

Postoperative Treatment of Children with Renal Form of Primary Hyperparathyroidism

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Abstract

Background: The metaphylactic measures carried out, including medical and dietary measures in 52 children with primary hyperparathyroidism. Reliably low rate of recurrent stone formation was recorded in patients who followed the recommendations compared with those who partially or did not follow the recommendations at all. **Subjects and Methods:** From 2011 to 2021, 2100 children with urolithiasis were studied retrospectively. 52 (2.47%) children were diagnosed with the renal form of primary hyperparathyroidism. **Results.** Rehabilitation was carried out individually for each patient, taking into account laboratory and clinical analyzes and the mineral composition of the removed calculus. **Conclusion.** Preventive measures were carried out individually for each patient, depending on the etiopathogenesis and complications of the disease. The diet was low in fat and sodium, which was the safest for normal calcium intake without increasing the risk of nephrolithiasis.

Keywords: Urolithiasis, Primary Hyperparathyroidism, Surgery, Pediatric Surgery, Endocrinology.

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Introduction

Urolithiasis is a common disease that affects people of any age. According to epidemiological studies. In various regions of the world the number of patients with urolithiasis ranges from 2 to 12% of the population,^[1,2] patients with urolithiasis make up 30-40% of the total contingent of urological hospitals.^[3,4] In childhood, urolithiasis occurs as often as among the adult population.^[5,6]

Many factors lead to impaired renal functions and the formation of stones, one of them is hyperfunction of the parathyroid gland - primary hyperparathyroidism. Primary hyperparathyroidism is a clinical syndrome with characteristic symptoms and signs caused by an increase in the production of parathyroid hormone by the parathyroid glands. One of the main points of application in the pathogenesis of primary hyperparathyroidism is the damage to the kidneys of the parathyroid hormone. Primarily parathyroid hormone affects the proximal convoluted renal tubules, and secondarily, the distal tubules.^[7]

A number of authors have noted that in 5-10% of children, renal stones formed as a result of hypercalciuria are caused by primary hyperparathyroidism.^[8,9]

There is no doubt that prolonged ischemia of the renal parenchyma with calculus, urostasis, pyelonephritis, sclerosis of the renal parenchyma under the influence of excess calcium and parathyroid hormone, injuries inflicted on the kidney during stone removal affect its further function.^[10-12]

It should be noted that for many patients, removal of stones or discharge of calculi and their fragments from the urinary tract does not mean their recovery.

The aim of the research was to improve the results of surgical treatment of the renal form of primary hyperparathyroidism in children.

Subjects and Methods

From 2011 to 2021, 2100 children with urolithiasis were studied. 52 of them (2.47%) were diagnosed with the renal form of primary hyperparathyroidism.

The objectives of the surgical treatment of the renal form of primary hyperparathyroidism in children were:

1. Determination of indications for primary surgical intervention in renal form of primary hyperparathyroidism in children.

2. Study of complications of primary surgical interventions (hypercalcemia and hypocalcemia) and development of diagnostic and treatment methods.
3. Development of an algorithm for the staging and timing of surgical treatment of the renal form of primary hyperparathyroidism in children.

The choice of the method of primary surgical interventions (treatment) was based on complications of urolithiasis and primary hyperparathyroidism, and was aimed at restoring the function of the kidneys and parathyroid gland. Preoperative preparation and postoperative treatment required an individual approach to each patient, and were aimed at restoring renal function and pathogenetic treatment of primary hyperparathyroidism.

In 23 (44.2%) children of 52 children with renal form, primary hyperparathyroidism was found to have occlusive stones with clinical and laboratory signs of acute pyelonephritis.

In 9 (39.1%) children, primary surgical care was performed using urine diversion by percutaneous puncture nephrostomy. The indication for high urine diversion in 6 children was a palpable, enlarged kidney with a sharp decrease in function ("silent kidney"). In 3 children, exacerbation of chronic calculous pyelonephritis was accompanied by high fever (38-39°C), vomiting, decreased appetite, dry skin, weakness, apathy, physical retardation and anemia of II, III degree. The kidney was enlarged and painful. There was an asymmetry of the abdomen with a lag in the act of breathing of the affected side. In this contingent of children, on the echodopplerogram, a sharp decrease in urine output through the UVS was observed, on the renogram and dynamic nephroscintigraphy, the decrease in kidney function averaged 48.5%.

