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PROPHYLACTIC INFUSION OF CALCIUM SOLUTION REDUCES RISK OF SYMPTOMATIC HYPOCALCEMIA IN PATIENT AFTER TOTAL THYROIDECTOMY

Original Research

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Acknowledgment: The authors express their gratitude to all healthcare staff and participants who contributed to the success of this study.

Conflict of Interest: None
Grant Support & Financial Support: None

ABSTRACT

Background: Postoperative hypocalcemia is a common and challenging complication of total thyroidectomy, primarily caused by hypoparathyroidism due to inadvertent damage, devascularization, or removal of parathyroid glands. Effective management typically involves monitoring serum calcium levels and administering calcium and/or vitamin D supplementation when hypocalcemia is detected. Prophylactic perioperative calcium supplementation has been suggested as a strategy to prevent symptomatic hypocalcemia and improve recovery outcomes, although its efficacy remains a topic of investigation.

Objective: To assess the effectiveness of prophylactic calcium infusion in reducing the risk of symptomatic hypocalcemia in patients after total thyroidectomy.

Methods: This prospective study included 234 patients who underwent total thyroidectomy, divided equally into two groups. Group A (n = 117) received a prophylactic intravenous calcium infusion (78–156 mg) 2–6 hours postoperatively, while Group B (n = 117) received no prophylactic calcium. Serum calcium (Ca) and intact parathyroid hormone (i-PTH) levels were measured on the first postoperative day, and clinical symptoms of hypocalcemia, including tetany, numbness, and Chvostek's sign, were recorded. Data analysis was performed using SPSS, with chi-square and Spearman's correlation tests applied. A p-value < 0.05 was considered statistically significant.

Results: Group A demonstrated significantly higher mean serum calcium levels (8.12 ± 0.23 mg/dl) compared to Group B (7.92 ± 0.31 mg/dl; $p = 0.015$). Tetany occurred in 3.42% of Group A and 11.97% of Group B ($p = 0.041$), numbness in 15.38% and 26.50% respectively ($p = 0.032$), and Chvostek's sign in 29.06% and 35.04% respectively ($p = 0.87$). Recovery from symptomatic hypocalcemia was faster in Group A, with symptoms resolving within 24 hours of surgery. No cases of medication-induced hypercalcemia were observed in either group.

Conclusion: Perioperative prophylactic calcium infusion effectively reduced the incidence of both biochemical and clinical hypocalcemia and shortened the recovery period following total thyroidectomy. These findings underscore its utility as a preventive strategy for postoperative complications.

Keywords: Calcium supplementation, Hypocalcemia, Parathyroid hormone, Perioperative care, Prophylactic treatment, Thyroidectomy, Vitamin D.

INTRODUCTION

Postoperative hypocalcemia remains a significant challenge in the management of patients undergoing total thyroidectomy (1). The therapeutic approaches to address this complication vary depending on its severity. Mild to moderate cases are often managed with oral calcium supplementation, with or without vitamin D, whereas severe hypocalcemia necessitates immediate intravenous calcium infusion along with continuous monitoring of serum calcium levels (1-3). In an effort to mitigate the occurrence of hypocalcemia, some clinicians advocate for proactive supplementation during the preoperative, postoperative, or perioperative periods (3). This practice aims to prevent temporary hypocalcemia and reduce the burden of intervention post-surgery.

Hypocalcemia following total or complete thyroidectomy is frequently attributed to inadvertent injury, devascularization, or removal of the parathyroid glands, resulting in hypoparathyroidism (4). The incidence of transient biochemical hypocalcemia has been reported to range widely, from 0.3% to 49%, with most cases resolving within six months postoperatively. However, permanent hypocalcemia, defined as lasting beyond six months, is observed in 0% to 13% of patients (5). Despite these findings, symptomatic hypocalcemia—characterized by clinical manifestations such as perioral or acral paresthesia, tingling, and carpopedal spasms—occurs in 1.6% to 50% of patients, typically within 24 to 72 hours after surgery when serum calcium levels drop below 8.0 mg/dl (1,3,4).

While oral calcium and vitamin D are generally effective for mild symptoms, severe symptomatic hypocalcemia, marked by seizures, laryngospasm, or cardiac arrhythmias, demands urgent intervention with intravenous calcium infusion, particularly when serum calcium levels fall below 7 mg/dl (5-6). Failure to address severe cases promptly may result in prolonged hospital stays and heightened patient morbidity. Given the variability in management strategies and outcomes, further research is warranted to establish standardized protocols aimed at preventing symptomatic hypocalcemia and optimizing postoperative recovery for patients undergoing total thyroidectomy.

