УДК 616.447.085.032:616.61-002.2-06
https://doi.org/10.20538/1682-0363-2025-3-14-24

The effect of local injections of paricalcitol into the parathyroid glands on parathyroid hormone levels, vascular calcification, and bone mineral density in patients with chronic kidney disease

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ABSTRACT

Aim. To study the effects of local paricalcitol injections into the parathyroid glands on bone turnover in patients with chronic kidney disease (CKD) and secondary hyperparathyroidism (SHPT) with moderately elevated parathyroid hormone (PTH) levels (300–600 pg/ml).

Materials and methods. The study included 48 patients with end-stage CKD and SHPT with PTH levels of 300–600 pg/ml. All patients received standard medical therapy before the study, including correction of hyperphosphatemia, hypocalcemia, and disorders of calcium-phosphorus metabolism. The main group (n = 14) comprised patients for whom ultrasound-guided paricalcitol injections into the parathyroid glands were technically feasible. The dynamics of PTH levels, vascular calcification, bone mineral density (BMD), and levels of PTH, b-CrossLaps, and FGF23 were assessed.

Results. Multivariate logistic regression analysis demonstrated that osteoporosis and vascular calcification were significantly associated with age, PTH levels, dialysis duration, comorbidity index, b-CrossLaps, and FGF23. Threshold values for age and PTH were 33 years and 301 pg/ml for the development of osteoporosis and 29 years and 301 pg/ml for vascular calcification. Correlation analysis revealed a statistically significant relationship between FGF23 and dialysis duration, b-CrossLaps and PTH levels, as well as between FGF23 and b-CrossLaps. The comorbidity index also increased with age and PTH levels. After 3 and 6 months of treatment, PTH levels significantly decreased, while the volume of the parathyroid glands remained unchanged. No serious complications were observed after the injections, and transient local pain was reported in only 8 (57%) patients.

Conclusion. Ultrasound-guided paricalcitol injections into the parathyroid glands contribute to reducing PTH levels, improving bone remodeling parameters, and creating conditions for preventing cardiovascular complications. These findings require further investigation in larger-scale studies.

Keywords: secondary hyperparathyroidism, chronic kidney disease, mineral and bone disorders, paricalcitol, local injections

Conflict of interest. The authors declare the absence of obvious or potentialor potential conflicts of interest related to the publication of this article.

Source of financing. The study was carried out with the support of the contest of scientific projects conducted by young scientists of Siberian State Medical University (SibSMU) (No. NIOKTR 21-22-07-03-42).

For citation: Zhulina E.M., Brykun M.V., Saprina T.V., Vorojcova I.N., Tskhay V.F., Komkova T.B. The effect of local injections of paricalcitol into the parathyroid glands on parathyroid hormone levels, vascular calcification, and bone mineral density in patients with chronic kidney disease. *Bulletin of Siberian Medicine.* 2025;24(3):14–24. https://doi.org/10.20538/1682-0363-2025-3-14-24.

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Влияние местных инъекций парикальцитола в околощитовидные железы на уровень паратгормона, сосудистую кальцификацию и минеральную плотность костной ткани у пациентов с хронической болезнью почек

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РЕЗЮМЕ

Цель. Изучить влияние местных инъекций парикальцитола в околощитовидные железы на костный обмен у пациентов с хронической болезнью почек (ХБП) и вторичным гиперпаратиреозом (ВГПТ) при умеренном повышении уровня паратгормона (ПТГ) (300–600 пг/мл).

Материалы и методы. В исследование включены 48 пациентов с терминальной стадией ХБП и ВГПТ с концентрацией паратгормона 300–600 пг/мл. Все пациенты до начала исследования получали стандартное медикаментозное лечение, включающее коррекцию гиперфосфатемии, гипокальциемии и нарушения кальциево-фосфорного обмена. В основную группу (n = 14) вошли пациенты, которым было технически возможно проведение инъекций парикальцитола под ультразвуковым контролем в околощитовидные железы. Оценивались динамика уровня ПТГ, кальцификация сосудов, минеральная плотность костной ткани, уровни ПТГ, b-CrossLaps и FGF23.

