

Research Article

Routine Calcium and Vitamin D Supplement Post Total Thyroidectomy Patients, Does It Worth? Prospective Randomized Study

Abouelnagah G¹, Ali RF^{2*}, Ahmed SF¹ and Fouad SM¹

¹Department of General Surgery, Faculty of Medicine, Alexandria University, Egypt

²Department of General Surgery, Faculty of Medicine, Kafrelsheikh University, Egypt

*Corresponding author: Reda Fawzy Ali, Kafr El Sheik Faculty of Medicine, 202 Gamal Abdel Naser st, Sidi Bishr, Alexandria, Egypt

Received: September 05, 2019; Accepted: October 23, 2019; Published: October 30, 2019

Abstract

Background: Thyroidectomy is the most common surgical procedure performed in the neck by surgeons. Hypocalcemia is the most frequent complication after total thyroidectomy, and it is the main cause of prolonged hospital stay. The value of routine postoperative oral calcium and vitamin D supplementation in preventing symptomatic hypocalcemia after total thyroidectomy is still controversy.

Material & Methods: Two hundred and seventy patients who underwent total thyroidectomy for goiters were randomly assigned to routinely receive or not receive oral calcium (3 g/d) and vitamin D (1 µg/d) for 4 weeks post-operatively. Hypocalcemic symptoms, signs, total serum calcium and parathormone levels were monitored and compared between two groups.

Results: The incidence of symptomatic and laboratory hypocalcemia was lower in the group receiving the supplement than in the group not receiving it: 9 of 135 patients (6.7%) versus 45 of 135 (33.3%). The hypocalcemic symptoms were minimal in the group receiving the supplement but more severe in the group not receiving it. Serum calcium levels decreased in both groups after surgery but were lower in the supplemented group.

Conclusion: Routine administration of oral calcium and vitamin D supplementation is effective in reducing the incidence and severity of hypocalcemia after total thyroidectomy.

Keywords: Calcium supplementation; Vitamin D; Hypocalcemia; Thyroidectomy

Introduction

Thyroidectomy is the most common surgical procedure performed in the neck by surgeons. Theodore Kocher recognized recurrent laryngeal nerve injury, myxedema, and tetany as the three main postoperative complications of thyroidectomy as early as 1883. Tetany was attributed to the deficiency of thyroid gland until Moussu (1898) could relieve it with an aqueous extract of parathyroid glands. Fourman and colleagues (1963) suggested persistent parathyroid insufficiency following transient hypocalcemia [1]. They observed persistent parathyroid insufficiency in 24% of patients after thyroidectomy based on depression of serum ionized calcium level by the ethylene diaminetetraacetic acid (EDTA) infusion test [2].

The immediate manifestations of hypocalcemia are mostly neuromuscular symptoms and occasionally psychotic states. Ectodermal changes leading on to alopecia, eczema, and cataract may occur as early as 6 months after the operation. Persistent hypocalcemia may cause intracranial lesions and cardiac arrhythmias. Permanent hypocalcemia causes a substantial impact on the health of patient along with the considerable financial loss.

The prevention of significant symptomatic hypocalcemia will allow early discharge of post-thyroidectomy patients from the

hospital [3]. A combined measurement of iPTH “intact parathyroid hormone” and serum calcium levels is recommended to identify patients at risk for developing hypocalcemia. Severe, progressive hypocalcemia is unlikely with a normal iPTH level, and thus iPTH can be used cautiously to facilitate early discharge for many patients [4].

Routine oral calcium and vitamin D supplements have been proposed to prevent the development of symptomatic hypocalcemia and to increase the likelihood of early hospital discharge after bilateral surgical treatment of the thyroid gland or exploration of the parathyroid glands [5,6].

Materials and Methods

This study included 270 (two hundred and seventy) patients suffering from thyroid enlargement who were admitted to the Department of Surgery at Alexandria and Kafrelsheik University hospitals, during a period from January 2016 to December 2017 excluding those patients suffering from chronic renal failure and parathyroid gland diseases.

