

Osteodystrophy in Children with the Renal form of Primary Hyperparathyroidism

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Authors' contributions

This work was carried out in collaboration between both authors. Author AAN designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author IZS managed the analyses of the study and the literature searches. Both authors read and approved the final manuscript.

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ABSTRACT

Introduction: PHPT was diagnosed on the basis of a study of the content of total calcium and inorganic phosphorus in the blood and in daily urine, ionized calcium in the blood, exercise tests with calcium and sodium chloride, the content of parathyroid hormone (PTH), calcitonin (CT), vitamin D and cyclic 3,5 β -adenosine monophosphate (cAMP) in serum.

Materials and Methods: A total of 2100 children aged 1 to 15 years with patients with urolithiasis were examined, of which 52 (2.5%) children were diagnosed with primary hyperparathyroidism (PHPT). The renal form (RF) of PHPT was 29 (55.7%) and the mixed form (MF) (damage to the kidneys and bones) of PHPT was 23 (44.2%) patients. To detect bone damage, we studied the activity of alkaline phosphatase (ALPL) and X-ray densitometry of the bones of the hand and ultrasound osteometry of the bones.

Results: High rates of alkaline phosphatase (ALPL) and low rates of echoosteometry were observed in children with impaired renal function and had a direct relationship with the number and size of formed stones and osteoporosis of bones.

Discussion: The study of alkaline phosphatase (ALPL) activity and bone echoostometry makes it possible to assess the severity of osteostrophy and accordingly, to differentiate PHPT by forms (renal and mixed) and the severity of the disease.

Keywords: Urolithiasis; primary hyperparathyroidism; kidneys; alkaline phosphatase; pediatric urology.

1. INTRODUCTION

In children suffering from urolithiasis, enamel destruction and tooth loss, pain and curvature of limbs, joints are noted. Attempts to identify the cause of these phenomena by studying the mineral composition of blood and urine do not give positive results [1-4]. In recent years, the hyperparathyroid nature of these changes has been mentioned more often, especially with a combination of bone demineralization and the formation of kidney stones [5,6]. Excessive production of parathyroid hormone enhances the activity of osteoclasts and bone resorption, which is accompanied by the mobilization of mineral substances from bone tissue (calcium and inorganic phosphorus) and their excessive excretion by the kidneys [7-9]. Aim of the study is to assess the degree of demineralization of bone tissue depending on the form of primary hyperparathyroidism (PHPT) and urolithiasis.

2. MATERIALS AND METHODS

A total of 2100 children aged 1 to 15 years with patients with urolithiasis were examined, of which 52 (2.5%) children were diagnosed with PHPT. The renal form (RF) of PHPT was 29 (55.7%) and the mixed form (MF) (damage to the kidneys and bones) of PHPT was 23 (44.2%) patients. PHPT was diagnosed on the basis of a study of the content of total calcium and inorganic phosphorus in the blood and in daily urine, ionized calcium in the blood, exercise tests with calcium and sodium chloride, the content of parathyroid hormone (PTH), calcitonin (CT), vitamin D and cyclic 3,5 β -adenosine monophosphate (cAMP) in serum. To detect bone damage, we studied the activity of alkaline phosphatase (ALPL) and X-ray densitometry of the bones of the hand and ultrasound osteometry of the tubular bones [8-11].

To clarify the severity of stone formation and assess the functional state of the kidneys, ultrasound, x-ray (survey, excretory or infusion urography), radioisotope (radioisotope renography, renal scanning, dynamic nephroscintigraphy) studies were used.

The activity of alkaline phosphatase (ALPL) was determined by the photocalorimetric method using reagents from "Lachema". Ultrasound examination of bone tissue was examined with

an EOM - 02 C echoosteometer, in four bones - tibial, radial, clavicle and lower jaw.

Ultrasound osteometry (echoosteometry) is a method for quantifying the state of bone density by measuring the transit time of ultrasound vibrations through the studied area of the bone. This method is based on the fact that the speed of sound transmission in different media is different and depends on the density: the denser the medium, the faster the sound passes through it, and vice versa. Echoosteometry is highly sensitive to changes in the mineral saturation of bone tissue, therefore, it allows you to obtain objective information about the density of the bone and evaluate its mechanical (strength) properties in a particular area. Ultrasonic osteometry is carried out using an "EOM-02 C" echoosteometer. A radio frequency of 1.2 MHz is transmitted to a transmitting ultrasound head, with the help of which a probe signal is transmitted through soft tissue to the bone. After passing a section of bone, the signal returns to the device for measurement.

3. RESULTS AND DISCUSSION

Clinical symptoms characteristic of bone changes was: pain in the limbs in 30 (57.65%) children, gait changes in 19 (36.5%) children, deformation and curvature of the bones of the skull, spine and limbs in 21 (40.3%) of the child, fractures of the tubular bones were observed in 7 (13.4%) children. In 50 (96.1%) children, the disease was complicated by pyelonephritis, in 24 (46.1%) children, gross renal dysfunction was noted. Patients with PHPT significantly lagged behind in physical development.

The activity of alkaline phosphatase (ALPL) in patients with urolithiasis without PHPT (comparison group) did not significantly differ from that in healthy children (Table 1).

