

Original Research Article

Potential indicators for hyperparathyroidism progression: Calcium, phosphorus, alkaline phosphatase, 25 hydroxyvitamin D and hemoglobin

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Abstract

Purpose: To compare the differences in perioperative biochemical indices between patients with primary hyperparathyroidism (PH) and secondary hyperparathyroidism (SH).

Methods: One hundred and ten patients with hyperparathyroidism who were treated in The Affiliated Hospital of Chengde Medical University, from June 2016 to April 2021, were enrolled and divided into two groups, viz, PH group (50 patients) and SH group (60 patients). Automatic biochemical analyzer was used to determine the levels of calcium, phosphorus, alkaline phosphatase and 25-hydroxyvitamin D, while hemoglobin was determined by liquid chromatography coupled with tandem mass spectrometry in the perioperative period.

Results: Compared to PH group, SH group had higher levels of indicators ($p < 0.05$). There were significant differences in body mass index (BMI), somatic cell index and blood albumin in patients from 18 to 70 years ($p < 0.05$). BMI and blood albumin increased significantly with age ($p < 0.05$). The complication rate was higher in SH than PH group ($p < 0.05$). The scores of pruritus and bone pain of patients after surgery were lower than those before the operation ($p < 0.05$). Blood calcium levels increased significantly with age, while ALP and iPTH levels decreased significantly ($p < 0.05$). SH group showed lower scores of physiological, emotional, social, and cognitive functions than PH group ($p < 0.05$).

Conclusion: Patients with PH and SH have differences in perioperative biochemical indicators. Furthermore, the levels of calcium, phosphorus, alkaline phosphatase, 25 hydroxyvitamin D, and hemoglobin may be used as indicators of disease progression, and this may facilitate the development of suitable therapeutic measures.

Keywords: Biochemical indices, Hyperparathyroidism, Perioperative, Renal failure

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INTRODUCTION

Available data show that the incidence of chronic renal failure is increasing annually and patients often develop complications such as secondary

hyperparathyroidism after long-term chemotherapy, which seriously affect patients' prognosis and quality of life [1]. Patients often develop symptoms such as metastatic calcification, bone pain, and multiple fractures,

which impact patient activity as well as quality of life [2]. Therefore, appropriate treatment options, such as drug and surgical treatments, should be selected. However, some patients develop drug resistance after long-term administration, which has a negative impact on treatment efficiency. Surgical treatment prevents drug resistance that develops over time [3].

Some scholars found that there are differences in perioperative biochemical indicators between patients with primary and secondary hyperparathyroidism [4]. However, there are few studies providing a comprehensive analysis.

This study investigates the differences in perioperative biochemical indices such as calcium and phosphorus, alkaline phosphatase, and 25 hydroxyvitamin D were analyzed, with the aim to provide a basis for the clinical treatment of hyperparathyroidism.

METHODS

Baseline data

One hundred and ten patients with hyperparathyroidism treated in the Affiliated Hospital of Chengde Medical University, Chengde, from June 2016 to April 2021 were selected, including 50 of the comprised patients with primary hyperparathyroidism (PH group) and 60 patients with renal failure and secondary hyperparathyroidism (SH group). Of the 110 patients, there were 45 males and 65 females, aged 17 - 77 years, with a mean age of (49.9 ± 1.1) years. The average dialysis time was (6.7 ± 0.5) years in 60 patients with secondary hyperparathyroidism, including 8 patients on peritoneal dialysis and 52 patients on hemodialysis. The patients' signed informed consent was obtained, and the study was approved by the Ethics Committee of Affiliated Hospital of Chengde Medical University (approval no. CYFYLL2019002). The study followed the ethical principles of the Declaration of Helsinki regarding human experimentation [5].

Inclusion criteria

The included subjects were patients who were clinically diagnosed with hyperparathyroidism; who had significant symptoms and met the diagnostic criteria of renal failure or hyperparathyroidism [6]; who had a normal cognitive function and did not participate in other studies during the study period; who had stable vital signs with an expected survival >12 months; and those who were available for prognostic follow-up.

Exclusion criteria

Patients with psychiatric disorders, coagulation disorders, cardiac dysfunction, patients who withdrew from the study, and pregnant or lactating patients, were excluded.

Procedures and treatments

Preoperatively, calcitriol was administered to increase the phosphorus and calcium concentration of osteocytes, and sodium bicarbonate tablets were used for acid-base balance treatment, avoiding acidosis. Heparin-free dialysis was performed one day before and after surgery, and phosphorus and calcium ions were tested on the day of surgery and the next day following surgery. Venous blood was drawn to determine hypocalcemia and evaluate the patient's self-perceived symptoms, and calcium supplementation was given immediately if hypocalcemia occurred.

