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Assessment of risk factors for post-operative hypocalcemia after thyroid surgery

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Abstract
Background and Aim: Early Hypocalcemia is the most frequent complication after thyroid surgery. Several studies have tried to identify factors affecting hypocalcemia following thyroid surgery. Present study was done to evaluate risk factors for post-operative hypocalcemia after thyroid surgery.
Material and Methods: This prospective study was conducted in the department of general surgery Tertiary care institute of Gujarat for the duration of 1 year in 80 patients who had undergone total, near-total thyroidectomy. Ultrasound imaging of the thyroid gland and the neck was conducted in order. Patients undergoing total/near-total thyroidectomy had their data collected through careful history collection, rigorous clinical examination, appropriate radiographic, hematological studies including serum calcium and serum albumin, operative findings, and post-operative hypocalcemia follow-up.
Results: Out of the total 80 surgeries done, 20 were hemithyroidectomy and 60 were total thyroidectomy. 37 patients with swelling/goiter, 16 patients with toxic features, and 14 patients with thyroiditis underwent thyroidectom. Based on the histopathological report, Hashimoto thyroiditis was higher in the study. 4 in 11 patients with toxic multinodular goiter had hypocalcemia, followed by 5 cases with Thyroid adenomas, 1 case with Graves' disease had hypocalcemia after thyroidectomy. 22 patients had hypocalcemia after thyroidectomy.
Conclusion: The findings reveal that the only variables that influence early hypocalcemia development are sex, surgical method, and perioperative changes in serum calcium. Thus, prophylactic and therapeutic management may be quite similar to the recommendations in primary total thyroidectomies.

Keywords: hypocalcemia, serum calcium, thyroidectomy, thyroid adenomas

Introduction
Total thyroidectomy is widely recommended for benign thyroid diseases, and as a result, the number of these treatments has risen considerably in previous decade [1-3]. Thyroid surgery (total/near-total thyroidectomy) might result in serious consequences such as transitory or permanent cordal palsy and severe bleeding. Hypocalcemia, on the other hand, is the most common consequence following thyroid surgery [4-6].
The prevalence of hypocalcaemia 6 months after surgery is 3.6% and the prevalence of permanent hypocalcaemia is 1.5–4% [7, 8]. However, what matters most to the patients is not only quality of life, but also prolonged hospital stays and an unfavourable prognosis.[9]Recent studies have identified various risk factors for postoperative hypocalcaemia, including perioperative parathyroid hormone (PTH) levels, incidental parathyroidectomy during thyroid resection, as well as postoperative vitamin D and magnesium levels [10-12].
Additional mechanisms, such as vitamin D deficiency, an acute increase in calcitonin serum levels (because of gland handling during surgery) or an "hungry bone syndrome" are believed to contribute to this process [13-17].
Etiological considerations include post-operative alkalosis-induced hypocalcemia resulting from hyperventilation triggered by postoperative pain, and diluition hypocalcemia [18]. Even though the perfect knowledge of thyroidal anatomy regarding the embriological origin of parathyroid glands is the most concrete element to decrease incidence of post-operative hypocalcemia [19]. Although the rate of hypocalcemia has decrease as parathyroid preserving techniques have developed, the rates of transient hypocalcemia still range between 6.9 and 49.0% of patient undergone thyroid surgery [20-22]. Surgeon's ability to predict the onset of postthyroidectomy hypocalcemia is very important for post-operative management. Early detection of any risk of developing hypocalcemia will reduce the hospital stay lenght and eliminate unnecessary

laboratory examinations. When hypocalcemia is predicted, treatment with profilactic calcium and vitamin D supplements can prevent the development of hypocalcemia symptoms and premature discharge of patients. Several studies tried to identify risk factors related to early hypocalcemia (EH) development after thyroid surgery, with different results.

The capacity of the surgeon to forecast the beginning of hypocalcemia after thyroidectomy is critical for post-operative care. Early diagnosis of any risk of hypocalcemia will shorten hospital stays and prevent the need for unnecessary laboratory tests. Regardless matter how brief this issue is, the risk of developing hypocalcemia necessitates constant monitoring to ensure correct care and the treatment.