This method of primary surgical treatment made it possible to avoid such formidable complications as sepsis, bacteriotoxic shock, purulent pyelonephritis, exacerbation of chronic renal failure, etc.

In 24 (46.2%) children, kidney stones did not cause acute occlusion and pyelonephritis attacks. These children began their primary surgical treatment with parathyroidectomy, which prevented the development of hypercalcemia and stone formation.

5 (9.6%) children underwent only parathyroidectomy, their kidney stones did not interfere with the outflow of urine.

Surgical treatment provided to children was carried out in stages and required an individual approach to each sick child, in this regard, we developed an algorithm for the surgical treatment of the renal form of primary hyperparathyroidism.

A retrospective analysis of the treatment of children with renal form of primary hyperparathyroidism showed the possibility of complications associated with the choice of surgical tactics.

Children in the postoperative period were divided into two groups: children who received metaphylactic measures, including drug and dietary treatment (43 / 82.6% /) and children who did not receive metaphylactic treatment (9 / 17.3% /). The control group consisted of children (54 children), patients with urolithiasis without primary hyperparathyroidism. Among children in the control group, 42 (77.7%) children received metaphylaxis, 12 (22.2%) children did not.

In the first year of observation after parathyroidectomy, general clinical and specialized examinations (ultrasound of the kidneys, examination of the level of calcium and inorganic phosphorus in the blood and in daily urine) were carried out monthly, the level of ionized calcium, parathyroid hormone, vitamin D and echoosteometry were investigated quarterly. In the second year and in subsequent periods of observation, the patients were examined twice a year.

Results

Prophylaxis, metaphylaxis and rehabilitation measures depended on the etiopathogenesis of urolithiasis and its complications, was carried out before and in the postoperative period (from the moment of admission of patients to the hospital), individually for each patient and included the following tasks:

1. To improve the functional ability of the kidneys by including the maximum number of nephrons, which will allow faster implementation of the function of homeostasis.
2. Evacuate microbial bodies and elements of purulent inflammation
3. Improve renal blood flow, change the rheological properties of blood, reduce viscosity, which is the prevention of renal vein thrombosis.
4. Conduct rational antibiotic therapy, taking into account the microflora of urine and increase the concentration of antibacterial drugs in the blood serum and in the area of inflammation (fight against pyelonephritis).
5. Anti-relapse therapy, which ensures the cessation of the growth of calculi and their removal from the body.
6. Treatment of concomitant diseases of the gastrointestinal tract, endocrine glands, nervous and musculoskeletal systems
7. Development of diet therapy individually for each patient

In all patients, operations on the kidneys (pyelo-calico-nephrolithotomy) were completed with the installation of drainage tubes into the collecting system of the kidney (nephro-pyelostomy), in order to control the functional state of the kidneys (diuresis), irrigation of the calyx-pelvic system with an aseptic solution (0.1 % dioxidine solution on 0.25% novocaine) to remove macroliths and calculus fragments.

Against pyelonephritis was carried out taking into account the excreted microflora and its sensitivity to antibiotics. According to which, antibiotics and uroantiseptics were used. They were changed every 7-8 days, under the control of a general urinalysis. Antibiotic therapy was carried out until the urine analysis was normalized (urine analysis was repeated every 7 to 10 days).

Kidney stones formed in an alkaline environment (in primary hyperparathyroidism, phosphate, oxalate and mixed stones are formed in an alkaline environment) and consist of the minerals calcium phosphate, calcium oxalate, or mixed minerals. To reduce the urine environment and crystallize phosphates and oxalates, urine output was increased (from 1 to 2 - 2.5 liters per day), taking into account the hydrolability of the child's body. The pH of the urine was investigated during the day, in a fresh portion of urine, at each act of urination. With an increase in urine alkalinity, methionine was used (0.25 mg, orally).

To reduce the excretion of calcium by the kidneys, the use of table salt (the main source of sodium in the human body) was limited (up to 80-100 mg / kg per day).

The state of hypercalcemia and hypercalciuria in primary hyperparathyroidism should have been eliminated after parathyroidectomy, but hypercalciuria persisted and was observed in the long-term follow-up period (2-5 years), which indicated a continuing low level of calcium reabsorption in the renal tubules. To restore this process, a thiazide diuretic was used (hypothiazide 12.5 mg / day).

