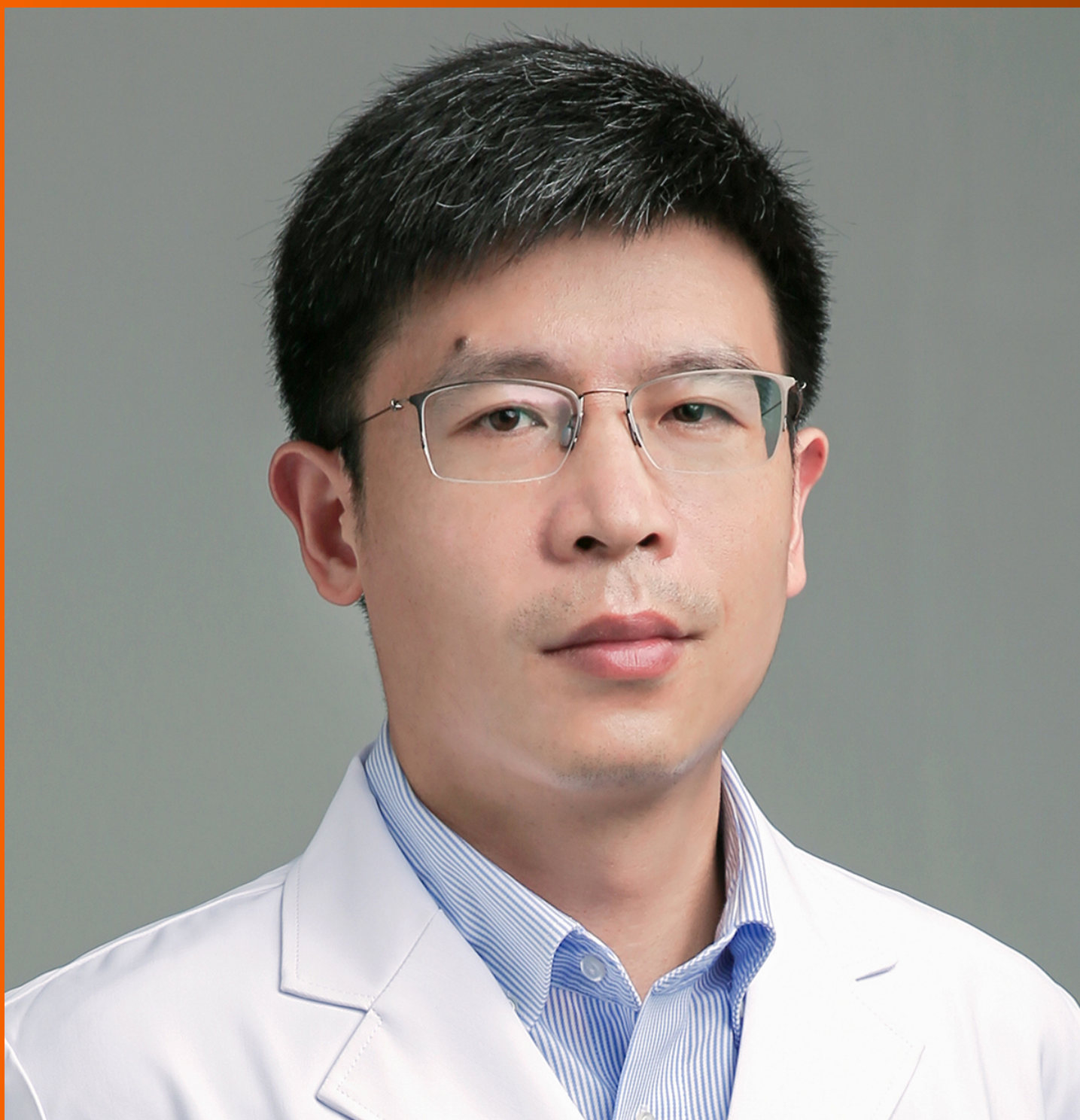


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ABOUT COVER

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Retrospective Study

Effect of calcium supplementation on severe hypocalcemia in patients with secondary hyperparathyroidism after total parathyroidectomy

Jun Liu, Xue-Feng Fan, Meng Yang, Lin-Ping Huang, Ling Zhang

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Abstract

BACKGROUND

Severe hypocalcemia (SH) is a dreaded complication of total parathyroidectomy (TPTX) without auto-transplantation.

AIM

To compare conventional and preventive calcium supplementation (CS) regimens in terms of SH occurrence after TPTX.

METHODS

This retrospective study included patients who underwent TPTX between January 2015 and May 2018 at the China-Japan Friendship Hospital. From January 2015 to May 2016, conventional CS was performed in patients who underwent TPTX, with calcium amounts adjusted according to postoperative serum calcium levels. From October 2016 to May 2018, preventive CS was performed according to preoperative alkaline phosphatase (ALP) levels. The patients were defined as low-risk (ALP < 500 U/L) and high-risk (ALP > 500 U/L) for SH. All preoperative blood samples were collected in the fasting state on the day before surgery. Postoperative blood samples were obtained at 6-7 AM from the first postoperative day.

