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Urolithiasis in Children (Literature Review)

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Abstract Urolithiasis is a common and important problem of childhood, and in recent years the prevalence of this disease has been especially increasing due to changes in the environment, lifestyle and nutrition. This disease has its own characteristics. One of them is that, unlike, for example, various surgical conditions, surgical removal of stones is not the final stage in the treatment of urolithiasis, since this disease has a tendency to relapse. In this regard, 50% of children have a new stone within 3-5 years after the first appearance.

Keywords Urolithiasis in children, Factors, Diagnosis, Treatment, Metaphylaxis, Prevention

1. Introduction

Urolithiasis (UL) – is a metabolic disease caused by various endogenous and / or exogenous causes, often of a hereditary nature, characterized by the formation of stones in the urinary system. Currently, urolithiasis in children is an urgent problem, since on the one hand it has an increasing tendency (the number of children around the globe is steadily growing), and on the other hand it has a number of features, for example, the recurrence of the disease after the removal of the concretion, which can lead to repeated surgical interventions and disability of children.

Urolithiasis in children is a serious disease that requires surgical treatment in most cases. The formation of stones often leads to repeated surgical interventions due to frequent complications and relapses, which in turn leads to a rapid decrease in the functional parameters of the kidneys and disability of children. The problem of child disability remains extremely relevant for all civilized countries of the world and is an indicator of the health status of the child population. Finding the causes of the formation of stones, the search for sparing methods of removing concrements and proper postoperative metaphylaxis are the main directions of modern study of urolithiasis all over the world.

Urolithiasis is one of the most common consequences of modern life, since many factors are involved in the formation of stones. The prevalence of urolithiasis may vary depending on culture and geographic regions. The development and composition of stones are significantly influenced by diet, lifestyle and related illnesses. It is widespread throughout the world. Children make up 2-5%. Countries such as India, Turkey, Pakistan, Iran, some countries of South Asia, Africa and the northern states of the United States are endemic. The incidence of urolithiasis among the child population of Uzbekistan tends to grow. Thus, according to statistical data, in the last 5 years, more than a thousand new cases are detected every year. The prevalence of urolitization per 1000 population in Uzbekistan is 45 cases. Among boys, illness occurs more often – 1:2–1:4, than among girls. The cause of urolithiasis can be detected in 67-92.6% of cases. The main factors of the development of urolithiasis are endogenous and exogenous factors.

The main directions of the study of UL all over the world are the search and finding of the causes of stone formation, sparing methods of removing concrements and adequate metaphylaxis. In recent years, the accumulation of knowledge in the field of molecular genetics made it possible to explain the mechanisms of the development of urolithiasis, which led to a new era of diagnosis and treatment of stones.

The method of predicting the occurrence of urolithiasis, based on the identification of molecular genetic markers based on DNA analysis, has certain and significant advantages. The biochemical research method used for these purposes allows, first of all, to diagnose an existing disease, that is, it is effective for a sufficiently long pathological process. Practice shows that even in the presence of obvious clinical manifestations of the disease, biochemical changes can be detected only in half – and two-thirds of the children studied.

The molecular genetic method of predicting the occurrence of urolithiasis allows us to identify a predisposition to the disease at any age, almost from the birth of a person, since the genotype of a particular individual does not change during life. With the help of this method, it is possible to establish a predisposition to the disease in the absence of any clinical or biochemical manifestations, that is, at the earliest preclinical stage of the development of pathology. This means that the earlier the presence of a genetic marker is detected, the more reliable and timely measures to prevent the disease will be.

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In cases of an existing UL disease, the study of the association of molecular genetic markers with recurrent forms of urolithiasis, as well as the establishment of pharmacokinetic interactions will contribute to a more effective postoperative metaphylaxis of urolithiasis. Early detection of a predisposition to urolithiasis will undoubtedly lead to a decrease in morbidity, effective postoperative metaphylaxis, which in turn will lead to a significant reduction in material costs for organizing and conducting therapeutic measures.

