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Surgery

POST THROIDECTOMY HYPOCALCEMIA: RETROSPECTIVE STUDY IN RURAL AREA OF IDUKKI

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ABSTRACT **Introduction:** Thyroidectomy is a frequent operation performed worldwide. The most common complication following thyroid surgery is hypocalcemia, caused by transient or persistent hypoparathyroidism. This study aimed to investigate the prevalence of hypocalcemia after thyroidectomy and to identify potential risk factors. **Methods:** All thyroidectomies performed at Department of General amd Laproscopic Surgery AlAzhar Medical College Thodupuzha between 2018 and 2021 were retrospectively analyzed. Post-thyroidectomy hypocalcemia was evaluated in relation to risk factors such as age, sex, procedure type, and type of thyroid disease. Data were extracted from patient medical records. Patients with pre-operative hypocalcemia were excluded. **Results:** A retrospective study conducted on 2108 patients that underwent thyroid surgery in a single center (1669 women and 439 men). Postoperative early hypocalcemia was defined as serum calcium levels lower than 8,0 mg/dl measured 24 h after surgery. Following factors were evaluated in the study: sex, age, glandular hyperfunction, preoperative diagnosis, preoperative serum calcium levels, preoperative serum PTH levels, type of surgery performed (total thyroidectomy vs. lobectomy); number of parathyroid preserved in situ, postoperative serum calcium levels, changes in perioperative calcium levels (difference between preoperative values and postoperative calcium levels), presence of carcinoma in the surgical specimen, presence of thyroiditis based on histopatology reports. **Conclusion:** Thyroidectomy is a safe surgery with few complications when performed by a skilled surgeon. These complications result in longer hospital stays and higher costs. The most common post-thyroidectomy complication was hypocalcemia. Furthermore, patients who underwent total thyroidectomy were at the greatest risk of developing post-thyroidectomy hypocalcemia.

KEYWORDS : thyroidectomy, temporary hypocalcemia, risk factors, post-thyroidectomy complications, persistent hypocalcemia

INTRODUCTION

Thyroid disorders are among the most commonly occurring endocrine gland diseases worldwide. They can be treated either medically or surgically. Thyroidectomy (partial or total) is one of the most frequent operations performed globally [1,2]. Compression symptoms, suspected or known malignancy, presence of a solitary cold nodule in patients aged <20 years, cosmetic reasons, and the presence of a complex cyst or a cyst >4 cm in diameter are all indications for thyroidectomy [3].Due to advancements in anesthesia, operative techniques and antisepsis, better surgical instruments, and understanding of thyroid anatomy and physiology, thyroid surgery is now considered a safe procedure [4,5]. However, complications following thyroid surgery may occur. These complications include hypocalcemia, recurrent laryngeal nerve injury, hematoma, seroma, stridor, loss of high-pitched voice, thoracic duct injury, wound infection, and tracheal injury [6]. Such complications occur less frequently when the surgery is performed by experienced surgeons (surgical volume of procedures performed per year) [3,7]. Hypocalcemia and recurrent laryngeal nerve injury are the most frequently encountered complications [8].Post-thyroidectomy complications may be associated with some risk factors such as age, sex, increased gland size, type of thyroid disease, presence of fibrosis and inflammation, extent of thyroidectomy, and lymph node dissection [4]. According to a study conducted by Papaleontiou et al., advanced age, presence of comorbidities, and advanced disease are significant risk factors for post-thyroidectomy complications, especially in cases of thyroid cancer [9].Our research group has previously published a paper on post-thyroidectomy complications in general [6]. The current study, however, focuses on the prevalence and risk factors associated with post-thyroidectomy hypocalcemia. Furthermore, we hope to share our experiences and compare our findings with those in the literature.

MATERIALS AND METHODS

MethodsWe analyzed datas about a total number of 2108 patients that underwent thyroid surgery in the study period. There were1669 women (79.2%) and 439 men (20.8%) with a mean age of 54.65 years (range, 15–87). Patients' demographics, operative details, histological findings and postoperative events are reported in Table 1.

