patients with US pathology, turns to disorders of oxalic acid metabolism, so called dysmetabolic nephropathies with oxalate-calcium crystallium (DN with ON) [1,2,5].

Progression of oxalate nephropathy often leads to development abacterial interstitial nephritis (IN), and as a result addition of secondary infection develops pyelonephritis. As much as possible pronounced dysmetabolic disorders can cause occurrence of urolithiasis disease (ULD), even in the early years of the child 's life [3,12,15].

Currently, the prevalence of crystalluria in children 's population in non-endemic areas are 32%, and in ecologically adverse reaches 47%, for the share of oxalate crystalluria 68-71%, uranium - 9-15%, phosphaturia - 9-10%, others - from 3 to 5% [9]. Clinical-genetic analysis conducted by M.S. Ignatova and others. [10], showed that cases of oxalate nephropathy in ULD endemic the region can be classified as a multi-factor pathology in which the share of hereditary factors is approximately 60%, medium - 40%.

One of the most important scientific and practical directions of social paediatrics and health organization is a regional approach to study of children's health. Its formation is influenced by impact of climate-geographical, environmental and economic conditions residence, degree of population migration, ethnic and sociocultural features as well as significant differences in logistics the basis of medical and preventive institutions in the regions.

According to a number of experts, dysmetabolic nephropathy with oxalate-calcium crystallium is considered as a model eco-dependent disease [11].

E.Yu. Pushkareva [12] when studying clinical-pathogenetic features of formation and mechanisms of progression dysmetabolic nephropathies in children depending on age found that living in areas with a high anthropogenic load increases the chance of DN development with ULD by 2 times. The author has proved that consumption of filtered drinking water may be considered as a preventive measure for the development of oxalate-calcium crystallory in children, living in industrial areas. Variability of dysmetabolic nephropathy prevalence with oxalate-calcium crystallory, according to various authors, is due to differences in the environmental situation in the area of residence children and can reach 31.4% [1,3,5,7,8]. Average for Russia the prevalence of dysmetabolic nephropathy is 1.4:1000 children's population and due to environmental degradation has upward trend [10].

The most studying factor in the development of dysmetabolic nephropathies in children are exposed to exogenous toxicants: severe metals, pesticides, components of cement production, which children living in ecologically disadvantaged regions, as well as in climate-adverse season's years of adaptation. Such versions of dysmetabolic nephropathies are worn name of eco-nephropathy [7].

Endogenous and exogenous causes of oxalate are isolated dysmetabolic nephropathy in children. Endogenous causes include increase of oxalate biosynthesis, hyperuricemia, exchange disorders cystine, phosphaturia, diabetes mellitus, vitamin metabolism disorders, ischemic nephropathies, electrolyte disorders, hyperparathyroidism. Exogenous causes include features of nutrition and drinking regimen, Ecopathogens (cadmium, lead, uranium, organic solvents, etc.), drugs, and climatic features of the region of residence. Persistent crystallory should be considered a specific feature disorders of calcium metabolism at the cellular level, even presence usually is combined with salt diathesis [1,2].

The trigger mechanism in tubulointerstitial damage is crystallization of calcium oxalate in canals due to its local toxicity and poor solubility [18]. Damaged cells renal epithelium actively bind to crystals, inducing regeneration and repair processes. Urothelia proliferating cellsexpressing "crystal-binding molecules" on its surface which act as stimulators of adhesion of crystals to epitheliocyte surfaces [20].

There are two etiopathogenetic versions of hyperoxaluria- primary and secondary. Primary hyperoxaluria is hereditary disease comprising three rare species of genetically induced glyoxylic acid metabolism disorders which are characterized by increased excretion of oxalates, recurrent oxalate - calcium urolithiasis and/or nephrocalcinosis and progressive reduced rate of tangle filtration with development of chronic renal failure [2]. Oxalate-calcium crystals are deposited in all tissues of the body, leading to oxalosis at age 10-30 years. The disease is inherited by autosomal-recessive type, however cases of dominant inheritance are known. These forms are diagnosed with using biochemical methods, their clinical manifestations are identical.

In pediatric observing, secondary, or spontaneous hyperoxaluria, which can be transitive (at the same nutrition, against the background of SRVI (severe respiratory viral infection), intercurrent diseases) or constant. Several mechanisms of its development are identified. Alimentary hyperoxaluria is associated with excessive consumption of products containing oxalic and ascorbic acids [14].