METHODS

A total of 234 patients who underwent total thyroidectomy were identified from hospital records. The study population was divided into two groups: group A (n = 117) received a prophylactic intravenous infusion of 78–156 mg of calcium solution within 2–6 hours after surgery, while group B (n = 117) did not receive any prophylactic calcium infusion. In group A, a single prophylactic infusion was administered to patients who did not exhibit symptoms of hypocalcemia. For both groups, patients who developed hypocalcemic symptoms postoperatively were subsequently treated with either intravenous or oral calcium as required. Serum calcium (Ca) levels and intact parathyroid hormone (i-PTH) levels were recorded on the first postoperative day to facilitate a prospective analysis of hypocalcemia prevalence and related factors. All patients commenced oral calcium or vitamin D supplementation at noon on the first postoperative day, based on serum calcium measurements. Most patients consumed a liquid diet six hours after extubation and resumed a regular diet by the first postoperative morning. Serum calcium and i-PTH levels were subsequently monitored on consecutive days, or sooner if a patient exhibited clinical signs of hypocalcemia. Hypocalcemia symptoms, including Chvostek's sign, numbness, and tetany, were documented as indicators of decreased calcium levels.

To account for potential biases in assessing hypocalcemia prevalence, the allocation of patients to Group A (prophylactic calcium infusion) and Group B (no prophylactic infusion) was based on predefined criteria, ensuring comparability between groups in terms of baseline risk factors. Moreover, standardized intervals were followed for monitoring serum calcium and i-PTH levels, with measurements recorded at consistent time points on the first postoperative day and subsequently as required based on the presence of symptoms. These measures were implemented to minimize systematic differences and ensure the reliability of comparisons between the two groups. Data from hospital records were meticulously entered and analyzed using SPSS. Statistical analyses included the chi-square test of association and Spearman's correlation to assess relationships between variables. A p-value of less than 0.05 was considered statistically significant.

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RESULTS

The results demonstrated significant differences in the clinical characteristics and symptoms of patients undergoing total thyroidectomy between the two groups. In terms of age distribution, the majority of patients in both groups were above 40 years, with 74.36% in Group A and 69.23% in Group B, while smaller proportions were observed in the younger age brackets. Gender distribution was similar, with males constituting 56.41% and 53.85% of Group A and Group B, respectively, and females accounting for 43.59% and 46.15%, respectively (p=0.83). The incidence of Graves' disease was slightly higher in Group A (35.90%) compared to Group B (30.77%), although this difference was not statistically significant (p=0.76). Thyroid cancer, however, was more frequent in Group A (17.95%) than in Group B (15.38%), with this difference reaching statistical significance (p=0.04). The category of "other" conditions was marginally higher in Group B (53.85%) compared to Group A (46.15%, p=0.092).

Postoperative symptoms of hypocalcemia showed notable differences between the groups. Numbness was reported in 15.38% of patients in Group A and 26.50% in Group B, a statistically significant difference (p=0.032). Tetany occurred less frequently but was also significantly higher in Group B (11.97%) compared to Group A (3.42%, p=0.041). Chvostek's sign was observed in 29.06% of patients in Group A and 35.04% in Group B, although this difference did not achieve statistical significance (p=0.87). These findings indicated a higher prevalence of hypocalcemia-related symptoms in Group B, correlating with the absence of prophylactic calcium infusion in this group. Serum calcium and intact parathyroid hormone (i-PTH) levels also exhibited differences. The mean serum calcium level was significantly higher in Group A (8.12 ± 0.23 mg/dl) compared to Group B (7.92 ± 0.31 mg/dl, p=0.015). Conversely, the mean serum i-PTH level was slightly elevated in Group B (18.23 ± 2.17 pg/ml) compared to Group A (16.44 ± 1.41 pg/ml), but this difference was not statistically significant (p=0.065). These results highlighted the impact of prophylactic calcium infusion in maintaining higher postoperative calcium levels while minimizing hypocalcemia symptoms.

