"Primary hyperparathyroidism in children: assessment of the state of bone tissue before and after treatment"

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Annotation
The purpose of the study. Evaluating the effectiveness of treatment of the bone form of primary hyperparathyroidism in children.
Research material and methods. In the study, 90 patients and children who applied to the clinic of the Republican Specialized Scientific and Practical Endocrinology Center, were treated in the hospital and were under ambulatory observation based on the diagnosis of primary hyperparathyroidism, were taken in the study. 50 patients were treated surgically (parathyroidectomy) (main group), 40 patients were under outpatient observation (with contraindications to surgery and refused surgery) (comparative group). The control group consisted of 20 healthy children without thyroid and parathyroid pathology
Research results. Skeletal changes in primary hyperparathyroidism are an important and very common symptom of this disease.
Systemic osteoporosis in 36% of the patients (90 people) under our observation, thinning of the cortical layer in 72% of cases, fibro-cystic osteitis in 21%, subperiosteal resorption of nail phalanges in 31%, decrease in bone mineral density in 76% were noted. The lag in bone age (23.3%) was 2-3 years
Conclusions.1.After parathyroidectomy, recovery of bone structure in long tubular bones (humerus and elbow) was noted within 1 year. Bone fractures were recorded in 17.5% of children who did not undergo surgery, and repeated bone fractures in 57.1%. Cystic changes in the bones of the pelvis and limbs (15%) caused gross deformities, which later required surgical interventions.
2. Bone-based treatment of primary hyperparathyroidism in children led to a positive increase in bone metabolism indicators.

Keywords: primary hyperparathyroidism, children, bone form.

Background In recent years, primary hyperparathyroidism (BHPT) has been steadily developing in the infrastructure of endocrine diseases and is increasingly attracting the attention of doctors of various specialties both in our country and abroad. This condition is undoubtedly related to the fact that primary hyperparathyroidism is a pathogenetic link in the development of various cardiovascular, uronephrological, traumatological, gastroenterological and other disorders. Primary hyperparathyroidism occurs in 1% of the adult population and 2% of the population over 55 years of age. The estimated incidence of BHPT in children is 2-5:100,000. In recent years, the incidence of primary hyperparathyroidism has increased 5-fold worldwide. According to medical statistics, in 30% of cases in families with primary hyperparathyroidism, the disease manifests itself in children. Epidemiological studies have shown that in the last 10 years, there has been a rapid increase in primary hyperparathyroidism in children, from 23% to 62%.

In children, BHPT manifested target organ damage in 25-50%, skeletal pathology in 9-89%. In children, the bone form of the disease is characterized by high activity of osteoclasts, fibrosis, formation of cystic cavities (fibrous-cystic osteitis), and diffuse demineralization of bone tissue is noted in many cases. Bone resorption was observed in long tubular bones and caused bone deformities. Often, in pediatric practice, primary hyperparathyroidism is described as incomplete osteogenesis, as it is associated with pathological bone fractures. Characteristic features of primary hyperparathyroidism in children are the predominance of the manifest form of the disease. Especially when primary hyperparathyroidism occurs in childhood and adolescence, during active growth and formation of the skeleton, bone manifestations of the disease come to the fore and pose a risk of disability in children.

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Therefore, the monitoring of bone mineral density indicators in children with primary hyperparathyroidism before and after treatment in the near and long term is of particular importance in the multifaceted evaluation of the treatment results.

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Research material and methods. In the study, 90 patients and children who applied to the clinic of the Republican Specialized Scientific and Practical Endocrinology Center, were treated in the hospital and were under ambulatory observation based on the diagnosis of primary hyperparathyroidism, were taken in the study. 50 patients were treated surgically (parathyroidectomy) (main group), 40 patients were under outpatient observation (with contraindications to surgery and refused surgery) (comparative group). The control group consisted of 20 healthy children without thyroid and parathyroid pathology (Figure 1).

