ORIGINAL RESEARCH PAPER
Volume-8 | Issue-9 | September - 2019 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

VITAMIN D STATUS AND RISK OF AFTER TOTAL THYROIDECTOMY HYPOCALCEMIA

General Surgery

Prapul Reddy — Assistant Professor, Department of General Surgery, Sri Lakshmi Narayana Institute of Medical Sciences, Affiliated to Bharath University, Pondicherry-605 502, India

Madhava Rao* — Assistant Professor, Department of General Surgery, Sri Lakshmi Narayana Institute of Medical Sciences, Affiliated to Bharath University, Pondicherry-605 502, India *Corresponding Author

E. Prabhakar Reddy — Professor, Department of Biochemistry, Sri Lakshmi Narayana Institute of Medical Sciences, Affiliated to Bharath University, Pondicherry- 605 502, India

ABSTRACT

Transient hypocalcemia is a well-recognized occurrence after thyroid surgery.We performed a cross-sectional review on 50 thyroidectomies from SLIMS hospital. Pre-operative vitamin D levels and post-operative calcium level were obtained. Early calcium and vitamin D supplementation had positive effects to treat hypocalcemia postoperative thyroidectomy. Transient hypocalcemia appears to occur less frequently in patients with LVD. Multivariate logistic regression analysis suggests that vitamin D could be predictive for post-thyroidectomy hypocalcemia, with lower vitamin D levels associated with less risk of hypocalcemia.

KEYWORDS

Thyroidectomy, Vitamin D levels; Hypocalcemia; Hypoparathyroidism

INTRODUCTION:

Transient hypocalcemia is a well-recognized occurrence after thyroid surgery.(1-5). It is generally considered to be due to early postoperative hypoparathyroidism,which occurs secondary to intraoperative trauma to parathyroid glands or their blood supplies, or inadvertent parathyroid removal. This condition leads to reduced circulating levels of parathyroid hormone (PTH). Low PTH levels lead to reduced reabsorption of calciumin the kidney and decreased release of calcium from bones, which in turn leads to reductions in serumcalcium levels. Without sufficient vitamin D, bones become thin, brittle, or misshapen. Vitamin D3 sufficiency prevents rickets in children and osteomalacia in adults. Together with calcium, vitamin D also helps protect older adults from osteoporosis (6). Vitamin D3 (cholecalciferol) . is synthesized in the human skin from 7-dehydrocholesterol upon exposure to ultraviolet (UV) radiation from sunlight. Vitamin D2 (ergocalciferol) is a vitamin D analog photosynthesized in plants, mushrooms and yeasts; it is also sometimes used in vitamin D food fortification. When vitamin D3 in skin is inadequate due to insufficient exposure to UV radiation, oral intake of vitamin D is necessary to meet vitamin D requirements (7-10).

It has been hypothesized that patients who are vitamin D deficient and who experience temporary hypoparathyroidism after thyroid surgery are at increased risk of developing symptomatic hypocalcemia due to the loss of this compensatory role of PTH in maintaining eucalcemia.(11) However,whether low or insufficient vitamin D levels affect the incidence of hypocalcemia after thyroid surgery is not clear. Only a small number of studies(12-15) have investigated this, with mixed results. Hypocalcemia is the most common complication after thyroid surgery (16). Low postoperative serum calcium has been attributed to transient hypo-parathyroidism due to intra-operative injury to the adjacent parathyroid tissue or its blood supply (17-18). 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 biomedical tests and multiple outpatient visits. The incidence of transient hypocalcemia has been estimated to occur between 3% to 30% of cases even after preservation of one or more parathyroids . Permanent hypocalcaemia, although much less frequent, still occurs, with an incidence of around 2-4% reported in the literature.

Traditionally, serum or ionized calcium levels are evaluated on the evening of surgery and again on postoperative day 1 to evaluate for low calcium. However,symptomatic hypocalcemia can frequently occur 48 to 72 hours after discharge. Discharging patients on calcium supplementation has been endorsed as a means to reduce symptomatic hypocalcemia (19). Therefore, the aim of this study was to evaluate the clinical usefulness calcium postoperative oral vitamin D and calcium supplements in the prevention of hypocalcemia after thyroidectomy 30 days and 90 days.