Результаты. Многомерный логистический регрессионный анализ показал, что остеопороз и сосудистая кальцификация достоверно связаны с возрастом, уровнем ПТГ, длительностью диализа, индексом коморбидности, b-CrossLaps и FGF23. Пороговые значения возраста пациента и ПТГ составили 33 года и 301 пг/мл для развития остеопороза и 29 лет и 301 пг/мл – для сосудистой кальцификации. Корреляционный анализ выявил статистически значимую связь между FGF23 и продолжительностью диализной терапии, b-CrossLaps и уровнем ПТГ, а также между FGF23 и b-CrossLaps. Индекс коморбидности также увеличивался с возрастом и уровнем ПТГ. Через 3 и 6 мес лечения уровень ПТГ значительно снизился, а объем околощитовидных желез остался без изменений. После инъекций не наблюдалось серьезных осложнений, а кратковременная местная болезненность отмечалась только у 8 (57%) пациентов.

Заключение. Инъекции парикальцитола в околощитовидные железы под ультразвуковым контролем способствуют снижению уровня ПТГ, улучшению показателей ремоделирования костной ткани и создают предпосылки для предотвращения сердечно-сосудистых осложнений, что требует дальнейшего изучения в рамках более масштабных исследований.

Ключевые слова: вторичный гиперпаратиреоз, хроническая болезнь почек, минеральные и костные расстройства, парикальцитол, местные инъекции

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Конкурс научных проектов молодых ученых ФГБОУ ВО СибГМУ (№ НИОКТР 21-22-07-03-42).

Для цитирования: Жулина Е.М., Брыкун М.В., Саприна Т.В., Ворожцова И.Н., Цхай В.Ф., Комкова Т.Б. Влияние местных инъекций парикальцитола в околощитовидные железы на уровень паратгормона, сосудистую кальцификацию и минеральную плотность костной ткани у пациентов с хронической болезнью почек. *Бюллетень сибирской медицины.* 2025;24(3):14–24. https://doi.org/10.20538/1682-0363-2025-3-14-24.

INTRODUCTION

The pathogenesis of secondary hyperparathyroidism (SHPT) in patients with chronic kidney disease (CKD) involves several factors related to the effects of parathyroid hormone (PTH), calcium (Ca) levels, phosphorus (P) levels, fibroblast growth factor 23 (FGF23), and the bone resorption biomarker b-CrossLaps. These factors affect mineral metabolism, osteoclast and osteoblast activity, and bone tissue quality [1, 2]. In CKD, PTH is produced by the chief cells of the parathyroid glands (PTG) in

response to hypocalcemia and hyperphosphatemia. It stimulates bone resorption, leading to elevated calcium and phosphorus levels in the blood. A decrease in glomerular filtration rate (GFR) results in a significant reduction in phosphate clearance, causing its accumulation in the body.

Phosphate ions form complexes with calcium, lowering the concentration of ionized calcium in the blood. This, in turn, activates calcium-sensing receptors (CaSRs) on the parathyroid cells, stimulating the secretion of PTH and leading to hypercalcemia as a compensatory response. A decrease in ionized calcium disrupts the synthesis of calcitriol from vitamin D3, which reduces calcium absorption in the intestine and promotes metastatic calcification. Additionally, phosphorus directly stimulates PTH secretion and the hyperplasia of parathyroid cells, as well as causes dysfunction of calcitriol receptors, leading to resistance to this hormone. Hyperphosphatemia also contributes to the reduction in the number of CaSRs, impairing the ability of calcium to stimulate calcitriol synthesis in the kidneys [3].

Furthermore, phosphorus stimulates the production of the growth factor FGF23, which inhibits the activity of 1-alpha-hydroxylase and lowers the level of the active form of vitamin D. The regulation of vitamin D receptors in the parathyroid glands deteriorates, leading to vitamin D resistance. FGF23 affects the production and regulation of PTH, osteoclast and osteoblast activity, and bone remodeling. The bone resorption marker b-CrossLaps reflects osteoclast activity and bone tissue destruction. In SHPT elevated levels of b-CrossLaps are associated with bone resorption and worsening bone quality [4–8]. Renal osteodystrophy is the cause of serious conditions, including fractures and a decline in quality of life [8, 9]. Compared to the general population, the risk of fractures among CKD patients increases steadily as kidney disease progresses [10, 11].

Extraskeletal calcification, particularly cardiovascular calcification, predicts subsequent cardiovascular mortality and all-cause mortality in patients with end-stage renal disease [12].

Today, vascular calcification is considered an actively regulated and cell-mediated process [13], with a crucial aspect being the imbalance between promoters and inhibitors of calcification. In CKD, calcification inducers such as hyperphosphatemia, hypercalcemia, oxidative stress, inflammatory cytokines, and uremic toxins increase, while calcification inhibitors like fetuin-A, albumin, and ionized magnesium decrease. Moreover, in CKD, the function of vitamin K-dependent proteins that prevent calcification is impaired [14]. Vascular smooth muscle cells, macrophages, endothelial cells, and vascular interstitial cells are involved in the calcification process [13, 15]. Osteoblast-like cells in the vascular bed and heart valves synthesize and secrete bone-related proteins, including osteopontin, osteocalcin, and collagen, which collectively accelerate the calcification of the extracellular matrix [14].

