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The Rate of Post-Thyroidectomy Hypocalcemia and its Relation to Vitamin D Level

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Abstract

Background and Aim: Hypocalcemia following total thyroidectomy is a common complication that is sometimes hard to correct. The aim of this study was to determine the rate of post-thyroidectomy hypocalcemia in a tertiary hospital in Riyadh, Saudi Arabia and trying to explore the relationship of pre-operative vitamin D level and the incidence of post-thyroidectomy hypocalcemia.

Methods: This retrospective study was conducted among 122 patients who underwent total thyroidectomy over one year (from January 2018 to December 2018) in Prince Sultan Military Medical City, Riyadh, Saudi Arabia. All patients were admitted and monitored for at least 24-48 hours after surgery. The postoperative hypocalcemia, vitamin D, Alkaline phosphatase (ALP), parathyroid hormone (PTH), phosphate (PO4) and vitamin D level were collected.

Results: A total of 122 (mean age 41.6 ±1.2 years; females 90.2 %) patients underwent total thyroidectomy in the year 2018. The rate of hypoparathyroidism in the first two days was 2.07 mmol/L and 2.01 mmol/L. Most of the cases of hypocalcemia happened on day 1 postoperatively. Hypoparathyroidism mainly happens in patients with benign pathology. The mean level of vitamin D was 54.6 ± 25. For those who had benign pathology the mean vitamin D level 49 ± 23 (mild deficiency) and malignant is 62 ± 25 (normal). There was no correlation between postoperative hypocalcemia with other variables.

Conclusion: The findings of this study evidently illustrated that a significant drop in calcium level after the surgery. Further, well-designed randomized controlled trials with higher sample sizes are essential to validate our findings.

Keywords

Post-thyroidectomy, Hypocalcemia, Vitamin D

Introduction

Total thyroidectomy is an effective treatment for patients with thyroid malignancies, thyrotoxicosis, multinodular goiter and chronic thyroiditis. The most common complications after thissurgery are hematoma, recurrent laryngeal nerve injury and hypocalcemia [1,2]. The hypocalcemia generally takes place in the first days after surgery and it can be symptomatic or asymptomatic. One of the most common causes of hypocalcemia after surgery is due to hypoparathyroidism. Even in an experience surgeon, the deletion of the thyroid gland with preservation of parathyroid might cause in transient or stable hypoparathyroidism due to cut of the blood supply to parathyroid gland during surgical handling or postoperative hematoma or inattentive removal of one or more parathyroid gland. The transient hypoparathyroidism defined as hypoparathyroidism which lasts less than 6 months, affects 25.4-83% of patients after neck surgery globally, in contrast with permanent hypoparathyroidism, defined as hypoparathyroidism which lasts more than 6 months, which disturbs 0.12-4.6% of patients [3,4].

The incident and prevalence of hypocalcemia is reliant on by the specific setting of patients [5]. The occurrence of hypocalcemia postoperatively in hospital setting has been detected up to 3%. Contrarily, hypocalcemia has been defined to touch a prevalence of 18% in hospitalized patients and up to 85% in the intensive care patients [6].There are numerous risk factors which might disturb the incidence of postoperative hypoparathyroidism such

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asetiology of the thyroidal illness, extent of the surgery, and the 25 hydroxy vitamin D level earlier to surgery. Severe hypocalcemia can lead life threatening problems such as seizures, laryngospasm and cardiac arrhythmias. Additional mechanisms, such as vitamin D deficiency, an acute rise in calcitonin serum levels (because of gland handling during surgery) or an "hungry bone syndrome" are assumed to contribute to this process [7]. In this study we determine the rate of hypocalcemia post total thyroidectomy in a tertiary hospital in Riyadh, Saudi Arabia and trying to explore the relationship of pre-operative vitamin D level and the incidence of hypocalcemia post thyroidectomy.

Methods

This retrospective study was conducted among 122 patients who underwent total thyroidectomy over one year (from January 2018 to December 2018) in Prince Sultan Military Medical City which is one largest tertiary hospital in Riyadh, Saudi Arabia. The study was conducted in accordance with the declaration of Helsink and study protocol was approved by the Research and Ethics Committee of Prince Sultan Military Medical City, Riyadh, Saudi Arabia.

Inclusion criteria: All patients who underwent total thyroidectomy during January 2018 to December 2018 were included in this analysis. Patients with history of previous hypoparathyroidism, thyroid surgery, presence of metabolic bone disease, presence of renal or liver diseases and patients on drugs known to cause hypocalcemia were excluded.