2. The Main Results and Findings

Possible risk factors contributing to the development of urolithiasis may be associated with differences in the diet of different strata and regions of the population that consume more salt, protein, calcium and purines. The analysis of the family history of urolithiasis suggests a genetic basis for its occurrence. Diabetes mellitus also contributes to the formation of kidney stones. The increase in the incidence and prevalence of urolithiasis occurs in parallel with the increase in the incidence of metabolic syndrome. In addition, there seems to be a positive association between obesity and the risk of first and recurrent stone formation with a decrease in the time to relapse in obese patients compared to the normal population. Moreover, dehydration (caused by a hot climate or for other reasons) can also cause the development of urolithiasis. Due to the low volume of urine and high osmolarity of urine, the content of calcium and oxalates in the urine increases. Similarly, working in hot and humid conditions contributes to the formation of kidney stones.

The cause of urolithiasis can be detected in 67-92.6% of cases. There are two groups of factors for the development of urolithiasis exogenous and endogenous.

Exogenous factors include the environment, the lifestyle of parents, the burden of a gynecological history, living in a hot climate, the racial, sexual and age profitability of the child, taking food, rich by animal-protein, a high-calorie diet, taking medicinal drugs. The endogenous factor includes anomalies of the structure of the organs of the urinary system, urinary infection, metabolic disorders, heredity and genetic predisposition.

These are factors that are well studied and do not cause doubts. However, it is important to note that many researchers in recent years have come to the conclusion that the genetic predisposition to metabolic disorders associated with the metabolism of stone-forming substances is the main determinant of the development of urolithiasis, while environmental and dietary factors that play an important role in the development of urolithiasis in adults remain insignificant in children.

Such, at first glance, important risk factors as: the environmental situation in the place of direct residence of patients' families, the lifestyle of parents, the burden of the gynecological history of the expectant mother and the nature of intercurrent diseases of the child itself can lead in some cases to the formation of various kinds of anomalies of the urinary system in children, a disorder of the metabolism of stone-forming substances and the development of a serious disease-urolithiasis.

The hereditary factor of the development of urolithiasis is increasingly widely discussed in the modern literature. The family history of the disease is traced in 46-83% of cases and is least pronounced in European countries (12-33% of cases); in North American children, this indicator is 33-69%, the highest frequency is observed in children from Asian countries (up to 83%). The role of genetic factors in the development of polygenically inherited membranopathies, congenital and acquired enzymopathies, tubulopathies and metabolic nephropathies, as well as some monogenic forms of metabolic disorders of lithogenic substances is proved.

Modern urology has a significant arsenal of methods for getting rid of kidney stones and urinary tract stones in most patients. However, the removal of a stone does not mean getting rid of urolithiasis, which is why the problems of metaphylaxis (prevention of relapse) of urolithiasis are extremely urgent. The treatment of most conditions in which stones form in the urinary organs is currently based mainly on the symptoms, and not on the causes. In this regard, it is relevant to study the distribution of genotypes of polymorphic markers of the vitamin D receptor, steopontin, Urokinase, Fetuin-A, interleukin-1bett, interleukin-18 genes in children with and without urolithiasis.

A full understanding of the molecular causes of these conditions, including the identification of mutant genes and their gene products, should lead to more rational treatment protocols. Great importance in the diagnosis of urolithiasis has the identification of the degree of participation of genetic factors. The results of the study and the literature data showed that the occurrence of metabolic disorders characteristic of urolithiasis is significantly influenced by a hereditary predisposition in combination with environmental factors.

The realization of a hereditary predisposition to urolithiasis is associated with genetically determined structural and functional features of metabolism, neurohumoral regulation, and local factors. In their epidemiological or clinical studies, foreign scientists note the participation of genetic factors in the occurrence of urolithiasis, which suggests the existence of specific genes responsible for the occurrence of urolithiasis. One of the candidate genes for UL is the vitamin D Receptor gene.