The activity of alkaline phosphatase (ALPL) in 46 (88.4%) children with PHPT was higher compared to the children in the control group. With renal form of PHPT, the activity of alkaline phosphatase (ALPL) significantly increased ($1,23 \pm 0,06 \mu\text{mol} / \text{liter}$) $p < 0,05$. If renal failure joined it, this indicator increased 2.17 times ($1,87 \pm 0,08 \mu\text{mol} / \text{liter}$) compared with children in the control group ($p < 0,01$).

Table 1. Alkaline phosphatase (ALPL) activity in examined children ($\mu\text{mol} / \text{liter}$)

Surveyed groups of children	#	Alkaline phosphatase activity ($\mu\text{mol} / \text{liter}$)	P
1. Healthy children	20	$0,82 \pm 0,04$	$p > 0,05$
2. Children with urolithiasis without PHPT (control)	20	$0,91 \pm 0,06$	
3. Children with renal form of PHPT	16	$1,23 \pm 0,06$	$p < 0,05$; $P1 < 0,05$
4. The mixed form of PHPT	12	$2,3 \pm 0,1$	$p < 0,01$; $p1 < 0,01$
5. The renal form of PHPT complicated by renal failure	13	$1,87 \pm 0,08$	$p < 0,01$; $p1 < 0,01$
6. A mixed form of PHPT complicated by renal failure	11	$6,38 \pm 0,22$	$p < 0,001$; $p1 < 0,001$

R - Compared with healthy children; P1- Compared with indicators of children with urolithiasis (control)

Table 2. Indicators of echoostometry in the examined children

Surveyed groups of children	#	Echoosteometry (meter / second)			
		Tibia	Ulna	Clavicula	Mandible
1 Healthy children	20	3898 ± 43	3786 ± 57	3591 ± 63	3642 ± 61
2 Children with urolithiasis without PHPT (control)	20	3609 ± 37	3447 ± 37	3492 ± 62	3501 ± 57
	p	$p < 0,05$	$p < 0,05$		
3 Renal form PHPT	16	3210 ± 43	3228 ± 41	3270 ± 38	3322 ± 49
	p	$p < 0,05$	$p < 0,05$	$p < 0,05$	$p < 0,05$
	P1	$p1 < 0,05$	$p1 < 0,05$	$p1 < 0,05$	$p1 < 0,05$
4 Mixed form PHPT	12	2208 ± 41	2354 ± 46	2482 ± 53	2456 ± 51
	p	$p < 0,01$	$p < 0,01$	$p < 0,01$	$p < 0,01$
	P1	$p1 < 0,01$	$p1 < 0,01$	$p1 < 0,01$	$p1 < 0,01$
5 Renal form PHPT complicated by renal failure	13	2786 ± 39	3049 ± 42	3152 ± 49	3040 ± 61
	p	$p < 0,05$	$p < 0,05$	$p < 0,05$	$p < 0,05$
	P1	$p1 < 0,05$	$p1 < 0,05$	$p1 < 0,05$	$p1 < 0,05$
6 Mixed PHPT complicated by renal failure	11	1888 ± 42	1960 ± 54	2080 ± 61	2070 ± 59
	p	$p < 0,001$	$p < 0,001$	$p < 0,001$	$p < 0,001$
	P1	$p1 < 0,001$	$p1 < 0,001$	$p1 < 0,001$	$p1 < 0,001$

R - Compared with healthy children; P1- Compared with indicators of children with urolithiasis (control)

With mixed form of PHPT, the activity of alkaline phosphatase (ALPL) was 2.8 times greater than $p < 0,001$. If renal failure was added, this indicator increased significantly and was equal to $6,38 \pm 0,22 \mu\text{mol} / \text{liter}$, which is 7.8 times higher than the indicator of children in the control group ($p < 0,001$).

An ultrasound examination of bones was performed to identify the degree of violation of bone mineral saturation with PHPT in children suffering from urolithiasis (Table 2).

The difference in echoosteometry in children with urolithiasis disease without PHPT with

healthy children was significant only in the tibia, in the other bones a downward trend was observed.

In children with renal form of PHPT, echoosteometry in all bones was significantly lower ($P < 0,05$). Bone tissue with a mixed form of PHPT was characterized by significantly low (1.8 times) conductivity of ultrasonic signals ($P < 0,001$) compared with children, the renal form of PHPT. Echoosteometry in children with renal form of PHPT complicated by renal failure was 1.41 times lower ($P < 0,05$), in children with a mixed form - 2.1 times ($P < 0,001$).

4. CONCLUSION

The analysis of the research results showed that the activity of alkaline phosphatase (ALPL) and echoostometry in children of patients with PHPT significantly different from that of children in the control group ($P < 0.05$), which is a characteristic sign that evaluates the process of bone demineralization. Significantly high levels of alkaline phosphatase (ALPL) and a low level of echoostometry were observed in children with a mixed form of PHPT, especially in children with impaired renal function ($P < 0.001$).

Thus, the study of alkaline phosphatase (ALPL) activity and bone echoostometry makes it possible to assess the severity of osteostrophy and, accordingly, to differentiate PHPT by forms (renal and mixed) and the severity of the disease [12-14]. High rates of alkaline phosphatase (ALPL) and low rates of echoostometry were observed in children with impaired renal function and had a direct relationship with the number and size of formed stones and osteoporosis of bones [15].

CONSENT

As per international standard, parents' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard, written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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