RESULTS

A total of 271 patients were included. These patients were 47.7 ± 11.1 years old,

and 57.6% were male. Their mean body mass index (BMI) was 22.9 ± 3.8 kg/m². There were no significant differences in sex, age, BMI, preoperative ALP, serum calcium, serum phosphorus, calcium-phosphorus ratio, and intact parathyroid hormone (iPTH) between the two CS groups. Compared with conventional CS, preventive CS led to lower occurrence rates of hypocalcemia within 48 h (46.0% *vs* 74.5%, $P < 0.001$) and SH (31.7% *vs* 64.1%, $P < 0.001$). Multivariable analysis showed that preoperative iPTH levels [odds ratio (OR) = 1.001, 95% confidence interval (CI): 1.000-1.001, $P = 0.009$], preoperative ALP amounts (OR = 1.002, 95% CI: 1.001-1.003, $P = 0.002$), preoperative serum phosphorus levels (OR = 8.729, 95% CI: 1.518-50.216, $P = 0.015$) and preventive CS (OR = 0.132, 95% CI: 0.067-0.261, $P < 0.001$) were independently associated with SH. In patients with preoperative ALP ≥ 500 U/L, only preventive CS (OR = 0.147, 95% CI: 0.038-0.562, $P = 0.005$) was independently associated with SH.

CONCLUSION

This study suggests that preventive CS could reduce the occurrence of SH, indicating its critical value for hypocalcemia after TPTX.

Key Words: End-stage renal disease; Secondary hyperparathyroidism; Parathyroidectomy; Hypocalcemia; Calcium supplementation

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Core Tip: Compared with conventional calcium supplementation (CS), preventive CS led to lower occurrence rates of hypocalcemia within 48 h and severe hypocalcemia (SH). Multivariable analysis showed that preoperative intact parathyroid hormone levels, preoperative alkaline phosphatase (ALP) amounts, preoperative serum phosphorus levels, and preventive CS were independently associated with SH. In patients with preoperative ALP > 500 U/L, only preventive CS was independently associated with SH.

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INTRODUCTION

Secondary hyperparathyroidism (SHPT), a common complication of end-stage renal disease (ESRD), is characterized by the progressive hyperplasia of parathyroid glands and increased secretion of parathyroid hormones[1,2]. After 3-10 and 20 years of hemodialysis, respectively, 20% and 40% of patients require parathyroidectomy (PTX)[3]. At present, subtotal and total PTX plus auto-transplantation are the standard procedures for the treatment of SHPT. In the context of dialysis, SHPT may recur; in this case, total PTX (TPTX) without auto-transplantation is an effective therapeutic option [3]. However, postoperative hypocalcemia limits its clinical application[4,5].

Despite monitoring serum calcium levels and adjusting the amounts of supplemented calcium and vitamin D, the incidence of hypocalcemia after TPTX remains high, *i.e.*, 72%-97%[6]. Hypocalcemia occurs due to the abrupt withdrawal of parathyroid hormones, which results in a sharp increase in bone remineralization (hungry bone syndrome), depleting calcium from the circulation[7-9]. The ensuing severe hypocalcemia (SH) is a critical condition that may result in convulsions, arrhythmias, and even sudden death. Therefore, the possible complications of hypocalcemia limit the clinical application of TPTX. Studies have examined the prognostic factors of hypocalcemia after PTX[10-13] but reported conflicting data due to different methods.

Maintaining adequate calcium levels after TPTX is required to avoid hypocalcemia complications and hungry bone syndrome[14]. Viaene *et al*[15] showed that high preoperative parathyroid hormone levels and low calcium amounts are predictive of SH after TPTX[15]. Previous studies have used alkaline phosphatase (ALP) levels to predict the level of calcium supplementation (CS), with apparent success in improving patient outcomes[16,17]. Nevertheless, efficient tools for reducing or preventing SH after TPTX have not been reported.

Therefore, this study aimed to identify risk factors for SH and compare conventional and preventive CS regimens for their effects on SH occurrence after TPTX. We found that preventive CS reduces the

occurrence of SH, indicating its critical value for hypocalcemia after TPTX.

MATERIALS AND METHODS

Study design and patients

This work was carried out in accordance with the Declaration of Helsinki (2000) by the World Medical Association. The current retrospective study was approved by the institutional review board of China-Japan Friendship Hospital (2019-SDZL-12). The requirement for written informed consent was waived due to the retrospective nature of this study. The records of patients who underwent TPTX between January 2015 and May 2018 were reviewed. The inclusion criteria were: (1) Age > 18 years; (2) ESRD complicated with SHPT; and (3) TPTX administration. The exclusion criteria were: (1) Severe complications before surgery; or (2) Incomplete medical records.

