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Original Research Article

Efficacy of calcitriol in the treatment of patients with renal osteodystrophy

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Abstract

Purpose: *To investigate the efficacy and prognosis of calcitriol in patients with renal osteodystrophy (ROD).*
Methods: *60 patients with ROD admitted to The Affiliated Huaian No. 1 People's Hospital of Nanjing Medical University, China between June 2020 and June 2021 were randomly grouped into control (n = 30) and study groups (n = 30). Patients in control group received routine management study group was treated with routine management plus calcitriol. The treatment duration was six months. Serological markers (parathyroid hormone (PTH), calcium (Ca), and phosphorus (Pi)), renal function indices (blood creatinine (SCr), urea nitrogen (BUN), and alkaline phosphatase (ALP)), as well as patients' skeletal conditions of the spine, pelvis, and extremities were investigated. Additionally, postoperative complications and clinical efficacy were also evaluated.*
Results: *Study group showed significant improvement in serological markers compared to control group ($p < 0.05$). Also, study group had significantly reduced SCr, BUN, and ALP levels ($p < 0.05$) compared to control group. There was significantly reduced incidence of complications and better skeletal conditions in study group compared to control group ($p < 0.05$).*
Conclusion: *Calcitriol effectively mitigates blood-bone mechanism dysfunction and reduces the occurrence of complications in patients with ROD. However, factors such as Scr, Hb, and blood pressure affect the clinical efficacy of calcitriol on renal bone disease by mechanisms that will be investigated in the future.*

Keywords: *Calcitriol, Renal osteodystrophy, Clinical efficacy, Prognostic factors*

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INTRODUCTION

Renal osteodystrophy (ROD) refers to skeletal damage caused by abnormalities in calcium, phosphorus and vitamin D metabolism, secondary hyperparathyroidism, and acid-base balance disorders following congenital renal hypoplasia, chronic nephritis and chronic renal failure [1,2]. With disease progression, skeletal lesions and tissue calcification may occur, resulting in joint pain, osteoporosis, and fractures, posing a significant health risk [3,4].

Treatment of ROD often involves removing phosphorus. Mild cases are managed with phosphorus-lowering drugs, while severe cases

require hemodialysis. However, side effects such as gastrointestinal discomfort, including nausea, vomiting, and diarrhea, have been reported after phosphorus-lowering medication [5,6]. Calcitriol, a metabolite of vitamin D, plays a crucial role in regulating blood calcium, and phosphorus concentrations, and prevents osteoporosis [7]. This study was therefore aimed at investigating the clinical efficacy of calcitriol in treatment of ROD patients.

METHODS

Participants

A total of 60 patients with renal ROD admitted to the Department of Orthopedics and Nephrology from June 2020 to June 2021 were randomly grouped equally into study and control groups with 30 patients in each group. Control group were treated with routine management, and study group received routine management in addition to calcitriol. The study was approved by the ethics committee of The Affiliated Huaian No.1 People's Hospital of Nanjing Medical University (approval no. LL28424A), and per the Declaration of Helsinki [8]. All patients and their families voluntarily took part in the study and signed informed consent forms.

Inclusion criteria

Patients who met the clinical diagnostic criteria for ROD [4], had a confirmed diagnosis of osteoporosis, no allergies to study drugs, patients with complete clinical data, and good treatment compliance.

Exclusion criteria

Patients with severe heart or lung diseases, hypercalcemia or diseases related to hypercalcemia, hyperparathyroidism, patients who used vitamin D-associated drugs within 1 month before study, and those who rescinded their consent.

