ORIGINAL RESEARCH

Role of Preoperative Calcium and Vitamin D Supplementation in Preventing Post-total Thyroidectomy Hypocalcemia

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Abstract

Introduction: Thyroidectomy is the commonest endocrine surgical procedure. Transient hypocalcemia occurs in the range of 19–38%. Though many parameters are being attributed to postthyroidectomy hypocalcemia, preoperative vitamin D and calcium supplementation seem to be debated. The objective of this study was to find out the benefits of preoperative calcium and vitamin D supplement in preventing postthyroidectomy hypocalcemia.

Subjects and methods: This was a prospective randomized study conducted from 1st April 2018 to 31st July 2019. Total thyroidectomy (TT) was performed in all patients for various thyroid disorders. Group A received no preoperative supplements and group B received 6 weeks 2 gm calcium carbonate with weekly cholecalciferol 60,000 units for 6 weeks before surgery. The preoperative biochemical panel, bone mineral density, intraoperative factors, postoperative blood parameters, and clinical effects were analyzed.

Results: Of 133 patients who underwent TT in the above period, 83 patients were included in the study, group A ($n = 42$) and group B ($n = 41$). Mean age was 41.6 ± 13.39 years (range: 18–74). Female:male was 11:1. Clinical hypocalcemia occurred in 37.3% ($n = 31$), group A ($n = 19$) vs group B ($n = 12$) ($p = 0.197$). Vitamin D deficiency was seen in 74.7% ($n = 62$), group A 76.2% ($n = 32$) vs group B 73.2% ($n = 30$) ($p = 0.804$). Postoperative calcium levels were significantly correlated to preoperative magnesium ($r = 0.222$, $p = 0.043$), and postoperative day (POD)-1 parathyroid hormone (PTH) levels ($r = 0.219$, $p = 0.047$). On multiple linear regression analysis, both were not statistically significant with preoperative magnesium levels ($\beta = 0.194$, $p = 0.077$) and POD-1 PTH ($\beta = 0.190$, $p = 0.083$). The number of parathyroid glands visualized was the only significant independent variable in a separate multiple linear regression analysis ($\beta = 0.598$, $p = 0.019$). When the number of parathyroid glands visualized was less than two, the hypocalcemia increased with an odds ratio (OR) 1.132, 95% confidence interval: 0.068–18.719.

Conclusion: Preoperative calcium and vitamin D supplementation did result in lowering post-TT hypocalcemia and hospital stay.

Keywords: Postoperative hypocalcemia, Thyroidectomy, Vitamin D deficiency.

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Introduction

Thyroidectomy is the most frequently performed endocrine surgery world over.[1] Hypocalcemia is the commonest complication post-TT. Temporary and permanent hypocalcemia post-TT ranges from 19% to 38% and 0.2% to 10%, respectively.[2,3] Factors responsible for hypocalcemia are devascularization or inadvertent removal of the parathyroid gland, surgery for malignancy, hyperthyroid state, and prolonged surgical time.[4] Of these, the most important is the number of parathyroid glands identified and preserved during thyroid surgery.

Identification of parathyroid glands and preservation of their vasculature is established causative factors for post-TT hypocalcemia. However, few factors attributable to post-TT hypocalcemia are still being debated. One such is vitamin D status. Vitamin D deficiency is prevalent in 40–99% population of the Indian subcontinent.[5,6] Retrospective studies observed low levels of 25-hydroxy (25-OH) vitamin D as one of the predictive factors for postoperative hypocalcemia.[7,8] Few retrospective studies in the past found a significant positive correlation of preoperative serum 25-OH vitamin D levels with post-TT hypocalcemia.[7,9–11] However, other studies did not establish any causal relationship of preoperative serum vitamin D with postoperative hypocalcemia.[12,13] Subsequently, few prospective trials have shown perioperative calcium and calcitriol supplementation to be beneficial in preventing immediate postoperative hypocalcemia.[14,15] Predicting and managing post-TT hypocalcemia given the varied etiology, taking vitamin D status into consideration among the Indian population, this study was intended to find if preoperative with oral cholecalciferol and calcium supplementation reduce post-TT hypocalcemia.