The vitamin D receptor is encoded by the VDR gene, which is characterized by genetic polymorphism, that is, the existence of various allelic variants of this gene in the population. The most significant polymorphisms of the VDR gene involved in the development of diseases were: Bsm I, For I, Tag I. Several studies have established the association of VDR gene polymorphism with urolithiasis. Data have been published demonstrating the significance of the presence of the ApalAA genotype, which determines sensitivity to vitamin B, in the development of calcium stones in the urinary organs. It is also reported that the incidence of HLA genes B13, B22 and B35 in patients

with urolithiasis is higher than in healthy individuals. Also candidate genes are the genes of steopontin, Urokinase, Futuna-A, interleukin-1beta, interleukin-18. Studies conducted by foreign scientists have shown that metabolic disorders of phosphorus metabolism lead to hypophosphatemia and often associated hypercalciuria and urolithiasis. This disorder was found to be associated with two different heterozygous mutations in the renal protein transporting sodium phosphate, encoded as the NPT2a gene. Each of the destroyed Huns was determined. Such disorders were found in patients with recurrent urolithiasis and a decrease in renal phosphate reabsorption. Interestingly, other genetic forms of urolithiasis associated with hypophosphatemia were established without the presence of mutations in the gene of the same name NPT2a, All these disorders have a very high level of the active product of vitamin D by the endocrine system, 1,25 dihydroxyvitamin D. Such high levels of 1,25 dihydroxyvitamin D can contribute to a higher than usual efficiency of calcium absorption through the gastrointestinal tract and a decrease in the synthesis and secretion of parathyroid hormone. Such physiological changes in calcium homeostasis speak in favor of hypercalciuria and thus can contribute to the formation of kidney stones.

Despite many population-based molecular genetic studies, the molecular genetic markers of urolithiasis in children are still insufficiently studied. Also, the issues of choosing diet therapy, as well as the effectiveness of diet therapy, depending on the genetic status of the patient, have not been sufficiently studied. Also, the pharmacogenetic aspects of urolithiasis, such as the choice of pharmacological drugs for conservative treatment and metaphylaxis of urolithiasis, depending on the genetically determined functional features of the metabolism, have not been sufficiently studied.

In this regard, it is relevant to study the distribution of genotypes of polymorphic markers of the genes of the vitamin D receptor, steopontin, Urokinase, Fetuin-A, interleukin-1bett, interleukin-18 in children of the Uzbek population with UL and children without UL. And based on the data of genetic and biochemical testing, to assess the differences in the state of phosphorus-calcium, metabolism, oxalate, uric acid and other substances in the group of patients with UL.

It is important to note that many researchers in recent years have come to the conclusion that the genetic predisposition to metabolic disorders associated with the metabolism of stone-forming substances is the main determinant of the development of urolithiasis, while environmental and dietary factors that play an important role in the development of urolithiasis in adults remain insignificant in children.

The study of the role of genetic factors and the deepening of knowledge in the field of molecular mechanisms underlying the formation of urine components, such as calcium, oxalates, cystine and uric acid, will improve the diagnosis, treatment and prevention of urolithiasis in children. The study of genetic factors will also allow the development of therapeutic measures aimed at eliminating the molecular genetic defect, which will further prevent the formation of kidney stones.

Thus, the main directions of studying urolithiasis all over the world are the search and finding the causes of stone formation, sparing methods of removing concrements and adequate metaphylaxis. In recent years, the accumulation of knowledge in the field of molecular genetics has made it possible to explain the mechanisms of the development of urolithiasis, which has led to a new era of diagnosis and treatment of stones. Unlike traditional diagnostic methods, the molecular genetic method of predicting the origin of urolithiasis allows you to deduce a predisposition to the disease at the preclinical stage in love to grow, almost with the birth of a person, since the genotype of a particular person does not change in the course of life. The earlier a similar genetic marker is obtained, the more reliable and timely the measures for pre-ordering the disease will be.

The diagnosis of ICD is based on the patient's complaints, anamnesis data, physical examination, and the results of their laboratory, radiological, radioisotope and ultrasound examination methods. These data allow us to choose the correct strictly individual management tactics; examination methods and subsequent treatment of children with urolithiasis should be carried out in accordance with the developed algorithms for managing patients and should include not only stone removal, but also proper postoperative metaphylaxis. A comprehensive examination of patients with urolithiasis must necessarily include the determination of metabolic disorders, parathyroid gland function, hormonal background, immune system, chemical composition of the nodule. Careful clinical observation of children in the long-term period after the independent removal of stones or the use of various methods of their removal allowed us to establish that the main factor of relapse of the disease is pronounced metabolic disorders. Taking this into account, first of all, the study of metabolic factors should be performed in children.