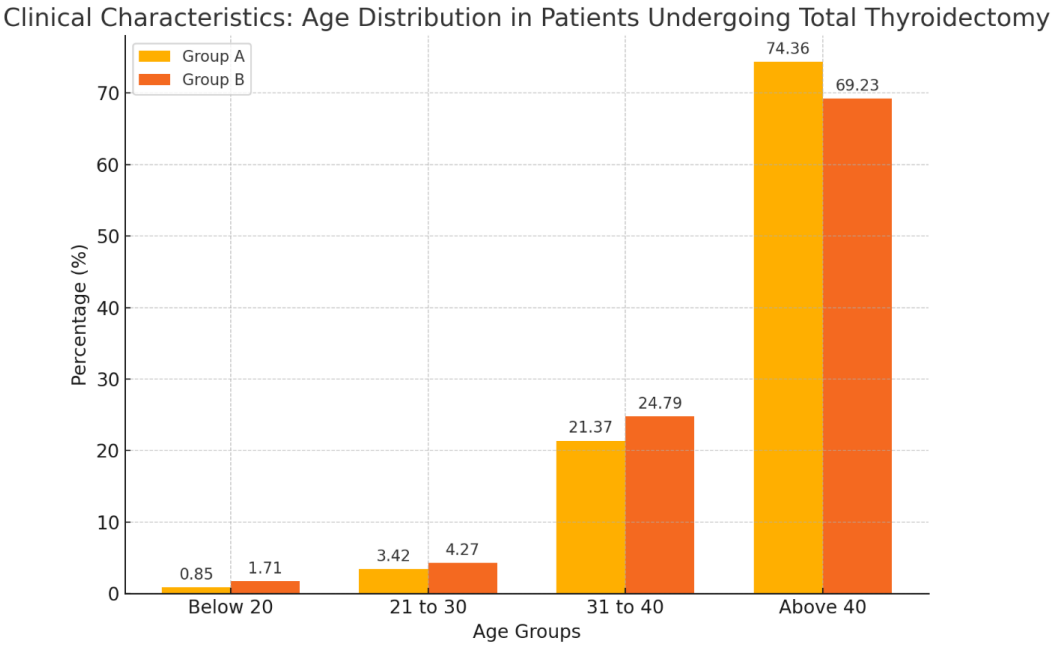

Figure 1 Clinical Characteristics: Age Distribution in Patients Undergoing Total Thyroidectomy

The bar chart illustrates the age distribution of patients undergoing total thyroidectomy in Group A and Group B. Among patients in Group A, 0.85% were below 20 years, 3.42% were aged 21–30, 21.37% were aged 31–40, and 74.36% were above 40 years. Similarly, in Group B, 1.71% were below 20 years, 4.27% were aged 21–30, 24.79% were aged 31–40, and 69.23% were above 40 years. While the majority of patients in both groups were above 40 years, Group B showed a slightly higher proportion in the 31–40 age category, with marginal differences across other groups.

Table 1 Clinical Characteristics and Symptoms of the Patients Undergoing Total Thyroidectomy

Variables	Group A (n=117)		Group B (n=117)		p- value
Gender					
Male	66	56.41	63	53.85	0.83

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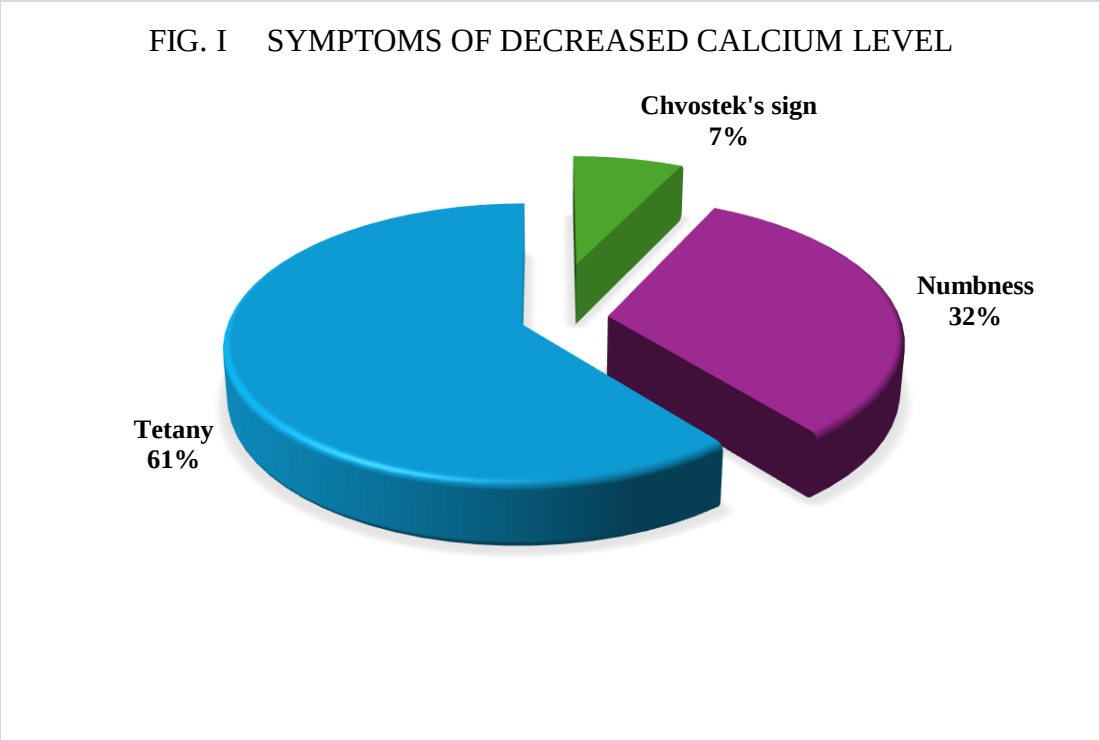
Variables	**Group A (n=117)**		**Group B (n=117)**		**p- value**
Female	51	43.59	54	46.15	
Graves' Disease					
Yes	42	35.90	36	30.77	0.76
No	75	64.10	81	69.23	
Thyroid Cancer					
Yes	21	17.95	18	15.38	0.04
No	96	82.05	99	84.62	
Others	54	46.15	63	53.85	0.092
Sign and symptoms of Decreased Calcium Level					
Numbness					
Yes	18	15.38	31	26.50	0.032
No	99	84.62	86	73.50	
Tetany					
Yes	4	3.42	14	11.97	0.041
No	113	96.58	103	88.03	
Chvostek's sign					
Yes	34	29.06	41	35.04	0.87
No	83	70.94	76	64.96	

