

## THE LOADING TESTS IN DIAGNOSTICS OF THE KIDNEY FORM OF PRIMARY HYPERPARATHYROIDISM IN CHILDREN

### ABSTRACT

**Background.** The aim of the research is to determine the value of stress tests in the diagnosis of the renal form of primary hyperparathyroidism in children.

**Materials and methods.** From 2018 to 2020, 800 children with urolithiasis arrived at our clinic. Based on clinical, biochemical and instrumental studies (the content of total calcium and inorganic phosphorus in the blood and in daily urine, ionized calcium, exercise tests with calcium and sodium chloride, the content of parathyroid hormone (PTH), calcitonin (CT), vitamin D and cyclic 3,5-adenosine monophosphate (cAMP) in serum. Of the instrumental methods: X-ray hand bones and ultrasound osteometry), 52 (2.47%) children were diagnosed with a renal form of primary hyperparathyroidism.

**Results.** Of the 52 children with a renal form of primary hyperparathyroidism, hypercalcemia was observed in 13 (25.0%) children, hypophosphatemia in 12 (23.0%) children. Normocalcemia was observed in 34 (65.3%) children, and in 5 (9.6%) children the calcium content was below normal. 35 (67.3%) children had normophosphatemia, and only 5 (9.6%) children had hyperphosphatemia. Hypercalciuria was observed in 41 (78.8%) children and hyperphosphaturia in 37 (71.1%) children; in other children, the indicators were within the normal range.

**Conclusion.** Thus, stress tests with calcium and sodium chloride are specific diagnostic tests and increase the efficiency of the diagnosis of the renal form of primary hyperparathyroidism, help to differentiate primary hyperparathyroidism from other hypercalcemic and hypercalciuric conditions.

**KEY WORDS:** kidney, primary hyperparathyroidism, hypercalciuria, load tests

### INTRODUCTION

Today, the pathogenesis of urolithiasis is a rather complex chain of biochemical disorders and is a polyetiological disease. Despite such an in-depth study of the pathogenesis of this disease, the diagnosis of ICD is carried out only by the fact of its complication, namely, by the presence of a stone in the urinary tract, detected by x-ray or ultrasound, or by direct discharge of the stone [1, 2, 3].

Stone formation in the kidneys can cause one, less often several factors, but, as a rule, when there are pathogenetic conditions conducive to this [4].

The basis of the pathogenesis of nephrolithiasis are metabolic disorders and, above all, the metabolism of lithogenic substances, as well as promoters and inhibitors of stone formation [5].

In this article, we tried to parse urolithiasis, which occurs against the background of hyperparathyroidism

The solution to the problem of diagnosing the renal form of primary hyperparathyroidism (RF PHPT) in children prevents the development of its complications [6]. The latent course of the process, the polymorphism of nosological forms, the absence of specific laboratory tests is the cause of the delayed and erroneous diagnosis of primary hyperparathyroidism, leading to the early formation of severe forms of urolithiasis [7, 8, 9]. It is known that the study of calcium and phosphorus in the blood and in daily urine is not enough to diagnose primary hyperparathyroidism, normal levels of calcium and phosphorus in the blood serum do not exclude primary hyperparathyroidism [10, 11, 12].

The aim of the research is to determine the value of stress tests in the diagnosis of the renal form of primary hyperparathyroidism in children.

## **MATERIALS AND METHODS**

From 2018 to 2020, 800 children with urolithiasis arrived at our clinic. Based on clinical, biochemical and instrumental studies (the content of total calcium and inorganic phosphorus in the blood and in daily urine, ionized calcium, exercise tests with calcium and sodium chloride, the content of parathyroid hormone (PTH), calcitonin (CT), vitamin D and cyclic 3,5-adenosine monophosphate (cAMP) in serum. Of the instrumental methods: X-ray hand bones and ultrasound osteometry), 52 (2.47%) children were diagnosed with a renal form of primary hyperparathyroidism. The article analyzes the results of a study of load samples with calcium and sodium chloride.

