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Original Research

Composition and structure of kidney stones in children with primary hyperparathyroidism

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***ABSTRACT*:**
Background: Urolithiasis in children is an important part of urological pediatric practice. Since it is recurring, every effort should be made to identify the underlying metabolic disorder causing her to ensure adequate treatment. In this article, we studied the chemical composition of urinary stones in children with kidney disease of primary hyperparathyroidism. **Materials and Methods:** The study was carried out using the method of X-ray diffraction analysis (X-ray diffraction), which was performed on a DRON-4 diffractometer (Russia). An analysis of the mineral composition of kidney stones was carried out in 54 children with nephrolithiasis (a comparison group) and 47 children with kidneys with primary hyperparathyroidism. **Results:** Unilateral kidney damage with calculus in patients with primary hyperparathyroidism occurred in 16 (15.1%) children, of which 4 (25%) children had multiple stones. Bilateral renal lesion with calculus was observed in 36 (69.2%) children, of which 12 (33.3%) had single-sided single stones, and 24 (67.6%) had multiple bilateral stones. In children with nephrolithiasis in primary hyperparathyroidism, 88 (kidneys) kidneys were affected by calculus. Among them, in 45 (51.1%) kidneys, coral stones were noted. **Conclusion:** A study showed that the mineral composition of kidney stones can be used to judge the damage to the skeletal system in primary hyperparathyroidism. They were characterized by phosphate stones, in the mineral composition of which apatites were found (81.1%) (hydroxylapatite, apatite, whitlockite, brushite, struvite-carbonate-apatite).
Key words: kidneys, urinary stones, urolithiasis, hyperparathyroidism, parathyroid hormone.

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INTRODUCTION

Urinary stones are concentrated layered crystalline aggregates. Concentrated layers are formed as a result of crystal growth, between which there are protein substances - mucoproteins and coloring (pigment) substances [1-3].

In healthy people urine can be detected oxalate, phosphate crystals, uric acid crystals, cystine crystals, etc. Their presence in the urine is not a diagnostic sign of urolithiasis. The composition of urinary stones is divided into mixed stones - calcium oxalate and calcium phosphate (41%), calcium oxalate stones (27%), calcium phosphate stones (7%), magnesium-ammonium phosphate stones (15%), uric acid stones (7 %) and cystine (2%) [4, 5]. According to authors, who studied the composition of kidney stones in 1392 patients, most often kidney stones were formed from calcium oxalate (n = 1041), mixed calcium-oxalate and calcium-apatite stones were detected in 485 (34.8%) patients and 146 (10.5%) of patients with calcium-apatite stones [6].

Calcium-apatite and mixed stones were formed due to renal tubular acidosis and primary hyperparathyroidism [7].

Oxalates (urine reaction is acidic or alkaline) - stones consisting of calcium salts of oxalic acid, usually dark in color, almost black with a prickly surface, very dense. Calcium oxalate is the most common and overly saturated stone forming component, even in normal urine it is 4-5 times higher than its solubility, which has a nephrotoxic effect on kidney epithelial cells [8]. In patients with calcium nephrolithiasis,

hypercalciuria is observed in 40-50% of cases, which develops as a result of increased absorption of alimentary calcium and disturbance of tubular reabsorption. Of these patients, in 40% of cases, idiopathic hypercalciuria is noted [9].
Other previous stone formation factors include calcium phosphate (hydroxylapatite) and calcium phosphate monohydrate, cystine, magnesium phosphate, ammonium phosphate and mucoproteins - these are unsaturated stone precursors. Stones from calcium phosphate are formed in an alkaline environment, cystine in acidic [10, 11].