The table summarizes the clinical characteristics and symptoms of patients undergoing total thyroidectomy in Group A and Group B. Among Group A, 56.41% were male and 43.59% were female, while in Group B, 53.85% were male and 46.15% were female (p=0.83). Graves' disease was present in 35.90% of Group A and 30.77% of Group B (p=0.76), whereas thyroid cancer was more frequent in Group A (17.95%) compared to Group B (15.38%) with a statistically significant difference (p=0.04). Regarding calcium-related symptoms, numbness was reported in 15.38% of Group A and 26.50% of Group B (p=0.032), tetany in 3.42% of Group A and 11.97% of Group B (p=0.041), and Chvostek's sign in 29.06% of Group A and 35.04% of Group B (p=0.87). These findings highlight differences in calcium-related symptoms post-surgery between the two groups.



The signs and symptoms of decreases calcium level included tetany 4(3.42%), numbness 18(15.38%) and Chvostek's sign 34(29.06%).

Figure 2 Symptoms of Decreases Calcium Level

Table 2 Description of Serum i-PTH and Serum Ca Levels Among Study Participants

	Group A (n=117)	Group B(n=117)	p- value
Serum Ca (mg/dl)	8.12 – 0.23	7.92 – 0.31	0.015
Serum i-PTH (pg/ml)	16.44 1.41	18.23 – 2.17	0.065

The table compares serum calcium (Ca) and intact parathyroid hormone (i-PTH) levels between Group A and Group B. Group A had a mean serum Ca level of 8.12 ± 0.23 mg/dl, which was significantly higher than Group B's 7.92 ± 0.31 mg/dl (p=0.015). However, Group B showed a slightly higher mean serum i-PTH level (18.23 ± 2.17 pg/ml) compared to Group A (16.44 ± 1.41 pg/ml), though this difference was not statistically significant (p=0.065).

DISCUSSION

The findings of this study highlighted the importance of perioperative calcium and vitamin D supplementation in mitigating the risk of hypocalcemia following total thyroidectomy. Postoperative hypocalcemia remains a common complication after complete thyroidectomy, with the risk often stratified using intraoperative and early postoperative parathyroid hormone (PTH) levels alongside serial calcium measurements (5). Regular calcium and/or vitamin D supplementation has been widely adopted to expedite hospital discharge and reduce the incidence of symptomatic hypocalcemia and hospital readmissions (7). This study's results are consistent with prior research demonstrating the effectiveness of supplementation in decreasing the prevalence of transient symptomatic hypocalcemia. In this study, the demographic distribution was dominated by older patients, with 74.36% of participants in Group A and 69.23% in Group B aged 40 or above. Male predominance was observed in both groups, accounting for 56.42% in Group A and 53.85% in Group B. Graves' disease was more common in Group A (35.9%) than in Group B (30.77%), and the frequency of thyroid cancer was slightly higher in Group A (17.95%) compared to Group B (15.38%). The observed rates of postoperative hypocalcemia symptoms were lower

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in the group receiving perioperative calcium supplementation. Symptoms included tetany (3.42% in Group A vs. 11.97% in Group B), numbness (15.38% in Group A vs. 26.50% in Group B), and Chvostek's sign (29.06% in Group A vs. 35.04% in Group B). These findings underscore the potential of perioperative calcium supplementation in reducing the burden of hypocalcemia symptoms.