Treatment modalities

Control group received routine management. Patients were advised to increase intake of calcium-rich foods (fish, dairy products, shrimp, oats), and reduce intake of high-phosphorus foods (peanuts, walnuts, and animal offal) to control calcium and phosphorus intake. Also, patients were instructed to receive calcium-containing (calcium carbonate, calcium acetate) or calcium-free (lanthanum carbonate, sevelamer), phosphorus-binding agents, to lower blood phosphorus if necessary. Small amounts and multiple doses were used to enhance absorption. Active vitamin D was administered intravenously or orally to prevent excessive hyperparathyroidism if thyroid hormone levels exceeded 150 - 300 pg/mL after calcium and phosphorus levels were controlled. Hemodialysis treatment was performed using 7102005 single pumps, 4008S, AK95S, Dialog+, Beltone Dialog type dialysis machine, and FB130 dialyzer to remove large molecule toxins. The blood flow was maintained at 150 - 200 mL/min, the amount of water removed was controlled at 500 - 1000 mL/h, and dialysis duration was 4 - 5 h/time. Dialysis treatment was scheduled 2 - 3 times a week. Serum-related indicators were tested regularly, and medication and hemodialysis regimen were adjusted according to patient's disease condition. Patients in study group received additional treatment with calcitriol (Shanghai Roche Pharmaceutical Co., Ltd., State Drug Administration). Dietary modification, oral calcium, vitamin D supplementation and hemodialysis were consistent with those of control group. Calcitriol was administered orally at an initial dose of 0.25 µg per day. For patients with normal or slightly low blood calcium levels, initial dose was reduced to 0.25 µg every 2 days. If no significant improvement in serum-related indicators was observed within 2 - 4 weeks of dosing, or if the patient's thyroid hormone exceeded 900 pg/ml, the dose was increased to 0.5 - 1.0 µg daily. During treatment, Ca and serum phosphorus (Pi) concentrations were measured at least once a week.

Evaluation of parameters/indices

Bone metabolism and biochemistry

Fasting venous blood samples were collected from patients before and after therapy. The blood samples were analyzed for parathyroid hormone (PTH), serum calcium (Ca), and serum phosphorus (Pi), which are key indicators of bone metabolism and biochemistry. The normal reference ranges for these analytes are as follows: PTH (1-10 pmol/L), Ca (2.25-2.75 mmol/L), and Pi (0.97-1.61 mmol/L). The closer the levels were to these normal ranges, the more effective the treatment outcome.

Blood creatinine (SCr), urea nitrogen (BUN), and alkaline phosphatase (ALP)

Blood creatinine (SCr), urea nitrogen (BUN), and alkaline phosphatase (ALP) were determined through an automated biochemical analyzer. Normal reference ranges for these analytes are as follows: SCr (41-111 umol/L), BUN (2.0-7.1 mmol/L), and ALP (35 - 135 U/L). Lower levels of

these markers indicated better treatment outcomes.

Skeletal conditions

Patients' skeletal conditions of the spine, pelvis, and extremities before and after treatment were examined, including bone pain, skeletal deformities, and pathological fractures.

Post-treatment complications

Both groups were monitored for post-treatment complications, including nausea and vomiting, dizziness and headache, muscle aches and pains, and hypercalcemia. The patient-related data were compared with the American Kidney Foundation guidelines for bone metabolism and bone disease control in chronic dialysis patients. Based on standard level, the patients were assigned to a standard group and non-standard group. Relationships between age, gender, body mass index, urea clearance index (Kt/v), hemoglobin (Hb), blood pressure, and high-sensitivity C-reactive protein (hs-CRP) were investigated.

Statistical analysis

Data was analyzed using Statistical Packages for Social Sciences (SPSS version 22.0). Measurement data were described as mean ± standard deviation (SD) and analyzed using independent sample t-test. Count data were presented as number of cases (%) and analyzed using the chi-square test. Univariate analysis was conducted to identify relevant factors that affected patients' prognosis, and multivariate logistic regression was conducted to identify risk factors that impacted patients' prognosis. $P < 0.05$ was considered statistically significant.

RESULTS

Patient characteristics

There was no significant difference in sex, age, disease duration and primary renal diseases between study and control groups ($p > 0.05$) (Table 1).

Serological indices

Study group showed significant increase in serological conditions (elevated Ca concentrations and reduced Pi and PTH levels) compared to control group ($p < 0.05$) (Table 2).

Renal function

As for superior renal function, study group had significantly reduced SCr, BUN, and ALP levels ($p < 0.05$) compared to control group (Table 3).

Skeleton conditions

Study group had better skeletal conditions compared to control group ($p < 0.05$) (Table 4).

Complications

Study group exhibited significantly lower incidence of complications compared to control group ($p < 0.05$) (Table 5).