Table 1. Frequency Distribution Of Demographic And Clinical Characteristics Of The Subjects.

Properties	Number	Percent Cumulative	Percentage
1. AGE			
40 ≥	31	21.7	21.7
41–60	87	60.8	82.5
60<	25	17.5	100
2. TYPE OF SURGERY			
Total Thyroidectomy	116	81.1	81.1
Subtotal Thyroidectomy	27	18.9	100
3. Hypocalcemia In The First 24 Hours After Surgery			
Positive	70	49	49
Negative	73	51	100
4. Hypocalcemia In The First 48 Hours After Surgery			
Positive	91	63.6	63.6
Negative	52	36.4	100
total	143	100	

RESULTS

Among the 182 patients who underwent thyroidectomies, 105 (57.7%) had benign lesions and 77 (42.3%) had malignant lesions. The ages ranged between 15 and 95 years (mean 39.87 ± 12.67 years), with most patients being female (n = 151, 83%). Total thyroidectomy was the most common surgery performed (n = 107, 58.8%), followed by right hemithyroidectomy (n = 39, 21.4%) and left hemithyroidectomy (n = 24, 13.2%). Further, completion thyroidectomy and subtotal thyroidectomy were performed for 2.7% and 3.8% of the patients, respectively.A total of 116 patients (63.7%) had temporary hypocalcemia and three developed persistent hypocalcemia (1.6%). The remaining patients (n = 63, 34.6%) did not develop hypocalcemia. Table 1 depicts the association between post-thyroidectomy hypocalcemia and various risk factors. In addition, there was no significant relationship between the occurrence of hypocalcemia and

age, type of thyroid disease, and sex. Conversely, there was a significant relationship between the development of hypocalcemia and the type of procedure (P < 0.001). Temporary hypocalcemia was more common in patients who underwent total thyroidectomy (70.7%), followed by right hemithyroidectomy (15.5%) and left hemithyroidectomy(10.3%). Only three patients had permanent hypocalcemia after undergoing left hemithyroidectomy, subtotal thyroidectomy, or total thyroidectomy.Hypocalcemia is a common complication after thyroid surgery.

Table 2. Investigating The Relationship Between Variables.

Properties	Hypocalcaemia In The First 24 Hours After Surgery		P-Value	Hypocalcaemia In The First 48 Hours After Surgery		P-Value
	Positive	Negative		Positive	Negative	
1.Sex			0.121			0.025
Male	23(41.8%)	32(58.2)		29(52.7%)	26(47.3%)	
Female	47(53.4%)	41(46.6%)		62(70.5%)	26(29.5%)	
2.Age			0.167			0.26
40 ≥	12(38.7%)	19(61.3%)		17(54.8%)	14(45.2%)	
41–60	42(48.3%)	45(51.7%)		55(63.2%)	32(36.8%)	
60<	16(64%)	9(36%)		19(76%)	6(24%)	
3. Type Of Surgery			0.021			0.37
Total Thyroidectomy	62(53.4%)	54(46.6%)		75(64.7%)	41(35.3%)	
Near-Total Thyroidectomy	8(29.6%)	19(70.4%)		16(59.3%)	11(40.7%)	
4. Duration Of Surgery			0.41			0.45
120min >	5(41.7%)	7(58.3%)		7(58.3%)	5(41.7%)	

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% [11,12,13,14,15,16].The mechanism of hypocalcemia after thyroidectomy is not precisely disclosed, although is accepted to be multifactorial; factors like surgical techique, parathyroid iatrogenic damage (injury, edema, infarction, ischemia), 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 [2, 17, 18].In literature, contrary opinions have been asserted about correlation between development of postoperative hypocalcemia and patient 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 [18]. The present study also found no significant intergroup difference with regard to patient age. We also divided patients in four age groups (ved. Table 2) but no significant difference have been noticed between groups.