For the diagnosis of UL, such research methods as ultrasound, biochemical blood tests, qualitative and quantitative analysis of urinary sediment, X-ray studies are widely used. An informative method of diagnosing UL is ultrasound examination of the kidneys and bladder. Another indirect symptom of a stone of the upper urinary tract is the expansion of the calyx-pelvic system.

An important value in the recognition of stones in the kidney or in the ureter is an X-ray examination. However, this method of research has a drawback – not all stones are radiopaque. Therefore, after a review urography, it is necessary to perform excretory urography, which allows you to clarify whether the shadow belongs to the urinary tract, as well as to determine the anatomical and functional state of the kidneys and the localization of the concretion (in the pelvis, ureter).

To diagnose the formation of stones, a general urinalysis in the absence of pyelonephritis is the least sensitive. Despite the fact that the formation of crystals is the first step in the

formation of a concrement, crystals of urinary sediment are a frequent laboratory sign and can be detected in the urine of both patients with UL and healthy children. During the period of formation and growth of the stone, crystalluria may be absent.

The study of quantitative urinary excretion of individual macromolecular inhibitors of stone formation, such as Tamm–Horsfall protein, uropontin, nephrocalcin and others, is practically not carried out due to their labor intensity and high cost. In addition, in most cases, anomalies of the structure, rather than the amount of the corresponding glycoproteins, are found in patients with UL. Determination of the daily urinary excretion of low-molecular-weight inhibitors-citrates is widely used in foreign clinics and is taken into account when calculating the indicator of urinary.

It is equally important to determine the functional state of the kidneys with UL, since it is often possible to observe and treat conservatively in patients with coral-like stones that occupy the entire kidney, and it is not necessary to operate on them at all. For example, there is no need to perform an operation if the stone occupies the entire pelvis, but the functional state of the kidney is satisfactory, there is no urinary tract infection, there are no pronounced clinical manifestations of the disease. Only the detection of a concrement is not an indication for the operation. Today, it has been proven that a 50% decrease in kidney function is considered a contraindication to such a modern method of UL treatment as remote lithotripsy (RLT).

Timely diagnosis of urinary tract infections with UL is also necessary, since the presence of such infections is also a contraindication to surgery. And at the same time, the infection itself can cause the formation of stones, mainly phosphate.

One of the most informative methods of diagnosing UL is spiral computed tomography (CT). With the help of it, not only the concretion is well visualized, but also the entire bundle, the cortical and cerebral layers. When conducting a spiral CT scan, it is possible to correct the image, for example, remove the image of the intestines, gases and leave only the vascular bed of the kidney or the upper urinary tract. The radiation load during CT does not exceed that of overview radiography.

Thus, most of the laboratory methods used in the diagnosis of UL is mainly aimed at determining the nature of metabolic disorders of crystal-forming substances. Since the process of stone formation depends on the interaction of various urine compounds that are promoters and inhibitors of stone formation, the search for integral indicators of UL activity is of the greatest practical interest.

The disadvantage of these research methods is that they allow you to diagnose an existing disease, i.e., these studies are effective for a sufficiently long pathological process.

The method of predicting the occurrence of urolithiasis, based on the identification of molecular genetic markers based on DNA analysis, has certain and significant advantages. The biochemical method used for these purposes for determining the violation of mineral metabolism allows, first of all, to diagnose an existing disease, that is, it is effective for a sufficiently long pathological process. Meanwhile, it was found that even in the presence of an obvious disease, biochemical changes are detected only in half – two-thirds of the studied patients.

The molecular genetic method of predicting the occurrence of urolithiasis allows us to identify a predisposition to the disease at any age, almost from the birth of a person, since the genotype of a particular individual does not change during life. In addition, a predisposition to the disease can be established using this method in the absence of any clinical or biochemical manifestations, that is, at the earliest preclinical stage of the development of pathology. This means that the earlier the presence of a genetic marker is detected, the more reliable and timely measures to prevent the disease will be. In cases of an existing UL disease, the study of the association of molecular genetic markers with recurrent forms of urolithiasis and the establishment of pharmacokinetic interactions will contribute to a more effective postoperative metaphylaxis of urolithiasis. Reducing the incidence of urolithiasis due to early effective detection of predisposition to it as well as more effective postoperative metaphylaxis of urolithiasis will lead to a significant reduction in material costs for organizing and conducting therapeutic measures.

