Metaphylaxy Of Urolithiasis Disease In Children With Renal Form Of Primary Hyperparathyroidism

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Summary: The conducted metaphylactic measures including medication and dietary measures in 52 children with ULD of PGPT genesis allowed to increase the efficiency of surgical treatment of urolithiasis and primary hyperparathyroidism. A significantly low rate of recurrent stone formation in patients who fulfilled the recommendations in full compared to those who fulfilled them partially or not at all was registered. Metaphylactic measures were carried out individually for each child depending on the etiopathogenesis and complications of the disease. A diet low in fat and sodium (table salt) was prescribed; this was the safest for normal calcium intake without increasing the risk of nephrolithiasis (for the growing organism).

Relevance: Urolithiasis disease (ULD) is a common disease occurring in people of any age. According to epidemiologic studies, in different regions of the world, the number of patients with ULD ranges from 2 to 12% of the population [1, 7], patients with urolithiasis make up 30-40% of the total contingent of urologic hospitals [3, 9]. ICH is as common in children as in adults [3, 5, 7, 9].

Many factors contribute to renal dysfunction and stone formation, one of which is parathyroid hyperfunction - primary hyperparathyroidism (PHPT). PHPT is a clinical syndrome with characteristic symptoms and signs due to increased production of parathyroid hormone (PTH) by the parathyroid glands. One of the main points of application in the pathogenesis of PHPT is renal damage by PTH. Primary parathyroid hormone affects proximal convoluted renal tubules and secondary affects distal tubules [2].

According to some authors among patients with urolithiasis (UL) in 5-15% of cases is determined PGPT, according to the results of the study of Soreide J. A. with a group of authors (1996) among patients with PHPT in 30% of cases is observed UL [6, 8]. A number of authors have noted that in 5-10% of children renal stones formed due to hypercalciuria are due to primary hyperparathyroidism [4, 6].

There is no doubt that prolonged ischemia of the renal parenchyma by a kidney stone, urostasis, pyelonephritis, sclerosis of the renal parenchyma under the action of excessive calcium and PTH, trauma inflicted on the kidney during stone removal, affect its further function.

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

Objective: To improve the results of surgical treatment of renal primary hyperparathyroidism (PHPT) in children.

Material and methods: 2100 children with urolithiasis were studied from 2002 to 2022. Of these, 52 (2.47%) children were diagnosed with renal form (RF) of PHPT, and they underwent surgical interventions: parathyroidectomy (PTE), percutaneous nephrostomy (PCNS) and removal of renal stones.

The choice of the method of primary surgical interventions (treatment) was based on the complications of ULD and PHPT, and was aimed at restoring renal function and thyroid function. Preoperative preparation and postoperative treatment required an individual approach to each patient and were aimed at restoration of renal function and pathogenetic treatment of PHPT.

Obturating stones with clinical and laboratory signs of acute pyelonephritis were detected in 23 (44.2%) children out of 52 children with RF PHPT. Retrospective analysis of treatment of children with showed the possibility of complications associated with the choice of surgical intervention tactics.
Children in the postoperative period were divided into two groups: children who received metaphylactic measures including medication and dietary treatment (43 /82.6/%) and children who did not receive metaphylactic treatment (9/17.3%/).

Children (54 children) with ULD without PHTP served as the control group. Among children in the control group, 42 (77.7%) children received metaphylaxis and 12 (22.2%) children did not.

In the first year of follow-up after PTE, general clinical and specialized examinations (renal ultrasound, calcium and inorganic phosphorus levels in blood and daily urine) were performed monthly, ionized calcium, PTH, vitamin D levels and echosteometry were examined quarterly. In the second year and in the subsequent periods of observation, the patients were examined twice a year.

RESULTS: Prophylaxis, metaphylaxis and rehabilitation measures depended on etiopathogenesis of urolithiasis and its complications, were carried out before and after the operation (from the moment of patients' admission to the hospital), individually for each patient and included the following tasks:

1. Improve the functional capacity of the kidneys by incorporating the maximum number of nephrons, allowing faster homeostasis function.
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 urine microflora and create the concentration of antibacterial drugs in the serum and in the area of inflammation (control of pyelonephritis).
5. Anti-recurrence therapy to ensure the cessation of growth of concrements and their excretion from the body.
6. Treatment of associated diseases of the gastrointestinal tract, endocrine glands, nervous and musculoskeletal system.
7. Development of dietary therapy is individualized for each patient.

In all patients renal surgeries (pyelo-calico-nephrolithotomy) were finished 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-lochanous system with an aseptic solution (0.1% dioxidine solution on 0.25% novocaine) to remove macroliths and fragments of the concrement.

Control of pyelonephritis was carried out taking into account the isolated 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 the general urine analysis. Antibiotic therapy was carried out until normalization of urine analysis (urine analysis was repeated every 7-10 days).

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

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

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

Diuretics allochol (1 tablet 3 times a day after meals), cholosas (¼-1/2 teaspoon 2-3 times a day) and corn stigmas (decoction of 1-2 tablespoons every 3-4 hours) helped to reduce calcium absorption in the intestine.

