

Single-dose preoperative vitamin D and calcium supplementation to prevent hypocalcemia after total thyroidectomy: a comparative clinical trial

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Background

Hypocalcemia is not a rare complication after total thyroidectomy. It may be predisposed by preoperative low serum calcium, malignancy, prolonged surgery, inexperienced surgeons, inappropriate use of diathermy, and lack of loop magnifier during surgery. It causes patient distress and may prolong hospital admission time. Calcium and vitamin D administration may help decrease its rate.

Patients and methods

Two groups of patients undergoing total thyroidectomy were included. Each group included 43 patients. One group was given a single dose of calcium 3 g and vitamin D 40 000 IU on the preoperative day (supplementation group), and no calcium or vitamin D was given to the other group (non-supplementation group). Patients were monitored for clinical hypocalcemia and serum calcium level at 6, 12, 24, and 48 postoperative hours, as well as postoperative vitamin D level and serum calcium after 1 month.

Results

In the supplementation group, the authors reported three cases of clinical hypocalcemia and seven cases of laboratory hypocalcemia. In the nonsupplementation group, the authors reported 19 patients with laboratory hypocalcemia and 10 patients with clinical hypocalcemia, with significant difference between groups. Postoperative calcium and vitamin D levels were significantly higher in the supplementation group.

Conclusion

A single-dose preoperative calcium and vitamin D administration is effective in prevention of postoperative hypocalcemia after total thyroidectomy, especially in simple cases. Complicated and malignant cases may need postoperative calcium administration.

Keywords:

calcium, hypocalcemia, supplementation, thyroidectomy, vitamin D

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Introduction

Total thyroidectomy is a common surgical operation carried out for the management of a variety of thyroid diseases [1–3]. One of total thyroidectomy complications is hypocalcemia with a rate ranging between 1.2 and 40% [1,4,5]. Hypocalcemia in this situation is mostly attributed to parathyroid gland injury, ischemia, or inadvertent excision [6]. The surgical techniques and surgeon's skills affect post-thyroidectomy hypocalcemia [7]. Surgery for malignancy has a higher rate of hypocalcemia than surgery for benign diseases [8,9]. Preoperative parathyroid dysfunction, previous parathyroid gland surgery, abnormal calcium homeostasis, systemic diseases such as renal failure, and chemotherapy all affect postthyroidectomy calcium level [10,11]. Hypocalcemia may be transient in the first postoperative 24 h or permanent if extended beyond the sixth postoperative month [12]. It can be diagnosed by clinical manifestations such as perioral

tingling, numbness, muscle twitches, and carpopedal spasm, changes in patient's emotions, and laboratory findings such as calcium level below 8.5 mg/dl or decreased serum parathyroid hormone level [13]. Hypocalcemia can affect the decision of patient discharge after total thyroidectomy, and also it may be a cause of readmissions [14]. Some studies advised vitamin D and calcium administration in the perioperative period to decrease postthyroidectomy hypocalcemia [14,15]. Here in this study, the investigators aimed at evaluation of the effect of single-dose preoperative vitamin D and calcium administration on post-total thyroidectomy calcium level.

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Patients and methods

This study is randomized controlled trial carried out on 86 patients undergoing total thyroidectomy in the period between January 2018 and November 2019, in Zagazig University Hospitals. Patients were randomly allocated into two groups, with 43 patients each. The first group was the supplementation group, where the patients received oral vitamin D 40 000 IU and 3 g of calcium tablets once the day before surgery, and the second group received placebo.

Patient included in this study are those above 18 years old undergoing total thyroidectomy.

Patients excluded from this study are those with the following:

- (1) Previous thyroid surgery.
- (2) Malabsorption diseases.
- (3) Pregnancy.
- (4) Previous parathyroid disease or surgery.
- (5) Vitamin D deficiency.
- (6) Renal impairment.
- (7) Hypocalcemia or hypercalcemia.
- (8) American Society of Anesthesiologists status 3 and 4.

All patients in this study were subjected to thorough history taking, full clinical examination, body mass index calculation, proper assessment of the original thyroid disease requiring surgery, preoperative investigations done as usual, in addition to serum calcium, serum magnesium, serum vitamin D, and serum parathormone level assessments.