Choleretic drugs allochol (1 tablet 3 times a day after meals), holosas ($\frac{1}{4}$ -1/2 teaspoon 2-3 times a day) and corn silk (decoction 1-2 tablespoon every 3-4 hours) helped to reduce the absorption of calcium in the intestine.

To increase the resistance of the renal tissue to hypoxia, inhibition of platelet aggregation, and accelerate the formation of collateral blood flow in the renal parenchyma, curantil and trental (in tablets, for 1-1.5 months) were used. They have antiplatelet, vasodilating properties, inhibit phosphotidyl esterase, reduce blood viscosity, increase oxygen exchange in the renal nephrons and normalize sodium reabsorption. The rheological properties of blood were increased by using rheopolyglucin (10 ml / kg, i.v.).

Dimephosphon is an antihypoxic, membrane-stabilizing, immunostimulating drug, has an anti-inflammatory, radio-protective effect (30-50 mg / kg, 2-3 times a day, by mouth). It restores the metabolic processes of the renal tissue, normalizes the acid-base state, improves blood circulation in organs and tissues.

Nicotinic acid was used to reduce the sclerotic processes of the renal tissue and blood vessels (20-30 days, twice a year). Venoruton promoted the free movement of venous blood through the vessels of the kidneys (300 mg, inside for 12-15 days, 2-3 courses with an interval of 20-30 days).

Anabolic steroid - retabolil (once every 15 days) stimulates the synthesis of proteins in the body, provides calcium retention in bones and increases the calcification of bone tissue in osteoporosis, improves appetite and general condition of children, promotes weight gain.

Almagel (1-2 teaspoons, 20-30 minutes before meals) helped to normalize the level of calcium and phosphorus in daily urine.

Cimetidine (150 mg, 4 times a day, orally), as a histamine-H2 antagonist, reduced gastroduodenal symptoms. The drug, which does not affect the pharmacokinetics of cimetidine, but reduces the toxic effect of calcium, amlodipine (Norvasc) was prescribed at 1.5 mg / kg per day by mouth.

Treatment aimed at preventing the development of recurrent stones and the growth of residual stones, their removal from the body was carried out individually, pathogenetically justified, taking into account the mineral composition of the calculus, microflora and urine pH.

The results of the study of the mineral composition of the removed stones, together with the data of the study of mineral metabolism, hormonal studies, formed the basis for the planning of metaphylaxis.

Metaphylactic measures were carried out individually for each child, taking into account age, physical development, the mineral composition of the removed stones, the results of metabolic assessment, the functional state of the kidneys, the presence of external and internal risk factors.

Nutrition plays a major role in the pathogenesis of calcium-formed stones (calcium oxalate and calcium phosphate). When formulating the diet, the consumption of foods low in fat and sodium (table salt) was encouraged; which was safe for normal calcium intake without increasing the risk of nephrolithiasis.

Correction with the help of dietary factors in urolithiasis, in our opinion, should consist in creating conditions that prevent the growth of existing stones and the formation of new ones, contributing to the spontaneous discharge of the latter. The effect of the therapeutic diet should ultimately potentiate the action of litholytic agents.

The recommended diet was based on the following principles: a) restoration and maintenance of (neutral or slightly acidic) urine reaction, thereby preventing microcrystallization; b) satisfy the sick child's need for proteins, fats, carbohydrates and other food components; c) correspond to the functional state of the kidneys; d) exclude fatty milk and fried (fatty) dishes; e) 7-9 meals a day during the day, in small portions within the diet.

The carried out therapeutic and prophylactic measures (metaphylactics) aimed at restoring kidney function, reducing the exacerbation of pyelonephritis, preventing the formation of

Table 1: Clinical evaluation of the results of metaphylaxis in children with urolithiasis

Analysis group	Clinical recovery		Recurrence of stones		of HPT*		Impaired renal function		Total		
	Abs	%	Abs	%	Abs	%	Abs	%	Abs	%	
Urolithiasis without PHPT n -54	Metaphylaxis +	42	77,7	1	1,85	-	-	1	1,85	44	81,5
	Metaphylaxis -	6	11,1	5	9,2	-	-	3	5,5	14	25,9
Urolithiasis with primary PHPT n-52	Metaphylaxis +	43	82,6	1	1,9	-	-	2	3,8	46	88,4
	Metaphylaxis -	2	3,8	5	9,6	3	5,7	5	9,6	15	28,8
Total		93		12		3		11		119	