Measures

All patients were admitted and monitored for at least 24-48 hours after surgery. The total calcium levels were detected by a centralized laboratory of our hospital through an automated analyzer. The postoperative hypocalcemia was defined according to the British Association of Endocrine and Thyroid Surgeons as postoperative hypocalcemia as a plasmatic calcium level less than 8.4 mg/dl (2.1 mmol/L) in the first day after surgery. Tardive hypocalcemia is defined as calcium or vitamin D treatment requirement in order to maintain normal calcium levels 6 months or more after surgery [8]. Further, the Alkaline phosphatase (ALP), parathyroid hormone (PTH), phosphate (PO4) and vitamin D level were also collected.

Statistical analysis

Data analysis was performed using Microsoft Excel 2013 (Microsoft Corporation, Seattle, WA, USA) and the Statistical Package for Social Sciences (version 22; SPSS Inc., Chicago, IL, USA). Two-tailed t test was conducted to determine the differences between the sets with respect to the different time points and groups (preoperativevs post-operative; Benign vs Malignant). Correlation among each variable was performed by Pearson correlation coefficient. A $p < .05$ was considered to be statistically significant.

Results

A total of 122 (mean age 41.6 ± 1.2 years; females comprised more than 90%,) patients underwent total thyroidectomy in the year 2018. The rate of hypoparathyroidism in the first two days was 2.07 mmol/L and 2.01 mmol/L. Most of the cases of hypocalcemia happened on day 1 postoperatively (45.1%). Hypoparathyroidism mainly happened in patients with benign pathology. The mean level of vitamin D was 54.6 ± 25. For those who had benign pathology the mean vitamin D level 49 ± 23 (mild deficiency) and malignant is 62 ± 25 (normal). There was no correlation between postoperative hypocalcemia with other variables. The malignancy rate, overall, of 40% (n = 46) (Figure 1-4). Table 1 shows the ALP, corrected calcium, PO4 and PTH level among benign and malignant patients. Significant differences were observed among malignant patients vitamin D level and 0 day corrected calcium level compared to benign.

Table 2 shows the pre and post-operative level ALP, corrected calcium, PO4 and PTH level. Significant differences were observed

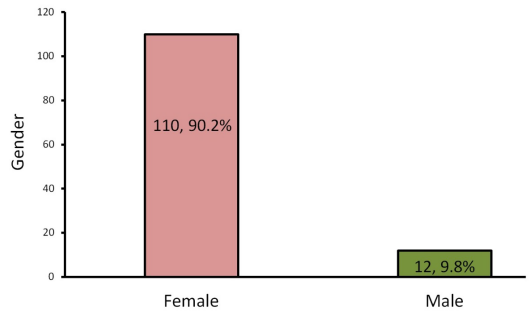

Figure 1: Gender wise distribution of the study population

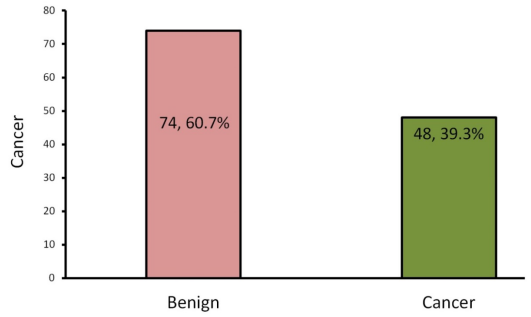

Figure 2: Malignant wise distribution of the study population

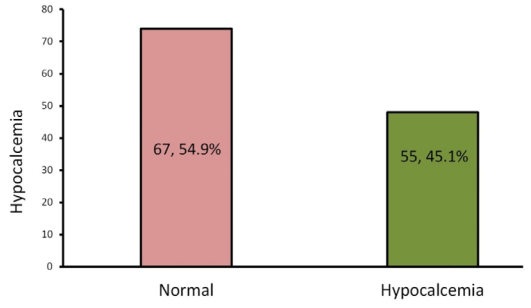

Figure 3: Hypocalcemia among the study population (day 1)