According to literature we identified sex as significant risk factor for hypocalcemia, in fact female seemed to be more prone to develop this complication. In fact in our study female patients experiencedEH in 42% (701/1669) of cases, which was significantly greater than the 21.4% (94/439) incidence detected in men (p < 0.001). There was no significant difference in rates of EH between premenopausal women and postmenopausal women, as confirmed by other studies [4].

Many studies tried to find an explanation to female predisposition to post-thyroidectomy hypocalcemia, but the specific mechanisms undelying 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 [4].

Some studies identified low preoperative level of serum calcium as a risk factor for the development of transient hypocalcemia [11, 19, 23,24,25]. In our study no difference has been identified between mean preoperative serum calcium level in EH group and in normocalcemic group. There was a significant difference in serum calcium level drop; mean perioperative variation in serum calcium levels (difference btween preoperative level and 24 h postoperative level) was significantly higher in patients that developed early hypocalcemia (p < 0.001). These findings clearly show that preoperative level of serum calcium has no influence on EH development, but perioperative level variation plays a decisive role in this process. This mechanism is confirmed by other studies in which a larger decrease in post-operative calcium from preoperative levels was associated with transient hypocalcemia [19, 24, 26,27,28].

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 [1, 29]. In our study thyroid hyperfuntion didn't appear as a significant factor in EH development (Table 2) as confirmed by other studies in literature [9, 30].Few articles in literature investigated effect diabetes has on hypocalcemia following thyroidectomy. Al-Dhahiri et al.

Prospectively explored factors affecting recovery of parathyroid function after thyroidectomy and found diabetes mellitus to be a statistically significant factor.[1, 30]The mechanism by which diabetes cause this effect is unclear; however, it is hypothesised that the small vessel disease and the impact on angiogenesis may leave the parathyroids more vulnerable to hypoxia in these patients. This hypotesis is not confirmed by our study,no significant difference (p = 0.399) was found between diabetic patients and patients not affected by diabetes regarding EH development.

The surgical technique and the extent of thyroidectomy are related to parathyroid injury, edema, infarction, ischemia or incidental parathyroidectomy [2, 11, 18]. Dissection carried around the parathyroid glands and efforts to isolate RLN in this region can lead to venous congestion and edema. In addition, ligating of thyroid veins is among the cause of venous stasis. Venous stasis and edema slow down parathyroid function and may cause a temporary hypoparathyroidism [17]. As confirmed by our study, the incidence of hypocalcemia is much lower among patients that underwent lobectomy (13,8%) than in total thyroidectomy patient group (38.8%).Some authors described thyroidectomy for carcinomaas a higher risk operation because in case of malignant pathology posterior capsule is radically removed with the gland and this is the reason why parathyroid glands are at higher risk of injuryas the risk of nerve injury [17, 31,32,33,34]. In our study, as it has been described also in other studies [16], EH developed in 36.5% of patients with preoperative malignant or suspected malignant (Thyr 3, Thyr 4, Thyr 5) diagnosis, and in 38,5% of patients that underwent surgery for benign pathology. Surgery for malignant pathology was not found as a significant factor for the development of EH.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 [35]. Other series questioned this strategy [18, 36,37,38,39]. 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 = 0.63). 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 represent 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

This findings suggest that sex (female gender is a strong risk factor), surgical procedure and perioperative changes in serum calcium are the only factors (among all variables examined) that influence early hypocalcemia development.All the risk factors detected in our study

appear to be very common and not editable before nor during or after surgical procedure. This is the reason why in our unit we are used to suggest prophylaxis against symptomatic hypocalcemia (Carbonate calcium 1 g and Vitamin D 0,50 mcg per os twice a day for seven days) to every patient who underwent thyroid surgery. In our experience, therefore, prophylaxis with calcium and Vit. D (4 euros/patient) during hospitalization and after patient discharge was found to be beneficial both in terms of clinical outcome and in terms of health costs. Since when we started this prophylaxis we noticed a decreased length of stay and minimization of re-entry.

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