Bone mineral density in children was determined by 2 different methods. It was evaluated by recording the ultrasound velocity through a specific segment of bone using a stationary exoosteometer EOM-02 (RIMEDA, Lithuania). The second method is the x-ray densitometry method. Initially, the x-ray image of the bones of the hand paw was taken along with clinical standards (clinic standard) on the device "EDR-750B" (Medicor-Budapest, Hungary), and the bone mineral density was determined by calculating the concentration of mineral salts using the densitometry method.The average age of the patients was 12.8±0.9. The duration of the study was 1-3-6 months in the short term and 1-5-10 years in the long term after the surgery. In order to study the results of long-term treatment, patients were re-examined at the RIIATEM center clinic at different times.

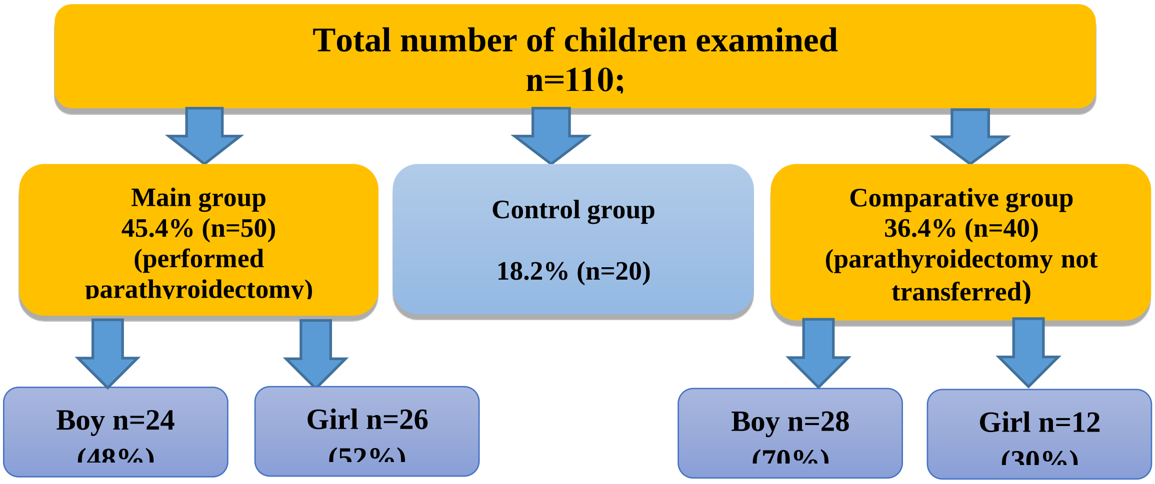

Figure 1. Research design.

Research results. Skeletal changes in primary hyperparathyroidism are an important and very common symptom of this disease. Skeletal changes in radiographs observed in primary hyperparathyroidism reflect pathologoanatomical changes to a certain extent.

Systemic osteoporosis in 36% of the patients (90 people) under our observation, thinning of the cortical layer in 72% of cases, fibro-cystic osteitis in 21%, subperiosteal resorption of nail phalanges in 31%, decrease in bone mineral density in 76% were noted. The lag in bone age (23.3%) was 2-3 years (Fig. 2).

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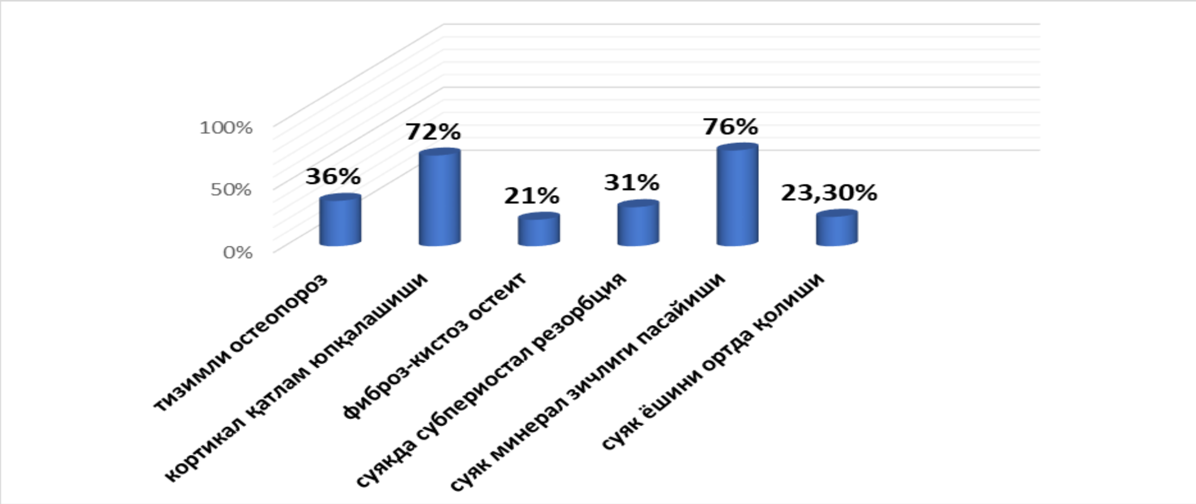