The clinical manifestations of urolithiasis in children are very variable. In uncomplicated cases, they are caused by the passage of the concretion through the urinary tract, which is accompanied by mild or severe pain due to spasm and the passage of the stone through the natural pathways. In the presence of larger stones in the urinary tract, the clinical symptoms of nephroureterolithiasis were more often caused not so much by the obturation of the calyx-pelvic system with stones or their passage through the ureter, as by the accompanying pathology, i.e. calculous pyelonephritis or chronic renal failure. Pain was the leading clinical manifestation of urolithiasis. They manifested themselves in different ways depending on the age, nature and localization of the stones. Children of the first three years of life responded to pain associated with spasms of the urinary organs in 80% of cases with general anxiety, crying, a rise in body temperature to 38℃ and above, sometimes dysuria and even macrohematuria. At the age of 4 to 11 years, patients with urolithiasis complained of abdominal pain. This is due to the fact that at this age the kidneys are located lower than in older children and there is still no differentiated innervation of the urinary tract and abdominal organs, Hence the irradiation of pain mainly in the abdominal area, disorders of the gastrointestinal tract. Older children localize pain in the lumbar region.

Dysuria with urolithiasis in children was significantly more often observed at an early age (58%) and rarely in older children (15%). The most common cause of dysuria is a combination of stones of the upper and lower urinary tract. In patients with low – lying ureteral stones, especially in the juxtapesical and intramural sections, pollakiuria, nocturia, and even acute urinary retention were noted during renal

colic. Dysuria with bladder stones is caused by irritation of the mucous membrane or acute cystitis that has occurred.

Hyperthermic reaction as a manifestation of the general reaction of the body to nephrolithiasis and its complications in children was observed quite often, and in children under 3 years old it is manifested twice as often as in older children. Hyperthermic reaction indicates the active phase of the course of calculous pyelonephritis or pionephrosis.

The syndrome of intoxication of the body can be considered the most characteristic manifestation of nephrolithiasis in childhood. Among young children, acute and chronic manifestations of intoxication were observed in 35%, and among children aged 3-15 years in 7% of cases. Acute intoxication is manifested by dryness of the skin, a decrease in tissue turgor, anorexia. As a rule, there is a hyperthermic reaction with deviations in the parameters of homeostasis. Chronic intoxication leads to a decrease in body weight, anemia, hypovitaminosis, a decrease in muscle tone, apathy.

Changes in urine in children with urolithiasis allow us to think approximately about the pathology of the urinary tract. Hematuria in nephrolithiasis is an important diagnostic sign and was detected in 67% of patients. Microscopically, it occurred in 85%. Pyuria, or leukocyturia, is also considered a symptom of urolithiasis, although it is more correct to consider uu as a symptom of a complication of calculous pyelonephritis, pyelonephritis, cystitis, and urethritis. Pyuria is detected in 95% of cases. Proteinuria is not typical for patients with nephrolithiasis.

The treatment of most conditions in which stones form in the urinary organs is currently based mainly on the symptoms, and not on the causes. A full understanding of the molecular causes of these conditions, including the identification of mutant genes and their gene products, should lead to more rational treatment protocols. The most significant radical changes in this direction occurred due to the identification of gene defects in PG1 (MsK 259900), for which enzyme replacement therapy with liver transplantation has become effective and long-term. The expansion of this direction, in which the identification of all defective genes in urolithiasis is carried out, cannot be implemented before the introduction of gene therapy as a "routine" procedure in treatment. The correspondence of gene mutations and severe forms of urolithiasis makes prenatal diagnosis possible and promising.

Oxalate metabolism in healthy people is well balanced. Even under normal circumstances, urine is super saturated with calcium oxalate and, accordingly, small changes in oxalate homeostasis lead to an imbalance in favor of crystallization. If the changes in normal metabolism are insignificant or non-specific, as in some familial forms of urolithiasis, the true signs of heredity may be masked by the influence of environmental factors, making it difficult for functional or positional cloning.