The risk factors of secondary hyperoxaluria include hereditary predisposition, which occurs in 70% of cases in children with hyperoxaluria. This is manifested not only by the pathology of oxalate exchange but also the tendency to instability of cytomembran [14]. In genesis membrane stabilising processes have an important role to play lipid

peroxidation intensification, activation endogenous phospholipases and oxidative metabolism of granulocytes. At degradation of acidic phospholipids of cell membranes is formed oxalate precursors.

Stage of oxalate nephropathy development in progression kidney lesions in the age aspect: from oxalate diathesis in early the age before development of chronic tubulointerstitial nephritis; urolithiasis in adults is shown in the works of M.S. Ignatova and others. (2000, 2006), N.V. Voronina and others. (2000, 2009). N.V. Voronina [5,6] emphasizes that in therapeutic practice this pathology, latently occurring in childhood and adolescence, detected more frequently in persons of working age.

In recent years, oxalate nephropathies have been considered as heterogeneous group of polygenically inherited and multifactor realized nephropathies related to the disruption of oxalic exchange acids. At the base of pathology is the membrane-pathological process, as family characters [5.6].

In recent years the local formation of oxalates in kidney in connection with cell membrane phospholipid degradation, thereby forming oxalate precursors (serine), and phosphates with which calcium forms insoluble salts [16].

The first manifestations of hyperoxaluria in children are possible already on the first year of life. Hyperoxaluria is most commonly recorded during periods intensive child growth - 7-8 and 10-14 years. In most cases oxalate crystallium is detected accidentally, sometimes against the background of SRVI, intercurrent diseases. It is not uncommon for parents to notice a decrease in the amount of the urine during the day, precipitation of a large amount of salts. When polling from children are exposed to recurrent abdominal pain. Sometimes develops genital inflammation due to constant skin and mucosa irritation, when urinating, there may be a sense of burning or other dysurine disorders. Against the background of crystalluria is often formed urinary system infection. Visual assessment of urine shows it saturated character, spontaneous formation of sediment is possible. Hyperstenuria (relative urine density above 1030) in absence glucosuria should be alarming with respect to hyperoxaluria. In further on the background of crystallium appear insignificant microhematuria and proteinuria, abacterial leukocyturia, that indicates kidney damage and is designated as "Dysmetabolic nephropathy" [4].

Biochemical study of daily urine (salt transport) allows clarifying the presence of hyperoxaluria and hypercalciuria. Normal level of oxalates is less than 0.57 mg/kg/day, calcium - less than 4 mg/kg/day. To diagnose hyperoxaluria and hypercalciuria It is also possible to use the definition of such an indicator in a single portion urine as calcium to creatinine ratio and oxalate to creatinine ratio creatins [4].

In children with hyperoxaluria in nephrological hospitals is carried out analysis for the anticrystal-forming capacity of urine to calcium oxalate; which is reduced. Urine peroxide test allows to estimate activity lipid peroxidation processes of cytomembran. At the examination of kidneys in some of children is detected echopositive inclusions in the pelvis and the cups.

For prevention of Oxalate Nephropatia and calcium nephrolithiase it is recommended dispensary surveillance of children from families with hereditary predisposition to urolithiasis, with regular prophylactic treatment, including dietary therapy, drinking regimen, vitamin therapy (A, E, B6) and other treatments, especially phytotherapy. Surveillance over 5 years of 130 children showed the effectiveness of this rehabilitation scheme in both treatment and prevention relapses of pyelonephritis, as well as in reduction of expression in children metabolic disorders (Dlin V.V., Ignatova M.S., Osmanov I.M., E.A. Yureva, S.L. Morozov).

Despite the recent advances in treatment dysmetabolic nephropathies, improved treatments, prevention of severe outcomes of the disease, introduction of effective prevention to date remains one of the most important problems of modern children's nephrology.

Multi pathogenetic damage mechanisms urinary system, severity caused by metabolic disorders of effects such as urolithiasis, pyelonephritis and etc. it makes scientists to search for new modern treatment technologies and prevention of these diseases.

Thus, the study of risk factors and basic etiopogenetic mechanisms of dysmetabolic nephropathy formation in children are particularly important because of their high prevalence and a serious prediction.

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