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Subjects and Methods

The study was conducted from 1st April 2018 to 31st July 2019 at King George's Medical University, India. Patients diagnosed with benign multinodular goiter (MNG), toxic nodular goiter, and Graves' disease planned for TT, were included in this study. Those patients with proven malignancy on fine-needle aspiration cytology (FNAC) before surgery, patients on steroids, concomitant hyperparathyroidism or any dual pathology, completion thyroidectomy (i.e., surgery for recurrent goiter), patients with serum creatinine level >1.5 mg/dL, patients less than 18 years of age, pregnant and lactating women, or those not consenting were excluded from this study.

Preoperatively

Patients were randomized into two groups A and B (as described below). Simple randomization was done by the principal investigator. Serum calcium (total and ionic), phosphorus, magnesium, albumin, alkaline phosphatase, 25-OH vitamin D, and serum intact parathyroid hormone (iPTH), were measured apart from the routine blood investigations. Bone mineral density (BMD)—three sites, (i.e., distal 1/3rd of radius-ulna, lumbar vertebrae L1–L4, and hip joint) was performed once, after allocating the group. After these tests, group "A" patients underwent surgery. Group "B" patients were supplemented with calcium and vitamin D for 6 weeks. After 6 weeks of supplementation, the above blood investigations were repeated, and then patients underwent surgery.

Supplementation

Group A received no calcium and vitamin D supplementation. Those in group B were supplemented with oral calcium in the form of calcium carbonate 2000 mg/day (elemental) in two divided doses for 6 weeks (each tablet consisted of 1500 mg of salt, with elemental calcium 500 mg with vitamin D 250 IU, a total of four tablets per day), and vitamin D in the form of oral gel capsule of cholecalciferol 60,000 units every week for 6 weeks before surgery, irrespective of the serum 25-OH vitamin D levels. Surgery in Group B was performed within 1 week of the last dose of medication. The consolidated standards of reporting trials (CONSORT) diagram is shown in Flowchart 1.