Calcium loading test was carried out by intravenous administration of 10% calcium chloride solution at the rate of 12.4 mg / kg. The serum calcium levels were examined before and after the test for 20 and 120 minutes.

The transport of calcium cation in the renal tubules is associated with a sodium cation. Sodium is an osmotically active substance. Under the influence of a hypertonic solution of sodium chloride, osmotic hypertension develops. In conditions of osmotic diuresis, the excretion of sodium and calcium occur interconnected, which based of the load test with 5% sodium chloride (0.125 ml / kg / min for 45 minutes).

## RESULTS

Of the 52 children with a renal form of primary hyperparathyroidism, hypercalcemia was observed in 13 (25.0%) children, hypophosphatemia in 12 (23.0%) children. Normocalcemia was observed in 34 (65.3%) children, and in 5 (9.6%) children the calcium content was below normal. 35 (67.3%) children had normophosphatemia, and only 5 (9.6%) children had hyperphosphatemia. Hypercalciuria was observed in 41 (78.8%) children and hyperphosphaturia in 37 (71.1%) children; in other children, the indicators were within the normal range. The content of total calcium in the blood in children of the control group (patients with urolithiasis) was  $2.31 \pm 0.12$  mmol / liter; at 20 minutes after the administration of calcium chloride, it increased to  $2.93 \pm 0.12$  mmol / liter ( $p < 0.02$ ), at 120 minutes from the moment of administration, the total calcium content returned to the initial level ( $2.36 \pm 0.13$  mmol / liter) (Table 1).

Table 1

### The results of the calcium test in the examined children (mmol / liter)

Analyzed groups	Total calcium (before the test)	Total calcium content at 20 Minutes	Total calcium at 120 minutes
Children with urolithiasis (n = 54)	2,31±0,12	2,93±0,12*	2,36±0,13
Children with kidney form of primary hyperparathyroidism (n = 52)	2,36±0,14	2,97±0,13*	3,03±0,1*

Note: \* - reliability in relation to the indicator before the sample

In children with a kidney form of primary hyperparathyroidism, the level of total calcium before the test was  $2.36 \pm 0.14$  mmol / liter; at 20 minutes it increased to  $2.97 \pm 0.13$  mmol / liter ( $p < 0.05$ ). At 120 minutes, the total calcium content was  $3.03 \pm 0.1$  mmol / liter ( $p < 0.02$ ).

The study of the effect of sodium on calcium homeostasis was carried out by intravenous administration of a 5% solution of sodium chloride (0.125 ml / kg / min for 45 minutes) which increases the excretion of calcium through the tubular apparatus of the kidneys. The study of calcium in the blood and in daily urine was performed before and after the test (table. 2).

Table 2

## Test results with a load of 5% sodium chloride in children

Analyzed groups	Calcium Content			
	before the test		after the test	
	in blood (mmol / l)	per day urine (mmol / day)	in blood (mmol / l)	per day urine (mmol / day)
<b>Children with urolithiasis (n = 54)</b>	2,41±0,17	2,22±0,21	2,38±0,135	<b>2,43±0,2</b>
<b>Children with kidney form of primary hyperparathyroidism (n = 52)</b>	<b>2,45±0,17</b>	<b>3,85±0,22</b>	<b>2,45±0,14</b>	<b>6,07±0,25*</b>

Note: \* reliability of indicators before and after the test

The calcium content in daily urine in children of the control group (patients with urolithiasis) before the test was  $2.22 \pm 0.21$  mmol / day, after the test this indicator increased to  $2.43 \pm 0.20$  mmol / day ( $p > 0.05$ )

In children with a renal form of primary hyperparathyroidism, the level of calcium in the daily urine before the test ( $3.85 \pm 0.22$  mmol / day) was higher compared with the indicator in children in the control group ( $2.22 \pm 0.21$  mmol / day) ( $p < 0.01$ ), the introduction of a 5% solution of sodium chloride (0.125 ml / kg for 45 minutes) contributed to a further increase in its level in the urine ( $6.07 \pm 0.25$  mmol / day) ( $p < 0.001$ ).