All patients included in this study were subjected to complete history taking, full clinical examination, serum T3, T4, TSH, Ultrasound neck. Blood samples were taken from every patient

preoperatively as well as postoperatively (days 2, 14, 30) for Serum calcium (total), Parathyroid hormone blood level. All patients in this study were submitted to total thyroidectomy with preservation of the four parathyroid glands. Post-operative histo-pathological details were also collected.

After total thyroidectomy patients were randomized by blind closed envelop technique into 2 groups: Group (A) = 135 patients received routine oral calcium (3gm/day) and oral vitamin D supplementation (alphacalcidol, 1 microgram /day) starting from the first postoperative day and continued for 4 weeks. Group (B) members = 135 patients served as a control group, these patients did not receive any supplementation of calcium or vitamin D.

All patients of both groups (A, B) were observed for any hypocalcemia manifestations as (carpopedal spasm, peri-oral tingling, and numbness). Both patients groups were informed about the manifestations of hypocalcemia. Serum calcium and serum parathormone level were measured after 48 hours, one month and three months postoperatively.

Chovostek's sign and trousseau sign were done for every patient on day 2 and 14 of the operation. Statistical analysis was done using the SPSS software package version 17.0 Statistical analysis was done to obtain the mean.

Results

The age of the studied patients ranged from 18-57 years. Among the patients included in this study, 54 cases (20%) were males and 216 cases (80%) were females. Pathological results of all patients with different indicated disease for surgery is shown in (Table 1).

All symptomatic hypocalcaemic patients were from group B, 18 patients (6.7%), statistically significant with P value = 0.007. The reported hypocalcemia symptoms including numbness (perioral and in both hands) were in 2 patients and 1 of them associated with carp pedal spasm, no cases have experienced laryngeal or bronchospasm.

There were 54 patients 20% with positive Chovostek's sign 9 from group A and 45 from group B, those are the same cases who have experienced hypocalcemia, however, 36 have given positive Trousseau sign, 9 from group A and 27 from group B.

Laboratory hypocalcemia was noted in 54 patients (20%) out of the 270 patients, 9 are from group A and 45 from group B.

In-group A patients 135 patients (supplement) the pre-operative calcium levels were normal; 48 hours postoperatively; serum calcium levels were ranging (7.3-9.9 mg/dl) mean = 9.41. Only 9 patients (6.7%) had none manifested laboratory hypocalcemia, with serum calcium less than 8 mg /dl. It showed a significant difference, P value = 0.007. After one month there were no manifestations of hypocalcemia with serum calcium levels range of (9.2-10.2 mg/dl) and after 3 months there were also no manifestations of hypocalcemia with serum calcium level range of (9.6 - 10.8). (Table 2).

In group B (non-supplement) the preoperative calcium levels were normal; 48 hours postoperatively it ranged of (6.5 - 9.3) mean = 8.45; 45 patients (33.3%) developed laboratory hypocalcemia and 36 of them with clinical manifest that needed urgent treatment with IV Ca gluconate infusion on the instant. After one month, 18 patients

Table 1: Distribution of the studied cases in-group A & B according to pathology results.

	Group A No (%)	Group B No (%)
Controlled Grave's	14 (10.4%)	10 (7.4%)
Controlled Secondary Toxic goiter	2 (1.5%)	3 (2.2)
Simple nodular goiter	81 (60%)	90 (66.7%)
Benign solitary thyroid nodule (size >2cm)	24 (17.7%)	19 (14.1%)
Malignant goiter	12 (8.9%)	9 (6.7%)
Hashimoto thyroiditis	2 (1.5%)	4 (2.9%)

Table 2: Comparison between the studied groups according to S-Ca level.

Serum Ca level	Group A (n = 135)	Group B (n = 135)	P
Pre-operative			
Min. – Max.	9.11 – 10.40	9.11 – 10.36	0.603
Mean ± SD.	9.72 ± 0.36	9.65 ± 0.40	
48 hours			
Min. – Max.	7.30 – 9.90	6.50 – 9.30	0.007
Mean ± SD.	9.41 ± 0.62	8.45 ± 1.07	
1 month			
Min. – Max.	9.20 – 10.20	8.70 – 9.80	<0.001
Mean ± SD.	9.79 ± 0.26	9.31 ± 0.33	
3 months			
Min. – Max.	9.60 – 10.80	9.40 – 10.60	0.017
Mean ± SD.	10.19 ± 0.33	9.87 ± 0.37	

(13.3%) continued to have only laboratory hypocalcemia. There was a significant decrease in serum calcium levels in the non-supplement group. P value = < 0.001. After 3 months there were no cases with manifested or even laboratory hypocalcemia in both groups (Table 2).