Methods of treatment of children with UL are diverse, but they can be divided into two main groups: conservative and operative. The choice of the treatment method depends on the following factors: the general condition of the patient, age, the clinical course of the disease, the size and localization of the stone, the anatomical and functional state of the kidney, the stage of chronic renal failure. But still, UL is primarily a surgical disease, so conservative therapy is not considered as an alternative to removing a stone using one of the modern methods of surgical treatment. The only exceptions are concretions consisting of uric acid salts-urates, which can be successfully dissolved with citrate mixtures. Types of surgical treatment: open operations (pyelolithotomy, ureterolithotomy, and others); remote shock wave lithotripsy (SWL); percutaneous nephrolitholapaxy; transurethral endoscopic operations. The algorithm for treating patients with UL is as follow. When a stone is recalled in the middle and lower third of the pelvis, the methods of SWL and contact lithotripsy can be considered equivalent, especially when the proportions of concretions are more than 2 cm. If the size of the stone does not exceed 2 cm, preference should still be given to SWL. With nephrolithiasis of the upper third of the pelvis, contact lithotripsy is not optimal, since the stones migrate downwards with the irrigation solution. If children with UL have uric acid stones, it is better to try to dissolve them. With a competent approach to such treatment, its effectiveness is 47%, therefore, in this case, it is recommended to conduct litolytic therapy first, and only if it is ineffective to use other methods. In turn, in coral nephrolithiasis, despite the presence of such promising treatment methods as SWL and contact lithotripsy, open surgical intervention, including nephrectomy and kidney resection, is indicated primarily.

Conservative therapy of UL includes: pharmacotherapy, diet therapy, detection and correction of metabolic disorders, anti-inflammatory therapy, effects on organ hemodynamics, immunomodulation. "Stone-expelling" therapy is indicated for small uncomplicated ureteral concretions that can move away on their own, as well as after remote lithotripsy. As a rule, it includes antispasmodics, non-steroidal anti-inflammatory drugs, and herbal medicines. The appointment of antibacterial drugs, taking into account the data of a bacteriological examination of urine and the clearance of endogenous creatinine, is indicated in the case of an attachment of a urinary tract infection.

Etiopathogenetic therapy can be aimed at preventing the recurrence of stone formation and growth of calculus, as well as at the dissolution of stones (litholysis). The diet of patients with UL provides for: the use of at least 2 liters of liquid per day; depending on the detected metabolic disorders and the chemical composition of the stone, it is recommended to limit the intake of animal protein, salt, products containing a large amount of calcium, purine bases, oxalic acid; the consumption of food rich in fiber has a positive effect on the state of metabolism. We can recommend some general principles in observing the diet and water balance: maximum restriction of the total volume of food; its variety; restriction of the consumption of food rich in stone-forming substances; intake of liquid in a volume that supports the daily amount of urine from 1.5 to 2.5 liters. Part of the liquid can be taken in

the form of cranberry or lingonberry fruit drinks, mineral water. Diet therapy for calcium-oxalate stones consists in limiting the use of coffee and cocoa products (chocolate, etc.), strong tea, sorrel, spinach, lettuce, black currants, strawberries, nuts, legumes, citrus fruits, cheese, cottage cheese, milk. With urate stones, it is necessary to limit the intake of protein (animal origin) food, chocolate, coffee, alcohol, fried and spicy dishes and the exclusion of offal (pates, liver sausages, etc.), meat food in the evening. In phosphorus-calcium stones the following groceries are excluded: alkaline mineral waters, milk, spices, spicy snacks; it is worth limiting yourself to eating potatoes, beans, pumpkin, berries, green vegetables, cottage cheese, cheese, cheese. Recommended: meat food, grapes, green apples, pears, lard, flour products, vegetable fats, sauerkraut, lingonberries, red currants, kefir, sour cream.