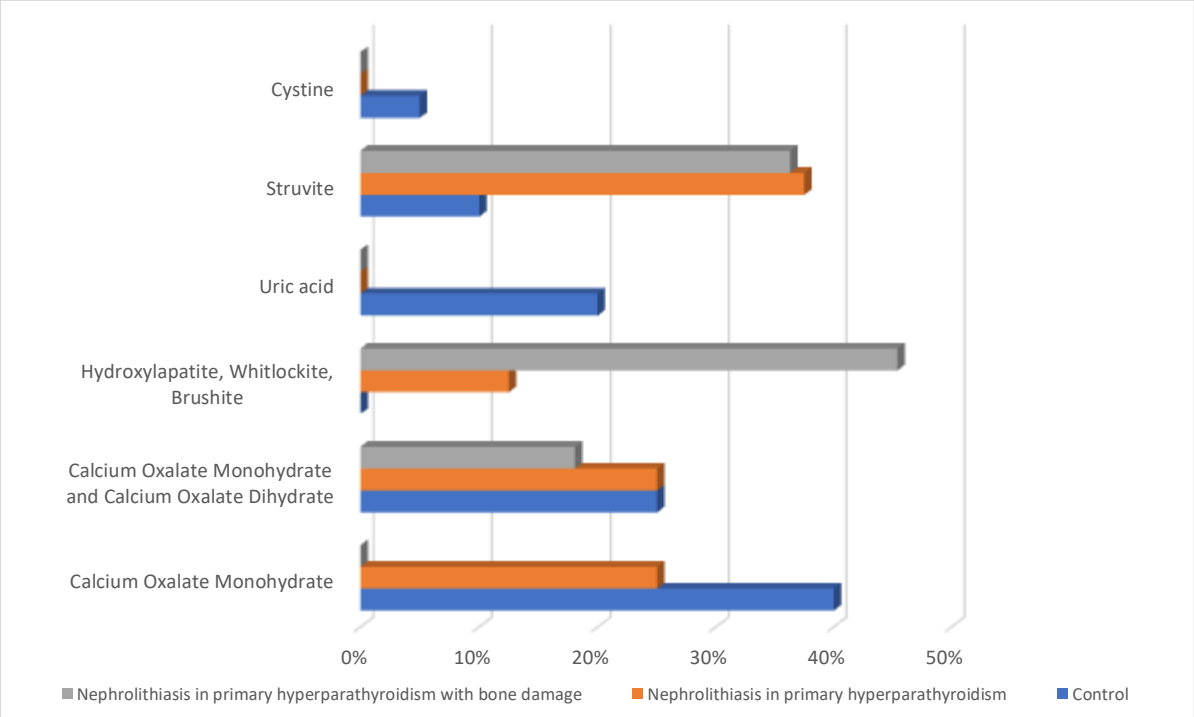
MATERIALS AND METHODS

In our study, an analysis was made of the mineral composition of kidney stones in the examined children. The study was carried out using the method of X-ray diffraction analysis (X-ray diffraction), which was performed on a DRON-4 diffractometer (Russia).
An analysis of the mineral composition of kidney stones was carried out in 54 children with nephrolithiasis (a comparison group) and 47 children with kidneys with primary hyperparathyroidism.

RESULTS

Unilateral kidney damage with calculus in patients with primary hyperparathyroidism occurred in 16 (15.1%) children, of which 4 (25%) children had multiple stones. Bilateral renal lesion with calculus was observed in 36 (69.2%) children, of which 12 (33.3%) had single-sided single stones, and 24 (67.6%) had multiple bilateral stones. In children with nephrolithiasis in primary hyperparathyroidism, 88 (kidneys) kidneys were affected by calculus. Among them, in 45 (51.1%) kidneys, coral stones were noted.
Of the 47 children with nephrolithiasis in primary hyperparathyroidism, in 21 (44.7%) children, according to clinical, biochemical and instrumental methods of investigation (echoosteometry, X-ray densitometry), changes in the skeletal system (osteoporosis) were found.
According to studies in 20 (37.0%) children with nephrolithiasis, monominerals were found in the removed stones - calcium oxalate monohydrate in 8 (40%), calcium oxalate dihydrate and calcium oxalate monohydrate in 5 (25%), uric acid in 4 (20%), struvite in 2 (10.0%) and cystine in 1 (5%) sick children (Fig. 1).
In 8 (30.7%) children with the renal form of primary hyperparathyroidism, monomineral calcium oxalate monohydrate was detected in 2 (25.0%) patients, calcium oxalate monohydrate and calcium oxalate dihydrate in 2 (25.0%) patients, hydroxylapatite, whitlockite, brushite - in 1 (12.5%) child, struvite - in 3 (37.5%) children.
In 11 (52.3%) children of patients with renal form of primary hyperpar-athyroidism with bone damage, stones consisting of monominerals were detected - calcium oxalate monohydrate and calcium oxalate dihydrate in 2 (18.1%) children, hydroxyapatite, whitlockite, and brushite in 5 (45.4%) of children, struvite in 4 (36.3%). In children with bone damage, monomineral stones in 18.1% of cases consisted of calcium oxalate, and 81.8% of calcium phosphate, against 90 and 10% of the children in the comparison group.