Serum calcium was tested after 6, 12, 24, and 48 postoperative hours. Patients were discharged on the third postoperative day, except if further hospitalization was indicated. After discharge, the patients were followed up in the outpatient clinic by one of the surgical team, and then, serum calcium was tested after 1 month.

The outcome of this study is vitamin D level and development of hypocalcemia, either clinically or laboratory.

Clinical hypocalcemia means development of perioral and/or acral tingling and numbness, twitches of the face muscles on tapping in front of the ear (Chvostek's sign), muscle twitches, and development of carpopedal spasm.

Laboratory hypocalcemia means serum calcium level less than 8.5 mg/dl.

Preoperative data, postoperative clinical follow-up, and laboratory data were collected and analyzed using paired *t* test and *Z* test in SPSS 22 program package (IBM Statistics for Windows, Version 22 Armonk, NY, USA).

Principles of total thyroidectomy were as follows:

Total thyroidectomy was performed under general anesthesia. Through lower neck collar incision, skin and platysma muscle flap was raised till the thyroid cartilage, followed by opening of the midline raphe, exploration of each thyroid lobe, and tracing the inferior thyroid artery while emerging from underneath the carotid artery. The inferior thyroid artery was identified with its branches supplying the parathyroid gland, which was identified and preserved with its blood supply. The recurrent laryngeal nerve was searched for in the triangle between the carotid artery, trachea, and the inferior thyroid artery. The external laryngeal nerve was identified and preserved 1 cm superior to the upper thyroid pole. If radical thyroidectomy was deemed, the same principles were applied for preserving parathyroid glands and their blood supply, as well as recurrent and external laryngeal nerves. If the surgeons are sure of damaging or removing the parathyroid glands, a half of one of them was minced and transplanted in the subcutaneous tissue of the left forearm.

All patients signed an informed written consent before participation in the trial. The study was approved by the Institutional Review Board and the Research Ethical Committee of our hospital. The study was registered in the clinical trials with the identifier number NCT04212533.

Results

In this study, as presented in Table 1, demographic data showed nonsignificant differences regarding age, sex distribution, BMI, and associated diseases between the groups. The mean±SD preoperative calcium level in the supplementation group was 9.96 ± 0.61 and in the nonsupplementation group was 10.19 ± 1.66 . Mean ±SD vitamin D level in the supplementation group was 58.65 ± 12.51 and in the non-supplementation group was 58.2 ± 12.59 , with nonsignificant differences between both groups. Total thyroidectomy in the supplementation group was indicated for malignancy in 25.59% and for benign thyroid disease in 74.41% of

Table 1 Demographic and preoperative data

	Supplementation group [n (%)]	Nonsupplementation group [n (%)]
Age	38.14±11.8	38.02±12.01
Sex [n (%)]		
Male	16 (37.2)	18 (41.9)
Female	27 (62.79)	25 (58.1)
BMI	28.21±3.77	28.37±3.9
Indication		
Benign	32 (74.41)	33 (76.4)
Malignancy	11 (25.59)	10 (23.6)
Preoperative Ca ⁺⁺ level	9.96±0.61	?10.19±1.66?
Preoperative vitamin D level	58.65±12.51	58.2±12.59?

Table 2 Postoperative and follow-up data

	Supplementation group [n (%)]	Nonsupplementation group [n (%)]	P value
Complication			
Hoarseness	2 (4.65)	1 (2.33)	>0.05
Lost high-pitched voice	1 (2.33)	1 (2.33)	>0.05
Tetany	3 (6.98)	10 (23.26)	<0.05
Laboratory hypocalcemia	7 (16.28)	19 (44.19)	< 0.05
Serum calcium follow-up			
6 h	9.7±1.87	8.6±1.18	<0.05
12 h	9.88±0.94	8.7±1.1624	<0.05
24 h	9.93±1.14	8.7±1.14	<0.05
48 h	9.73±0.92	8.63±1.13	<0.05
1 month	8.79±1.12	8.64±1.15	>0.05
Postoperative Serum vitamin D follow-up			
6 h	65.32±11.73	58.81±13.3	<0.05

P<0.05, significant difference.

cases, whereas in the nonsupplementation group, it was indicated for malignancy in 23.6% and for benign diseases in 76.4% of cases, without any significant differences. In the supplementation group, there were three diabetic and two hypertensive cases, whereas in the nonsupplementation group, there were four diabetic and two hypertensive cases.