The diagnosis of SHPT was based on hypocalcemia or normocalcemia with elevated parathyroid hormone levels in patients with chronic kidney disease, vitamin D deficiency, or inadequate calcium intake or absorption[18,19]. Hypocalcemia and SH were defined as total calcium corrected for albumin < 2 mmol/L and < 1.875 mmol/L, respectively.

TPTX

Indications for TPTX in patients with ESRD complicated with SHPT were: (1) Intact parathyroid hormone (iPTH) amounts exceeding 800 pg/mL before surgery; (2) Uncontrollable hypercalcemia with hyperphosphatemia or refractory PTH accompanied by clinical symptoms such as bone pain and itchiness; (3) Previous resistance to active vitamin D; and (4) Doppler ultrasound showing more than one parathyroid gland enlarged by over 1 cm, and abundant blood flow[10]. Surgeries were performed by surgeons with > 10 years of experience. Under general anesthesia, the back of the cervical thyroid was explored to identify all four parathyroid glands, which were completely removed. The thymus was not routinely explored or removed. If less than four parathyroid glands were found, the thymus was explored, and the suspected parathyroid glands were removed.

The CS protocol

Between January 2015 and May 2016, conventional CS was performed in patients who underwent TPTX. The amounts of supplemented calcium were adjusted according to postoperative serum calcium levels. The CS protocol in our hospital changed after October 2016 due to a significant number of patients developing hypocalcemia after surgery. From October 2016 to May 2018, preventive CS was performed in patients with ESRD complicated by SPTH after TPTX. According to preoperative ALP levels, the patients were defined as low-risk (ALP < 500 U/L) and high-risk (ALP > 500 U/L) for SH. Low-risk cases received supplementation with 50 mL of 10% calcium gluconate daily, and the level of CS was adjusted according to daily serum calcium amounts. In high-risk patients, supplementation with 100 mL of 10% calcium gluconate was performed daily, with the level of CS also adjusted according to daily serum calcium amounts. In both the low- and high-risk groups, CS was started on the day of surgery.

Data collection

All preoperative blood samples were collected in the fasting state on the day before surgery. Postoperative blood samples were obtained at 6-7 AM from the first postoperative day (within 48 h after TPTX) to monitor daily blood calcium. Postoperative CS was administered at around 8 AM daily. Age, sex, body mass index (BMI), preoperative serum calcium amounts, serum phosphorus levels, calcium-phosphorus ratio, ALP amounts, and iPTH levels were recorded.

Statistical methods

Statistical analysis was performed with SPSS 21.0 (IBM, Armonk, New York, United States). Continuous data are presented as mean \pm SD and analyzed using the Student's *t*-test. Categorical data are presented as numbers and percentages and analyzed using the chi-square test. Factors with *P* < 0.10 in univariable analysis were included in multivariable logistic regression analysis to determine risk factors for SH. *P* < 0.05 was considered statistically significant.

RESULTS

Patient characteristics

A total of 271 patients administered TPTX with confirmed SHPT were included in this study. These patients were 47.7 \pm 11.1 years old, and 57.6% were male. Their mean BMI was 22.9 \pm 3.8 kg/m². There were no significant differences in sex, age, BMI, preoperative ALP, serum calcium, serum phosphorus, calcium-phosphorus ratio, and iPTH between the two CS groups (Table 1).

Table 1 Patient characteristics

	All patients (n = 271)	Conventional CS group (n = 145)	Preventive CS group (n = 126)	P value
Male (n)	156 (57.6%)	95 (65.5%)	61 (48.4%)	0.489
Age (yr)	47.7 ± 11.1	47.4 ± 11.4	48.1 ± 10.7	0.577
BMI (kg/m ²)	22.9 ± 3.8	23.2 ± 4.0	22.7 ± 3.7	0.407
Preoperative iPTH levels (pg/mL)	1838.61 ± 933.60	1773.38 ± 934.49	1932.33 ± 928.01	0.143
Preoperative serum calcium amounts (mmol/L)	2.58 ± 0.24	2.60 ± 0.25	2.55 ± 0.22	0.075
Preoperative serum phosphorus levels (mmol/L)	2.24 ± 0.57	2.24 ± 0.60	2.22 ± 0.53	0.775
Preoperative calcium-phosphorus ratio	5.75 ± 1.52	5.81 ± 1.58	5.67 ± 1.45	0.444
Preoperative ALP amounts (U/L)	412.22 ± 415.14	409.18 ± 399.46	416.58 ± 438.28	0.878

CS: Calcium supplementation; BMI: Body mass index; iPTH: Intact parathyroid hormone; ALP: Alkaline phosphatase.