Figure 2. Changes in the bone system of patients during X-ray examination.

Spuzyak M.I. according to his opinion, subperiosteal resorption is a characteristic and rather early sign of primary hyperparathyroidism, and its diagnostic value is equal to the symptom of hypercalcemia. Changes in bone mineral density were examined before and after treatment using x-ray densitometry and exoosteometry. In the control group, healthy children without thyroid pathology (20 people), the mineral density of the porous substance was 55.0±0.3 mg/mm3, and the mineral density of the compact substance was 94.1±0.3 mg/mm3.

The mineral density of compact (91.7±0.4; r<0.05) and porous (51.2±0.6; r<0.05) substance before surgery in the main group of children was 64% and 72%, respectively. decrease to One year after the operation, the dynamic observation showed that the bone mineral density was restored and approached the control values. In the long term (5-10 years), the bone is compact (94.1±0.5; p<0.05; 94.2±0.4; p<0.05) and porous (55.2±0.5; p<0.05). (p<0.05; 55.7±0.3; p<0.05) mineral density recovery remained stable (Table 1).

Table 1

Indicators of bone mineral density in children in the main group

Field of investigation		Control group n=20	From the operation before n=50	o/k 6 months n=50	o/c 1 year n=50	o/k 5 years n=50	o/c 10 years n=50
mg/mm3	Compact substance	94.1±0.3	91.7±0.4*	93.4±0.1^	93.9±0.4^	94.1±0.5^	94.2±0.4^
	A pore substance	55.0±0.3	51.2±0.6*	54.3±0.4^	54.8±0.5^	55.2±0.5^	55.7±0.3^

Note: *-significant difference compared to the control group (p<0.05)

^ - the difference compared to the indicators before surgery is reliable (p<0.05)

In children in the comparative group, mineral density of compact (91.4±0.3; r<0.05) and porous (51.2±0.4; r<0.05) substance was 62.5% (25) and decreased by 65% (26 people), and in early and long-term follow-up it was found that the mineral density of bone compact and porous substance decreased (Table 2).

Table 2

Bone mineral density indicators in children in the comparison group

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Field of investigation		Control group n=20	Preliminary examination indicators n=40	After 6 months n=40	After 1 year n=40	After 5 years n=40	After 10 years n=40
mg/mm3	Compact substance	94.1±0.3	91.4±0.3*	91.6±0.1*	91.2±0.4*	88.1±0.3^	84.3±0.5^
	A pore substance	55.0±0.3	51.2±0.4*	51.9±0.4*	51.1±0.5*	50.8±0.5^	50.1±0.4^

Note: *-significant difference compared to the control group ($p<0.05$)
^ - the difference compared to the initial test indicators is reliable ($p<0.05$)

The obtained data showed long-term recovery of bone structure after parathyroidectomy in the main group of children treated with surgery for primary hyperparathyroidism. On the contrary, in the patients of the comparative group, a decrease in mineral density indicators was noted during the observation.

According to the results of exoosteometry, in the main group of children with primary hyperparathyroidism, before treatment, a decrease in ultrasound wave propagation was observed in 60% in the tibia, 52% in the ulna, 40% in the vertebral bone, and 82% in the lower jaw bone. One year after parathyroidectomy, a significant recovery of bone tissue structure was noted in elbow (3438.8±105.6; r<0.05) and tibia (3465.2±108.5; r<0.01). By the 5th year of follow-up, complete recovery of the bone tissue structure was found in the bones of the spine (3319.1±102.1; r<0.05) and lower jaw (3293.6±106.6; r<0.01) (3 -table).