Material and Methods

This prospective study was conducted in the department of general surgery Tertiary care institute of Gujarat for the duration of 1 year in 80 patients who had undergone total, near-total thyroidectomy. Convenient sample size was taken for this study; patients presenting during the study period were included in the study. Ethical approval was taken from the institutional ethical committee and written informed consent was taken from all the participants. Ultrasound imaging of the thyroid gland and the neck was conducted in order. When clinical evidence of mediastinal extension was found, a plain helical computerized tomography was performed. Patients undergoing total/near-total thyroidectomy had their data collected through careful history collection, rigorous clinical examination, appropriate radiographic, hematological studies including serum calcium and serum albumin, operative findings, and post-operative hypocalcemia follow-up. The study excluded patients with primary parathyroid disorders, past neck irradiation, and currently taking calcium supplements.

Statistical analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2007) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). For all tests, confidence level and level of significance were set at 95% and 5% respectively.

Results

In this study, 80 patients who underwent thyroidectomy were studied. Patients with altered calcium before surgery were excluded. 74 female and 6 male patients were included as shown in the Table 1. 23 patients between 30 years of age underwent thyroidectomy (Table 2), and 41 were between 30 to 50 years old. Out of the total 80 surgeries done, 20 were hemithyroidectomy and 60 were total thyroidectomy. 37 patients with swelling/goiter, 16 patients with toxic features, and 14 patients with thyroiditis underwent thyroidectom. Based on the histopathological report, Hashimoto thyroiditis was higher in the study. 4 in 11 patients with toxic multinodular goiter had hypocalcemia, followed by 5 cases with Thyroid adenomas, 1 cases with Graves' disease had hypocalcemia after thyroidectomy. 22 patients had hypocalcemia after thyroidectomy as shown in the Table 4.

Table 1: Gender wise Distribution of Study Participants

Gender	Number	Percentage
Male	74	92.5
Female	6	7.5
Total	80	100

Table 2: Age distribution of study patients

Age Group (Years)	Number	Percentage
<30	23	28.75
31-40	27	33.75
41-50	19	23.75
>51	11	13.75
Total	80	100

Table 3: Post-thyroidectomy hypocalcemia in the study population

Post-thyroidectomy hypocalcemia	Number	Percentage
Yes	22	
No	58	
Total	80	

Table 4: Distribution of diagnosis in post-operative hypocalcemia

HPE report	No of cases	No. of hypocalcemia cases	Percentage
Thyroid malignancy	14	3	21.4
Thyroid adenoma	16	5	31.25
Toxic MNG	11	4	36.3
Graves' disease	5	1	20
Hashimoto thyroiditis	8	5	62.5
Lymphocytic thyroiditis	6	0	0
Nodular/colloid goiter	20	4	200
Total	80	22	

Discussion

Hypoparathyroidism has been confirmed as an independent risk factor for hypocalcaemia after thyroid surgery because the function of the parathyroid gland directly affects serum calcium levels [23, 24]. Damage to the parathyroid gland may be primarily due to the anatomical location of the parathyroid gland. Most parathyroid glands are located at the posterior margin of the lateral lobe of the thyroid in the loose connective tissue between the true and false capillaries. The blood supply of the parathyroid gland comes from the inferior thyroid artery and its anastomotic branch with the superior thyroid artery. However, 80% of the inferior thyroid artery is the only blood vessel supplying the parathyroid gland. The parathyroid gland may be damaged if the inferior thyroid artery is ligated near the inferior pole of the thyroid gland or if vascular spasm is caused by careless surgical procedures.

Hypocalcemia is a common complication after thyroid surgery. It usually occurs in first days after surgery and it can be symptomatic or asymptomatic. The frequency of transient hypoparathyroidism after thyroid surgery is between 6.9 and 49% [20-22].