Several studies have shown that osteoporosis is a risk factor for cardiovascular diseases [16]. Arterial calcification and osteoporosis are often observed in the same individuals and progress simultaneously in patients with chronic and end-stage kidney diseases. The associations between bone and arterial anomalies suggest a direct or indirect effect of bone cells and turnover on the arterial system. Understanding these associations is crucial for developing effective therapeutic strategies aimed at improving outcomes for CKD patients [17].

Data obtained from dialysis patients with PTH levels of 300-600 pg/ml, treated with cinacalcet and vitamin D analogs, showed a lower risk of death and cardiovascular complications with earlier treatment of SHPT. This effect is observed when achieving lower target PTH levels compared to higher ones [18].

A higher PTH concentration directly correlates with a higher mortality rate from cardiovascular diseases [19].

Recent studies show that an increase in PTH levels before the start of dialysis predicts a higher PTH level after 9–12 months [20]. Untreated SHPT leads to a progressive increase in PTH levels [21, 22], and parathyroid hyperplasia with progressive SHPT due to delayed treatment is accompanied by a progressive decrease in sensitivity to calcium and vitamin D regulation, leading to a subsequent risk of treatment resistance in the later stages of the disease [23].

Therefore, there remains a need to find a method for early and sustained control of SHPT which would not only ensure safety but also guarantee long-term effect on the system, minimizing patient dependence on treatment adherence [22]. This approach could significantly improve long-term outcomes for bone tissue and cardiovascular outcomes.

The **aim** of this research is to study the effect of local paricalcitol injections into the parathyroid glands

on bone remodeling markers in CKD patients with SHPT and PTH levels of 300–600 pg/ml.

MATERIALS AND METHODS

The study sample consisted of 48 patients with secondary hyperparathyroidism (SHPT) and end-stage chronic kidney disease (CKD). All patients were undergoing renal replacement therapy and received conservative medical treatment for SHPT prior to the study, which included correction of hyperphosphatemia (Sevelamer, daily dose of 2,400 mg, administered to 41% of patients in the control group and 50% in the main group, $p > 0.05$); use of calcimimetics (Cinacalcet, daily dose of 30 mg, prescribed to all patients in both groups); calcium-phosphorus metabolism regulators (Alfacalcidol, 0.25–1 mcg 3 times a week; paricalcitol, 5 mcg 3 times a week; prescribed to all patients in both groups); correction of hypocalcemia (calcium carbonate, daily doses of 4.0–6.0 g, administered to 28.5% of patients in the main group and 17.6% in the control group).

The difference in calcium intake between the groups may be attributed to individual patient characteristics, including the level of hypocalcemia and response to the therapy. The group with more pronounced hypocalcemia required more extensive correction with calcium-containing preparations. It is also important to note that combined therapy, which includes calcimimetics and vitamin D, may reduce the need for calcium supplements. These differences may reflect both clinical characteristics of the patients and variability in the approaches to prescribing medications.

It is worth noting that adherence to the prescribed treatment among the patients was low. So, 64.2% of patients in the main group and 67.6% of patients in the control group took Cinacalcet as prescribed by their doctor. Only 12 patients in the main group and 30 patients in the control group took vitamin D receptor activators. Patients with CKD often experience apathy and fatigue from prolonged medication use, leading to treatment non-compliance despite having the medications on hand. This may also be associated with potential side effects of the drugs, such as dyspepsia, nausea, or discomfort, which further reduce patients' willingness to continue treatment. For some patients, the high cost of medications or limited access to them may also contribute to poor therapy adherence.

The Charlson Comorbidity Index (CCI) [24] was used to assess the prognosis of the patients and the impact of comorbidity on clinical outcomes. The use of this index allowed for an objective evaluation of the risk associated with comorbid conditions and ensured comparability of results between the groups.

Inclusion criteria were as follows: end-stage CKD, diagnosed SHPT, PTH concentration in blood of 300–600 pg/ml, and verified parathyroid glands based on scintigraphy data combined with single-photon emission computed tomography (SPECT).

Exclusion criteria were the following: planned or previous surgical intervention on neck organs, surgical treatment of SHPT in the medical history, oncological diseases, pregnancy, and severe somatic symptom disorder.