MATERIAL AND METHODS:

This longitudinal, cross-sectional study included patients with total thyroidectomy at SLIMS Hospital, Bharath University. The study protocol was approved by IEC. The procedure was explained completely to the guardians, and written informed consents were obtained before their participation. Typical diagnoses of patients in this hospital include retrosternal goiter, multinodular goiter, thyroids cancers, and/or other severe thyroidal illness. A total of 50 patients were admitted to the hospital for thyroidectomy during the study period. 50 patients met eligibility criteria and enrolled. We used pre-operative serum vitamin D level and early (< 24 hours) post-operative measurements of s-Ca levels. s-Ca < 8 mg/dl (< 2 mmol/l) after surgery (30 days and 90 days) were considered post-operative hypocalcemia. During hospitalization days, s-Ca and hypocalcemic symptoms were checked. Due to the fact that these symptoms may correspond to other reasons else hypocalcemia that is prone to remit within few days after surgery assessment for s-Ca was done on discharge. The threshold of 8 for s-Ca was selected according to the results of many studies in western and eastern countries. Age, sex, and fetal medical problems were asked. S-Ca before operation was measured. Based on s-Ca, 24 hours after surgery prevalence of post-thyroidectomy hypocalcemia was measured. The potential risk factors for post-thyroidectomy hypocalcemia were investigated and compared between the two groups (before operation and after operation) using Pearson's chi-squared test (corrected by Fisher Exact for small samples). The level of significance was set throughout the study at $P \leq 0.050$. Data entry was carried out on Microsoft Excel. Data analysis was performed using the software SPSS 11.0 version.

RESULTS:

Table. 1: Characteristics of the patients participants

Table. 2: Serum biochemical measurements level in pre-and postoperative patients

Hypocalcemia occurred in 4.4% (4 of 50) patients with LVD and 11.8 (12 of 50) patients with OVD. None of the 16 VDD patients developed hypocalcemia.Univariate analysis suggested vitamin D to be a predictive variable for hypocalcemia but did not show age ($P = 0.525$), sex ($P = 0.426$), proceedure ($P = 0.159$), malignancy ($P = 0.379$), thyroiditis ($P = 0.413$), number of preserved parathyroids ($P > 0.669$), parathyroid autotranplantation ($P = 0.143$), preoperative PTH ($P = 0.259$) to be significantly predictive.

Multivariable analysis confirmed that age, sex, proceedure, malignancy,number of preserved parathyroids, autotransplantation, preoperative PTH, preoperative corrected calcium where not significant confounding factors to the association between vitamin D and hypocalcemia. When controlling for each of the above variables, except for preoperative calcium, vitamin D was significantly correlated with hypocalcemia with P </= 0.041. Correlation was P = 0.064 with preoperative calcium controlled.

DISCUSSION:

Transienthypocalcemia is acommonoccurrence after total thyroidectomy.The reported incidence of this phenomenon is highly variable (0%-65%) and depends to a large extent on the definition of hypocalcemia used (20).The causewould appear to be postoperative hypoparathyroidism due to intraoperative trauma to parathyroid glands or their vasculature or inadvertent parathyroid removal. With increasing economic pressures to shorten the length of hospital stay in patients undergoing total thyroidectomy, there has beenmuchrecent interest in studying risk factors for the development of postoperative hypocalcemia.

Vitamin D plays an important role in calcium metabolism by increasing calcium absorption for the gastrointestinal tract. Patients with vitamin D deficiency thus have impaired gastrointestinal tract calcium absorption. These patients commonly have a secondary hyperparathyroidism, which restores calcium levels by increasing renal calcium reabsorption and increasing bone turnover. It has been suggested that preoperative secondary hyperparathyroidism in patients with medically treated Graves disease and vitamin Ddeficiency can render patients especially susceptible to postthyroidectomy tetany due to loss of a compensatory role of PTH in maintaining calcium levels concomitantwith continued increased demand for bone restoration (21). Therefore, it would seem reasonable to hypothesize that lowvitaminDlevels in all patients undergoing thyroidectomy may predispose patients to increased risk of hypocalcemia.

Few studies have explored the relationship between vitamin D stores and risk of hypocalcemia after thyroid surgery. These studies have suggested that VDD is a risk factor for hypocalcemia after total thyroidectomy (22-25). In contrast, the present paper suggests that LVD does not increase the risk of early postoperative hypoparathryoidism, but may even be a protective factor. In this study, none of the patients who were VDD became hypocalcemic. Lower vitamin D was associated with decreased risk of hypocalcemia by univariate and multivariable analysis.This data suggests that patients with suboptimal vitamin D levels may have parathyroids at are better able to compensate for injury or loss that occurs during thyroid surgery. Although the reason for this is unclear,parathyroid hypertrophy and/or an ability to enhance PTH production in those with prolonged VDD could account for this.