HPT = Hyperparathyrenemia

Table 2: Standards for the rehabilitation treatment of children with primary hyperparathyroidism urolithiasis

Symptoms and syndromes	Clinical manifestations	Medicinal product (dose and duration)
Hypercalcemia < 2.5 mmol / L	Drowsiness, weakness, stupor, psychosis, nausea, anorexia, constipation	0.9% NaCl (400-600 ml / day), aminophylline 2.4% 3-5 ml IV. Furasemide 20-40 mg IV. Dimphosphone 30 mg / kg 3-4 times a day, Almagel 1 h / 1 30 minutes before meals. Indomethacin 25 mg 3 times orally, after meals
Hypocalcemia > 2.0 mmol / L	Numbness of limbs, sensation of twitching, muscle twitching, positive symptom of Khvostek, Trousseau	Calcium chloride 1-1.5 g, or calcium gluconate 4-5 g per day, Vitamin D3 individually (2-3 capsules per day). Limiting milk and dairy products. Weekly monitoring of blood calcium levels
Bone and joint pain, osteoporosis (bone ultrasound < 3050 m/sec)	Arthralgia, ossalgia, myalgia, bone and joint pain	Retabolil 5% 10-20 mg / m 1 time in 3-5 days No. 5. Ergocalciferol 3000 IU 15-30 days under medical supervision
Recurrent kidney stones	Pain in the abdomen and lumbar region, dysuria, changes in urinalysis	Herbal diuretic diuretic, 1 ca-psule 3p per day for 2 months), diet (exclude fatty, fried foods and table salt), preparations: magnesium oxide 0.1 g / day, cystenal 2-3 drops for sugar, cyston 1/2 t. 3 p. In a day. Marelin 1 t. 3 r. per day, kanephron 1 dr. 3 r., allopurinol 150-200 mg / day, spilled 2 t. 3 r., phytolysin 1 h / 1 for 1/2 cup boiling water 3 r., urolesan 6-8 drops for sugar, 4-6 p. per day, ATP 1.0 ml / m No. 30, KKB 0.05 g / day, / m, No. 30.
Renal dysfunction (urea >13-15 mmol/l, creatinine 130-150 μmol/l)	Weakness, lethargy, malaise, retardation in physical development, anemia, uremia.	Broad-spectrum antibiotics based on urine culture. Ca D ₃ nycomed 1 t. 3 r., Lespinephril 1 h / 1 4 r. Depyridamole 2 mg / kg. Unitol 3.0 ml, i / m, 1 time. Trenthal mornings. 2 other in the afternoon and in the evening 1 other int. Vitamins of group B, A, and E. Paraffin applications in the region. kidneys. Protein and sodium restricted diet.

recurrent stones, dissolving and removing residual and fragments of calculus gave positive results.

Of 52 children with urolithiasis 43 (82.6%) children followed the doctor's recommendations in a timely manner and in full, 9 (17.3%) children did not attend dispensary observation and did not follow the recommendations of doctors or did not fully [Table 1].

Clinical recovery was observed in 2 (22.2%) children out of 9 who did not receive metaphylaxis.

In children who received metaphylaxis in a timely manner, a relapse of stone formation was recorded in 1 (2.3%) case, in children who did not receive metaphylaxis, a relapse of stone formation was recorded in 5 (55.6%) children ($P < 0.05$).

In the long-term follow-up, 3 (33.3%) children showed an increase in the level of parathyroid hormone (72.8 ± 7.0 pg / ml), vitamin D (11.4 ± 1.3 pg / ml) and calcium in urine (3.9 ± 0.25 mmol / day). In 2 (22.2%) children who did not receive metaphylaxis, the development of renal dysfunction was observed in the postoperative period.

For rehabilitation of children with primary hyperparathyroidism urolithiasis the standards of rehabilitation treatment were applied, which are shown in [Table 2].

Conclusion

Thus, the performed metaphylactic measures, including medication and dietary measures, made it possible to increase the efficiency of surgical treatment of urolithiasis and primary hyperparathyroidism. A reliably low rate of recurrent stone formation was recorded in patients who followed the recommendations in full compared with those who partially or did not follow them at all.

Preventive measures must be carried out individually for each child, depending on the etiopathogenesis and complications of the disease. Prescribe a diet low in fat and sodium; it is the safest route to normal calcium intake without increasing the risk of nephrolithiasis (for a growing body).

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