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POST-OPERATIVE CALCIUM LEVELS IN PATIENTS UNDERGOING THYROIDECTOMY: AN OBSERVATIONAL STUDY

Surgery

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ABSTRACT

Background: Hypocalcaemia causing transient or definitive hypoparathyroidism is the most frequent complication following thyroidectomy. We aimed to assess the pre-op and post op serum calcium levels in patients undergoing total/ near total thyroidectomy.

Method: A prospective review of retrospectively collected data was analyzed to study the post-operative hypocalcaemia in patients undergoing total/ near total thyroidectomy.

Results: The post-operative mean corrected calcium level at 6, 12 and 24 hours after thyroidectomy was 8.37 mg/dl, 8.47 mg/dl and 8.77 mg/dl respectively with the nadir for hypocalcaemia occurring at 24 hours post operatively. Post-operative hypocalcaemia had a female preponderance.

Conclusion: Post-operative hypocalcaemia is one of a dreaded complications of hypothyroidism. Meticulous attempts at surgery to identify and preserve the parathyroid must be made. Early diagnosis and treatment can reduce the post-operative morbidity and mortality associated with hypocalcaemia.

KEYWORDS

Hypocalcaemia, Thyroidectomy

INTRODUCTION

Hypocalcaemia is the most common complication after thyroidectomy. The reported incidence of transient hypocalcaemia ranges from 1.6 % to 50 %, while that of permanent hypocalcaemia is 0.5- 2.0 %. The differences in definitions of hypocalcaemia, operative procedure and surgeon expertise is responsible for the wide range of incidence of hypocalcaemia. Hence, strategies like biochemical tests to assess calcium levels, routine use of oral calcium and/ or Vit D post- operatively, have to be adopted to minimize the incidence of hypocalcaemia, which in turn reduce the cost and duration of hospital stay as well as the number of follow up visits to the hospital.

MATERIALS AND METHODS

A retrospective review of prospectively collected data was performed in 20 patients who underwent total/ near total thyroidectomy from Jan 2016 to Mar 2018 at a tertiary care hospital in southern India.

INCLUSION CRITERIA-

1. All patients who underwent total/ near total thyroidectomy with/ without neck dissection
2. Patient who had undergone calcium level monitoring during post-operative period for 48 hours

EXCLUSION CRITERIA-

1. All patients undergoing lobectomy/ hemi thyroidectomy
2. Patients with no previous history of parathyroid disease/ medical renal disease

Serum calcium and albumin level were determined the day before the surgery. The corrected serum calcium was measured at 8 hours, 24 hours and 48 hours after the surgery. Corrected serum calcium was calculated with the following equation: Corrected serum calcium = Serum Ca (mg/dl) + 0.8 x [4 – Albumin(mg/dl)]

RESULTS

In our study we had included 20 patients who had undergone thyroidectomy. There was female preponderance of patients undergoing thyroidectomy with 17(85%) patients being female and 03(15 %) patients being male (Graph 1). The majority of patients operated were above 40 years (Chart 1) and the mean age of patient analyzed in the study was 45.05 years. 18 patients underwent near total thyroidectomy, one patient underwent total thyroidectomy and one underwent total thyroidectomy + central compartment neck dissection.

In this study the calcium levels of all the 20 patients in the pre-operative ranged from 8.6 to 9.3 mg/dl. The post-operative mean corrected serum calcium level at 6, 24 and 48 hours after surgery was 8.37 mg/dl, 8.46 mg/dl and 8.77 mg/dl respectively. At 6 hours after the surgery, 08 patients (40%) had mean corrected serum calcium level < 8.5 mg/dl, while 12 patients (60%) had serum calcium levels in the range of 8.5-10 mg/dl. Out of the eight patients who developed hypocalcaemia, 3 were males (37.5%) and 5 (62.5%) were females [Table 4] At 24 hours after the surgery, 14 patients (70%) had mean corrected serum calcium level < 8.5 mg/dl while 06 patients (30%) had mean corrected serum calcium level in the range of 8.5-10 mg/dl. Of these 14 patients developing hypocalcaemia, 6 were males (42.85%) and 8 patients were females (57.14%). However, all the patients with serum calcium < 8.5 mg/dl where asymptomatic.