Table 2 Postoperative characteristics

Variable	All patients (n = 271)	Conventional CS group (n = 145)	Preventive CS group (n = 126)	P value
Postoperative serum calcium levels (mmol/L)	1.91 ± 0.34	1.81 ± 0.32	2.02 ± 0.32	< 0.001
Patients with postoperative hypocalcemia (n, %)	166 (61.3)	108 (74.5)	58 (46.0)	< 0.001
Patients with postoperative SH (n, %)	133 (49.1)	93 (64.1)	40 (31.7)	< 0.001
Patients with postoperative critical hypocalcemia (n, %)	26 (9.6)	21 (14.5)	5 (4.0)	0.003

CS: Calcium supplementation; SH: Severe hypocalcemia.

Postoperative characteristics of the patients

In all patients, the hypocalcemia occurrence rate within 48 h after surgery was 61.3% (166/271), and serum calcium levels were lower than normal (< 2 mmol/L). Postoperative serum calcium levels within 48 h were higher in the preventive CS group compared with the conventional CS group (2.02 ± 0.32 *vs* 1.81 ± 0.32 mmol/L, *P* < 0.001). In addition, the postoperative occurrence rates of hypocalcemia (46.0% *vs* 74.5%, *P* < 0.001), SH (31.7% *vs* 64.1%, *P* < 0.001) and critical hypocalcemia (4.0% *vs* 14.5%, *P* = 0.003) were lower in the preventive CS group (Table 2).

Risk factors for SH

Variables with *P* < 0.1 in univariate analysis (Table 3) were included in multivariate logistic regression analysis to determine the risk factors for SH (Table 4). The results showed that preoperative iPTH levels [odds ratio (OR) = 1.001, 95% confidence interval (CI): 1.000-1.001, *P* = 0.009], preoperative ALP amounts (OR = 1.002, 95%CI: 1.001-1.003, *P* = 0.002), preoperative serum phosphorus levels (OR = 8.729, 95%CI: 1.518-50.216, *P* = 0.015) and the preventive CS regimen (OR = 0.132, 95%CI: 0.067-0.261, *P* < 0.001) were independently associated with SH.

Characteristics of the patients with preoperative ALP ≥ 500 U/L

In patients with ALP > 500 U/L, the occurrence rate of hypocalcemia within 48 h after surgery was 93.5% (72/77), and serum calcium levels were lower than control values (Table 5). Compared with the conventional CS group, the preventive CS group displayed higher postoperative serum calcium levels within 48 h (1.76 ± 0.22 *vs* 1.55 ± 0.17 mmol/L, *P* < 0.001) and lower occurrence rates of postoperative SH (62.9% *vs* 90.5%, *P* = 0.005) and critical hypocalcemia (8.6% *vs* 33.3%, *P* = 0.012).

Logistic regression analysis was performed to determine the risk factors for SH in patients with preoperative ALP levels > 500 U/L (Table 6). As shown in Table 6, only the preventive CS regimen (OR = 0.147, 95%CI: 0.038-0.562, *P* = 0.005) was independently associated with SH.

Table 3 Univariable analysis of factors associated with severe hypocalcemia in all patients

	Univariate		
	t	χ^2	P value
Sex	-	3.079	0.079
Age	3.533	-	< 0.001
BMI	0.181	-	0.856
Preoperative iPTH levels	-7.260	-	< 0.001
Preoperative ALP amounts	-6.800	-	< 0.001
Preoperative serum calcium amounts	1.520	-	0.130
Preoperative serum phosphorus levels	-2.872	-	0.004
Preoperative calcium-phosphorus ratio	-2.163	-	0.031
CS regimen	-	28.304	< 0.001

BMI: Body mass index; iPTH: Intact parathyroid hormone; ALP: Alkaline phosphatase; CS: Calcium supplementation.

Table 4 Multivariable analysis of risk factors for severe hypocalcemia in all patients

	Multivariate		
	OR	95%CI	P value
Sex			0.447
Female	Ref		
Male	1.275	0.682-2.381	
Age	0.994	0.963-1.025	0.684
Preoperative iPTH levels	1.001	1.000-1.001	0.009
Preoperative ALP amounts	1.002	1.001-1.003	0.002
Preoperative serum phosphorus concentration	8.729	1.518-50.216	0.015
Preoperative calcium-phosphorus ratio	0.577	0.306-1.087	0.089
CS regimen			
Conventional CS	Ref		
Preventive CS	0.132	0.067-0.261	< 0.001

OR: Odds ratio; CI: Confidence interval; iPTH: Intact parathyroid hormone; ALP: Alkaline phosphatase; CS: Calcium supplementation; Ref: Reference.

DISCUSSION

SH is a dreaded complication of TPTX[14], and tools for its prevention are scarce[15-17]. This study aimed to identify risk factors for SH and to compare conventional and preventive CS regimens in terms of SH occurrence after TPTX. The results suggested that preventive CS could reduce the occurrence of SH, indicating its critical value for hypocalcemia after TPTX.