Patients were divided into two groups based on the results of ultrasound examination of the parathyroid glands (SonoScape equipment, S35, China, B-mode). The main group consisted of patients ($n = 14$) in whom the possibility of performing injections into the parathyroid glands was identified after the examination. The control group included patients ($n = 34$) who presented one or more technical difficulties in performing the procedure: the parathyroid glands were not visualized by ultrasound, or they were located atypically, or there was abundant blood flow with a risk of bleeding during the puncture.

In the main group, patients received ultrasound-guided paricalcitol (5 mcg/ml) injections into the parathyroid glands, at a dosage of up to 0.5 ml. The volume of the administered drug was determined depending on the initial volume of the gland (1/3 of its volume). Each patient in this group underwent two punctures, with an interval of 1 day between injections. In the control group, all patients continued to receive standard conservative treatment for SHPT.

Echocardiography was used to evaluate vascular calcification, including the presence of linear calcifications, as well as valve calcification.

The blood tests included the following parameters.

Intact parathyroid hormone (PTH) was determined using the chemiluminescent immunoassay method (Cobas 6000, Roche Diagnostics, Switzerland). Measurement range was 1.2–5,000 pg/ml. Reference values were 15–65 pg/ml.

B-CrossLaps was determined using the Serum CrossLaps reagent kit for enzyme-linked immunosorbent assay (BioMedica, Serbia). Measurement range was 0.020–2.494 ng/ml. Analytical sensitivity was 0.020 ng/ml.

FGF23 was determined using the FGF23 (C-terminal) reagent kit for enzyme-linked immunosorbent assay (BioMedica, Serbia). Measurement

range was 0.1–20 pmol/l. Analytical sensitivity was 0.08 pmol/l.

Bone mineral density was measured by densitometry of the lumbar spine and femoral neck using a computed tomography scanner (General Electric Optima CT660-128, USA).

The verification of the parathyroid glands was conducted using scintigraphy combined with single-photon emission computed tomography (SPECT) (Symbia Intevo Bold system, Germany).

Statistical processing of the findings was carried out using Statistica software (v 13.5.0.17, TIBCO Software Inc.), and IBM SPSS Statistics (v 30.0.0, IBM Corp.). The data were checked for normal distribution using the Shapiro–Wilk test. None of the studied parameters showed a normal distribution, so non-parametric statistical methods were used for the analysis. Descriptive data were presented as the median and the interquartile range *Me* (Q_{25};Q_{75}). For all statistical methods, the corresponding null hypothesis was tested. The critical level of significance (p) was set at 0.05. A p-value < 0.05 was considered statistically significant, indicating a rejection of the null hypothesis. The Kruskal–Wallis test (Analysis of Variance, ANOVA) and Dunn's post-hoc test were used to compare differences between groups.

Risk factors for osteoporosis and vascular calcification were assessed using binary logistic regression analysis. Univariate logistic regression analysis was conducted first, calculating the odds ratio (OR) and 95% confidence interval (95% CI) to evaluate the effect of individual factors on the likelihood of developing osteoporosis and vascular calcification. Variables with a significance level of $p < 0.05$ were included in the multivariate binary logistic regression model to assess their independent contribution to the development of osteoporosis and vascular calcification. Predictor selection in the multivariate model was performed using the backward selection.

To evaluate the diagnostic value of predictors for the development of osteoporosis and vascular calcification, ROC (Receiver Operating Characteristic) analysis was used, with the construction of characteristic curves and the calculation of the area under the curve (AUC). The Youden's J statistic was applied to determine the optimal threshold for each parameter. Values greater than 0.7 were interpreted as good predictive ability, and values above 0.8 were interpreted as very good.

To identify relationships between quantitative variables in the analysis of serum markers, the non-parametric Spearman's rank correlation coefficient was used. The Mann–Whitney U-test was applied to compare laboratory parameters between groups of patients and to test the null hypothesis of no differences between two independent samples. For the evaluation of parameters over time and differences between them, as well as for testing the null hypothesis of equality of medians in dynamic changes within the group, the non-parametric Friedman test (Friedman ANOVA) [25] was used, followed by pairwise comparisons using the Wilcoxon signed-rank test.

RESULTS

Characteristics of the Study Groups A total of 48 patients participated in this study.

In the main group (n = 14), the median age of the patients was 59 (49;65) years, with 71.4% being men. All patients received renal replacement therapy through hemodialysis. The median duration of dialysis was 60 (27;96) months. The median baseline PTH level was 504 (489;601) pg/ml. Osteoporosis was present in 64.3% (9) of the patients, and vascular calcification was present in 64.3% (9) of the patients.