Thus, today, in some cases, open surgical interventions are allowed. This applies to complex situations (reconstruction of the urinary tract, purulent-inflammatory process, coral stones complicated by kidney failure, etc.). The professionalism of urologists in carrying out such operations on the kidneys and ureters should be very high. No matter how fast the improvement and development of new minimally invasive methods of stone removal are carried out, it is impossible to solve the issues of treatment of urolithiasis without using a comprehensive interdisciplinary approach to the postoperative treatment of children (consultations of a urologist, pediatrician, endocrinologist, nutritionist). After successful removal of the stone, an extremely important stage of metaphylaxis of urolithiasis begins, which must necessarily include: treatment of concomitant diseases of the gastrointestinal tract, liver, endocrine glands, musculoskeletal system; active antibacterial therapy of urinary tract infection, conducted on the basis of a study of urine cultures (especially in children with phosphate nephrolithiasis); restoration of kidney function; litolytic therapy (especially effective in urate nephrolithiasis).

There are many methods of getting rid of kidney stones and urinary tract. Until recently, this disease was treated mainly by open, often repeated and traumatic surgery, requiring certain surgical experience and often accompanied by the development of complications. The treatment required a long stay of patients in the hospital and prolonged rehabilitation of patients.

Currently, new surgical aids have been mastered and continue to be developed, allowing in most cases to avoid open surgery, and, without changing the fundamental principles and basics of treatment, to achieve the same result, but with significantly less risk for the organ and the patient. One of the promising methods of treating ureterolithiasis is contact lithotripsy, based on the fragmentation of the concretion by its contact destruction.

There are several types of contact lithotripters exist: electrohydraulic, laser, ultrasonic, pneumatic. Their difference lies in the source and physical and mechanical parameters of the generated shock wave. The method of pneumatic lithotripsy is recognized as the "gold standard" of contact ureterolithotripsy regarding the effectiveness and safety.

However, in the course of accumulating experience and analyzing the long-term results of treatment of ureterolithiasis by contact destruction, it was revealed that the frequency of intraoperative complications of a traumatic and mechanical nature is quite high. The total percentage of such complications reaches 10%. These include – ballistic shock (3%), hematoma formation (3%), ureteral perforation (1%), tear (2%), wall rupture and complete separation of the ureter (1%) [30-35]. According to the research of foreign colleagues, it was noted that the frequency of complications depends on the size of the concretion and the level of its localization. So, with a stone size of up to 5 mm, complications occur in isolated cases. With an increase in the diameter of the concretion, the frequency of intraoperative complications increases significantly.

Endoscopic ureterolithotripsy, along with the destruction of the concrement, should ensure minimal traumatic impact on the ureter wall. However, under the same conditions, a number of patients still experience the above complications, the cause of which is not sufficiently studied. Presumably, it depends on the choice of the lithotripter power, the biomechanical properties of various ureters, the strength of the stone and its chemical composition, as well as the state of the blood coagulation system and the immune system. The biomechanical properties of the ureter depend on the age group of patients, the anatomical level of the ureter, as well as on the genetically determined biomechanical properties of the pacienta connective tissue.

Pediatric patients with stones in the urinary system are considered a high-risk group for the development of recurrent stones. Therefore, studies of the biochemical and genetic status of patients with UL for the presence of stones, as well as metabolic abnormalities play a crucial role.

We studied the effectiveness of surgical treatment of urolithiasis in children, depending on the biochemical and molecular genetic status of patients. The most important stage in the treatment of urolithiasis is the early removal of the stone, especially if this leads to such serious complications as kidney failure, urinary retention, etc. It is very important that the collecting system is freed from stones.

Until now, patients suffering from ICD have been treated mainly by open, often repeated and traumatic surgery, often accompanied by a large number of complications. That is, the only method of treating urolithiasis is mainly surgical treatment. Open traditional surgical interventions for urolithiasis are currently used for purulent-inflammatory complications, scarring of the upper urinary tract, coralloid nephrolithiasis, pionephrosis and kidney shrinking. But the study of this problem has shown that the most effective treatment is an integrated approach. Thus, in the future, the treatment of urolithiasis as a polyethological disease should be complex, but in any case, it is necessary to influence the causal factor (etiotropic treatment) and the mechanisms that contribute to the formation of a concretion (pathogenetic

treatment) as early as possible. Indications for surgical removal of kidney stones and urinary tract stones in children are: pain in the lumbar region, exhausting the child; frequent attacks of pyelonephritis or a progressive course of chronic; recurrent macrohematuria; hydronephrotic transformation; progression of chronic renal failure in bilateral nephrolithiasis.