After admission, 3 mL of fasting venous blood was collected and centrifuged at 3,500 rpm for 10 min to obtain serum. Hitachi 7600 automatic biochemical analyzer was used to determine the indices of calcium, phosphorus, alkaline phosphatase and 25-hydroxyvitamin D by liquid chromatography coupled with tandem mass spectrometry.

The kit was provided by Haikehua Dongling Diagnostic Supplies Co., Ltd. The related operations were carried out in strict accordance with the instructions. The remission of signs and clinical symptoms was observed, and the safety of treatment was followed up.

Evaluation of parameters/indices

Nutrient metabolism

The nutrient metabolism and blood biochemical indices in patients with varying ages were analyzed.

Complications

The complications of the two groups, including wound infection, lung infection, hypocalcemia, and hoarseness were recorded and compared.

Pruritus and bone pain score

The skin pruritus and bone pain scores before and after parathyroidectomy were compared. The lower score represented the lower degree of skin pruritus and bone pain.

Bone metabolism

The indices of bone metabolism at different ages were compared. Blood calcium and blood phosphorus levels were measured in patients at the age of ≤ 18 , 19 - 30, 41 - 50, 51 - 60, 61 - 70, and ≥ 70 , respectively.

Quality of life

The SF-36 scale [7] was applied to assess the quality of life of patients between the two groups, including physical function, emotional function, social function, and cognitive function scores, covering 0 - 100 points. The higher score represented a better quality of life.

Statistical analysis

Statistical Package for Social Science (SPSS) 19.0 statistical software (SPSS Inc., Chicago, IL, USA) was used for data analysis. The statistical data was analyzed using a two-sided test;

Quantitative data was expressed as mean \pm standard deviation (SD), and was analyzed using *t*-test while ANOVA was used for comparison between the two groups with post hoc LSD test.

Qualitative data was tested using χ^2 test, while graphs were made using Graphpad Prism 8 (La Jolla, CA, USA). The differences were considered significant at $p < 0.05$.

RESULTS

Differences in perioperative biochemical indicators

Compared with the first day after surgery, the indicators of calcium and phosphorus, alkaline phosphatase, 25 hydroxyvitamin D, and hemoglobin (%) were significantly lower at 7 days, 1 month, and 6 months postoperatively, but the indicators were relatively higher in the SH group than in the PH group ($p < 0.05$) Table 1.

Nutrient metabolism and blood biochemical indices

There were significant differences in BMI and blood albumin among patients of varying ages ($p < 0.05$). The BMI and blood albumin increased significantly with age, but there were no significant differences in hemoglobin, erythrocyte specific volume, triacylglycerol, and total cholesterol among patients of varying ages ($p > 0.05$) (Table 2).

Complications

The complication rate was 40.0 % in the SH group, which was higher than 14.0 % in the PH group ($p < 0.05$) (Table 3).

Skin pruritus and bone pain scores

The scores of pruritus and bone pain of patients after operation were lower than those before operation, and there were statistically significant differences in the scores of pruritus and bone pain of patients before and after operation ($p < 0.05$) (Table 4).

Bone metabolic indices

There were no significant differences in bone metabolic indices among patients of varying ages ($p > 0.05$). There were significant differences in blood calcium, ALP, and iPTH among patients of varying ages. The blood calcium levels increased significantly with age, and ALP and iPTH levels decreased significantly ($p < 0.05$), (Figure 1).

Quality of life

The scores on physical function, emotional function, social function, and cognitive function scores were lower in SH group than in PH group ($p < 0.05$; Figure 2).

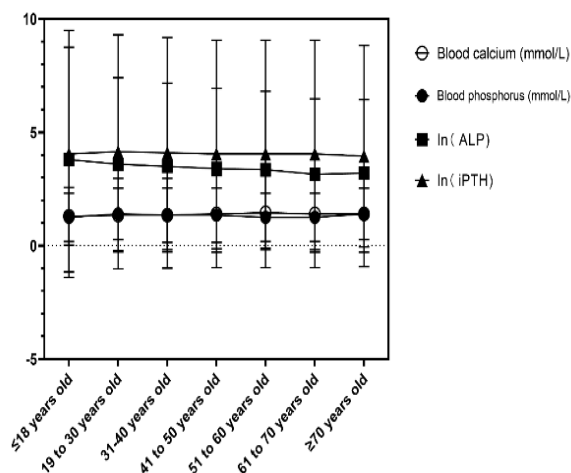


Figure 1: Comparison of bone metabolic indices by age. There were no significant differences in blood phosphorus levels by age ($p > 0.05$), However there were significant differences in blood levels of calcium, ALP and iPTH levels by age, and with increasing age, blood calcium levels increased significantly, and ALP and iPTH levels decreased significantly ($p < 0.05$)