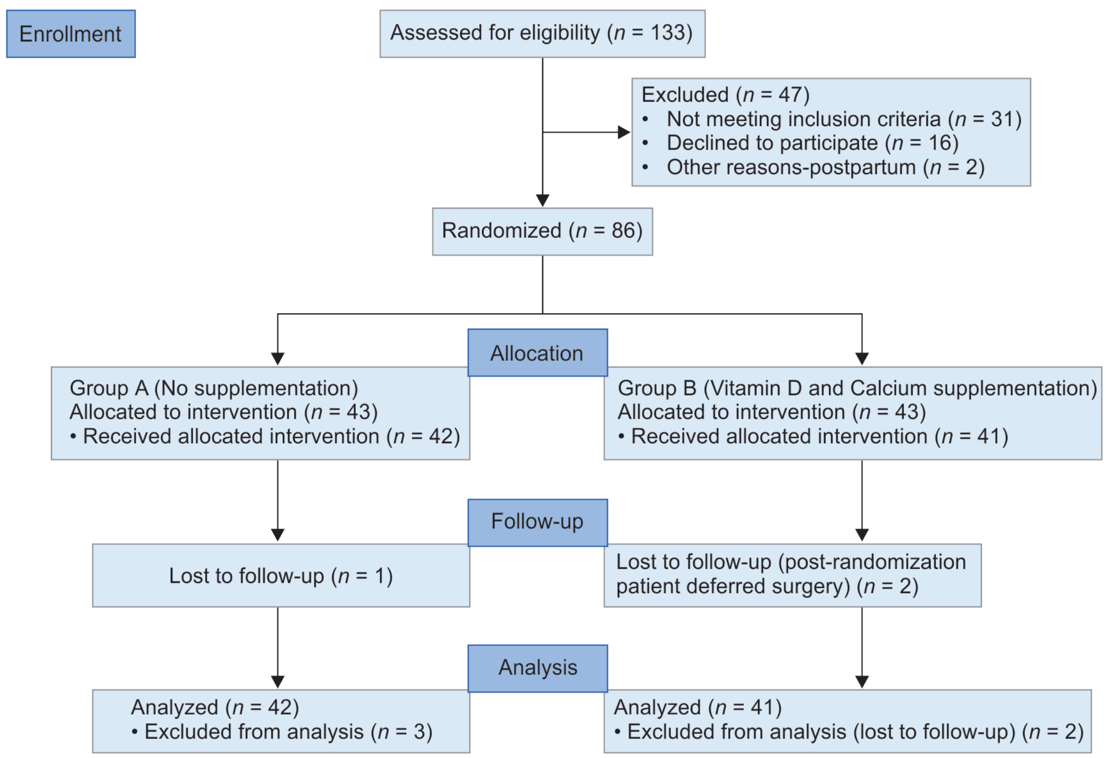
Surgical Procedure

Surgical procedure (TT) was done by one of the three senior consultants by standard technique. All visualized parathyroid glands were saved. Intraoperative parathyroid score system (IPSS) was used to assess the status of each parathyroid gland. A score of zero was given to complete loss of gland or when gland was not identified, when the gland was identified but was discolored and dark was scored one, mild discoloration was scored two, and normal gland with intact vascularity was scored three. The total score was 12 for all 4 well-preserved parathyroid glands. In case of inadvertent injury or removal of the parathyroid gland(s), the gland was autotransplanted (AT) immediately into the sternocleidomastoid muscle.

Postoperatively

None of the patients were given postoperative prophylactic supplements and were monitored for clinical features of hypocalcemia, like perioral tingling, numbness in fingers, and Trousseau sign. On POD-1, serum iPTH, calcium (total and ionic), phosphorus, magnesium, and albumin were checked. On POD-2, 3, 10, and 30, serum calcium and phosphorus were monitored. Biochemical hypocalcemia is defined as serum total calcium (albumin corrected) levels <8.2 mg/dL (lower limit of the laboratory range).

Flowchart 1: Flow diagram of patients enrolled in this study, and those patients who underwent the intervention in both groups, followed by surgery, follow-up, and analysis



Asymptomatic patients were discharged on POD-3 after checking their calcium levels. Symptomatic patients with tingling or numbness were started on oral calcium carbonate (1 gm thrice a day) with or without calcitriol supplementation (calcium carbonate in the form of elemental calcium 500 mg with vitamin D 250 IU and calcitriol titrating dose according to hypocalcemia, starting from 0.75 µgm a day in three divided doses to a maximum of 1.5 µgm per day in divided doses).

Departmental protocol for the calcium (oral and i.v.) supplement mentioned in Table 1. These patients were discharged after clinical hypocalcemia was resolved. Patients were followed-up on POD-10 and 30 with monitoring of serum calcium (total and ionic) and phosphorus levels. The primary outcome was to see clinical hypocalcemia rates and compare between both groups and the secondary outcome was to see if preoperative parameters (mentioned above) had any effect on postoperative hypocalcemia.

The study was done after obtaining university ethical clearance vide reference code 90th ECM II B-Thesis/P8.

Statistical Analysis

Statistical analysis was done by using IBM-SPSS version 23.0 (Chicago. Inc, USA). The categorical variables were expressed as percentages and were analyzed by the Chi-square test. Continuous data were expressed as mean ± SD (standard deviation) was analyzed using independent *t*-test. Pearson's correlation coefficients were calculated between POD-1 serum calcium and age, sex, body mass index (BMI), preoperative blood parameters, BMD, and intraoperative parameters (weight of thyroid gland, number of parathyroid glands visualized). Of these variables which were significantly associated with POD-1 calcium, multiple linear regression analysis was done. A *p*-value of <0.05 was taken as statistically significant and all the tests were two-tailed.