The content of total calcium in the blood serum in children of the comparison group (children with urolithiasis) before and after the test almost remained at the same level ( $2.41 \pm 0.17$  and  $2.38 \pm 0.13$  mmol / liter, respectively), in the daily urine after the test, there is a slight increase in this indicator ( $2.22 \pm 0.21$  and  $2.43 \pm 0.2$  mmol / day, respectively).

In children of patients with a renal form of primary hyperparathyroidism, the level of serum calcium in the blood before and after the test, as well as in the comparison group, remained at the same level ( $2.45 \pm 0.17$ ), but in daily urine there was a significant increase in this indicator after the test was 1.6 times ( $p < 0.001$ ). When comparing the calcium content in daily urine after a test in this group of sick children with the comparison group, a significant increase of 2.5 times ( $p < 0.001$ ) was noted, in the blood its level increased slightly ( $p > 0.05$ ).

## DISCUSSION

Artificial increase in the level of calcium in the blood, reduces the function of the parathyroid gland, stops the absorption of calcium through the walls of the

intestine, decreases the reabsorption of calcium. The calcitonin produced by the thyroid gland contributed to the normalization of serum calcium levels in children of the control group.

After the introduction of calcium chloride (12.4 mg / kg), its blood level was examined at 20 and 120 minutes. The calcium content in children of the comparison group at 120 minutes returned to its original level, in patients with renal form (RF PHPT) its level was 1.3 times higher. The test was sensitive and made it possible to detect hypercalcemia in 39 children, in whom there was normal and hypocalcemia. Impaired renal function did not affect the significance of the sample.

Under the influence of a hypertonic solution of sodium chloride, osmotic hypertension develops. Under conditions of osmotic diuresis, the elimination of calcium and sodium cations is interconnected. An increase in the level of sodium in the loops of Henley and the distal renal tubules stimulates the excretion of sodium, reducing its reabsorption, which leads to an increase in the level of calcium in daily urine in children with PHT.

A sample with sodium chloride made it possible to detect hypercalciuria in 11 (21.1%) children who had normocalciuria

In primary hyperparathyroidism, adenomatous and (or) hyperplastic parathyroid glands, working autonomously, produce excess parathyroid hormone, the latter increases the absorption of calcium through the intestinal wall, promotes the release of calcium from bone tissue into the blood, and increases the reabsorption of calcium in the distal renal tubules.

Thus, in the body of children of patients with a renal form of primary hyperparathyroidism after calcium administration, its level remains within high numbers. The test turned out to be sensitive and made it possible to detect hypercalcemia in the examined children who had normocalcemia (34 children) and hypocalcemia (5 children). Impaired renal function did not affect the significance of the sample.

The transport of calcium cation in the renal tubules is associated with a sodium cation. The content of these cations in the renal tubules varies proportionally. Under the influence of a hypertonic solution of sodium chloride, osmotic hypertension develops. Under conditions of osmotic diuresis, the elimination of calcium and sodium cations is interconnected.

Obviously, increasing the level of sodium in the loops of Henley and the distal renal tubules stimulates the excretion of sodium, reducing its reabsorption, which leads to an increase in the level of calcium in daily urine in children with primary hyperparathyroidism.

The sample with sodium chloride turned out to be a sensitive method, and made it possible to detect hypercalciuria in 11 (21.1%) children in whom normocalciuria was observed.

## **CONCLUSION**

Thus, stress tests with calcium and sodium chloride are specific diagnostic tests and increase the efficiency of the diagnosis of the renal form of primary hyperparathyroidism, help to differentiate primary hyperparathyroidism from other hypercalcemic and hypercalciuric conditions.

## **ETHICAL APPROVAL**

The ethical approval for the study was granted by the Committee of Ethical Approval for Researches under the Ministry of Health of the Republic of Uzbekistan.

## **CONSENT**

Written informed consent was obtained from all participants' parents of the research for publication of this paper and any accompanying information related to this study. A copy of the written consent is available for review by the authors.

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