



## “A STUDY TO ASSESS USEFULNESS OF PRE- AND POST-OPERATIVE CALCIUM AND VITAMIN D SUPPLEMENTATION IN PREVENTION OF HYPOCALCEMIA AFTER TOTAL THYROIDECTOMY”

### Surgery

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### ABSTRACT

**Background:** The aim of this randomized controlled trial was to ascertain the usefulness of routine pre- and post-operative calcium and Vitamin D supplementation in prevention of hypocalcemia after TT.

**Materials and Methods:** Sixty consecutive patients who underwent total or near TT from January 2016 to August 2016 were included in the study.

**Results:** Twelve patients from Group 2, and 3 patients from Group 1 developed symptomatic hypocalcemia ( $P < 0.01$ ). Laboratory hypocalcemia within postoperative 24 h was comparable between two groups, but more patients of Group 2 compared to Group 1 developed hypocalcemia at 48 h (6 and 13, respectively;  $P = 0.04$ ) and at 72 h after surgery (5 and 14, respectively;  $P = 0.01$ ).

**Conclusion:** Routine pre- and post-TT calcium and Vitamin D supplementation can significantly reduce postoperative hypocalcemia.

### KEYWORDS:

Calcium supplementation, thyroidectomy

#### Introduction:

We know that Total thyroidectomy (TT) is a commonly performed surgery worldwide.[1] It is the definitive management option for thyroid malignancies and also for benign diseases such as multinodular goiter symptomatic of compression.[2] The incidence of transient hypocalcemia, defined as hypocalcemia occurring within 6 months of surgery, has been variably reported to be 13%–38%.[3,4] It occurs because of transient hypoparathyroidism due to parathyroid gland manipulation or impairment of its blood supply. The development of postoperative hypocalcemia after TT is unfavorable not only since it is a cause of morbidity but also because it occurs 24–72 h postoperatively and hence necessitates repeated biochemical testing and prolonged in-hospital stay. Many risk factors have been identified for postoperative hypocalcemia including age  $>50$  years, female gender, thyroid malignancy, Grave's disease, lymph node dissection, nonidentification of parathyroid glands intraoperatively, reoperation, and Vitamin D deficiency.[5,6,7] Although 1-h and 4-h postoperative intact parathormone (iPTH) testing has been shown to stratify patients into high- and low-risk for hypocalcemia and expedite an early discharge after TT,[8,9,10] rapid iPTH measurement facility is not routinely available in many resource-poor settings and is hence not feasible.

A high prevalence of Vitamin D deficiency has been demonstrated in some North Indian states,[11] and is a known risk factor for postoperative hypocalcemia after TT.[5,6,7] Although routine postoperative oral calcium and Vitamin D supplementation has been shown to prevent the development of hypocalcemia after TT and facilitate an early discharge,[12,13] the role of preoperative supplementation has seldom been tested.[14] The aim of the present randomized controlled trial was to ascertain the usefulness of pre- and post-operative calcium and Vitamin D supplementation in prevention of hypocalcemia after TT.

#### Materials and methods:

This prospective randomized controlled study was performed, from January 2016 to August 2016, on sixty consecutive patients who underwent total or near TT in the department of General Surgery in a tertiary hospital in central India. Prior Ethical Committee approval was sought and each patient gave an informed written consent before being enrolled in the study. The included patients had no history of prior thyroid or neck surgery. Those patients who underwent lobectomy or sub-TT were excluded from the study. Preoperatively, patients were randomly divided into two groups, Group 1 received oral calcium and Vitamin D and Group 2 did not receive supplementation.

The reference range for serum calcium was 8.5–10.5 mg/dl. Serum calcium level  $\leq 8.5$  mg/dl was considered as laboratory hypocalcemia. Data was analysed using SPSS and appropriate statistical tests were applied.

#### Results:

During the study period, sixty consecutive patients referred for TT

were recruited. Baseline characteristics of patients belonging to the two groups are shown in Table 1. The mean age, sex ratio, type of thyroid disease, surgical procedure performed, and preoperative calcium profiles were comparable between the two groups. Twelve patients from Group 2, and 3 patients from Group 1 [Table 2] developed symptomatic hypocalcemia ( $P < 0.01$ ). Intravenous calcium was given to four patients who developed tetany and all these belonged to Group 2. Hypercalcemia or other side effects did not develop in any of the patients' receiving oral calcium and Vitamin D. Total calcium levels were lower in the group who did not receive any supplement than in the supplemented group [Table 2]. The Pearson's correlation coefficients and two-tailed P values are depicted in Table 3. On multiple linear regression analysis, preoperative serum calcium was the only independent significant variable in the development of 24 h post-TT hypocalcemia (standard coefficient  $\beta = 0.62$ ;  $P < 0.001$ ) while grade of goiter approached significance ( $\beta = -0.226$ ;  $P = 0.056$ ). The risk of 24 h post-TT hypocalcemia was increased 2.78-fold for patients who had a preoperative calcium  $<9.00$  mg/dl (odds ratio 8.14; 95% confidence interval 1.47–45.18).

#### Discussion:

In this randomized controlled study, we have shown that 7 day preoperative oral calcium and Vitamin D supplementation continued into the postoperative period after TT significantly reduced laboratory and symptomatic hypocalcemia. Moreover, the need for intravenous calcium administration due to carpopedal spasm was completely eliminated in the supplemented group while four patients of the control group required the same. Although the improvement in calcemia at all tested post-TT time points was modest, it did not reach statistical significance. This may be explained by the small sample size and it would be constructive to include more patients in each group to elicit statistically significant results. Hence, our study suggests the role of routine pre- and post-operative oral calcium and Vitamin D supplements in decreasing the incidence and severity of hypocalcemia after TT although it does not completely eliminate the occurrence of postoperative hypocalcemia.