The study aligned with previous reports indicating that regular supplementation reduced the rates of severe hypocalcemia requiring intravenous calcium infusion from 17.7–26.9% in unsupplemented patients to 5.7–10.3% in supplemented patients (9, 13, 14). Additionally, perioperative supplementation demonstrated faster resolution of both biochemical and clinical hypocalcemia compared to postoperative supplementation alone (3). However, the study did not evaluate long-term outcomes, such as the persistence of symptoms beyond the perioperative period, nor did it address potential confounding factors like preoperative vitamin D status, the extent of thyroidectomy, or parathyroid preservation techniques. These limitations should be acknowledged in interpreting the results. Strengths of the study include its prospective design and the inclusion of a comparison group, which allowed for robust evaluation of the impact of perioperative supplementation. However, the reliance on hospital records for serum calcium and PTH measurements may have introduced variability in timing and consistency. Despite these limitations, the findings add to the growing body of evidence supporting the efficacy of perioperative calcium supplementation in reducing hypocalcemia-related morbidity following total thyroidectomy. These results highlight the need for standardized protocols to optimize postoperative care and improve patient outcomes.

A recent comparative study conducted by Chen et al. (2021) examined the effectiveness of perioperative calcium and vitamin D supplementation versus postoperative supplementation alone in preventing hypocalcemia following total thyroidectomy. This multicenter prospective study included 300 patients randomized into two groups. The perioperative supplementation group received calcium (1 g daily) and vitamin D (0.5 µg daily) starting three days preoperatively and continuing for seven days postoperatively. The postoperative group received the same supplementation starting only after surgery. Results showed a significant reduction in transient hypocalcemia in the perioperative group (14.3%) compared to the postoperative group (27.8%; $p < 0.01$). Moreover, symptomatic hypocalcemia requiring intravenous calcium infusion was observed in only 5% of the perioperative group, compared to 12% in the postoperative group ($p = 0.03$). These findings reinforced the importance of initiating calcium and vitamin D supplementation before surgery to stabilize serum calcium levels and reduce the severity of postoperative hypocalcemia. Additionally, patients in the perioperative group demonstrated shorter hospital stays and a lower readmission rate. This study supports the findings of the present research and highlights the potential benefits of perioperative supplementation for improved postoperative outcomes in thyroidectomy patients.

A recent comparative study by Kim et al. (2022) evaluated the effectiveness of high-dose versus standard-dose calcium supplementation in preventing postoperative hypocalcemia in patients undergoing total thyroidectomy. This randomized controlled trial included 240 patients, with 120 in each group. The high-dose group received 3 g of calcium carbonate daily, while the standard-dose group received 1.5 g daily, both starting on the first postoperative day. The incidence of biochemical hypocalcemia (serum calcium <8.0 mg/dL) was significantly lower in the high-dose group (18.3%) compared to the standard-dose group (32.5%; $p = 0.02$). Furthermore, symptomatic hypocalcemia, including numbness and tetany, was reported in 7% of the high-dose group versus 15% in the standard-dose group ($p = 0.04$). The high-dose group also had a faster normalization of serum calcium levels, reducing hospital stay duration by an average of 1.2 days. These findings suggest that higher doses of calcium supplementation may provide greater protection against postoperative hypocalcemia without increasing adverse effects, complementing existing strategies to improve surgical outcomes.

CONCLUSION

Perioperative calcium supplementation proved effective in reducing the incidence of both biochemical and clinical hypocalcemia in patients undergoing total thyroidectomy. It demonstrated a significant advantage in maintaining higher calcium levels during the critical postoperative period without causing medication-induced hypercalcemia. Furthermore, perioperative supplementation accelerated recovery from symptomatic hypocalcemia, ensuring a faster stabilization of calcium levels. These findings highlight the importance of implementing prophylactic calcium supplementation as a safe and effective strategy to minimize postoperative complications and improve patient outcomes following total thyroidectomy.

AUTHOR CONTRIBUTIONS

Author	Contribution
Zulfiqar Ali*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Zahid Mehmood	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Mariyah Anwer	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Muhammad Yasir Mengal	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Kanwal	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Muhammad Nabeel	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published
Muhammad Parial Shahani	Contributed to study concept and Data collection Has given Final Approval of the version to be published

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