Although, PTH blood levels were within normal range in all cases postoperatively, those cases who showed decreases of PTH blood levels > 50% of the preoperative value were the same 54 cases who suffered from hypocalcemia while in the other 216 patients, the decrease in the PTH level was ≤ 50% of the preoperative value.

Discussion

Hypocalcemia is a well-known complication and concern following thyroid surgery. Although in most cases it is only temporary, post-thyroidectomy hypocalcemia can lead to an increased cost by prolonging the length of stay and increasing the need for expensive medications, frequent biochemical tests, and multiple outpatient visits [7].

Experienced thyroid surgeons nowadays take the greatest possible care to meticulously localize, dissect and preserve in situ the parathyroid glands, attempting to avoid injury to the blood supply of parathyroid glands, despite this progress, postoperative hypocalcaemia remains a fact of the present and still constitutes clinical challenge which complicates postoperative follow up, and potentially has deleterious long-term repercussion for patients. Despite the pathogenesis of post-thyroidectomy hypocalcemia being multifactorial which makes the prediction of postoperative hypocalcemia is difficult, these causes include previous thyroid status

(thyrotoxicosis), the extent of surgery (completion, neck dissection, retrosternal extension) and removal of more than one parathyroid gland, macrodilution, hypomagnesemia, medications, and general anesthesia [8].

In patients with hyperthyroidism, when the normal parathyroid function can be documented, "hungry bone syndrome" appears to be the most probable cause of hypocalcemia in hyperthyroid patients. The risk of hypocalcemia is not alleviated by the correction of hyperthyroidism within a few weeks before thyroidectomy. It is correlated with the pretreatment serum levels of free thyroxin and with markers of bone turnover rate, such as serum alkaline phosphatase levels and urinary hydroxyproline levels [9,10].

Hypocalcemia is the feared complication after total thyroidectomy. Common symptoms of hypocalcemia like numbness, tingling, and carpopedal spasm occur in the postoperative period due to primary parathyroid deficiency or due to relative causes like dehydration or transient ischemia. Parathyroid glands control the amount of calcium in the blood and within the bones. At surgery, it is harder to differentiate between thyroid, fat and parathyroid gland and inadvertent damage can occur to the gland. This can result in hypoparathyroidism and hence hypocalcemia. Transient asymptomatic hypocalcemia occurs in most patients undergoing thyroidectomy. Acute symptomatic hypocalcemia and permanent hypocalcemia were once quite common with thyroid surgery especially in patients having a total thyroidectomy [11].

Rates of these problems have decreased dramatically as the understanding of the anatomy and physiology of the parathyroid glands increased. Large series of thyroid operations have been reported in which the rates of permanent hypocalcemia due to hypoparathyroidism are less than 1- 2% [11].

Thyroidectomy has become a safe operation with little risk of mortality and long-term morbidity. With meticulous operative technique and careful attention to detail, injury to the recurrent laryngeal nerves and Superior laryngeal nerves and permanent hypoparathyroidism can be minimized. This is even true in settings such as reoperations where the risks of injury to these structures are greater from scarring and distorted anatomy. Symptoms of acute postoperative hypocalcemia usually develop from 1 – 7 days postoperatively. Symptom occurrence is variable and depends on the rate and decrement of the drop in ionized calcium.

It is important to be in the lookout for symptoms of hypocalcemia and one should be aware of the possible time of occurrence of these symptoms so that prompt steps can be taken to institute effective treatment [11].