The post-operative histopathological examination revealed that 90% of the patients had Multinodular goiter, 5 % had lymphocytic thyroiditis and the rest 5 % had papillary carcinoma thyroid (Table 3)

TABLE 1- Gender wise distribution of patient undergoing Thyroidectomy

Sex	Number	Percentage
Males	03	15 %
Females	17	85%

TABLE 2- Post-operative serum calcium levels in patients undergoing Thyroidectomy

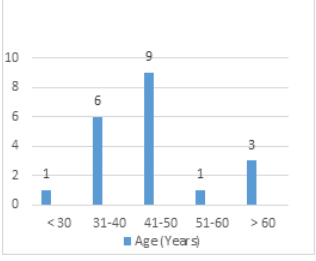
Corrected Calcium levels	After 8 hours	After 24 hours	After 48 hours
< 8.5 mg/dl	08	14	05
8.5-10.5 mg/dl	12	06	15

TABLE 3- Post –op diagnosis of patients undergoing Thyroidectomy

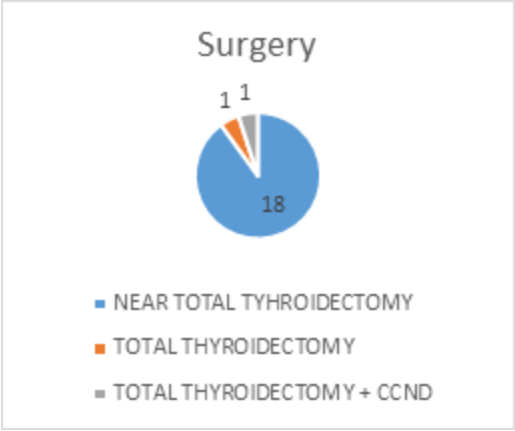
Diagnosis – HPE exam	No. of patients	Percentage
Multinodular Goiter	18	90 %
Lymphocytic Thyroiditis	01	5 %
Papillary carcinoma	01	5 %

TABLE 4. Gender wise distribution of patient developing post-op Hypocalcaemia

	At 6 hours	At 24 Hours
Females	62.5 %	57.15 %
Males	37.5 %	42.85 %



GRAPH 1 - Distribution of age in the study population



GRAPH 2- Type of thyroidectomy

DISCUSSION

Post-operative hypocalcaemia is one of the most frequent complications following total or near thyroidectomy. The incidence varies, with transient hypocalcaemia ranging from 1.6 % to 50 %, while that of permanent hypocalcaemia from 0.5- 2.0 % [14]. The causes of hypocalcaemia after total/ near total thyroidectomy are multifactorial which include devascularization and unintentional excision of parathyroid glands during surgery owing to the close proximity of the thyroid capsule , destruction of the parathyroid glands as a result of lymphadenectomy along the recurrent laryngeal nerve (RLN), or hypoparathyroidism due to hematoma formation, hyperthyroidism secondary to Graves' disease or a functioning adenoma, , retrosternal goiter and preoperative low serum Vit D (low sunlight, alcoholism).

There is no definitive evidence on the impact of age on the development of post-operative hypocalcaemia in the literature. Some studies suggest that temporary post-operative hypocalcaemia is more common in younger patients [15, 16], while others suggest it is more common in older patients [17, 18]. A meta-analysis of five studies with 2576 patients revealed no significant association between patient age and temporary hypocalcaemia [15, 19–20, 22]. While a meta-analysis of 10 studies involving 3443 patients showed that temporary postoperative hypocalcaemia was more common in women [12, 15-18, 23, 25]. In our study the incidence of hypocalcaemia was more common in females with 62.55 % females developing hypocalcaemia at 6 hours after the surgery while 57.56 % developing hypocalcaemia at 24 hours after the surgery [Table 4].

Several studies have found that temporary post-operative hypocalcaemia develops more often in patients who have a markedly decreased level of calcium before surgery [32, 35]. However, a meta-analysis of six studies with 2493 patients did not reveal a statistically reliable association between pre-operative calcium and the frequency of temporary hypocalcaemia [1-5, 7]. A sharp decrease in calcium after Total Thyroidectomy is associated with temporary hypocalcaemia [6,8-12]. In a multicenter study with 1157 patients, Hallgrimsson et al. found that patients who experienced a 2–3% decrease in postoperative calcium in the 24 hours following surgery, in comparison with the pre-operative level of calcium, had a 94% chance of developing temporary hypocalcaemia. Changes in the levels of calcium in the blood during the first 24 hours following surgery allow prediction of temporary hypocalcaemia with 19–91% sensitivity [3, 35, 36]. A blood calcium concentration of 1.88 mmol/L (7.52 mg/dl) or less during the first 24 hours after surgery has been associated with permanent hypocalcaemia [13, 14, 31]. Two other studies have demonstrated that there is an increased risk of developing permanent hypocalcaemia if the level of calcium in the blood remains at 2 mmol/L or less, 1–3 weeks after surgery [32]. Tartaglia et al. revealed that measurement of ionized calcium was more reliable than measurement of calcium in post-TT patients, in the immediate and long-term follow-up [37].