Table 1: The levels of perioperative biochemical indicators between two groups (mean \pm SD)

Group	Post-surgery day	Calcium phosphorus (mg/dL ²)	Alkaline phosphatase (U/L)	25-hydroxyvitamin D (ng/mL)	Hemoglobin (%)
Primary hyperparathyroidism (n=50)	1 day after surgery	66.3 \pm 19.9	389.8 \pm 20.3	12.7 \pm 5.5	8.3 \pm 1.7
	7 days after surgery	37.4 \pm 13.9 ^a	421.6 \pm 22.5 ^a	11.4 \pm 4.9 ^a	7.9 \pm 1.8 ^a
	1 month postoperatively	30.2 \pm 13.4 ^{ab}	529.1 \pm 26.2 ^{ab}	10.3 \pm 4.8 ^{ab}	7.2 \pm 1.4 ^{ab}
	6 months postoperatively	27.5 \pm 12.1 ^{abc}	320.6 \pm 24.1 ^{abc}	8.9 \pm 3.7 ^{abc}	5.3 \pm 0.4 ^{abc}
Renal failure with secondary hyperparathyroidism (n=60)	1 day after surgery	68.5 \pm 22.5	402.6 \pm 21.8	13.6 \pm 5.7	8.7 \pm 1.9
	7 days postoperative	39.6 \pm 14.2 ^a	431.4 \pm 23.6 ^a	11.8 \pm 5.2 ^a	8.2 \pm 2.0 ^a
	1 month postoperatively	31.5 \pm 14.7 ^{ab}	536.7 \pm 28.5 ^{ab}	10.9 \pm 4.7 ^{ab}	7.5 \pm 1.6 ^{ab}
	6 months postoperatively	28.2 \pm 12.5 ^{abc}	322.5 \pm 24.7 ^{abc}	9.4 \pm 3.9 ^{abc}	4.8 \pm 0.3 ^{abc}

Compared with 1 day after surgery, ^a $p < 0.05$; compared with 7 days after surgery, ^b $p < 0.05$; compared with 1 month after surgery, ^c $p < 0.05$

Table 2: Analysis of nutrient metabolism and blood biochemical indices in patients of different ages (mean \pm SD)

Parameter	≤ 18 years	19-30 years old	31-40 years old	41-50 years old	51-60 years old	61-70 years old	>70 years old	P-value
Hemoglobin (g/L)	95.7 \pm 23.7	95.2 \pm 20.0	104.7 \pm 19.5	100.6 \pm 18.1	104.0 \pm 19.4	103.4 \pm 20.9	102.6 \pm 18.8	>0.05
Erythrocyte volume (%)	28.8 \pm 6.1	29.7 \pm 6.2	32.5 \pm 5.9	31.4 \pm 5.6	32.4 \pm 6.0	32.4 \pm 6.7	31.6 \pm 5.2	>0.05
BMI (kg/m ²)	20.5 \pm 3.0	20.7 \pm 3.2	21.7 \pm 4.3	21.8 \pm 3.2	21.8 \pm 4.0	22.8 \pm 3.2	21.9 \pm 2.8	<0.05
Blood albumin (g/L)	35.0 \pm 3.0	39.1 \pm 4.3	39.3 \pm 4.5	38.0 \pm 4.2	38.0 \pm 4.0	37.3 \pm 4.0	35.0 \pm 3.0	<0.05
Triacylglycerol (mmol/L)	1.5 \pm 1.0	1.1 \pm 0.4	1.6 \pm 1.0	1.6 \pm 1.2	1.4 \pm 0.8	1.5 \pm 1.1	0.9 \pm 0.2	>0.05
Total cholesterol (mmol/L)	4.8 \pm 0.5	4.0 \pm 0.8	4.2 \pm 0.9	4.2 \pm 0.9	4.1 \pm 0.9	4.0 \pm 1.0	3.5 \pm 1.1	>0.05

Table 3: Comparison of complications between the two groups (cases, %)

Group	Number of cases	Wound infection	Pulmonary infection	Hypocalcemia	Hoarse voice	Incidence
Primary hyperparathyroidism	50	2 (4.0)	2(4.0)	1 (2.0)	2 (4.0)	14.0%
Renal failure with secondary hyperparathyroidism	60	2 (3.3)	5 (8.3)	10 (16.7)	7 (11.7)	40.0%
χ^2		0.035	0.860	6.519	2.134	9.109
P-value		0.852	0.354	0.011	0.144	0.006