Results

A total of 133 patients underwent TT in this period. Of which 47 were excluded, those who did not meet the inclusion criteria (n = 31), declined to participate (n = 16), postpartum, and lactating (n = 2). After randomization and surgery, one patient in group A and two patients in group B did not comply with the follow-up protocol. A total of 83 patients were included for analysis with 42 patients in group A and 41 patients in group B (Flowchart 1). All patients underwent TT, with no lymph node dissection. The mean age of all patients was 41.6 ± 13.39 years (range: 18–74). Female to male was 11:1. Overall BMI of the patients was 23.66 ± 4.6 kg/m^2 (range: 13.3–36.52). The mean thyroid stimulating hormone (TSH) of all patients was 1.49 ± 1.38 µIU/mL (range: 0.01–5.93).

Table 2 compares demographics, preoperative, and intraoperative parameters between two groups, which were comparable between two groups. Table 3 compares the postoperative blood parameters between two groups, which were comparable between two groups. Table 4 explains biochemical and clinical hypocalcemia. Biochemical hypocalcemia occurred in a total of 53 (63.85%) patients. On POD-1, 39 (73.6%) and on POD-2, 14 (26.4%) patients had biochemical hypocalcemia.

Clinical hypocalcemia occurred in 31 (37.3%) patients. Of these, 19 (61.3%) were in group A and 12 (38.7%) belonged to group B (p = 0.197). Among those who developed clinical hypocalcemia, only signs (i.e., tingling and numbness) appeared in five patients, of which three (7.1%) were in group A and two (4.9%) in group B. Clinical symptoms were positive (along with Trousseau sign) in 26 (83.87%) patients (31.3% of 83 patients), of which 16 (38.1%) among group A and 10 (24.4%) among group B patients, so these patients received intravenous calcium infusion along with oral calcium and calcitriol supplements. All patients developed clinical symptoms within 72 hours post-TT.

The number of parathyroid glands visualized in all patients was correlated with clinical hypocalcemia. At least one parathyroid gland was identified in all patients. Single gland was identified in 3.8% (n = 2), two glands in 25.3% (n = 21), three glands in 44.6% (n = 37), and all four glands in 27.7% (n = 23). Hypocalcemia occurred in n = 1, n = 6, n = 19, and n = 5 when the visualized parathyroid glands were one, two, three, and four, respectively. The incidence of hypocalcemia between the two groups was not statistically significant with respect to the number of parathyroid glands visualized.

Pearson's correlation of postoperative calcium level is depicted in Table 5, in which preoperative magnesium (r = 0.222, p = 0.043), and POD-1 PTH levels (r = 0.219, p = 0.047) were found to be significantly associated with POD-1 calcium levels. On multiple linear regression analysis, both were not statistically significant with preoperative magnesium levels (β = 0.194, p = 0.077) and POD-1 PTH (β = 0.190, p = 0.083). In a separate multiple linear regression analysis, the number of parathyroid glands visualized was the only significant independent variable (β = 0.598, p = 0.019). When the number of parathyroid glands visualized was less than two, the hypocalcemia increased with an OR 1.132, 95% confidence interval: 0.068–18.719.