Controversy exists concerning the most relevant measurements and the best time for their determination in predicting postoperative transient or permanent hypoparathyroidism. Some studies describe decreasing serum calcium levels within the first 48 hours after surgery as a safe predictor of post-operative hypoparathyroidism. In our study hypocalcaemia was more common at 24 hours after thyroidectomy (70 %).

The nadir for hypocalcaemia occurs at around 24-48 hours post operatively but may be delayed up to post –operative day 04. Acute hypocalcaemia results in decreased ionized calcium and increased neuromuscular excitability. Patient initially develop circumoral and fingertip numbness and tingling. Physical examination reveals positive Chvostek's sign – contraction of facial muscles elicited by tapping on the facial nerve and Trousseau's sign – Carpal spasm induced by inflation of a blood pressure cuff to 20 mmHg above the patient's systolic blood pressure for 3 min. Tetany, which is characterized by tonic-clonic seizures, carpopedal spasms, and laryngeal stridor may prove fatal and should be avoided. Severe hypocalcaemia can induce seizures, carpopedal spasm, bronchospasm, laryngospasm, and prolongation of the QT interval. Most patients with post-operative hypocalcaemia can be treated with oral calcium and Vit D supplementation. Intravenous calcium should be reserved for severe or symptomatic hypocalcaemia and can be administered as Calcium chloride or calcium gluconate, but calcium gluconate is typically favored due reduced risk of tissue toxicity. While treating severe or symptomatic hypocalcaemia 1 -2 gm of calcium gluconate mixed in 50—100 ml of 5% Dextrose is administered over 10 – 20 minutes followed by continuous infusion of 0.5-1.5 mg/kg/hr of elemental calcium.

The primary function of PTH is to maintain the extracellular fluid (ECF) calcium concentration within a narrow normal range. The hormone acts directly on bone and kidney and indirectly on intestine through its effects on synthesis of 1,25 (OH)2D to increase serum calcium concentrations; in turn, PTH production is closely regulated by the concentration of serum ionized calcium. This feedback system is the critical homeostatic mechanism for maintenance of ECF calcium.

The measurement of post-operative PTH is useful in predicting the need for calcium and Vit D after total thyroidectomy. There is no consensus on the optimal timing of the measurement of postoperative PTH, the cut off for high risk classification, or the percentage drop of PTH in literature. PTH checked one to six hours after thyroidectomy has been shown to have an excellent accuracy in identifying which patients will have symptomatic hypocalcaemia [18, 21, 26, 27]. PTH has a short half-life (2-5 minutes) and owing to its rapid turnover, serum PTH is a good marker of immediate parathyroidism function.

The measurement of post-operative PTH is useful for the need of calcium and Vit D after total thyroidectomy. Perioperative PTH is currently the most emphasized biomarker of impending post-operative hypocalcaemia. In the systematic review and meta-analysis by Edafe et al, a low post-operative PTH level (defined as less than 6-35pg/mL) between 1 hour and one day after thyroidectomy had a high sensitivity (69%-100%) and specificity (81%-100%) for predicting post-operative hypocalcaemia.

Hypocalcaemia in patients with hyperthyroidism secondary to Graves' disease or a functioning adenoma is due brisk uptake of calcium into the bones postoperatively as euthyroid state is achieved. The multivariate analysis by Thomusch et al. demonstrated that, in patients with Graves' disease, both temporary and permanent hypocalcaemia developed more often following TT [20]. Further, a meta-analysis of four studies with 6681 patients showed a greater frequency of post-operative temporary hypocalcaemia in patients with Graves' disease [20, 24, 26, 36]. Makaieff et al.[23] reported a 4.6 % incidence of permanent hypoparathyroidism after 117 re-operations and a 2.1 % incidence after surgery on 220 substernal goiters. In a series of 180 cases of thyroid cancer, Schwartz and Friedman [35] reported a 2.3 % permanent hypoparathyroidism rate. Sim and Soo reported a rate of 3.4 % in 149 cases while Hundahl et al. [25] reported a rate of 10 %.