TPTX is an effective method for treating SHPT, but postoperative hypocalcemia occurs in 20%-85% of the treated patients[11,20-22], which limits its clinical application. SH may lead to laryngeal stridor, spasms, arrhythmias, congestive heart failure, and tetany, which could be life-threatening in severe cases. In this study, the occurrence rate of hypocalcemia in patients administered conventional CS was 74.5% (108/145) within 48 h after surgery; in addition, the occurrence rates of SH and critical hypocalcemia were 64.1% (93/145) and 14.5% (21/145), respectively. These findings indicated that SH occurrence after surgery is very high with conventional CS.

Studies have reported the prognostic factors of hypocalcemia after PTX[10-13], but surgical methods were different among these studies, which yielded conflicting findings. In addition, the effect of age on postoperative serum calcium amounts remains controversial[10-13]. Furthermore, studies reported that older patients with SHPT are more likely to develop postoperative hypocalcemia[23,24]. The reason

Table 5 Hypocalcemia in patients with alkaline phosphatase ≥ 500 U/L

Variable	All patients (n = 77)	Conventional CS group (n = 42)	Preventive CS group (n = 35)	P value
Postoperative serum calcium levels (mmol/L)	1.65 \pm 0.22	1.55 \pm 0.17	1.76 \pm 0.22	< 0.001
Patients with postoperative hypocalcemia (n, %)	72 (93.5)	41 (97.6)	31 (88.6)	0.171
Patients with postoperative SH (n, %)	60 (77.9)	38 (90.5)	22 (62.9)	0.005
Patients with postoperative critical hypocalcemia (n, %)	17 (22.1)	14 (33.3)	3 (8.6)	0.012

CS: Calcium supplementation; SH: Severe hypocalcemia.

Table 6 Multivariate analysis of risk factors for severe hypocalcemia in patients with preoperative alkaline phosphatase > 500 U/L

	Multivariate		
	OR	95%CI	P value
Sex			0.142
Female	Ref		
Male	2.610	0.726-9.380	
Age	0.993	0.938-1.050	0.795
Preoperative iPTH levels	1	0.999-1.001	0.965
Preoperative ALP amounts	1.001	0.999-1.003	0.202
Preoperative serum phosphorus concentration	3.851	0.094-157.237	0.877
Preoperative calcium-phosphorus ratio	0.848	0.227-3.168	0.973
CS regimen			
Conventional CS	Ref		
Preventive CS	0.147	0.038-0.562	0.005

OR: Odds ratio; CI: Confidence interval; iPTH: Intact parathyroid hormone; ALP: Alkaline phosphatase; CS: Calcium supplementation; Ref: Reference.

might be that such patients are prone to vitamin D deficiency and inadequate nutrition intake[23,25,26]. Other studies suggested that younger age is a risk factor for postoperative hypocalcemia[11,14,20,24]. Few reports considered the male gender as a risk factor for hypocalcemia after TPTX[11]. Investigations revealed preoperative PTH levels to be an independent risk factor for SH; under excessive PTH stimulation, despite a significant negative balance, bone formation and bone resorption are increased[11, 15]. Postoperatively, due to the rapid decline in PTH levels, reduced bone resorption and increased bone formation also occur rapidly, and hypocalcemia occurrence is consistent with such changes. ALP encompasses a group of isoenzymes that are mainly present in the liver and bones. High serum levels of ALP are characteristic of bone disease with enhanced osteogenic activity. In SHPT patients, both osteogenic and bone resorption activities are significantly increased[23,27]. After PTX, osteoclast activity is significantly reduced, while osteoblast activity remains unchanged for a short time after surgery[28, 29]. The relative balance of bone metabolism is thus altered, inducing hypocalcemia. Therefore, high preoperative ALP levels may be an independent risk factor for SH after PTX[11,30]. Nevertheless, these findings remain controversial in different reports[11,13].

Few studies have examined the prognostic factors of hypocalcemia after PTX. As shown above, following univariable analysis, age, preoperative iPTH amounts, ALP levels, serum phosphorus concentration, calcium phosphate product, and preventive CS were significantly associated with SH after surgery; however, only preoperative iPTH levels, preoperative ALP amount, preoperative serum phosphorus levels, and preventive CS independently predicted postoperative SH in multivariable analysis.

In this study, after preventive CS, the occurrence rates of postoperative hypocalcemia, SH, and critical hypocalcemia were all significantly decreased. The occurrence of SH was reduced from 64.1% to 31.7%, and that of critical hypocalcemia from 14.5% to 4.0%, with no life-threatening hypocalcemia. Based on the present findings, selective enforcement of preventive CS in patients with ALP ≥ 500 could

significantly reduce the occurrence rates of SH and critical hypocalcemia, easing the control of hypocalcemia after TPTX as a simple and feasible tool. In high-risk patients with ALP ≥ 500 U/L, the incidence rates of postoperative hypocalcemia were 97.6% and 88.6% in the conventional and preventive CS groups, respectively, indicating a slight but not statistically significant decrease. Nevertheless, the occurrence rates of SH and critical hypocalcemia were significantly decreased by the preventive CS regimen, from 90.5% and 33.3% to 62.9% and 8.6%, respectively. Although selective enforcement of preventive CS significantly improved the calcium status of patients at high risk of hypocalcemia, the incidence of life-threatening critical hypocalcemia remained as high as 8.6%, and further investigation is warranted to develop tools to reduce this rate. In addition, applying CS or selecting subtotal PTX or TPTX combined with auto-transplantation should be studied. However, although TPTX with auto-transplantation is a more rational therapy than TPTX, some patients decline auto-transplantation mostly because of high cost. Therefore, tools should be developed to prevent hypocalcemia in such individuals.