This hypothesis is supported by Henry et al's animal study suggesting that decreased vitamin D levels are correlated with parathyroid hypertrophy and hyperplasia independently of serum calcium21. In our study, preoperative PTH levels had a tendency to be greater in the group with LVD when compared to those in the group with OVD levels (P = 0.061). This may be because patients with less than optimal levels of vitamin D maintain serum calcium levels by a compensatory increase in PTH output. A significant limiting factor in our study is inherent in our protocol for surveillance and treatment (26). We treat some patients who are hypoparathyroid prophylactically in order to prevent hypocalcemia from occurring. As a result, we cannot be certain about the true rate of hypocalcemia that would have evolved naturally after thyroidectomy. However, our results are based on the assumption that any overtreatment would apply for all groups equally.

We examined many different cutoff levels for vitamin D without finding any significant effect on postthyroidectomy hypocalcemia, because the number of patients with sufficient vitamin D levels was low, we cannot discount the possibility that there might be a difference in postthyroidectomy calcium levels in patients with sufficient as opposed to insufficient vitamin D levels. Third, this was a singlesurgeon series of thyroid operations. Thus, it is possible that our findings may not be applicable to thyroidectomy performed by different techniques to those used by the senior author.The PTH control calcium, phosphorus and vitamin D levels in the blood and regulate bone growth. In brief, PTH increases the calcium concentration in the blood by reducing the excretion of calcium though the kidneys and increasing the influx of calcium from the skeleton .

CONCLUSION:

Early calcium and vitamin D supplementation had positive effects to treat hypocalcemia postoperative thyroidectomy. Transient hypocalcemia appears to occur less frequently in patients with LVD. Multivariate logistic regression analysis suggests that vitamin D could be predictive for post-thyroidectomy hypocalcemia, with lower vitamin D levels associated with less risk of hypocalcemia. Future study observing a larger population is required to confirm whether low vitamin D is truly associated with reduced risk for hypocalcemia, and to define a threshold that is clinically useful for risk stratification.The findings of our study suggest that perioperative vitamin D levels do not have any significant effect on the incidence of postthyroidectomy hypocalcemia.

Table. 1: Characteristics of the patients participants

Variable (n = 30)		Number	%
Age	18 to 30 years	6	20.0
	31 to 40 years	8	26.7
	41 to 50 years	8	26.7
	> 51 years	8	26.7
	Total	30	100
Gender	Male	6	20.0
	Female	24	80.0
Anthropometric measurements		Mean	SD
Weight, Kg		69.76	16.39
Height, m		160.96	8.63
BMI, Kg/m^2		26.91	5.77

Table. 2. Serum biochemical measurements level in pre-and postoperative patients

		Postoperative				
Biomedical measurements		**Preoperative**	**30 D**	**90 D**	**P-value***	**P-value****
Vit D3 (pmol/L)	Mean ± SD	43.62± 28.27	54.59± 25.97	75.59± 35.21	0.001	0.000
Ca (mmol/L)	Mean ± SD	2.25±0. 30	2.12±0. 19	2.37±0 .18	0.404	0.004
PTH (ng/L)	Mean ± SD	8.63±1. 20	14.26± 2.17	20.95± 2.42	0.000	0.000
TSH (µU/L)	Mean ± SD	2.46±2. 44	1.79±1. 60	1.49±1 .20	0.003	0.025
T3 (nmol/L)	Mean ± SD	7.07±1 0.62	3.85±1. 60	3.74±1 .01	0.046	0.000
T4 (nmol/L)	Mean ± SD	157.78 ±25.31	168.24 ±23.79	168.21 ±40.10	0.037	0.038
Alb (g/L)	Mean ± SD	31.02± 14.29	36.42± 4.02	40.19± 3.81	0.049	0.003

REFERENCES:

1. Sheahan P, Mehanna R, Basheeth N, MurphyMS.Is systematic identification of all four parathyroid glands necessary during total thyroidectomy? a prospective study. Laryngoscope.2013;123(9):2324-2328.
2. Abboud B, Sleilaty G, Braidy C, et al. Careful examination of thyroid specimen intraoperatively to reduce incidence of inadvertent parathyroidectomy during thyroid surgery. Arch Otolaryngol Head Neck Surg. 2007;133(11):1105-1110.
3. Page C, Strunski V. Parathyroid risk in total thyroidectomy for bilateral, benign, multinodular goitre: report of 351 surgical cases. J Laryngol Otol.2007;121(3):237-241.
4. Sakorafas GH, Stafyla V, Bramis C, Kotsifopoulos N, Kolettis T, Kassaras G. Incidental parathyroidectomy during thyroid surgery: an underappreciated complication of thyroidectomy.World J Surg. 2005;29(12):1539-1543.
5. Sitges-Serra A, Ruiz S, Girvent M, Manjón H,Dueñas JP, Sancho JJ. Outcome of protracted hypoparathyroidism after total thyroidectomy. Br J Surg. 2010;97(11):1687-1695.
6. IMO, 2010. Institute of Medicine, Food and Nutrition Board. Dietary Reference Intakes for Calcium and Vitamin D. Washington, DC: National Academy Press.
7. Cranney, C., T. Horsely, S. O'Donnell, H. Weiler,D. Ooi, S. Atkinson, L. Ward, D. Moher, D. Hanley,M. Fang, F. Yazdi, C. Garritty, M. Sampson,N. A.Tsertsvadz and V.Mamaladze, 2007.Effectiveness and safety of vitamin D in relation to bone health.. Evid. Rep. Technol. Assess.,(158): 1-235.
8. Cmilansky, P. and L. Mrozova, 2014. Hypocalcemia -the most common complication after total thyroidectomy. Bratisl LekListy, (3): 175-178.
9. Falk, S., 1990. Complications of Thyroid Surgery:hypocalemia, hypoparathyreoidism. New York, NY:Raven Press.
10. Reeve, T. and N.W. Thompson, 2000.Complications of thyroid surgery: how to avoid them, how to manage them and observations on their possible effect on the whole patient. World J. Surge.,24(8): 971-975.
11. Shahai, A., A. Symes and T. Jedd, 2005. Short stay thyroid surgery. Br. J. Surg., 92: 58-59.
12. Pappalardo, G., A. Guadalaxara, F.M. Frattaroli,G. Illomei and P. Falaschi, 1998. Total compared with subtotal thyroidectomy in benign nodular disease: personal series and

review of published reports. Eur. J. Surg., 164(7): 501-506.
13. Yamashita H, Murakami T, Noguchi S, et al.Postoperative tetany in Graves disease: important role of vitamin Dmetabolites. Ann Surg. 1999;229(2):237-245.
14. Chia SH,Weisman RA, Tieu D, Kelly C, Dillmann WH, Orloff LA. Prospective study of perioperative factors predicting hypocalcemia after thyroid and parathyroid surgery. Arch Otolaryngol Head Neck Surg. 2006;132(1):41-45.
15. Erbil Y, Barbaros U, Temel B, et al. The impact of age, vitamin D3 level, and incidental parathyroidectomy on postoperative hypocalcemia after total or near total thyroidectomy. Am J Surg. 2009;197(4):439-446.
16. Cashman KD, Muldowney S, McNulty B, et al.Vitamin D status of Irish adults: findings from the National Adult Nutrition Survey. Br J Nutr.2013;109(7):1248-1256.
17. Silverberg SJ. Vitamin D deficiency and primary hyperparathyroidism. J Bone Miner Res. 2007;22(suppl 2):V100-V104.
18. Kirkby-Bott J, El-Khatib Z, Soudan B, Caiazzo R,Arnalsteen L, Carnaille B. 25-Hydroxy vitamin D deficiency causes parathyroid incidentalomas. Langenbecks Arch Surg. 2010;395(7):919-924.
19. Lin Y, Ross HL, Raeburn CD, et al. Vitamin D deficiency does not increase the rate of postoperative hypocalcemia after thyroidectomy. Am J Surg. 2012;204(6):888-894.
20. Mehanna HM, Jain A, Randeva H,Watkinson J,Shaha A. Postoperative hypocalcemia: the difference a definition makes. Head Neck.2010;32(3):279-283.
21. Palestini N, Borasi A, Cestino L, Freddi M,Odasso C, Robecchi A. Is central neck dissection a safe procedure in the treatment of papillary thyroid cancer? our experience. Langenbecks Arch Surg. 2008;393(5):693-698.
22. Kirkby-Bott J, Markogiannakis H, Skandarajah A, et al. Preoperative Vitamin D Deficiency Predicts Postoperative Hypocalcemia After Total Thyroidectomy. World J Surg 2011; 35(2):324-30.
23. Erbil Y, Bozbora A, Ozbey N, et al. Predictive value of age and serum parathormone and vitamin d3 levels for postoperative hypocalcemia after total thyroidectomy for nontoxic multinodular goiter. Arch Surg. 2007;142(12):1182-1187.
24. Erbil Y, Barbaros U, Temel B, et al. The impact of age, vitamin D(3) level, and incidental parathyroidectomy on postoperative hypocalcemia after total or near total thyroidectomy. Am J Surg 2009;197:439–446.
25. Yamashita H, Noguchi S, Murakami T, et al. Predictive Risk Factors for Postoperative Tetany in Female Patients with Graves' Disease. J Am Coll Surg 2001;192:465–468.
26. Cote V, Sands N, Hier M, et al. Cost savings associated with post-thyroidectomy parathyroid hormone levels. Otolaryngol Head Neck Surg 2008;138(2):204-8.