Incidental parathyroidectomy is not so uncommon during thyroidectomy. Most authors believe that a single functioning gland is enough to restore normal parathyroid activity, but some believe that at least 3 glands are necessary for the normal functioning of the parathyroid activity. The use of immediate parathyroid implantation of 1 mm fragments of saline chilled tissue into pockets made in sternocleidomastoid muscle or brachioradialis muscle is extremely effective in avoiding permanent hypocalcaemia. The greater the number of parathyroid gland found during surgery, the lower the chance of hypocalcaemia. The study by Thomusch et al. determined that permanent post-operative hypocalcaemia was more likely to develop if less than two parathyroid glands were found during surgery [40]. On the other hand, other studies have found that more parathyroid gland found during surgery may be associated with temporary hypocalcaemia [12, 25].

CONCLUSION

Post-operative hypocalcaemia is one of a frequent and dreaded complications of thyroidectomy. Preoperative preparation, meticulous attempts at surgery to identify and preserve the parathyroid can help to prevent the complications. Early diagnosis with serial monitoring of serum calcium levels along with careful monitoring of the signs and symptoms of hypocalcaemia is an efficient and cost effective tool to reduce the post-operative morbidity and mortality associated with hypocalcaemia associated with thyroidectomy.

Conflicts of interest

The authors declare no conflicts of interest

REFERENCES

1. Wang TS, Roman SA, Sosa JA. Postoperative calcium supplementation in patients undergoing thyroidectomy. Curr Opin Oncol 2012;24:22–8.
2. Chow TL, Choi CY, Chiu AN. Postoperative PTH monitoring of hypocalcemia expedites discharge after thyroidectomy. Am J Otolaryngol 2014;35:736–40.
3. Hallgrimsson P, Nordenström E, Bergenfelz A, Almquist M. Hypocalcaemia after total thyroidectomy for Graves' disease and for benign atoxic multinodular goitre. Langenbecks Arch Surg Dtsch Ges Für Chir. 2012 Oct;397(7):1133-7
4. Raffaelli M, De Crea C, Carrozza C, et al. Combining early postoperative parathyroid hormone and serum calcium levels allows for an efficacious selective post-thyroidectomy supplementation treatment. World J Surg 2012;36:1307–13.
5. 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;204:888–93
6. Wu J, and Harrison B. hypocalcemia after thyroidectomy: the need for improved definitions. World j End Surg. 2010. 2:17-20.
9. 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 J Surg 2000;24:971–5.
10. Nahas ZS, Farrag TY, Lin FR, et al. A safe and cost-effective short hospital stay protocol to identify patients at low risk for the development of significant hypocalcemia after total thyroidectomy. Laryngoscope 2006;116:906–10.
11. Grodski S, Serpell J. Evidence for the role of perioperative PTH measurement after total thyroidectomy as a predictor of hypocalcemia. World J Surg 2008;32:1367–73.
12. Carr AA, Yen TW, Fareau GG, et al. A single parathyroid hormone level obtained 4 hours after total thyroidectomy predicts the need for postoperative calcium supplementation. J Am Coll Surg 2014;219:757–64.
13. Lecerf P, Orry D, Perrodeau E, et al. Parathyroid hormone decline 4 hours after total thyroidectomy accurately predicts hypocalcemia. Surgery 2012;152:863–8.
14. Bellantone R, Lombardi CP, Raffaelli M, et al. Is routine supplementation therapy (calcium and vitamin D) useful after total thyroidectomy? Surgery 2002;132:1109–13.
15. Yamashita H, Noguchi S, Tahara K, Watanabe S, Uchino S, Kawamoto H, et al. Postoperative tetany in patients with graves' disease: a risk factor analysis. Clin Endocrinol. 1997;47:71–7.
16. Gentileschi P, Gacek IA, Manzelli A, Cascarella G, Sileri P, Lirosi F, et al. Early (1 hour) post-operative parathyroid hormone (PTH) measurement predicts hypocalcaemia after thyroidectomy: a prospective case-control single institution study. Chir Ital. 2008;60:519–28.