This study had some limitations. First, this was not a randomized trial, with differences in indications and periods for the two CS regimens. In addition, the study period was relatively short, and the sample size was small. Furthermore, as a single-center study in China, the results may not be suitable for other dialysis patients, as most patients in our center had end-stage disease with severe symptoms and delayed surgical opportunities. Furthermore, postoperative iPTH levels were not assessed in this study, although they are more important than preoperative iPTH amounts, showing an association with SH [31].

CONCLUSION

In conclusion, these findings suggest that preventive CS significantly reduces the occurrence rates of SH and critical hypocalcemia after TPTX for SHPT.

ARTICLE HIGHLIGHTS

Research background

Total parathyroidectomy (TPTX) without auto-transplantation is an effective therapeutic option for treating secondary hyperparathyroidism. However, postoperative hypocalcemia limits its clinical application.

Research motivation

Identify risk factors for severe hypocalcemia (SH) after TPTX, and find efficient tools for reducing or preventing SH.

Research objectives

To identify risk factors for SH after TPTX and compare conventional and preventive calcium supplementation (CS) regimens for their effects on SH occurrence after TPTX.

Research methods

From January 2015 to May 2016, conventional CS was performed in patients who underwent TPTX, with calcium amounts adjusted according to postoperative serum calcium levels. From October 2016 to May 2018, preventive CS was performed according to preoperative alkaline phosphatase (ALP) levels. Continuous data are presented as mean \pm SD and analyzed by the Student's *t*-test. Categorical data are presented as numbers and percentages and analyzed using the chi-square test. Factors with $P < 0.10$ in univariable analysis were included in multivariable logistic regression analysis to determine the risk factors for SH.

Research results

A total of 271 patients were included. Compared with conventional CS, preventive CS led to lower occurrence rates of hypocalcemia within 48 h (46.0% *vs* 74.5%, $P < 0.001$) and SH (31.7% *vs* 64.1%, $P < 0.001$). Multivariable analysis showed that preoperative iPTH levels [odds ratio (OR) = 1.001, 95% confidence interval (CI): 1.000-1.001, $P = 0.009$], preoperative ALP amounts (OR = 1.002, 95%CI: 1.001-1.003, $P = 0.002$), preoperative serum phosphorus levels (OR = 8.729, 95%CI: 1.518-50.216, $P = 0.015$) and preventive CS (OR = 0.132, 95%CI: 0.067-0.261, $P < 0.001$) were independently associated with SH. In patients with preoperative ALP ≥ 500 U/L, only preventive CS (OR = 0.147, 95%CI: 0.038-0.562 $P = 0.005$) was independently associated with SH.

Research conclusions

Preventive CS is an efficient tool for reducing the occurrence of SH after TPTX.

Research perspectives

Preventive CS could reduce the occurrence of SH after TPTX, which might contribute to the clinical application of TPTX.

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FOOTNOTES

Author contributions: Liu J, Yang M, and Fan XF carried out the studies, collected data, and drafted the manuscript; Liu J and Yang M performed the statistical analysis and critically reviewed the manuscript for important intellectual content; Huang LP and Zhang L participated in the acquisition, analysis, or interpretation of data and drafted the manuscript; and all authors read and approved the final manuscript.

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REFERENCES

- 1 **Cunningham J**, Locatelli F, Rodriguez M. Secondary hyperparathyroidism: pathogenesis, disease progression, and therapeutic options. *Clin J Am Soc Nephrol* 2011; **6**: 913-921 [PMID: 21454719 DOI: 10.2215/CJN.06040710]
- 2 **Ketteler M**, Martin KJ, Cozzolino M, Goldsmith D, Sharma A, Khan S, Dumas E, Amdahl M, Marx S, Audhya P. Paricalcitol versus cinacalcet plus low-dose vitamin D for the treatment of secondary hyperparathyroidism in patients receiving haemodialysis: study design and baseline characteristics of the IMPACT SHPT study. *Nephrol Dial Transplant* 2012; **27**: 1942-1949 [PMID: 21931122 DOI: 10.1093/ndt/gfr531]
- 3 **Yuen NK**, Ananthakrishnan S, Campbell MJ. Hyperparathyroidism of Renal Disease. *Perm J* 2016; **20**: 15-127 [PMID: 27479950 DOI: 10.7812/TPP/15-127]
- 4 **Ho LY**, Wong PN, Sin HK, Wong YY, Lo KC, Chan SF, Lo MW, Lo KY, Mak SK, Wong AK. Risk factors and clinical course of hungry bone syndrome after total parathyroidectomy in dialysis patients with secondary hyperparathyroidism. *BMC Nephrol* 2017; **18**: 12 [PMID: 28073343 DOI: 10.1186/s12882-016-0421-5]
- 5 **Moldovan D**, Racasan S, Kacso IM, Rusu C, Potra A, Bondor C, Patiu IM, Gherman-Căprioară M. Survival after parathyroidectomy in chronic hemodialysis patients with severe secondary hyperparathyroidism. *Int Urol Nephrol* 2015; **47**: 1871-1877 [PMID: 26377492 DOI: 10.1007/s11255-015-1106-x]
- 6 **Tsai WC**, Peng YS, Chiu YL, Wu HY, Pai MF, Hsu SP, Yang JY, Tung KT, Chen HY. Risk factors for severe hypocalcemia after parathyroidectomy in prevalent dialysis patients with secondary hyperparathyroidism. *Int Urol Nephrol* 2015; **47**: 1203-1207 [PMID: 26025063 DOI: 10.1007/s11255-015-1016-y]