Table 3

Dynamics of exoosteometry indicators before and after parathyroidectomy in children of the main group

The field under investigation	Control group n=20	Before the operation n=50	6 months after surgery n=50	1 year after surgery, n=50	5 years after surgery, n=50
Lower jaw bone, m/s	3293.3±15.4	2998.3±98.5	3173.2±96.4	3186.7±104.5	3293.6±106.6^
Vertebral bone, m/s	3318.3±22.9	3070.1±53.7	3202.9±103.3	3226.7±102.4	3319.1±102.1^
Elbow bone, m/s	3440.4±29.9	3122.2±34.6*	3349.8±108.9^	3438.8±105.6^	3440.5±108.6^^
Greater tibia m/s	3451.0±21.5	3131.1±34.6*	3385.5±105.8^	3465.2±108.5^^	3459.2±109.1^^

Note: * -significant difference compared to the control group ($p<0.01$)
^ - the difference compared to the indicators before surgery is reliable (^-$p<0.05$; ^^ - 0.01)

In children in the comparative group with primary hyperparathyroidism, during the initial examination, a decrease in ultrasound wave propagation was observed in 75% in the tibia, 65% in the ulna, 55% in the spine, and 80% in the mandible.Patients in the comparison group complained of constant pain during physical activity due to different pathological changes in the bones. The pain was observed especially in the spine, legs, waist, shoulder area. From the 4-5th year of the disease, the erosion of the cortical layer increased, and the bone mass in the tibia (2957.1±95.9; r<0.05) and elbow (2965.4±100.7; r<0.05) a sharp decrease was noted. A trend of decreasing bone mineral density was noted for 5 years (Table 4).

Table 4

Dynamics of exoosteometry indicators during long-term follow-up in children of the comparative group

The area under investigation	Control group n=20	In the initial examination n=40	After 6 months n=40	After 1 year n=40	After 5 years n=40
Lower jaw bone, m/s	3293.3±15.4	3150.7±24.5	3005.2±83.4	2989.8±96.8*	2789.8±96.8**^
Vertebral bone, m/s	3318.3±22.9	3271.7±24.4	3102.9±43.3	3001.8±97.5*	2801.8±97.5**^
Elbow bone, m/s	3440.4±29.9	3315.8±40.5	3249.8±38.9	3165.4±100.7*	2965.4±100.7**^
Calf bone m/s	3451.0±21.5	3365.2±25.8	3285.5±45.8	3157.1±95.9*	2957.1±95.9**^

Note:* -significant difference compared to the control group (* - p<0.05, ** - p<0.01)
^ - the difference compared to the initial test indicators is reliable (^ - p<0.05)

The obtained data showed a long-term recovery of bone tissue after parathyroidectomy in the main group of children treated with surgery for primary hyperparathyroidism. On the contrary, in the children of the comparative group that did not undergo parathyroidectomy, 2 years after the diagnosis of the disease, 7 (17.5%) patients had bone fractures, and 4 (57.1%) of them had repeated bone fractures. Cystic changes in the bones of the pelvis and limbs caused gross deformities in 6 (15%) patients by 5 years of disease and subsequently required surgical correction.
The frequency of postoperative hypocalcemia in children who underwent parathyroidectomy was 58% (29 patients). A decrease in the level of calcium is explained by "hungry bones syndrome". This syndrome was manifested by severe bone manifestations of primary hyperparathyroidism in the early postoperative period. This is due to the active transfer of minerals (calcium, magnesium, phosphorus) from the blood to the regenerating bone tissue after the stimulatory effect of parathyroid hormone on bones has decreased. Decreased calcium level was transient and was corrected with vitamin D and calcium preparations in an outpatient setting.

Conclusions.1.After parathyroidectomy, recovery of bone structure in long tubular bones (humerus and elbow) was noted within 1 year. Bone fractures were recorded in 17.5% of children who did not undergo surgery, and repeated bone fractures in 57.1%. Cystic changes in the bones of the pelvis and limbs (15%) caused gross deformities, which later required surgical interventions.
2. Bone-based treatment of primary hyperparathyroidism in children led to a positive increase in bone metabolism indicators.

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