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Original Article

Hypocalcemia Following Total Thyroidectomy: An Observational Study

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Abstract

Background: Hypocalcemia has become a common complication following thyroid surgeries ever since the widespread use of total thyroidectomy for the treatment of thyroid disorders. This problem, although lifethreatening at times, can be adequately treated in the vast majority with no long term sequelae if recognized early in the post-operative period. Sometimes hypocalcemia becomes permanent when it results from removal or damage of all the parathyroid glands leading to a prolonged morbidity and extended periods of the requirement for calcium supplementation. This can largely be avoided by following a meticulous surgical technique. Our study aims to determine the incidence of post-operative hypocalcemia and the effect of inadvertent removal of parathyroid glands in its occurrence.

Materials and Methods: A total of 136 patients undergoing total thyroidectomy during a 3 years period in our tertiary hospital were evaluated and the incidence of post-operative hypocalcemia was assessed using post-operative serum calcium values with 8 mg/dL as cutoff. This was then correlated with the number of parathyroid glands identified and preserved intraoperatively.

Results: The incidence of post-operative hypocalcemia was 12.5%, with temporary hypocalcemia in 11.76% and permanent in 0.74%. There was an inverse correlation found between the number of parathyroid glands identified and preserved during surgery and the occurrence of hypocalcemia.

Conclusion: Hypocalcemia following total thyroidectomy although common is usually transient and self-limiting. A few cases of permanent hypocalcemia result and these can largely be prevented by identifying and preserving the parathyroid glands with their intact blood supply.

Keywords: Hypocalcemia, Hospital, Thyroidectomy

INTRODUCTION

A total thyroidectomy has become one of the most common surgical procedures performed for thyroid pathologies, both benign and malignant.[1-4] It has become the standard of care in thyroid disorders due to its ease of performance and also due to the predictable hypothyroidism that results following a total thyroidectomy, which can be effectively managed with a fixed dose of thyroid replacement therapy. Total thyroidectomy has been proven safe in experienced hands and obviates the need for a re-exploration and its associated complications, in case a benign etiology on fine needle aspiration cytology (FNAC) turns out to be malignant on histopathological examination (HPE), following a less complete excision.[5] Even though this procedure has many advantages, there are two major complications which are worrisome and are almost exclusive to total thyroidectomy. One is bilateral recurrent laryngeal nerve palsy resulting in voice loss or respiratory obstruction, while the other is hypocalcemia, which can be either permanent or transient. Both these complications can be potentially fatal and can result in long-lasting morbidity for the patient. These complications can be avoided by giving proper attention to identifying vital anatomic structures during surgery.

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Hypocalcemia is a relatively common complication following total thyroidectomy, and in the vast majority of cases, it is transient. Hypocalcemia usually manifests itself on the 1st post-operative day, when the patient develops weakness of muscles, tetany and other signs of hypocalcemia. It results from various causes such as hemodilution, increased urinary excretion due to surgical stress, calcitonin release secondary to thyroid gland manipulation or due to spasm of the vessels supplying the parathyroid glands and is usually self-limiting. It requires therapy only if the patient becomes symptomatic. Transient hypocalcemia may sometimes take months to resolve but by definition lasts for <6 months.

Permanent hypocalcemia following total thyroidectomy is quite rare and is defined as hypocalcemia that persists beyond 6 months of surgery.[6] It results from inadvertent removal of the parathyroid glands or due to the disruption of vessels that supply these glands which arise as branches of inferior thyroid artery. In this study, we try to determine the incidence of hypocalcemia following total thyroidectomy.

MATERIALS AND METHODS

An observational study was conducted on 136 patients undergoing total thyroidectomy in our tertiary care hospital in Southern India. The study was conducted from January 2014 to December 2016 for 3 years.

Inclusion Criteria

1. All female patients >18 years age undergoing total thyroidectomy irrespective of the indication for surgery.
2. All patients giving consent for the procedure.

Exclusion Criteria

1. All male patients undergoing total thyroidectomy.
2. Patients who have had previous neck surgeries.
3. Patients undergoing concurrent neck dissection.
4. Patients with pre-existing hypocalcemia.
5. Patients with renal dysfunction.