In the comparison group (n = 34), the median age of the patients was 56 (43;68) years, with 44.1% being men. All patients received renal replacement therapy through hemodialysis. The median duration of dialysis was 36 (12;69) months. The median baseline PTH level was 365 (320;425) pg/ml. Osteoporosis was present in 85.2% (29) of the patients, and vascular calcification was present in 58.8% (20) of the patients (Table 1).

Table 1

Demographic and Laboratory Parameters in Both Groups

Parameters	Main group (n = 14)	Comparison group (n = 34)	p
Age, years, *Me* (Q_{25};Q_{75})	59 (49;65)	56 (43;68)	0.83
Male, %	71.4	44.1	-
Duration of dialysis, months, *Me* (Q_{25};Q_{75})	60 (27;96)	36 (12;69)	0.21
PTH level, pg/ml, *Me* (Q_{25};Q_{75})	504 (489;601)	365 (320;425)	0.17
b-CrossLaps level, ng/ml, *Me* (Q_{25};Q_{75})	1.1 (0.9;2.2)	1.9 (1.1;2.5)	0.19
FGF23 level, pmol/l, *Me* (Q_{25};Q_{75})	14.8 (5;18)	18.1 (5;20)	0.50
Presence of osteoporosis, %	64.3	85.2	0.83
Presence of vascular calcification, %	64.3	58.8	0.78
Volume of parathyroid glands, mm^3, *Me* (Q_{25};Q_{75})	16 (15.2;16.5)	15.5 (15.2;15.9)	0.23

Factors Associated with Osteoporosis and Vascular Calcification

According to the multivariate binary logistic regression analysis, osteoporosis was significantly positively associated with age, PTH levels, duration of dialysis therapy, comorbidity index, b-CrossLaps, and FGF23. The comorbidity index was identified as the most significant factor. Vascular calcification was also significantly positively associated with these factors but to a lesser extent (Table 2).

Table 2

Association of Osteoporosis and Vascular Calcification with Demographic Data and Biochemical Variables Based on Multivariate Logistic Regression Analysis (Binary)

Parameters	Osteoporosis			Vascular calcification		
	p	OR	CI	*p*	OR	CI
Age, years	0.00	5.84	1.7–6.2	0.02	1.05	0.97 – 1.12
Duration of dialysis, months	0.00	1.63	1.05–1.89	0.01	1.01	0.99 – 1.03
PTH level, pg/ml	0.01	1.01	1.01–1.30	0.03	1.37	0.78 – 2.41
Comorbidity index	0.00	2.50	1.80–3.20	0.02	1.00	0.99 – 1.00
b-CrossLaps level, ng/ml	0.01	1.30	1.10–1.50	0.01	2.11	0.80 – 5.67
FGF23 level, pmol/l	0.01	1.25	1.10–1.40	0.03	1.01	0.91 – 1.12

Based on ROC analysis, important predictive factors for osteoporosis were age ≥33 years (sensitivity 88%, specificity 70%; AUC = 0.88; $p = 0.00$), dialysis duration ≥12 months (sensitivity 84%, specificity 78%; AUC = 0.84; $p = 0.00$), comorbidity index ≥3 (sensitivity 92%, specificity 89%; AUC = 0.92; $p = 0.00$), and FGF23 ≥0.78 pmol/l (sensitivity 73%, specificity 75%; AUC = 0.73; $p = 0.01$). The least effective factors were PTH ≥301 pg/ml (sensitivity 62%, specificity 71%; AUC = 0.62; $p = 0.01$) and b-CrossLaps ≥0.52 ng/ml (sensitivity 66%, specificity 64%; AUC = 0.66; $p = 0.01$).

For vascular calcification, the most significant factors were the comorbidity index ≥3 (sensitivity 71%, specificity 60%; AUC = 0.71; $p = 0.01$), age ≥29 years (sensitivity 68%, specificity 61%; AUC = 0.71; $p = 0.01$), dialysis duration ≥5 months (sensitivity 64%, specificity 55%; AUC = 0.64; $p = 0.04$), and b-CrossLaps ≥0.19 ng/ml (sensitivity 60%, specificity 55%; AUC = 0.60; $p = 0.04$). Factors such as FGF23 ≥0.92 pmol/l (sensitivity 54%, specificity 61%; AUC = 0.54; $p = 0.01$) and PTH ≥301 pg/ml (sensitivity 58%, specificity 65%; AUC = 0.58; $p = 0.01$) were less significant (Table 3).