17. Kamer E, Unalp HR, Erbil Y, Akguner T, Issever H, Tarcan E. Early prediction of hypocalcemia after thyroidectomy by parathormone measurement in surgical site irrigation fluid. Int J Surg. 2009;7:466–71.
18. Moriyama T, Yamashita H, Noguchi S, Takamatsu Y, Ogawa T, Watanabe S, et al. Intraoperative parathyroid hormone assay in patients with graves' disease for prediction of postoperative tetany. World J Surg. 2005;29:1282–7.
19. Sitges-Serra A, Ruiz S, Girvent M, Manjón H, Dueñas JP, Sancho JJ. Outcome of protracted hypoparathyroidism after total thyroidectomy. Br J Surg. 2010; 97:1687–95.
20. Thomusch O, Machens A, Sekulla C, Ukkat J, Brauckhoff M, Dralle H. The impact of surgical technique on postoperative hypoparathyroidism in bilateral thyroid surgery: a multivariate analysis of 5846 consecutive patients. Surgery. 2003;133:180–5.
21. Pfleiderer AG, Ahmad N, Draper MR, Vrotsou K, Smith WK. The timing of calcium measurements in helping to predict temporary and permanent hypocalcaemia in patients having completion and total thyroidectomies. Ann R Coll Surg Engl. 2009;91:140–6.
22. Sands NB, Payne RJ, Cote V, Hier MP, Black MJ, Tamilia M. Female gender as a risk factor for transient post-thyroidectomy hypocalcemia. Otolaryngol Head Neck Surg. 2011;145:561–4.
23 Makeieff M, Rubinstein P, Youssef B, Crampette L, Guerrier B. Repeat surgery for thyroid nodules. Ann Chir 1998;52:970–7
24 Schwartz AE, Friedman EW. Preservation of the parathyroid glands in total thyroidectomy. Surg Gynecol Obstet 1987;165:327–32 16 Sim R, Soo KC. Surgical treatment of thyroid cancer: the Singapore General Hospital experience. J R Coll Surg Edinb 1998;43:239–43
25 Hundahl SA, Cady B, Cunningham MP, Mazzaferri E, McKee RF, Rosai J et al. 44. Serpell JW, Phan D. Safety of total thyroidectomy. ANZ J Surg. 2007;77:15–9. 45. Welch KC, McHenry CR. Total thyroidectomy: is morbidity higher for graves' disease than nontoxic goiter? J Surg Res. 2011;170:96–9.
26. Chiang FY, Lin JC, Wu CW, Lee KW, Lu SP, Kuo WR, et al. Morbidity after total thyroidectomy for benign thyroid disease: comparison of graves' disease and non-graves' disease. Kaohsiung J Med Sci. 2006;22:554–9
27. Moriyama T, Yamashita H, Noguchi S, Takamatsu Y, Ogawa T, Watanabe S, et al. Intraoperative parathyroid hormone assay in patients with graves' disease for prediction of postoperative tetany. World J Surg. 2005;29:1282–7.
28. Sitges-Serra A, Ruiz S, Girvent M, Manjón H, Dueñas JP, Sancho JJ. Outcome of protracted hypoparathyroidism after total thyroidectomy. Br J Surg. 2010; 97:1687–95.
29. Kamer E, Unalp HR, Erbil Y, Akguner T, Issever H, Tarcan E. Early prediction of hypocalcemia after thyroidectomy by parathormone measurement in surgical site irrigation fluid. Int J Surg. 2009;7:466–71
30. Erbil Y, Barbaros U, Temel B, Turkoglu U, Issever H, Bozbora A, et al. The impact of age, vitamin D(3) level, and incidental parathyroidectomy on. Am J Surg. 2009;197:439–46.
31. Erbil Y, Bozbora A, Ozbey N, Issever H, Aral F, Ozarmagan S, 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: 118 2–7.
32. Walsh SR, Kumar B, Coveney EC. Serum calcium slope predicts hypocalcaemia following thyroid surgery. Int J Surg. 2007;5:41–4.
33. Yamashita H, Murakami T, Noguchi S, Shiiba M, Watanabe S, Uchino S, et al. Postoperative tetany in graves disease: important role of vitamin D metabolites. Ann Surg. 1999;229:237–45.
34. Luu Q, Andersen PE, Adams J, Wax MK, Cohen JI. The predictive value of perioperative calcium levels after thyroid/parathyroid surgery. Head Neck. 2002;24:63–7.
35. Bentrem DJ, Rademaker A, Angelos P. Evaluation of serum calcium levels in predicting hypoparathyroidism after total/near-total thyroidectomy or parathyroidectomy. Am Surg. 2001;67(3):249-252.
36. Marohn MR, La Civita KA. Evaluation of total/near-total thyroidectomy in a short stay hospitalization: safe and cost-effective. Surgery. 1995;118(6):943-948.