Fig. 1 Composition of kidney stones consisting of monominerals in the examined children



Monominerals, calcium oxalate monohydrate and calcium oxalate dihydrate, joining calcium cations, in 6 (12.7%) children out of 47 children with primary hyperparathyroidism formed oxalate stones. Of these, 4 (66.6%) patients were children without bone damage and 2 (33.3%) with bone damage.

Stones consisting of calcium phosphate monominerals were noted in 6 (12.7%) children, of which 5 (83.3%) children showed bone lesions. It should be noted that in the comparison group of children, these monominerals were not found in the composition of renal stones.

Infectious stones (struvit-hydroxylapatite) were observed in 10 children, of which 7 (70.0%) children were treated with patients with renal form of primary hyperparathyroidism, of which 4 (57.1%) children had a lesion of the skeletal system. During bacteriological examination of the urine of these children, urease pathogens of the staphylococcus producing bacteria, Proteus and Klebsiella were seeded.

Monomineral urate stones with primary hyperparathyroidism were not observed.

DISCUSSION

The study of stone-forming oxalate and calcium markers in daily urine gives a significant effect in the diagnosis and treatment of the disease.

However, the frequency and nature of stone formation during primary hyperparathyroidism remains controversial, the composition of the detected urinary stones does not always correspond to generally accepted ideas.

Specific signs and symptoms of primary hyperparathyroidism are manifested mainly from the kidneys and skeleton. In 60–70% of patients with primary hyperparathyroidism, kidney pathology was found due to either calcium deposition in the renal parenchyma or recurrent nephrolithiasis [12].

Kidney stones usually consist of oxalate or calcium phosphate. Repeated stone formation or the formation of large stones can lead to obstruction of the urinary tract and infection and impair renal function. Increased urinary calcium excretion predisposes to nephrolithiasis formation. Nephrocalcinosis also reduces renal function and causes phosphate retention. Increased parathyroid function is manifested by damage to the kidneys and skeletal system. Under the direct influence of excess calcium and parathyroid hormone on the kidney tissue, its mitochondrial activity decreases, which contributes to the excessive accumulation of mucoproteins in them [13]. Mucoproteins lead to urothelial necrosis and the accumulation of protein compounds in the renal tubules. Protein compounds form an organic basis - the matrix, the accumulation of calcium crystals in them contributes to the formation of spherulites, increasing in size, they turn into macrolites, which, descending on the collective system of the kidneys, form the nucleus of future calculi. The accumulation of mineral salts on macrolites forms a stone.

Parathyroid hormone and excess calcium, affecting purine metabolism, are involved in the formation of urate stones. However, the frequency and nature of stone formation during primary hyperparathyroidism remains controversial, the composition of the detected urinary stones does not always correspond to generally accepted ideas.

Increased calcium ions contribute to the formation of urinary stones containing calcium (primarily oxalates). An increase in uric acid and PO3-4 ions in the urine can lead to the formation of urinary stones in the form of urates and phosphates. In addition, increasing the concentration of uric acid in urine leads to a decrease in the solubility of oxalates [14].

Analyzing the mineral composition of kidney stones consisting of mixed minerals, it was found that in the comparison group they were found in 34 (53.1%) children (calcium oxalate monohydrate, calcium oxalate dihydrate, ammonium urate, ammonium dihydrate, struvite), in 18 (69 , 2%) children with renal form of primary hyperparathyroidism (calcium oxalate monohydrate, calcium oxalate dihydrate, ammonium urate, ammonium dihydrate, struvite, vitlocite, hydroxylapatite, brushite, dollite) and in 10 (47.6%) children with a mixed form of primary hyperparathyroidism (whitlockite, brushite, hydroxylapatite, struvite, calcium oxalate monohydrate) (Table 1).