Table 4: Comparison of pruritus and bone pain scores before and after surgery (mean \pm SD, points)

Parameter	Number of cases	Preoperative	After 1 week	1 month after surgery	6 months after surgery	12 months after surgery
Bone pain score	110	5.1 \pm 0.8	4.9 \pm 0.6 ^a	4.7 \pm 0.7 ^{ab}	3.2 \pm 0.4 ^{abc}	2.6 \pm 0.3 ^{abcd}
Pruritus score	110	3.6 \pm 0.5	1.8 \pm 0.3 ^a	1.7 \pm 0.2 ^{ab}	1.6 \pm 0.4 ^{abc}	0.7 \pm 0.2 ^{abcd}

Compared with preoperative, ^a $p < 0.05$; compared with 1 week after operation, ^b $p < 0.05$; compared with 1 month after operation, ^c $p < 0.05$; compared with 6 months after operation, ^d $p < 0.05$.

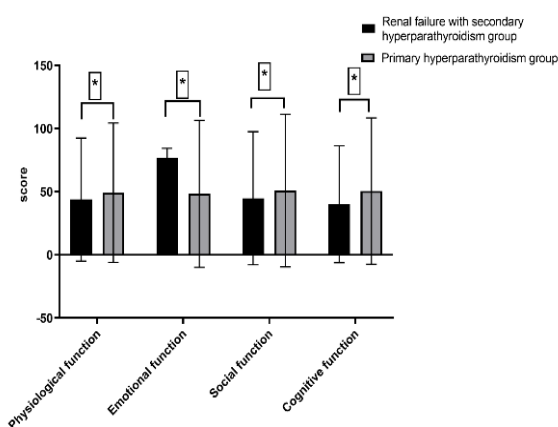


Figure 2: Comparison of quality of life between the two groups. Scores for the physical function, emotional function, social function, and cognitive function were lower in the renal failure with secondary hyperparathyroidism group than in PH group ($p < 0.05$).

DISCUSSION

Chronic renal failure disrupts calcium and phosphorus metabolism, which stimulates parathyroid cell proliferation and induces hyperthyroidism [8-10]. Data show that the incidence of hyperthyroidism in patients with end-stage renal failure is as high as 80 % [11]. Therefore, clinical staff should be highly concerned about this phenomenon [12]. In this study, the scores of skin pruritus and bone pain were significantly reduced after treatment. The results indicate that there were differences in the degree of improvement of clinical symptoms,

depending on the severity of the condition. The study examined changes in bone metabolic indices in patients with PH and SH, and the results showed that blood calcium increased significantly, and ALP and iPTH decreased significantly with increasing age. The results confirm that the surgical treatment of patients may improve their bone metabolic indices. However, the recovery time of bone metabolic indices is relatively longer with increase in age, therefore, the physicians should pay some attention to individual condition of the elderly and develop targeted treatment options [13,14]. Currently, there are three treatment options: total parathyroidectomy with auto-transplantation, sub-total parathyroidectomy, and total parathyroidectomy. Physicians should consider the indicators for surgery and choose the appropriate treatment options [15,16].

Patients with end-stage renal failure need dialysis treatment, which is often accompanied by adverse emotions due to the long duration of dialysis, and which is not conducive to recovery [17,18]. In this study, the changes in quality of life were investigated, and the results showed that patients' physical, emotional, social, and cognitive functions improved significantly, but the quality of life scores were lower in the SH group than in the PH group, indicating that secondary hyperparathyroidism affects patients' daily quality of life to a greater extent [19-21]. Therefore, accurate and early treatment should be carried out [22]. The results of this study also showed that the complication rate in the SH group was significantly higher than in the PH group. Hypoproteinemia and hypercalcemia can affect

the outcome and safety of patients, and can be clinically treated and recovered by oral or intravenous calcium [23]. This study also showed that perioperative biochemical indices were higher in the SH group than in the PH group, and there were significant differences in BMI and blood albumin among patients of varying ages, and these indices were elevated with increasing age. These results indicate that the clinical analysis of calcium and phosphorus, alkaline phosphatase, BMI, and blood albumin levels can play a very key role in the prognostic evaluation of patients.

CONCLUSION

There are significant differences in perioperative biochemical indices between SH and PH groups. The levels of calcium, phosphorus, alkaline phosphatase, 25 hydroxyvitamin D, and hemoglobin may be used as indicators of disease progression to facilitate the development of therapeutic measures. There will however, be need to carry out this investigation in other centers using larger numbers of patients and procedures to validate these findings.

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

The authors 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 them.

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