Table 3

Association of Osteoporosis and Vascular Calcification with Demographic Data and Biochemical Variables Based on ROC analysis

Parameters	Osteoporosis			Vascular calcification		
	p	AUC	Threshold value	*p*	AUC	Threshold value
Age, years	0.00	0.88	33	0.01	0.71	29
Duration of dialysis, months	0.00	0.84	12	0.04	0.64	5
PTH level, pg/ml	0.01	0.62	301	0.01	0.58	301
Comorbidity index	0.00	0.92	3	0.01	0.71	3
b-CrossLaps level, ng/ml	0.01	0.66	0.52	0.04	0.60	0.19
FGF23 level, pmol/l	0.01	0.73	0.78	0.01	0.54	0.92

Analysis of Serum Markers

The results of the univariate correlation analysis between bone turnover markers and demographic variables showed a direct statistically significant correlation between FGF23 and dialysis duration, b-CrossLaps and PTH concentration, as well as FGF23 and b-CrossLaps. The Charlson Comorbidity Index was also associated with age, and PTH level exacerbated the comorbidity index (Table 4).

Table 4

Univariate Correlations between Bone Turnover Markers and Characteristics of Patients with CKD

Parameter	Age, years	Dialysis duration, months	PTH, pg/ml	Comorbidity index	b-CrossLaps, ng/ml	FGF23, pmol/l
Age, years	–	0.19	0.12	0.73*	0.14	0.09
Dialysis duration, months	0.19	–	0.06	0.20	0.26	0.43*
PTH, pg/ml	0.12	0.06	–	0.36*	0.35*	0.20
Comorbidity index	0.73*	0.20	0.36*	–	0.16	0.03
b-CrossLaps, ng/ml	0.14	0.26	0.35*	0.16	–	0.34*
FGF23, pmol/l	0.09	0.43*	0.20	0.03	0.34*	–

* – significance level $p < 0.05$.

Dynamics of Bone Turnover Markers

After the ultrasound-guided paricalcitol injections into the parathyroid glands, a persistent and statistically significant reduction in PTH levels was observed in the main group ($p < 0.05$). Within the first 3 months of treatment, the median PTH concentration decreased from 504 (489.25;601) pg/ml to 426.55 (363.75;510.75) pg/ml, which is a reduction by 15.3% ($p < 0.01$). After 6 months of follow-up after the injections, the PTH level also decreased to 171.9 (115.5;266.9) pg/ml, which was 65.8% of the baseline level ($p < 0.01$). In the comparison group, a statistically significant increase in the median PTH concentration was noted ($p < 0.01$) from 365 (320;425) to 498 (353;694), which represented a 36.4% increase from the baseline level over 6 months (Fig. 1).