- 7 **Tominaga Y**, Uchida K, Haba T, Katayama A, Sato T, Hibi Y, Numano M, Tanaka Y, Inagaki H, Watanabe I, Hachisuka T, Takagi H. More than 1,000 cases of total parathyroidectomy with forearm autograft for renal hyperparathyroidism. *Am J Kidney Dis* 2001; **38**: S168-S171 [PMID: [11576947](#) DOI: [10.1053/ajkd.2001.27432](#)]
- 8 **Tominaga Y**, Numano M, Tanaka Y, Uchida K, Takagi H. Surgical treatment of renal hyperparathyroidism. *Semin Surg Oncol* 1997; **13**: 87-96 [PMID: [9088064](#) DOI: [10.1002/\(sici\)1098-2388\(199703/04\)13:2<87::aid-ssu4>3.0.co;2-y](#)]
- 9 **Park JH**, Kang SW, Jeong JJ, Nam KH, Chang HS, Chung WY, Park CS. Surgical treatment of tertiary hyperparathyroidism after renal transplantation: a 31-year experience in a single institution. *Endocr J* 2011; **58**: 827-833 [PMID: [21804261](#) DOI: [10.1507/endocrj.ej11-0053](#)]
- 10 **Sun X**, Zhang X, Lu Y, Zhang L, Yang M. Risk factors for severe hypocalcemia after parathyroidectomy in dialysis patients with secondary hyperparathyroidism. *Sci Rep* 2018; **8**: 7743 [PMID: [29773914](#) DOI: [10.1038/s41598-018-26142-9](#)]
- 11 **Yang M**, Zhang L, Huang L, Sun X, Ji H, Lu Y. Factors predictive of critical value of hypocalcemia after total parathyroidectomy without autotransplantation in patients with secondary hyperparathyroidism. *Ren Fail* 2016; **38**: 1224-1227 [PMID: [27359159](#) DOI: [10.1080/0886022X.2016.1202731](#)]
- 12 **Strickland PL**, Recabaren J. Are preoperative serum calcium, parathyroid hormone, and adenoma weight predictive of postoperative hypocalcemia? *Am Surg* 2002; **68**: 1080-1082 [PMID: [12516813](#)]
- 13 **Torer N**, Torun D, Torer N, Micozkadioglu H, Noyan T, Ozdemir FN, Haberal M. Predictors of early postoperative hypocalcemia in hemodialysis patients with secondary hyperparathyroidism. *Transplant Proc* 2009; **41**: 3642-3646 [PMID: [19917359](#) DOI: [10.1016/j.transproceed.2009.06.207](#)]
- 14 **Goldfarb M**, Gondek SS, Lim SM, Farra JC, Nose V, Lew JI. Postoperative hungry bone syndrome in patients with secondary hyperparathyroidism of renal origin. *World J Surg* 2012; **36**: 1314-1319 [PMID: [22399154](#) DOI: [10.1007/s00268-012-1560-x](#)]
- 15 **Viaene L**, Evenepoel P, Bammens B, Claes K, Kuypers D, Vanrenterghem Y. Calcium requirements after parathyroidectomy in patients with refractory secondary hyperparathyroidism. *Nephron Clin Pract* 2008; **110**: c80-c85 [PMID: [18758187](#) DOI: [10.1159/000151722](#)]
- 16 **Kang BH**, Hwang SY, Kim JY, Hong YA, Jung MY, Lee EA, Lee JE, Lee JB, Ko GJ, Pyo HJ, Kwon YJ. Predicting postoperative total calcium requirements after parathyroidectomy in secondary hyperparathyroidism. *Korean J Intern Med* 2015; **30**: 856-864 [PMID: [26552461](#) DOI: [10.3904/kjim.2015.30.6.856](#)]
- 17 **Goh BL**, Yudisthra MG, Hisham AN. Alkaline phosphatase predicts calcium requirements after total parathyroidectomy in patients receiving dialysis. *Br J Surg* 2010; **97**: 185-188 [PMID: [20035536](#) DOI: [10.1002/bjs.6818](#)]
- 18 **Fraser WD**. Hyperparathyroidism. *Lancet* 2009; **374**: 145-158 [PMID: [19595349](#) DOI: [10.1016/S0140-6736\(09\)60507-9](#)]
- 19 Erratum: Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Update Work Group. KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). *Kidney Int Suppl*. 2017; **7**: 1-59. *Kidney Int Suppl (2011)* 2017; **7**: e1 [PMID: [30681074](#) DOI: [10.1016/j.kisu.2017.10.001](#)]