The majority of patients, that is, 74.7% (n = 62) were vitamin D deficient. In group A, 76.2% (n = 32) were in deficient range

Table 1: Protocol for calcium and vitamin D supplementation in postoperative period on the basis of hypocalcemia (hypocalcemia: corrected calcium <8.2 mg/dL)

Signs (Chovstek's/ Trousseau)	*Symptoms (perioral numbness/paresthesia/tingling/ spontaneous carpopedal spasm)*	*Oral supplementation*	*I.V. supplementation*
No	No	Nil	Nil
Yes	No	Calcium carbonate	Nil
Yes	Yes	Calcium carbonate + calcitriol	100 mL 10% calcium gluconate in 400 mL of 5% dextrose at 1 mL/kg/hr

(serum 25-OH vitamin D < 30 ng/mL) and 23.8% ($n = 10$) were in the sufficient range. In presupplemental group B, 73.2% ($n = 30$) were in deficient range and 23.8% ($n = 11$) were in the sufficient range (postsupplementation, serum 25-OH vitamin D levels in group B were 42.39 ± 11.49 ng/mL vs 17.61 ± 10.44 ng/mL as compared to presupplement value; $p < 0.001$). None of the group B patients had any features suggestive of vitamin D levels in the toxic range after supplementation. There was no statistical significance between the distribution of these patients in both groups ($p = 0.804$). Biochemical hypocalcemia on POD-1 was found in 48.4% ($n = 30$) of vitamin D deficient and in 42.9% ($n = 9$) of vitamin D sufficient group ($p = 0.801$). Clinical hypocalcemia occurred in 38.7% ($n = 24$) of vitamin D deficient group and in 33.3% ($n = 7$) in vitamin D sufficient group ($p = 0.58$). Clinical hypocalcemia rates among the two groups were not statistically significant among vitamin D deficient patients ($p = 0.59$) and vitamin D sufficient patients ($p = 0.9$). Of the 31/83 patients with clinical hypocalcemia, 28 (33.7%) were discharged on oral calcium and calcitriol supplementation, whereas three patients (3.6%) were discharged with oral calcium supplementation only (each tablet of calcium carbonate consisted of 500 mg elemental calcium with 250 IU vitamin D). The mean hospital stay of group A patients was longer (4.19 ± 1.97 days) compared to group B (3.83 ± 2.65 days), though was not statistically significant ($p = 0.48$). Those patients with hyperthyroid vs nonhyperthyroid patients in the postoperative period were found to have similar rates of hypocalcemia ($p = 0.556$)

Discussion

The current study showed post-TT, serum total calcium levels on POD-1 between both groups were comparable as mentioned in Table 3, as well as other parameters measured on POD-1. Though clinical hypocalcemia in group B was found to be less. This finding was partially similar to a previous study from India, where they did not observe a significant difference between serum calcium level on POD-1 ($p = 0.21$) between supplement and nonsupplementation

Table 2: Comparison of preoperative and intraoperative parameters

Parameter	*Group A (n = 42)*	*Group B (n = 41)*	*p-value*
Age (years)	43.45 ± 13.89	39.74 ± 12.79	0.244
Sex F:M	41:1	35:6	0.1
BMI (kg/m^2)	23.79 ± 4.33	23.52 ± 4.91	0.754
BMD			
T-score—total	−1.54 ± 1.56	−1.96 ± 1.29	0.18
Z-score—total	−1.11 ± 1.5	−1.52 ± 1.08	0.18
Blood investigations			
S. TSH (µIU/mL)	1.69 ± 1.43	1.29 ± 1.23	0.198
S. total calcium (mg/dL)	8.89 ± 0.99	8.98 ± 0.52	0.24
S. ionic calcium (mg/dL)	4.8 ± 0.33	4.99 ± 0.28	0.05
S. phosphorus (mg/dL)	3.38 ± 0.58	3.19 ± 0.55	0.15
S. magnesium (mg/dL)	2.08 ± 0.88	2.15 ± 0.82	0.36
S. albumin (mg/dL)	4.29 ± 0.39	4.43 ± 0.21	0.06
S. alkaline phosphatase (IU/L)	225.35 ± 64.89	219.93 ± 46.20	0.77
25-OH vitamin D (ng/mL)	15.42 ± 9.85	17.71 ± 10.33	0.13
Intraoperative parameters			
Size of largest nodule (cm)	4.21 ± 2.08	3.68 ± 3.47	0.09
Weight of thyroid (gm)	125.69 ± 109.25	152.77 ± 273.34	0.935
Number of PTH glands visualized	3.07 ± 0.77	2.88 ± 0.81	0.33
IPSS	8.38 ± 2.4	8.05 ± 2.3	0.77
PTH–AT (*n*)	3	2	1
Diagnosis in final histopathology			
MNG	33 (78.6%)	31 (75.6%)	0.2
Graves' disease	2 (4.8%)	7 (17.1%)	
Toxic MNG	3 (7.1%)	3 (7.3%)	
Malignancy*	4 (9.5%)	0 (0)	