To increase renal tissue resistance to hypoxia, inhibition of platelet aggregation, acceleration of collateral blood flow formation in renal parenchyma we used curantil, trental (in tablets, for 1-1.5 months). They have antiaggregant, vasodilator properties, inhibit phosphotidyl esterase, reduce blood viscosity, increase oxygen
exchange in renal nephrons and normalize sodium reabsorption. Blood rheological properties were increased by using rheopolyglULin (10 ml/kg, intravenously).

Dimefosfon is an antihypoxic, membrane-stabilizing, immunostimulating, anti-inflammatory, radioprotective effect (30-50 mg/kg, 2-3 times a day, orally). It restores metabolic processes of renal tissue, normalizes acid-base state, improves blood circulation in organs and tissues.

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

Anabolic steroid - retabolil (once every 15 days) stimulates protein synthesis in the body, provides calcium retention in the bones and increases 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 normalize calcium and phosphorus levels in daily urine.

Cimetidine (150 mg, 4 times a day, orally) as a histamine-H2 antagonist reduced gastroduodenal symptoms. The drug not affecting pharmacokinetics of cimetidine, but redULing the toxic effect of calcium amlodipine (Norvasc) was administered at 1.5 mg/kg per day orally.

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

The results of the study of mineral composition of removed stones together with the data of mineral metabolism study, hormonal studies formed the basis for planning 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 evaluation, the functional state of the kidneys, and the presence of external and internal risk factors.

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

Correction with the help of dietary factors in ICD, in our opinion, should be to create conditions that prevent the growth of existing stones and the formation of new ones, promoting the spontaneous passage of the latter. The effect of the therapeutic diet should eventually potentiate the effect of litholytic agents.

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

The treatment and prophylactic measures (metaphylaxis) aimed at restoring renal function, redULing the exacerbation of pyelonephritis, preventing the formation of recurrent stones, dissolution and excretion of residual and fragments of the nodule gave positive results.

Out of 52 children with ICD of PHPTgenesis, 43 (82.6%) children fulfilled doctor's recommendations in time and in full, 9 (17.3%) children did not attend dispensary observation and did not fulfill doctor's recommendations or did not fulfill them in full (Table 1).

Only 2 (22.2%) children out of 9 who did not receive metaphylaxis showed clinical recovery.

| Table 1 |
| Clinical evaluation of metaphylaxis results in children with ULD of the PHPT genesis |
### Table 1

<table>
<thead>
<tr>
<th>Analysis Group</th>
<th>Clinical recovery- lengths</th>
<th>Relapse stones</th>
<th>Hyperparatirin emiya</th>
<th>Dysfunction. Kidneys</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Abs</td>
<td>%</td>
<td>Abs</td>
<td>%</td>
<td>Abs</td>
</tr>
<tr>
<td><strong>ULD with out PHPT n -54</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Those receiving metaphylaxis</td>
<td>42</td>
<td>77,7</td>
<td>1</td>
<td>1,85</td>
<td>-</td>
</tr>
<tr>
<td>Not receiving metaphylaxis</td>
<td>6</td>
<td>11,1</td>
<td>5</td>
<td>9,2</td>
<td>3</td>
</tr>
<tr>
<td><strong>ULD witht PHPT n-52</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Those receiving metaphylaxis</td>
<td>43</td>
<td>82,6</td>
<td>1</td>
<td>1,9</td>
<td>-</td>
</tr>
<tr>
<td>Not receiving metaphylaxis</td>
<td>2</td>
<td>3,8</td>
<td>5</td>
<td>9,6</td>
<td>3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>93</td>
<td>12</td>
<td>3</td>
<td>11</td>
<td>119</td>
</tr>
</tbody>
</table>

In children who timely received metaphylaxis, recurrence of stone formation was registered in 1 (2.3%) case; in children who did not receive metaphylaxis, recurrence of stone formation was registered in 5 (55.6%) children (P<0.05).

In the remote follow-up period, 3 (33.3%) children had elevated levels of PTH (72.8±7.0 pg/mL), vitamin D (11.4±1.3 pg/mL), and urinary calcium (3.9±0.25 mmol/d). In 2 (22.2%) children who did not receive metaphylaxis, the development of renal dysfunction was observed in the postoperative period.

Rehabilitation was carried out individually for each sick child, taking into account laboratory and clinical analyses and the mineral composition of the removed nodule.

**Conclusion:** Thus, metaphylactic measures, including medication and dietary measures, allowed to increase the effectiveness of surgical treatment of urolithiasis and primary hyperparathyroidism. There is a significantly low rate of recurrent stone formation in patients who implemented the recommendations in full compared to those who implemented them partially or not at all.

Metaphylactic measures should be carried out individually for each child depending on the etiopathogenesis and complications of the disease. A diet low in fat and sodium (table salt) is the safest way to achieve normal calcium intake without increasing the risk of nephrolithiasis (for the growing body).

**Literature**