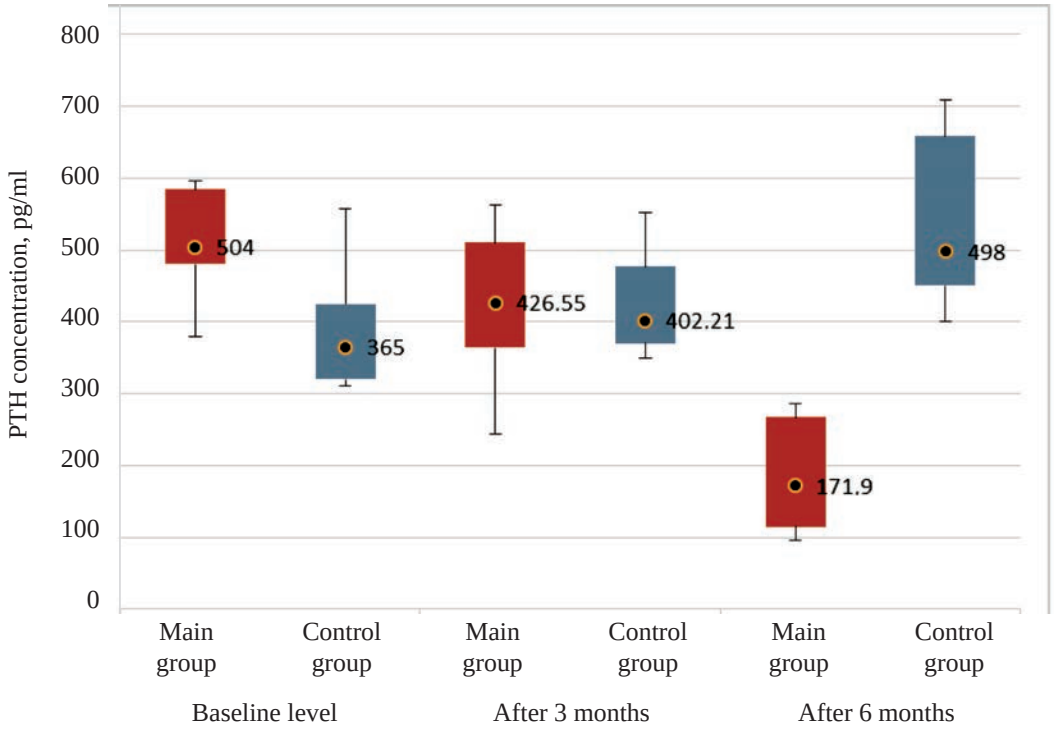

Fig. 1. Dynamics of parathyroid hormone concentration in both groups over 6 months

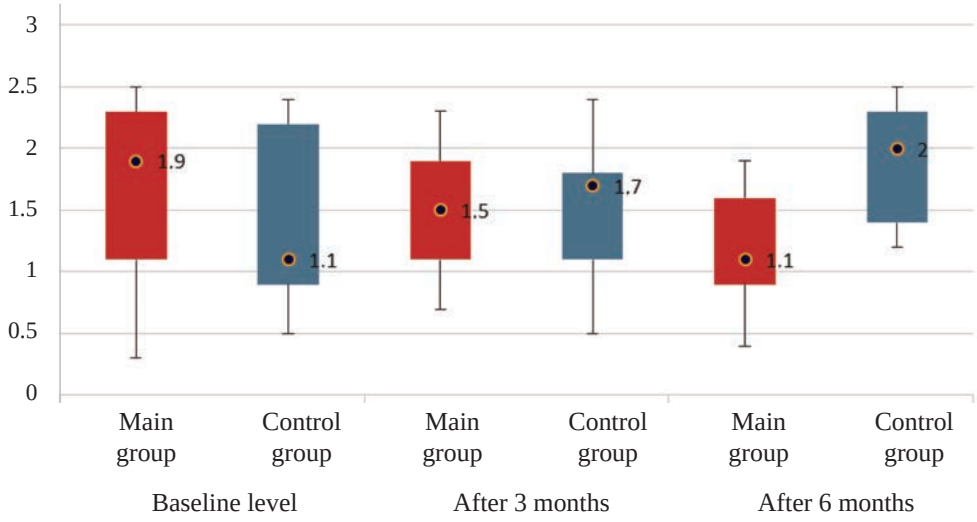

Fig. 2. Dynamics of b-CrossLaps concentration in both groups over 6 months, ng/ml. ANOVA Chi-Square in the main group was 24.03, and in the comparison group it was 38.80. Here and in Fig. 3, $p < 0.01$.

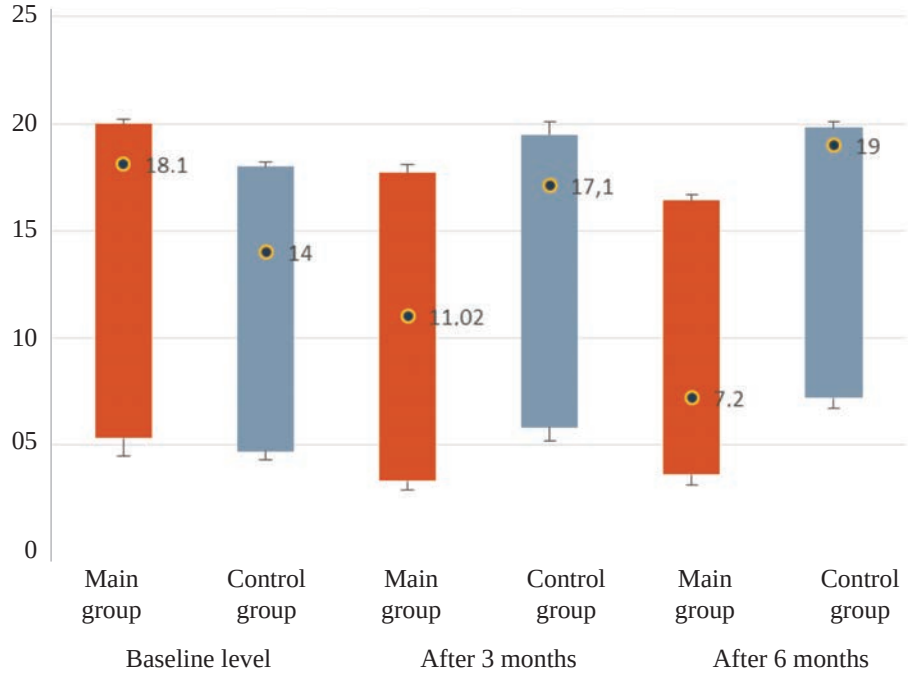

Figure 3. Dynamics of FGF23 concentration in both groups over 6 months, pmol/l. ANOVA Chi-Square in the main group was 33.00, and in the comparison group it was 65.61