*Preoperatively FNAC was benign, hence, included in study, postoperative histopathology showed non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) ($n = 4$, in one of the nodules of MNG) considered as malignant, without any high-risk features

Table 3: Comparison of postoperative parameters between two groups

Parameter	*Group A (n = 42)*	*Group B (n = 41)*	*p-value*
POD-1 PTH	22.37 ± 22.33	30.25 ± 26.39	0.08
S. total calcium (mg/dL)			
POD-1	8.13 ± 1.03	7.99 ± 0.76	0.33
POD 2	8.11 ± 1.04	8.17 ± 0.77	0.82
POD-3	8.26 ± 0.79	8.28 ± 0.71	0.39
POD-10	8.51 ± 0.55	8.62 ± 0.55	0.89
POD-30	8.56 ± 0.65	8.71 ± 0.39	1
S. ionic calcium (mg/dL)			
POD-1	4.3 ± 0.47	4.42 ± 0.42	0.33
POD-2	4.45 ± 0.5	4.47 ± 0.4	0.79
POD-3	4.46 ± 0.47	4.57 ± 0.43	0.2
POD-10	4.66 ± 0.34	4.66 ± 0.37	0.72
POD-30	4.76 ± 0.3	4.79 ± 0.32	0.56
S. phosphorus (mg/dL)			
POD 1 PO4	3.93 ± 0.78	3.77 ± 0.71	0.52
POD-2 PO4	3.99 ± 0.97	3.82 ± 0.86	0.41
POD-3 PO4	3.96 ± 1.04	3.93 ± 0.84	0.85
POD-10 PO4	3.93 ± 1.3	3.79 ± 0.67	0.4
POD-30 PO4	3.57 ± 0.88	3.43 ± 0.55	0.87
S. magnesium (mg/dL) POD-1	1.78 ± 0.65	1.89 ± 0.72	0.54
S. albumin (mg/dL) POD-1	3.99 ± 0.35	4.9 ± 0.3	0.08
Post-op discharge (days)	4.19 ± 1.96	3.83 ± 2.65	0.08

Post-op, postoperative

Table 4: Comparison of biochemical and clinical hypocalcemia between two groups with respect to postoperative day

Parameter	*Group A (n = 42), (%)*	*Group B (n = 41), (%)*	*Total number of patients*	*p-value*
Biochemical hypocalcemia				
POD-1 (*n*)	18 (42.9)	21 (51.2)	39	0.51
POD-2 (*n*)	20 (47.6)	22 (53.7)	42	0.66
POD-3 (*n*)	13 (31)	16 (39)	39	0.49
POD-10 (*n*)	7 (16.7)	7 (17.1)	14	1
POD-30 (*n*)	7 (16.7)	4 (9.8)	11	0.52
Manifestation of clinical hypocalcemia on POD				
POD-0 (*n*)	1 (5.3)	3 (25)	4	
POD-1 (*n*)	11 (57.9)	7 (58.3)	18	
POD-2 (*n*)	7 (36.8)	2 (16.7)	9	
Total	19 (100)	12 (100)	31	0.197