Severe hypocalcemia remains the limiting factor for such a short in-hospital stay policy, as tetany may affect a relevant number of patients after early discharge. Identification of pre- and perioperative risk factors associated with a high risk of postoperative tetany is an important step for patient selection. Intra- and postoperative monitoring of intact parathyroid hormone has been embraced with enthusiasm by many surgeons as a means to detect patients at highest risk of severe hypocalcemia [12].

Monitoring declines in serum calcium or intact parathyroid hormone (iPTH) levels have been suggested to predict which patients

are at risk of hypocalcemia, but this may not be feasible if the patient is discharged too early [5].

Routine oral calcium and vitamin D supplements have been proposed to prevent the development of symptomatic hypocalcaemia and to increase the likelihood of early hospital discharge after bilateral surgical treatment of the thyroid gland or exploration of the parathyroid glands, because symptomatic hypocalcemia usually develops as late as 24 hours to several days after surgery, postoperative treatment with oral calcium and vitamin D may be a useful approach for avoiding the risk of postoperative hypocalcaemic crisis. This may, in turn, reduce the cost associated with multiple blood samplings in monitoring the development of hypocalcemia as well as costs associated with prolonged hospitalization [9,13].

Conclusion

The routine use of calcium and vitamin D after total thyroidectomy for 4 weeks after operation could prevent or decrease the incidence of clinically relevant post-thyroidectomy hypocalcemia and also maybe cost-effective by reducing postoperative hospital stay as it can reduce its incidence that can postpone the patient discharge.

References

1. Wade JS, Fourman P, Deane L. Recovery of parathyroid function in patients with transient hypoparathyroidism after thyroidectomy. *Br J Surg.* 1965; 52: 493-496.
2. Michie W, Stowers JM, Frazer SC, Gunn A. Thyroidectomy and the Parathyroids. *Br J Surg.* 1965; 52: 503-514.
3. Stiges Serra A, Ruiz S, GirventM, Manjón H, Dueñas JP, Sancho JJ. Outcome of protracted hypoparathyroidism after total thyroidectomy. *Br J Surg.* 2010; 97: 1687-1695.
4. Grodski S, Serpell J. Evidence for the role of perioperative PTH measurement after total thyroidectomy as a predictor of hypocalcemia. *World J Surg.* 2008; 32:1367-1373.
5. Lo CY, Luk JM, Tam SC. Applicability of intraoperative parathyroid hormone assay during thyroidectomy. *Ann Surg.* 2002; 236: 564-569.
6. Grodski S, Lundgren CI, Sidhu S, Sywak M, DelbridgeL. Postoperative PTH measurement facilitates day 1 discharge after total thyroidectomy. In *Clinical Endocrinology.* 2009; 70: 322-325.
7. Roh JL, Park JY, Park CI MD. Prevention of postoperative hypocalcaemia. *Cancer. Asian Medical Center & Chungnam National University Hospital in Asian Medical Center Chungnam National University in Korea.* 2009; 115: 251-258.
8. Reeve T, Thompson NW. Complications of thyroid surgery: how to avoid them, how to manage them, and observations on their possible effect on the whole patient. *World Journal of Surgery.* 2000; 24: 971-975.
9. Bellantone R, Lombardi CP, Raffaelli M, Boscherini M, Alesina PF, De Crea C, et al. Is routine supplementation therapy (calcium and vitamin D) useful after total thyroidectomy? *2002; 132: 1109-1112.*
10. Testa A, Fant V, De Rosa A, Fiore GF, Grieco V, Castaldi P, et al. Calcitriol plus hydrochlorothiazide prevents transient post-thyroidectomy hypocalcemia. *HormMetab Res.* 2006; 38: 821-826.
11. Nair CG, Babu MJ, Menon R, Jacob P. Hypocalcaemia following total thyroidectomy: An analysis of 806 patients. *Indian J EndocrinolMetab.* 2013; 17: 298-303.
12. Lindblom P, Wester Dahl J, Bergenfelz A. Low parathyroid hormone level after thyroid surgery: a feasible predictor of hypocalcaemia. *2002; 131: 515-520.*
13. Moore FD. Oral calcium supplements to enhance early hospital discharge after bilateral surgical treatment of the thyroid gland or exploration of the parathyroid glands. *J Am CollSurg.* 1994; 178: 11-16.