Thus, among the many factors, the main factors for the development of urolithiasis are hereditary, environmental and prematurity factors.

The presence of a hereditary factor of stone formation in itself may not always lead to stone formation in children. The hereditary factor manifests itself indirectly in combination with other factors of stone formation, the main of which are various anomalies of the urinary system at all its levels.

The complex of therapeutic measures aimed at correcting disorders of the metabolism of stone-forming substances in the body includes: diet therapy, maintaining an adequate water balance, phytotherapy, medicines aimed at dissolving a number of stones, stone-expelling agents, surgical and spa treatment.

In the course of studying this problem, an algorithm for the prevention and metaphylaxis of urolithiasis has also been developed, depending on the main pathogenetic factors.

In most of the patients studied by us (children), the presence of uric acid in the urine in a significant amount was revealed during biochemical analysis. Therefore, we have developed a method for managing patients with uric acid stones. For the purpose of prevention and metaphylaxis, it is necessary to dilute urine by recommending compliance with the water regime (abundant drinking), as well as alkalinization – the appointment of potassium citrate 3-7 mmol x 2-3 times a day.

Metaphylaxis of urolithiasis is a complex of permanent, alternating therapeutic measures for a long time and the same for all types of stone formation. They can only be individual, and their effectiveness should be constantly monitored and corrected. At the same time, both risk factors for stone formation and the functional state of the kidneys and urinary tract, individual sensitivity to medications and concomitant somatic pathology are taken into account.

The main criterion for determining the volume and duration of urolithiasis metaphylaxis measures is the severity of kidney damage: the stage of calculous pyelonephritis, calculous hydronephrosis and their combination and the stages of chronic renal failure (CRF).

When calculous pyelonephritis is activated, the patient is indicated inpatient treatment. One of the important stages of metaphylaxis of urolithiasis is the correction of the pH of urine. It is carried out with the help of a diet, proteolytic enzymes, medicines and mineral water.

Metaphylaxis is a complex task and in each case depends on the form of the disease, the method of removing the stone, the results of additional research methods. Nevertheless, dynamic monitoring of the patient's condition in the process of metaphylaxis is quite effective. Studies show that in patients who were under the supervision of a doctor and received anti-relapse treatment, the frequency of relapses of the disease was 3 times lower compared to those who were not prescribed this treatment.

3. Conclusions

1. In conclusion, it should be noted that the formation of stones in the urinary tract is a pathological condition that affects more and more people around the world, So urolithiasis is a serious problem of the health system. The recurrent nature of the disease focuses not only on the removal of stones from the urinary tract and assistance in the spontaneous exit of stones, but also on suitable ways to correct metabolic disorders, taking into account the biochemical and genetic status of patients with urolithiasis.
2. The effectiveness of UL treatment increases with the use of concrement removal and prevention of primary (for uric acid nephrolithiasis) and recurrent stone formation. Currently, the leading methods in the treatment of UL are aimed at eliminating the concrement. Conservative therapy, which aims to chemically dissolve the stone and prevent its further growth, is ineffective and is used in cases where surgical treatment for one reason or another cannot be performed or complete disintegration of the stone is not achieved. When studying the genetic factor of the development of urolithiasis in children, it became possible to clearly identify the main indications for surgical intervention in children and develop a set of conservative measures to prevent the development of urolithiasis in children after studying the genetic factor.
3. Practice shows that despite the surgical interventions performed to remove the stone in urolithiasis, it is very important to carry out preventive and metaphylactic measures. The role of prevention here will be to prevent the recurrence of concretions in both sick and healthy children, and metaphylaxis is necessary in case of frequent recurrence of the disease due to persistent crystalluria.
4. Interdisciplinary cooperation of general practitioners, surgeons, endocrinologists, pediatricians, nutritionists and urologists is of no small importance in the management of children at risk of developing urolithiasis and postoperative treatment of children.

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