Table 5: Pearson's correlation for POD-1 calcium levels with various parameters

Parameter	*Pearson's coefficient*	*p-value*
Group	–0.154	0.165
Age	–0.133	0.231
Sex	–0.078	0.484
BMI	–0.104	0.351
TSH	–0.091	0.415
BMD T-score	0.004	0.974
BMD Z-score	–0.009	0.974
Pre-op total calcium	0.181	0.101
Pre-op ionic calcium	0.050	0.650
Pre-op phosphorus	0.069	0.535
Pre-op magnesium	0.222	0.043
Pre-op alkaline phosphatase	–0.060	0.589
Presupplement serum 25-hydroxy vitamin D	–0.064	0.563
Weight of thyroid	0.055	0.621
Largest nodule	0.001	0.990
No. of PTG	0.185	0.095
IPSS	0.126	0.258
PTH-AT	0.105	0.343
POD-1 PTH	0.219	0.047

BMI, body mass index; TSH, thyroid stimulating hormone; BMD, bone mineral density; Pre-op, pre-operative; Ca, calcium; Mg, magnesium; ALP, alkaline phosphatase; Vit-D, serum 25-hydroxy Vitamin D; PTG, parathyroid gland; IPSS, intra-operative parathyroid scoring system; PTH-AT, parathyroid gland auto-transplantation; PTH, parathyroid hormone

groups. They found that on POD-2, three serum calcium levels were significantly lower in the nonsupplemented group ($p = 0.04$ and 0.01, respectively). Their study found clinical hypocalcemia rates higher in patients without supplementation 12 vs 3 patients ($p \leq 0.01$). Also, they found a significant correlation between preoperative calcium and postoperative calcium levels ($r = 0.618$, $p < 0.001$),[14] whereas the current study did not find any significant correlation of any preoperative parameters with POD-1 calcium ($r = 0.181$, $p < 0.101$). The rate of clinical hypocalcemia in this study (37.3%) was comparable to previous studies 19–38%.[2]

Clinical hypocalcemia was found higher in patients with three glands being identified 51.3% (n = 19 of 31), this may be due to parathyroid stunning. The other mechanisms are possibly due to reduced bone resorption, reduced calcium reabsorption from ascending thick loop of Henle, or reduced conversion of 1,25-OH vitamin D, which in turn reduces intestinal absorption of calcium.[16] Hypocalcemia was resolved in these patients and none had clinical manifestations of hypocalcemia at the end of 1 month. Incidentally, POD-1 serum calcium was lower in group B, however, it was not found to be significant. It is likely because of the outliers/extreme values which is evident as the group B patients had higher PTH and also higher standard deviation. Also, serum electrolytes including calcium apart from PTH are affected by perioperative fluid management, the fluid balance which is dependent on the duration of fasting, was not taken into account.

Another study from India found post-TT hypocalcemia to have a significant association with POD-1 PTH[17] and hyperthyroid vs nonhyperthyroid state which was similar to our study. Vitamin D deficiency was not found to be a predictive factor of post-TT hypocalcemia in our study which was similar to previous study.[17] On discharge, these patients were advised oral cholecalciferol 60,000 units weekly for 6 weeks for vitamin D deficiency. Vitamin D deficiency was comparable to previous studies with community-based having a prevalence of 50–94% and in patients having 37–99%.[6]

There are a few limitations to this study. The serum PTH levels were done on POD-1 due to logistic issues at the start of this study. Later on, the laboratory test was available for immediate postoperative value. So, only 46 patients had the value, hence is being evaluated as a part of another prospective study, which is not included in this study.