Methodology

All patients presenting with a thyroid swelling underwent a FNAC and were posted for total thyroidectomy if indicated. A pre-operative serum albumin and serum total calcium were measured.

The patients then underwent a total thyroidectomy under general anesthesia. It was a routine in all the patients to identify and preserve the recurrent laryngeal nerves and the parathyroid glands intraoperatively. The number of parathyroid glands identified and the total duration of surgery were documented in each case. Repeat serum total calcium was performed 6 h after surgery and on the mornings of post-operative day 1 and day 2 at 7 am.

Post-operative hypocalcemia was defined as a serum total calcium of <8 mg/dL within 24-72 h after surgery.[7] All patients with asymptomatic hypocalcemia received oral calcium therapy with 500 mg elemental calcium along with 250 IU calcitriol. Patients with neuromuscular symptoms received intravenous infusion of injection calcium gluconate (0.5 mg elemental calcium/kg/h).

Patients with hypocalcemia were then followed up for 6 months to see if the condition was transient or permanent.

RESULTS

A total of 136 patients were included in this study, who underwent total thyroidectomy. All patients were explained the need for lifelong thyroid hormone supplementation, and an informed written consent was taken.

The median age in our study was 39 years with 46 patients belonging to the 31-40 years age group, 25 in the 21-30 years group, 41 in the 41-50 years group, 16 in the 51-60 years, 6 in the >60 years, and 2 in the <20 years age group. Age distribution of patients is shown in Figure 1.

Among the 136 patients, 94 had a pre-operative diagnosis of multinodular goiter (69.12%), 19 had solitary nodule of thyroid (13.97%) while 23 patients (16.91%) were diagnosed to have a diffuse thyroid enlargement. The pathological diagnoses being colloid goiter in 86 patients (63.24%), autoimmune thyroiditis in 22 patients (16.18%), papillary carcinoma of thyroid in 16 patients (11.76%), and follicular neoplasm in 12 patients (8.82%). Pre-operative diagnoses are shown in Figure 2.

The average pre-operative serum total calcium was 9.41 mg/dL with a range of 8.2 mg/dL to 10.3 mg/dL, and the average serum albumin level was 4.34 g/dL with a range of 3.60 g/dL to 5.10 g/dL.

Intraoperatively, all four parathyroid glands were identified in 55 patients (40.44%) while three were identified in 61 patients (44.85%), 2 in 16 patients (11.77%), and 1 in 4 patients (2.94%). The mean duration of surgery was 86 min with a range of 53-118 min.

Post-operative hypocalcemia was seen in 17 patients (12.5%) of which 16 developed temporary hypocalcemia (11.76%) and one patient developed permanent hypocalcemia (0.74%) which required continued calcium

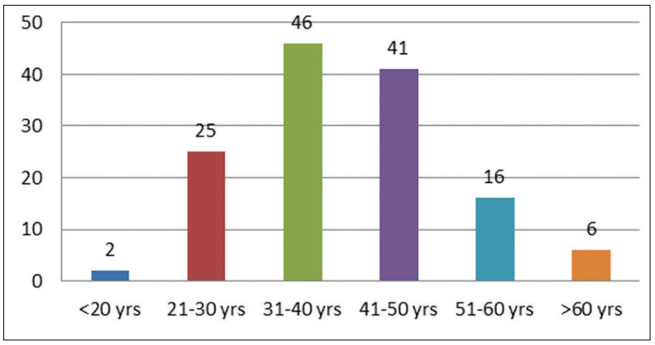

Figure 1: Age distribution of patients

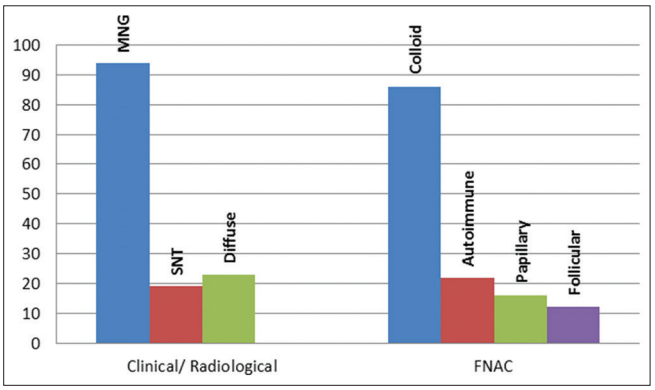

Figure 2: Pre-operative diagnoses

supplementation at 6 months duration post-surgery. Among the 17 cases with post-operative hypocalcemia, 3 were seen in those patients in whom 3 glands were identified (4.92%), 11 in those in whom 2 glands were identified (68.8%), and 3 in patients in whom one gland was identified (75%). Incidence of hypocalcemia relative to the number of parathyroid glands identified is shown in Table 1.