Total thyroidectomy was accomplished successfully in all patients. We noticed nonsignificant differences in the rate of general postoperative complication rates. In the supplementation group, we have two cases of transient hoarseness and one case of loss of high pitched voice, whereas in the nonsupplementation group we have one case of transient hoarseness and one case of lost high pitched voice. In the early postoperative period, clinical and laboratory data showed statistically significant difference regarding serum calcium level, as laboratory hypocalcemia was found in 7 cases; three of them developed tetany in the supplementation group as they underwent total thyroidectomy for malignancy, but in the non supplementation group, laboratory hypocalcaemia was found in 19 cases, 10 of them developed Tetany, six cases of those 10 underwent total thyroidectomy with central neck dissection for

malignancy and four cases underwent total thyroidectomy for grave's disease, we have got no cases of permanent hypocalcemia. The mean±SD serum calcium level after 6 h postoperatively was 9.7±1.87 and serum vitamin D level was 65.32±11.73 in the supplementation group and in the nonsupplementation group, calcium serum level was 8.6±1.18 and serum vitamin D was 58.81±13.3. Statistical analysis of serum calcium levels shows nonsignificant difference between preoperative and postoperative levels in both groups but significant difference between supplementation and nonsupplementation. Moreover, there was a significant difference between the preoperative and postoperative values of serum vitamin D in the supplementation group and between the postoperative values of both groups. Sequential levels of serum calcium at 12, 24, and 48 h show significant differences between both groups, but follow-up after one month shows nonsignificant difference between both groups; the follow-up data are presented in Table 2.

Discussion

In this study, we found that preoperative vitamin D supplementation significantly prevented

hypovitaminosis D in the early postoperative period; hence, this together with calcium supplementation added to the prevention of postoperative laboratory and clinical hypocalcemia. Hypocalcemia after total thyroidectomy was predisposed by preoperative hypovitaminosis D level, decreased calcium level, prolonged surgery, previous thyroid or parathyroid surgery, and if surgery is associated with neck dissection. In the current study, intravenous calcium administration was required only in three patients of the supplementation group and in 10 patients of the nonsupplementation group. In the study of Jaan *et al.* [16], there was no need to give intravenous calcium, but in their study, they gave oral calcium for one week postoperatively; this helped decrease the rate and severity of clinical hypocalcemia. Many studies recommended postoperative calcium administration after total thyroidectomy, such as Moore *et al.* [17], who in their study demonstrated that 4 of 124 patients developed hypocalcemia and only one patient required intravenous calcium administration. Moreover, Bellantone *et al.* [11] recommended preoperative vitamin D together with post-operative calcium oral administration at 3g daily dose after total thyroidectomy. In addition, Decimo *et al.* [18] recorded 6% hypocalcemia cases in their study after preoperative and postoperative vitamin D and calcium supplementation and 10% hypocalcemia cases in the nonsupplementation group.

There were no enough studies on preoperative single dose calcium and vitamin D administration for prevention of postoperative hypocalcemia after total thyroidectomy. In this study, the differences between both study groups reached statistical significance regarding rate of postoperative clinical and laboratory hypocalcemia, and postoperative vitamin D level. The sequential serum calcium level in the first postoperative week was significantly higher in the supplementation group, as we detected from our results most cases of postoperative hypocalcemia occurred in patients with prolonged surgery or surgery for malignancy or difficult surgeries. Thus, single-dose vitamin D and calcium administration was not sufficient in this situations and those patients were in need for more calcium doses.

Conclusion

Single-dose preoperative calcium and vitamin D administration is effective in prevention of postoperative hypocalcemia after total thyroidectomy, especially in simple cases,

Complicated and malignant cases may need postoperative calcium administration.

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Conflicts of interest

There are no conflicts of interest.

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