Table 1: Comparison of patient baseline data (N = 30 in each group)

Group	Sex		Age (year)	Disease duration (months)	Primary renal diseases			
	Male	*Female*			*Glomerulo-nephritis*	*Chronic pyelonephritis*	*Hypertensive kidney damage*	*Diabetic nephropathy*
Control	15	15	42.24±6.68	20.46±4.96	18	5	3	4
Study	17	13	41.76±7.10	21.23±5.35	17	7	2	4
t/χ^2	0.268	0.270	0.578	0.341				
***P*-value**	0.605	0.788	0.565	0.560				

Table 2: Comparison of serological indices (mean ± SD) (N = 30 in each group)

Group	Ca (mmol/L)		Pi (mmol/L)		PTH (pg/L)	
	Before treatment	*After treatment*	*Before treatment*	*After treatment*	*Before treatment*	*After treatment*
Control	2.07±0.22	2.15±0.27	2.00±0.24	1.81±0.15	286.37±50.61	260.52±48.18
Study	2.04±0.18	2.43±0.25	1.98±0.25	1.60±0.12	288.34±50.77	210.50±45.06
T-value	0.578	4.168	0.316	5.988	0.151	4.153
P-value	0.565	0.001	0.753	0.001	0.881	0.001

Note: PTH (parathyroid hormone), Ca (calcium) Pi (phosphorus)

Table 3: Comparison of renal function (mean ± SD) (N = 30 in each group)

Group	SCr (μmol/L)		BUN (mmol/L)		ALP (U/L)	
	Before treatment	***After treatment***	***Before treatment***	***After treatment***	***Before treatment***	***After treatment***
Control	445.58±14.66	400.60±10.75	25.22±8.50	21.71±8.46	80.46±2.51	75.11±2.33
Study	448.65±15.10	380.89±11.13	24.89±8.62	17.12±8.15	80.55±2.64	70.45±2.41
T-value	0.800	6.977	0.150	2.140	0.135	7.614
P-value	0.428	0.001	0.882	0.037	0.893	0.001

SCr (blood creatinine), BUN (urea nitrogen), ALP (alkaline phosphatase)

Table 4: Comparison of skeleton conditions (N = 30 in each group)

Group	Bone pain		Bone deformity		Pathological fracture		Post-treatment inefficiency
	Before treatment	***After treatment***	***Before treatment***	***After treatment***	***Before treatment***	***After treatment***	
Control	16	7	7	1	7	1	9
Study	15	2	6	0	9	0	2
χ^2	-	-	-	-	-	-	5.455
P-value	-	-	-	-	-	-	0.020

Table 5: Comparison of complications (N = 30 in each group) (N, %)

Group	Nausea and vomiting	Dizziness and headache	Muscle aches and pains	Hypercalcemia	Total incidence
Control	6(0.20)	0(0)	2(0.07)	0(0)	8(0.27)
Study	2(0.07)	0(0)	0(0)	0(0)	2(0.07)
χ^2	-	-	-	-	4.320
P-value	-	-	-	-	0.038

Table 6: Univariate analysis (mean ± SD)

Group	Standard group	Non-standard group	t/x^2	*P*-value
Scr (μmol/L)	445.58±14.66	471.84±27.06	6.609	0.001
Hb (g/L)	108.51±11.23	99.82±12.50	4.006	0.001
Hs-CRP (mg/L)	7.66±6.79	8.58±9.45	0.612	0.541
BMI (kg/m^2)	22.54±3.31	25.06±3.45	4.083	0.001
Age (years)	45.15±5.24	46.22±5.10	1.133	0.259
Kt/v	1.30±0.09	1.28±0.10	1.152	0.252
Gender (Male/Female)	10/6	22/22	0.737	0.391
Hypertension (n)	9	40	7.241	0.007

SCr (blood creatinine), Hb (hemoglobin), HS-CRP (high-sensitivity C-reactive protein), BMI (body mass index), Kt/v (urea clearance index).

Univariate analysis

Before treatment, there were 32 cases (53.3 %) with serum Ca concentration, 24 cases (40.0 %) with serum Pi concentration, 36 cases (60.0 %) with Ca Pi product, and 18 cases (30.0 %) with intact PTH that reached the required level set by the guideline, but only 16 cases (26.7 %) reached the required level for all indices. There was no significant difference in age, gender, Kt/v as well as HS-CRP between the two groups ($p > 0.05$). However, Scr, Hb, BMI, and blood pressure were significantly different ($p < 0.05$) (Table 6).

Multivariate analysis

Risk factors that impacted patients' prognosis of renal osteodystrophy were Scr, Hb and hypertension (Table 7).