Among the post-operative specimens sent for HPE, colloid goiter was found in 82 patients (60.29%), autoimmune thyroiditis including Hashimoto's thyroiditis in 22 patients (16.18%), benign hemorrhagic cyst in 1 patient (0.74%), benign colloid cyst in 1 patient (0.74%), papillary carcinoma of thyroid in 14 patients (10.29%), follicular adenoma in 10 patients (7.35%), and follicular thyroid carcinoma in 6 patients (4.41%). Post-operative pathological diagnoses are shown in Table 2.

The mean age of patients developing hypocalcemia was 46.2 years. There was no significant correlation between the histopathological diagnosis and the occurrence of hypocalcemia. Patients were followed up for 6 months. There was no loss to follow-up and no mortality in the study.

DISCUSSION

Hypocalcemia is one of the most common complications following a total thyroidectomy. This complication can

Table 1: Parathyroid glands identified

Number of parathyroid glands identified	Number of patients	Incidence of hypocalcemia	Percentage
4	55	0	0
3	61	3	4.92
2	16	11	68.8
1	4	3	75

Table 2: Post operative pathology

Post-operative pathology	Number of patients (%)
Colloid goiter	82 (60.29)
Autoimmune thyroiditis	22 (16.18)
Benign hemorrhagic cyst	1 (0.74)
Benign colloid cyst	1 (0.74)
Papillary carcinoma	14 (10.29)
Follicular adenoma	10 (7.35)
Follicular carcinoma	6 (4.41)

be lifethreatening if not diagnosed and treated correctly. Although the majority of the cases are temporary and correct themselves over time, most of them still need calcium supplementation to prevent or treat the symptoms associated with hypocalcemia. Few patients are left with permanent hypocalcemia postoperatively needing prolonged monitoring and indefinite calcium supplementation. This post-operative hypocalcemia usually results from damage to the blood supply of the parathyroid glands or to the glands themselves during surgery. We conducted this study to determine the incidence of hypocalcemia and to assess the importance of intraoperative identification of the parathyroid glands during thyroid surgery in the prevention of this complication.

We included only female patients in this study because of the increased incidence of thyroid disorders in the female population and also to determine if there would be any difference in the incidence of post-operative hypocalcemia in this particular patient population compared to a mixed male and female patient population included in most previous studies. It was also found in a study conducted by Thomusch *et al.* that hypoparathyroid complications were more in female patients compared to male patients.[8] All patients with previous neck surgeries and needing concurrent neck dissection were excluded as they were a known predisposition for inadvertent injury to parathyroid glands during the thyroid surgery.[8,9] Similarly, patients with renal failure have a known abnormality in calcium homeostasis and hence were excluded from the study.

The median age in our study was 39 years, and the most common age group was 31-40 years. Middle-aged women are most commonly affected with thyroid

disorders. This was reiterated in many other studies like the one conducted by Bhattacharyya and Fried who reported a mean age of 48.3 years in their study on 517 patients conducted for the assessment of morbidity and complications of total thyroidectomy.[10]

The most common pre-operative clinical/radiological diagnosis in our study was multinodular goiter seen in 69.12% of patients, while the most common pathological diagnosis ascertained by FNAC was colloid goiter, seen in 63.24%. This was similar to the results obtained in the study conducted by Nair *et al.* who showed a diagnosis of multinodular goiter in 69.35%.[11]

The mean duration of surgery in our study correlates well with the average duration of surgery reported in other studies. In our study, the mean operating time was 86 min. We identified four parathyroid glands in 55 patients, three glands in 61 patients, two in 16 patients, and one in 4 patients with the average number of glands identified being 3.23. The incidence of hypocalcemia was highest in patients with one intraoperatively identified gland, and this incidence reduced with the increasing number of glands identified. Identification of all the parathyroid glands was earlier recommended to reduce the incidence of hypoparathyroidism postoperatively,[12,13] but this has been questioned in recent studies, like the ones conducted by Shaha and Jaffe[14] and Almquist *et al.*,[15] which claim that mere identification does not reduce this incidence.