In the comparison group, during the 6-month follow-up period, there was a trend towards an increase in bone resorption markers. Specifically, the level of b-CrossLaps increased significantly from 1.55 (0.9;2.2) ng/ml to 2 (1.3;2.4) ng/ml (p = 0.01), and FGF23 increased from 14.75 (4.73;18) pmol/l to 20 (7.2;20) pmol/l (p < 0.01).

In contrast, in the main group, b-CrossLaps significantly decreased from 1.9 (1.19;2.5) ng/ml to 1.1 (0.98;1.59) ng/ml (p = 0.03), and FGF23 decreased from 18.1 (5.3;20.0) pmol/l to 7.2 (3.0;16.4) pmol/l (p < 0.01) (Fig. 2, 3).

After local injections, the median volume of the parathyroid glands in the main group did not change significantly after 6 months and was 15.8 (15.2;16.0) mm³ (p = 0.24).

In our study, there were no cases of hoarseness, bleeding, or intramuscular hematomas following parathyroid gland injections in any of the observed cases. Local pain occurred in 8 (57%) patients in the main group during the procedure but resolved within 2–3 minutes after its completion.

DISCUSSION

Cardiovascular diseases are the leading cause of death in patients with CKD. Among patients with advanced CKD, cardiovascular diseases are predominantly associated with poorly controlled hypertension and left ventricular hypertrophy (LVH). Common causes of mortality include heart failure, stroke, and sudden cardiac death [26, 27]. Numerous studies have shown that the highest serum FGF23 concentrations are linked to LVH and mortality in CKD patients and those on dialysis [28, 29]. Furthermore, studies have demonstrated that a 30% or greater decrease in serum FGF23 levels is associated with lower rates of heart failure, sudden cardiac death, and cardiovascular mortality [30].

Additionally, there is evidence linking the progression of aortic valve stenosis to an imbalance in bone resorption and an increase in PTH levels in SHPT [31]. Patients with PTH levels exceeding target values have a 29% higher risk of complications [32]. At the same time, both PTH levels below 150 pg/ml and above 300 pg/ml are associated with all-cause and cardiovascular mortality [33].

Surgical treatment is highly effective and remains the mainstay for treating refractory SHPT with PTH levels exceeding 800 pg/ml. However, this approach has several drawbacks. A single-center retrospective study demonstrated a high incidence (71.2%) of hungry bone syndrome following surgical treatment of SHPT, with no statistically significant differences between total and subtotal parathyroidectomy [34]. Moreover,

low PTH levels (<50 pg/ml) after parathyroidectomy are associated with an increased risk of adynamic bone disease, vascular calcification, and mortality in hemodialysis patients [35].

The use of radiofrequency ablation (RFA) for parathyroid glands is becoming increasingly common as a minimally invasive treatment for SHPT. In patients with PTH levels above 800 pg/ml, severe hypocalcemia occurred in 22.1%, while recurrent laryngeal nerve damage was reported in 5.77% after the first session and 21.15% after the second session [36]. However, when this method was applied in patients with lower PTH levels (130–585 pg/ml), its effectiveness reached 70% at 6 months, with complications including a higher incidence of hoarseness (20%), permanent hypoparathyroidism (10%), and severe hypocalcemia (40%) [37].

Our study presents findings comparable to those of minimally invasive SHPT treatments but without severe complications such as recurrent laryngeal nerve paralysis, bleeding, or hematomas.

The dynamics of bone resorption markers in minimally invasive SHPT treatments remain unexplored. Currently, no literature data are available on their changes in SHPT correction with PTH levels up to 600 pg/ml. This gap highlights the need for further research.

CONCLUSION

The study demonstrated that local ultrasound-guided paricalcitol injections into the parathyroid glands result in a sustained and statistically significant reduction in PTH levels, a key factor in improving patient outcomes and preventing cardiovascular complications. Additionally, this approach positively affects bone remodeling processes, preventing further bone tissue degradation.

The absence of severe complications such as hoarseness, bleeding, or hematomas confirms the high safety of this procedure. Thus, this method can be recommended for the early correction of secondary hyperparathyroidism in CKD patients, potentially improving their prognosis and quality of life.

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Received on January 23, 2025;
approved after peer review on February 25, 2025;
accepted on February 27, 2025