Studies in past found benefits of routine prophylactic postoperative calcium and vitamin D supplementation.[15,18–21] Whereas, this study was designed to predict post-TT hypocalcemia by administering 6 weeks of oral calcium and cholecalciferol supplements. Also, our

Table 6: Showing comparison of various studies for calcium supplementation and hypocalcemia with their significant findings

			Inference		
Sl. no	*Author, country, year, {protocol of supplementation} [reference]*	*Groups*	*Incidence of clinical hypocalcemia*	*Incidence of biochemical hypocalcemia*	*Overall incidence of hypocalcemia*
1	Osman Kurukahveciouglu et al., Turkey, 2007 ($n = 487$)[18]	Group 1: no supplementation ($n = 244$)	11/ 244 (4.5%) i.v. calcium—7/244 (2.86%)	Data not available	4.3%
		Group 2: oral calcium 600 mg/day + Vit D3—400 IU/day ($n = 243$)	10/243 (4.3%) i.v calcium—zero ($p < 0.001$)		
2	Nemade et al., Pune, India, 2012 ($n = 48$) {supplementation 1 week prior to surgery to postoperatively 2 weeks}[19]	Group 1: calcium 2 gm/day ($n = 24$)	10/24 (41.6%)	7/24 (29.17)	29.17%
		Group 2: Calcium 2 gm/day with Vit D 60,000 U thrice/week ($n = 24$)	3/24 (12.5%) ($p = 0.023$)	1/24 (4.17%) ($p = 0.0201$)	
3	Arer et al., Turkey, 2016 ($n = 106$) {supplementation immediate postoperative and tapered off}[20]	Group 1: 2500 mg calcium/day + 880 IU Vit D3 ($n = 53$)	1/53 (1.9%)	POD-7 calcium levels 9.09 ± 0.69	17.92 %
		Group 2: only if symptomatic ($n = 53$)	18/53 (33.9%) ($p < 0.001$)	9.43 ± 0.49 ($p = 0.014$)	
4	Langner et al., Brazil, 2017 ($n = 47$) {supplementation starting on POD-1 to POD-6}[21]	Group 1: no supplementation ($n = 27$)	10/27 (37%)	17/27 (62.9%)	29.8%
		Group 2: calcium 3 gm/day ($n = 20$)	4/20 (20%) ($p < 0.01$)	6/20 (30%)	
5	Ravikumar et al., Chennai, India, 2017 ($n = 208$) Calcium: 2 gm/day Calcitriol: 1 µgm/day Cholecalciferol: 60,000 IU/day {supplementation started 6 hrs after surgery till 5th postoperative day}[15]	Group 1: no supplementation ($n = 52$)	67/208 (32.2%)	30/52 (57.69%)	34.6%
		Group 2: oral calcium ($n = 52$)		26/52 (50%)	
		Group 3: oral calcium + calcitriol ($n = 52$)		8/52 (15.38%)	
		Group 4: oral calcium + calcitriol + cholecalciferol ($n = 52$)		8/52 (15.38%) ($p < 0.001$)	
6	Jaan et al., Kashmir, India, 2017 ($n = 46$) {supplementation started 7 days prior to surgery and till 7 days postoperatively}[14]	Group 1: oral calcium 2 gm/day + oral calcitriol 1 µgm/day ($n = 24$)	3/24 (12.5%)	6/24 (25%)	32.6%
		Group 2: no Supplementation	12/22 (54.5%) ($p < 0.01$)	13/22 (59%) ($p = 0.04$)	
7	Current study, 2018–2019; Lucknow, India{6 weeks prior to surgery}	Group A: no supplementation	19 (45.2%)	18 (42.9%)	37.5%
		Group B: calcium 2 gm/day + cholecalciferol 60,000 IU/week	12 (29.26%) ($p = 0.195$)	21 (51.2%) ($p = 0.51$)	

study did not start routine prophylactic postoperative calcium and vitamin D supplements. Table 6 shows the comparison of various studies of perioperative oral calcium and vitamin D supplementation with their significant findings with temporary hypocalcemia rates described. Hypocalcemia rate though was higher than previous studies, but results are comparable.[22,23]

Conclusion

Preoperative vitamin D deficiency was not found to be predictive of post-TT hypocalcemia. Irrespective of preoperative vitamin D levels, 6 weeks of supplementation of oral cholecalciferol and calcium may result in lowering post-TT hypocalcemia morbidity and hospital stay in some patients.

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