- 20 **Mittendorf EA**, Merlino JI, McHenry CR. Post-parathyroidectomy hypocalcemia: incidence, risk factors, and management. *Am Surg* 2004; **70**: 114-9; discussion 119 [PMID: [15011912](#)]
- 21 **Stewart ZA**, Blackford A, Somervell H, Friedman K, Garrett-Mayer E, Dackiw AP, Zeiger MA. 25-hydroxyvitamin D deficiency is a risk factor for symptoms of postoperative hypocalcemia and secondary hyperparathyroidism after minimally invasive parathyroidectomy. *Surgery* 2005; **138**: 1018-25; discussion 1025 [PMID: [16360386](#) DOI: [10.1016/j.surg.2005.09.018](#)]
- 22 **Li JG**, Xiao ZS, Hu XJ, Li Y, Zhang X, Zhang SZ, Shan AQ. Total parathyroidectomy with forearm auto-transplantation improves the quality of life and reduces the recurrence of secondary hyperparathyroidism in chronic kidney disease patients. *Medicine (Baltimore)* 2017; **96**: e9050 [PMID: [29245308](#) DOI: [10.1097/MD.0000000000009050](#)]
- 23 **Brasier AR**, Nussbaum SR. Hungry bone syndrome: clinical and biochemical predictors of its occurrence after parathyroid surgery. *Am J Med* 1988; **84**: 654-660 [PMID: [3400660](#) DOI: [10.1016/0002-9343\(88\)90100-3](#)]
- 24 **Erbil Y**, Barbaros U, Temel B, Turkoglu U, Issever H, Bozbora A, Ozarmagan S, Tezelman S. The impact of age, vitamin D(3) level, and incidental parathyroidectomy on postoperative hypocalcemia after total or near total thyroidectomy. *Am J Surg* 2009; **197**: 439-446 [PMID: [19324110](#) DOI: [10.1016/j.amjsurg.2008.01.032](#)]
- 25 **Farese S**. [The hungry bone syndrome--an update]. *Ther Umsch* 2007; **64**: 277-280 [PMID: [17685087](#) DOI: [10.1024/0040-5930.64.5.277](#)]
- 26 **Erbil Y**, Bozbora A, Ozbey N, Issever H, Aral F, Ozarmagan S, Tezelman S. Predictive value of age and serum parathormone and vitamin d3 levels for postoperative hypocalcemia after total thyroidectomy for nontoxic multinodular goiter. *Arch Surg* 2007; **142**: 1182-1187 [PMID: [18086985](#) DOI: [10.1001/archsurg.142.11.1182](#)]
- 27 **National Kidney Foundation**. K/DOQI clinical practice guidelines for bone metabolism and disease in chronic kidney disease. *Am J Kidney Dis* 2003; **42**: S1-201 [PMID: [14520607](#)]
- 28 **Guo CY**, Holland PA, Jackson BF, Hannon RA, Rogers A, Harrison BJ, Eastell R. Immediate changes in biochemical markers of bone turnover and circulating interleukin-6 after parathyroidectomy for primary hyperparathyroidism. *Eur J Endocrinol* 2000; **142**: 451-459 [PMID: [10802521](#) DOI: [10.1530/eje.0.1420451](#)]
- 29 **Sun L**, He X, Liu T. Preoperative serum alkaline phosphatase: a predictive factor for early hypocalcaemia following parathyroidectomy of primary hyperparathyroidism. *Chin Med J (Engl)* 2014; **127**: 3259-3264 [PMID: [25266524](#)]
- 30 **Cheng SP**, Liu CL, Chen HH, Lee JJ, Liu TP, Yang TL. Prolonged hospital stay after parathyroidectomy for secondary hyperparathyroidism. *World J Surg* 2009; **33**: 72-79 [PMID: [18953601](#) DOI: [10.1007/s00268-008-9787-2](#)]
- 31 **Cannizzaro MA**, Okatyeva V, Lo Bianco S, Caruso V, Buffone A. Hypocalcemia after thyroidectomy: iPTH levels and iPTH decline are predictive? *Ann Med Surg (Lond)* 2018; **30**: 42-45 [PMID: [29946457](#) DOI: [10.1016/j.amsu.2018.04.032](#)]



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