Consequently, the highest percentage of detection of stones consisting of mixed minerals is recorded in the group of children with renal hyperparathyroidism i.e. in children without damage to the skeletal system, and the difference is 21.6%.

Analysis of the mineral composition of stones in 28 (53.8%) children of patients with PHPT consisting of mixed minerals showed that the occurrence of minerals ammonium hydrate, ammonium dihydrate in the composition of urate lithiasis was recorded in 19 (67.8%) children, of which 15 (78.9%) cases were children without bone damage and in 4 (21.0%) cases children with bone damage.

Consequently, urate monomineral stones do not form during PHPT; they, when combined with oxalates and phosphates, form stones from mixed minerals.

Parathyroid hormone directly affecting bone tissue, has a demineralizing effect, increases the resorption of bone minerals, thus contributing to a significant increase in the concentration of calcium in serum. Inorganic mineral crystals, hydroxylapatites - reinforcing elements of bone tissue - enter calcium together with calcium from bone tissue, bone demineralization, osteoporosis, and bone tissue are replaced by fibrous tissue.

Table 1 The composition of kidney stones consisting of mixed minerals in the examined children

Minerals	Urolithiasis (n = 34) (comparison group)	Renal form of primary hyperparathyroidism (n = 18)	Renal form of primary hyperparathyroidism with bone damage (n = 18)
1. Calcium Oxalate Monohydrate, Calcium Oxalate Dihydrate, Ammonium Urate	4 (11,7%)	1 (5,5%)	-
2. Calcium Oxalate Dihydrate, Ammonium urate	9 (26,4%)	-	-
3. Calcium Oxalate Monohydrate, Ammonium Dihydrate	2 (5,8%)	1 (5,5%)	-
4. Calcium Oxalate Monohydrate, Ammonium Urate	7 (20,5%)	2 (11,1%)	-
5. Struvite, Ammonium Urate	6 (17,6%)	-	-
6. Calcium Oxalate Monohydrate, Dollite	-	-	1 (10,0%)
7. Struvite, Calcium Oxalate Monohydrate	6 (17,6%)	-	
8. Struvit, Whitlockite	-	1 (5,5%)	2 (20,0%)
9. Struvit, Calcium Oxalate Dihydrate, Ammonium Urate	-	2 (11,1%)	-
10. Hydroxylapatite, Calcium Oxalate Monohydrate, Ammonium Urate	-	7 (38,8%)	4 (40,0%)
11. Brushite, Whitlockite, Calcium Oxalate Monohydrate	-	-	2 (9,5%)
12. Hydroxylapatite, Calcium Oxalate Monohydrate	-	1 (5,5%)	-
13. Struvite, Brushite, Sodium Urate	-	1 (5,5%)	-
14. Hydroxylapatite, Struvite	-	-	1 (10,0%)
15. Hydroxylapatite, Ammonium Urate	-	1 (5,5%)	-
16. Hydroxylapatite, Calcium Oxalate Monohydrate, Calcium Oxalate Dihydrate	-	1(5,5%)	-
Total	34 (53,1%)	18 (69,2%)	10 (47,6%)

In 21 (44.6%) children with a renal form of primary hyperparathyroidism, bone osteoporosis was revealed. Kidney stones in these children are presented in the form of mono and mixed minerals, consisting of hydroxylapatite, apatite, whitlockite, brushite, struvite-carbonate-apatite and dolite. They had an irregular shape, in 83% of cases they were coral-shaped and 69% bilateral.

CONCLUSION

A study showed that the mineral composition of kidney stones can be used to judge the damage to the skeletal system in primary hyperparathyroidism. They were characterized by phosphate stones, in the mineral composition of which apatites were found (81.1%) (hydroxylapatite, apatite, whitlockite, brushite, struvite-carbonate-apatite).

Researchers who studied the composition and structure of urinary stones, including recurrent, noticed one characteristic feature: in relapses of urolithiasis, the composition of the cameos was often phosphate. The stones, consisting of apatites, were coral and multiple. Kidney stones, consisting of calcium oxalate monohydrate, calcium oxalate dihydrate, ammonium urate, ammonium dihydrate, struvite, vitlocite, brushite, were characteristic of nephrolithiasis in primary hyperparathyroidism without bone damage and amounted to 87.5%.

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