The mechanism of hypocalcemia after thyroidectomy is not precisely disclosed, although is accepted to be multifactorial; factors like surgical techique, parathyroid iatrogenic damage, extent of thyroidectomy, hyperthyroidism, malignancy, patient gender, perioperative serum calcium drop, presence of

thyroiditis, diabetes, number of identified parathyroid gland during surgery can be considered as etiological factors [25, 26]. Most studies underline the significance of expertise and surgeon's experience.

In this study, the data of 80 patients that underwent thyroid surgery were retrospectively reviewed and hypocalcemia was detected in 22 cases. The incidence of hypocalcemia in our study comes in agreement with the incidence reported in the literature. In literature, some studies were found that states transient hypocalcemia to be associated with advanced age, whereas others reported an association with younger age. Some studies, found transient hypocalcemia to be associated with advanced age, whereas others reported an association with younger age. A systematic review performed by Edafe *et al* observed no significant difference in mean age between patients who had transient hypocalcemia and those who did not [27].

We found gender as a key risk factor for hypocalcemia in the literature, with females appearing to be more prone to developing this problem [28]. In this present study, it is seen that females contribute more to this disorder compared to men. The exact cause beyond that phenomenon is still under debate. In most studies women were found to have significant higher rates of hypocalcemia, whereas other studies showed that gender has no significant effect on the incidence of hypocalcemia [29-31]. According to literature we identified sex as significant risk factor for hypocalcemia, in fact female seemed to be more prone to develop this complication. Many studies tried to find an explanation to female predisposition to post-thyroidectomy hypocalcemia, but the specific mechanisms underlying this gender difference can only be assumed. The gender disparity may be related to effects of sex steroids on PTH secretion, genetic variation among cell-signaling pathways or anatomic differences that can cause more frequent iatrogenic damages because of a more diminutive operative field.

In literature hyperthyroidism is described as a risk factor for EH development; it is unclear why thyrotoxic thyroidectomies have an increased rate of hypocalcemia; however, it is perhaps unsurprising as the thyroid gland in thyrotoxicosis tends to be larger than normal and very highly vascularised leading to a more challenging operation [32]. In the current study, toxic goiter was a significant risk factor for hypocalcemia.

Thyroidectomy for carcinoma is described by some authors as a higher-risk procedure since the posterior capsule is drastically removed with the gland in the case of malignant disease, which is why parathyroid glands are at higher risk of injury due to the danger of nerve injury [33]. In our investigation, like in others, we found that hypocalcemia developed in 21.4% of patients with preoperative malignant or suspected malignant diagnosis and 31.25% of patients who underwent surgery for benign pathology (thyroid adenoma).

Although the benefits and risks of total thyroidectomy are still debated, it is becoming more common. Hypocalcemia was much less common among lobectomy patients than among total thyroidectomy patients in our study.

The importance of systemic identification of all 4 parathyroid glands during thyroid surgery is one of the most controversial factors debated in the literature. Some authors recommend routinary physical identification and preservation of as many of parathyroid glands as possible [34]. Other series questioned this strategy [35-37]. Among our patients we noticed an increasing rate of EH when a higher number of parathyroid gland have been identified during surgery, but statistical analysis didn't show significant results (p>0.05). To avoid potential injury to the parathyroid glands, every surgeon must be thoroughly aware of their anatomic complexity that contributes to difficulty of identification and possible injury. Strict adherence to capsular dissection represents the optimum method for safe preservation of parathyroid glands without necessitating their systemic identification. Distal ligation of all terminal branches of the superior and inferior thyroid arteries, close to the thyroid capsule, enables reliable separation of all tissues carrying parathyroid gland away from the thyroid surface. Continued dissection in this tissue, with the aim to identify all parathyroid glands may increase the risk of their mechanical injury or devascularization.

Conclusion

In the majority of cases, clinically significant hypocalcemia following thyroid surgery is transitory. The findings reveal that the only variables that influence early hypocalcemia development are sex, surgical method, and perioperative changes in serum calcium. Thus, prophylactic and therapeutic management may be quite similar to the recommendations in primary total thyroidectomies.

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