We chose to measure the serum calcium on the first 2 post-operative days because post-operative hypocalcemia occurred from 24 h after the surgery to about 72 h following it.[7] The time for measurement was chosen to be 7 am because the serum calcium shows a slight diurnal variation compared to baseline and has a nadir early in the morning.[16] Furthermore, parathormone which influences serum calcium levels has a diurnal variation and has a peak at around 2-4 am and reaches baseline values at around 8 am.[17]

The incidence of post-operative hypocalcemia in our study was 12.5%, i.e., 17 patients among 136 overall, of which 16 cases were transient (11.76%) and 1 case was permanent (0.74%). In another study conducted by Thomusch *et al.*, the incidence of transient parathyroid hypofunction was 6.4% while permanent dysfunction occurred in 1.5% of patients.[8] They concluded that hypoparathyroidism could be predicted based on the degree of thyroid dissection, presence of autoimmune thyroid antibodies and dietary iodine status. In another study by van Zuidewijn *et al.*, initial symptomatic hypocalcemia necessitating supplementation was encountered in 12.5% while the incidence of permanent symptomatic hypocalcemia was 6% and this was not influenced by the extent of thyroid resection.[18] In our study, we observed that the incidence of hypocalcemia postoperatively could be reduced if proper care was taken to visualize the parathyroid glands and preserve their blood supply which comes from the inferior thyroid artery. Historically, it was suggested that the branches of the inferior thyroid artery should be ligated on the thyroid capsule distal to their supply of the parathyroid glands rather than ligating the artery as a single trunk which was associated with a higher incidence of ischemia of parathyroid glands and increased incidence of post-operative hypocalcemia,[19,20] but this has not shown to be of much significance in many studies thus making proper identification and preservation of glands all the more important.[21,22]

We observed an association between anatomic variations in the location of parathyroid glands and the occurrence of post-operative hypocalcemia resulting from their inadvertent removal. This was reiteration of the results obtained in the study by Akerstrom *et al.* who found that the parathyroid glands were intrathyroidal in 50% of the thyroidectomy specimens.[23] Furthermore, there appeared to be an increased incidence in cases associated with significant intraoperative hemorrhage. We did not find any association between the post-operative pathological diagnosis and the occurrence of post-operative hypocalcemia although such occurrence was found to occur in a study conducted by Nair *et al.*[11] In their study, there was a higher association of post-operative hypocalcemia in cases with a final diagnosis of Grave's disease.

We observed a reduced incidence of hypocalcemia with increasing number of parathyroid glands identified during surgery and recommended that at least one parathyroid gland should be preserved during thyroidectomy with an intact blood supply. In a study by Sheahan *et al.*, there was a higher incidence of permanent hypoparathyroidism if <3 parathyroid glands were identified and preserved.[24] In the study by Thomusch *et al.*, <2 parathyroid glands identified and preserved intraoperatively resulted in an increased incidence of permanent post-operative hypoparathyroidism.[8] Chisthi *et al.*, in their study, concluded that preservation of maximum number of parathyroids *in situ* can counter and normalize post-operative hypocalcemia.[25]

Although not performed in our study, implantation of the parathyroid in the sternocleidomastoid muscle must be attempted in cases of recognized inadvertent removal or in glands with questionable vascularity at the end of thyroidectomy as this procedure has been reported to improve outcomes in various studies.[26,27]

To conclude, hypocalcemia occurs relatively commonly following total thyroidectomy and usually results from

the inadvertent removal of parathyroid glands or injury or spasm of the blood vessels supplying them. The majority of these are transient and patients recover fully within 6 months. Few cases of permanent hypocalcemia result and pose a management problem needing prolonged supplementation and monitoring. This can be largely avoided by following a meticulous surgical technique, routine identification of the parathyroid glands intraoperatively, and proper hemostasis during the procedure.

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