The literature is replete with studies evaluating the effect of post-TT calcium and Vitamin D supplementation on hypocalcemia. Moore[12] administered calcium at a dosage of 5 g/day to patients after bilateral thyroid resection and found that only 4 of 124 patients developed hypocalcemia and one required administration of intravenous calcium. Hence, he recommended prophylactic use of oral calcium to reduce the risk of hypocalcemic crisis and increase the likelihood of early hospital discharge. Bellantone et al.[15] conducted a prospective control study and reported that only 3 of 26 patients (11%) receiving oral calcium supplement (3 g/day) had symptoms related to hypocalcemia after TT, whereas 11 of 27 patients (40%) not receiving calcium supplement had symptoms. They also showed that the addition of Vitamin D to oral calcium supplements was associated with significantly higher serum calcium concentrations on postoperative day 2 and 3, with a lower incidence of hypocalcemia. Therefore, they recommended the early use of Vitamin D in addition to calcium supplement in patients

undergoing TT. These studies suggest that hypocalcemia after thyroidectomy can be prevented by routine administration of calcium supplements. A systematic review and meta analysis on nine such studies also showed a significant decrease in postoperative hypocalcemia in patients who received routine supplementation of oral calcium or Vitamin D.[16] The incidence decreased even more with the combined administration of both supplements. However, the effect of preoperative calcium and Vitamin D has seldom been tested. Docimo et al.[14] supplemented fifty consecutive patients undergoing TT with pre- and post-operative calcium and Vitamin D. They found the incidence of symptomatic hypocalcemia to be 6% and that of laboratory hypocalcemia to be 10%. No permanent hypocalcemia developed.

The dosage and duration of calcium and Vitamin D intake are also of concern. In the study by Moore,[12] patients were given oral calcium on an empirical basis as 5 g/day for 2 weeks. On this dose, one elderly patient became lethargic and developed hypercalcemia. In the trial conducted by Bellantone et al.,[15] the dosage of calcium was 3 g/day and Vitamin D was 1 µg/day for 7 days after surgery and it did not lead to any complication. In our study, oral calcium 2 g/day and calcitriol 2 µg/day were given preoperatively for 1 week and continued 1 week postoperatively.

**Conclusions:**

The results of this study indicate that routine pre and post TT calcium and Vitamin D supplementation can significantly reduce post operative hypocalcemia. We, therefore, suggest the same in the prevention of post TT hypocalcemia, which ultimately can also decrease prolonged hospitalization of patients and costs associated with multiple blood sampling.

**Tables:**

**TABLE 1: Baseline characteristics of supplemented (Group 1) and not supplemented (Group 2)**

Variables	Group 1 (supplemented)	Group 2 (not supplemented)	P
Sex ratio (male/female)	6/24	8/22	0.76
Mean age±SD (years)	36.43±11.54	38.13±15.71	0.64
Thyroid disease benign/malignant (n)	7/23	8/22	0.5
Malignancy (n)			
Papillary	18	14	0.24
Follicular	2	7	
Medullary	1	0	
Hurthle	2	1	
Benign disease (n)			
Grave's disease	0	1	0.25
Multinodular goiter	0	2	
Colloid goiter	7	5	
Surgery			
Near total thyroidectomy	2	1	0.84
Total thyroidectomy	24	25	
Lymph node dissection	4	4	
Preoperative tests (mg/dl)			
Calcium	10.08±0.78	9.88±0.66	0.29
Phosphorus	3.05±0.7	3.09±0.57	0.82
Magnesium	2.42±0.39	2.61±0.28	0.35

SD: Standard deviation

**Table 2: Postoperative calcium levels and hypocalcemia in supplemented (Group 1) and not supplemented (Group 2)**

Variables	Group 1 (supplemented)	Group 2 (not supplemented)	P
Mean serum calcium±SD (mg/dl)			
6 h	9.47±0.77	9.31±0.73	0.40
12 h	9.09±0.79	8.94±0.84	0.48
24 h	8.88±0.76	8.53±0.96	0.12
48 h	8.96±0.72	8.70±0.76	0.19
72 h	8.97±0.70	8.78±0.74	0.32
30 days	9.05±0.58	8.83±0.40	0.09
Postoperative hypocalcemia (≤8.5 mg/dl), n (%)			
6 h	2 (6.7)	4 (13.3)	0.34
12 h	7 (23.3)	7 (23.3)	0.62
24 h	8 (26.7)	12 (40)	0.21
48 h	6 (20)	13 (43.3)	0.04
72 h	5 (16.7)	14 (46.7)	0.01
30 days	5 (16.7)	9 (30)	0.18
Symptomatic hypocalcemia, n (%)	3 (10)	12 (40)	<0.01

SD: Standard deviation

**Table 3: Correlation between 24 h postoperative calcium and other parameters**

Variables	Pearson's correlation coefficient	P (two-tailed)
Group	-0.200	0.126
Age	-0.113	0.39
Gender	-0.057	0.664
Height	0.076	0.566
Weight	0.215	0.099
BMI	0.200	0.125
Lymph node dissection	-0.108	0.411
Goiter grade	-0.261	0.044
Malignant histopathology	-0.260	0.045
Preoperative calcium	0.618	<0.001

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