DISCUSSION

Renal osteodystrophy (ROD) is not absolutely cured, as a result, active control, regular and periodic monitoring becomes the only effective means of management [9,10]. Primary principle of clinical treatment of ROD is to correct secondary hyperparathyroidism and regulate calcium and phosphorus metabolism levels [11,12].

Studies have shown that calcitriol provides superior therapeutic benefits compared to conventional treatment for patients with ROD, effectively improves body metabolism, and alleviates clinical symptoms [13,14].

Table 7: Multivariate analysis

Index	B	OR	OR 95 % CI	*P*-value
Scr (μmol/L)	0.005	1.005	1.002-1.008	0.010
Hb (g/L)	0.044	0.957	0.923-0.987	0.010
Hs-CRP (mg/L)	0.007	1.007	0.960-1.055	0.739
BMI (kg/m^2)	0.005	1.005	0.872-1.153	0.935
Age (years)	0.012	0.986	0.945-1.020	0.482
Kt/v	4.787	0.008	0.000-3.050	0.110
Gender (Male/Female)	0.385	0.668	0.230-1.948	0.460
Hypertension (n)	1.670	0.188	0.057-0.590	0.003

SCr (blood creatinine), Hb (hemoglobin), HS-CRP (high-sensitivity C-reactive protein), BMI (body mass index), Kt/v (urea clearance index)

In this present study, patients treated with calcitriol showed more improvements in serological conditions (elevated Ca concentrations and reduced Pi and PTH levels) than those receiving routine management. Additionally, calcitriol was found to enhance renal function (significant decrease in serum concentrations of SCr, BUN, and ALP) more effectively than routine management. Moreover, patients treated with calcitriol exhibited better skeletal conditions, and a significantly reduced incidence of complications compared to routine therapy.

The above results indicated that calcitriol effectively ameliorated patients' symptoms, played a significant role in regulating patients' blood-bone metabolic dysfunction, and reducing complications in the treatment of ROD. In addition, the study identified several factors that may be associated with renal bone disease, including age, gender, body mass index, Scr, Kt/v, Hb, HS-CRP, and blood pressure. The findings revealed that high Scr, low hemoglobin, high blood pressure, and high BMI were identified as independent risk factors for chronic renal failure complicated by renal bone disease. Among these factors, Scr, Hb and high blood pressure were independent as risk factors for the development of renal bone disease. Vitamin D regulates Ca and Pi metabolism in the body, and promotes bone formation and skeletal calcification [15].

Calcitriol, the biologically active form of vitamin D, stimulates intestinal calcium transport, leading to the transfer of Ca and Pi from the blood to the circulation. This process promotes the absorption of Ca and Pi in the proximal tubules of the kidney, maintaining the dynamic balance of Ca and Pi in the body. [16,17]. In addition, calcitriol directly affects the skeletal, intestinal, renal, and parathyroid systems. It enhances the sensitivity of the parathyroid glands to calcium and inhibits transcriptional activity of PTH gene and proliferation efficiency of parathyroid cells, thereby reducing secretion and synthesis of PTH [18,19]. However, it is essential to closely monitor patients' blood Ca and Pi concentrations when using calcitriol. If blood Ca and Pi concentrations remain elevated, dosing adjustments or medication discontinuation may be necessary to prevent potential complications such as myocardial infarction due to vascular calcification [20].

Limitations of this study

This study used a limited number of patients in a single study center. It is therefore difficult to apply these findings in a general scale. Furthermore, the scope of this study did not cover the molecular mechanism of calcitriol in ROD and kidney function which will be very important in arriving at clear scientific conclusion about its action.

CONCLUSION

Calcitriol effectively ameliorates dysfunction of blood-bone metabolism and reduces incidence of complications in patients with ROD. However, while correcting Ca and Pi metabolism disorders and secondary hyperparathyroidism, it is also necessary to achieve standard levels of blood pressure and Hb, comprehensively control bone metabolism in chronic renal failure patients, and reduce occurrence of renal bone disease. These will for the basis for future investigations.

DECLARATIONS

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Ethical approval

None provided.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Haitao Jiang and Haiyuan Lu conceived and designed the study, and drafted the manuscript. Haitao Jiang, Xiaoming Tang, Cheng Zhang and Jian Dai collected, analyzed and interpreted the experimental data. Haitao Jiang and Xiaoming Tang revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

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