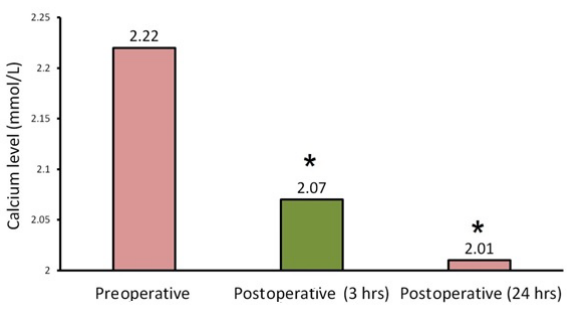

Figure 4: Calcium level of pre and post-surgery

	Benign	Malignant	P Value	Reference Range
Preoperative ALP	79.5 ± 40	80 ± 33	0.975	40 – 129 U/L
Preoperative Vitamin D	49 ± 23	62 ± 25	**0.009**	**50 – 150 nmol/L**
Preoperative corrected calcium	2.01 ± 0.13	2.03 ± 0.17	0.702	2.15 – 2.50 mmol/L
Preoperative PO4	1.04 ± 0.20	1.03 ± 0.17	0.833	0.81 – 1.45 mmol/L
Preoperative PTH	81.5 ± 62	79 ± 71	0.962	15 – 65 pg/ml
Postoperative PO4	2.90 ± 11.1	1.26 ± 0.26	0.460	0.81 – 1.45 mmol/L
Corrected calcium day 0	2.19 ± 0.14	2.12 ± 0.45	**0.053**	2.15 – 2.50 mmol/L
Corrected calcium day 1	2.18 ± 0.12	2.14 ± 0.15	0.162	2.15 – 2.50 mmol/L
Postoperative day1 PTH	23.5 ± 15.1	24.7 ± 13.3	0.681	15 – 65 pg/ml
Postoperative ALP	77.5 ± 36.3	67.8 ± 22.8	0.217	40 – 129 U/L

Table 1: Biochemical level of benign and malignant

	Preoperative	Postoperative	P Value	Reference Range
ALP	79.8 ± 38	74 ± 32	0.307	40 – 129 U/L
Corrected calcium	2.22 ± 0.12	2.07 ± 0.03	**0.006**	2.15 – 2.50 mmol/L
PO4	1.14 ± 0.23	2.31 ± 8.9	0.248	0.81 – 1.45 mmol/L
PTH	80.5 ± 74	24 ± 14	**0.001**	15 – 65 pg/ml

Table 2: Pre and post-operative biochemical level of the study population

	Age	Gender	Preoperative ALP	Preoperative Vitamin D	Preoperative corrected calcium	Preoperative PO4	Preoperative PTH	Postoperative PO4
Age								
Gender ***p* value**	-.086 .361							
Preoperative ALP ***p* value**	.022 .847	.004 .975						
Preoperative Vitamin D ***p* value**	.162 .117	.266 **.009**	-.148 .220					
Preoperative c. calcium ***p* value**	.387 **.000**	.042 .702	.303 **.008**	.079 .503				
Preoperative PO4 ***p* value**	-.275 .014	-.024 .833	.002 .985	.099 .412	-.032 .779			
Preoperative PTH ***p* value**	.104 .692	-.013 .962	.491 .074	-.147 .588	-.100 .723	-.091 .452		
Postoperative PO4 ***p* value**	.163 .168	-.088 .460	.076 .580	.165 .205	-.055 .686	-.180 .121	-.230 .552	
Postoperative c calcium ***p* value**	**.449** **.015**	-.288 .130	.393 .052	.115 .591	.453 **.026**	.006 .965	.365 .762	.121 .602

Table 3: Correlation of biochemical parameters

between pre-operative corrected calcium level and PTH. Table 3 demonstrated the correlation of different variables. Significant correlation was found between age *vs* pre-operative corrected calcium level and post-operative corrected calcium level. Gender significantly correlated with pre-operative vitamin D level and pre-operative ALP significantly correlated with pre-operative corrected calcium level.

Discussion

Thyroidectomy has been revealed to be a safe surgery in the hands of specialist and experienced surgeons [9]. The entire morbidity is very low and mortality currently is almost an anecdotal incidence with many centers discharging patients as early the first post-operative day [10]. Transient hypocalcemia initiated by inadvertent parathyroidectomy (IP) or disruption of the blood supply to the parathyroid glands (PG) is one of the most commonly happening complication of thyroidectomy procedures [11]. In this present study, aimed to determine the rate of post-thyroidectomy hypocalcemiain and trying to explore the relationship of pre-operative vitamin D level and the incidence of post-thyroidectomy hypocalcemia.

The mean age of the study population was 41.6 ± 1.2 years, and the females comprised more than 90% of the total sample (thyroid disease is very common condition and affects more women), this findings suggests that being female is likely a risk factor for transient post-thyroidectomy hypocalcemia. Although this association is statistically significant, its magnitude and clinical relevance are uncertain and may be trivial, similar results were also observed from the previous studies [12].

The purpose of the present study was not only to examine the

reasons of hypocalcemia following total thyroidectomy but also to find, at an initial stage, patients at huge threat of emerging post-operative hypocalcemia, in order to start thetherapy and thereby avoid the clinical manifestations of the condition and allow a reduction in hospitalization time. Due to this purpose, we did not select patients type of thyroid disease and did not consider whether or not lateral or central neck dissection was performed. In this present study we found a significant drop in calcium level after the surgery, which is confirm by many earlier studies [13,14]. It should be noted here that a recent study stated that post-operative hypocalcemia has an incidence of 1.2-40% and the permanent hyoparathyroidism is recorded in 3% of cases [14]. This study focusing on the levels of calcium after performing a thyroidectomy in a tertiary hospital and the need of calcium supplements under these circumstances. This problem, even it appears rather harmless initially, in fact it signifies an imperative factor to hospitalization delay and, especially for severe forms, to poor quality of life, comprising the risk of life threatening episodes which is agreement with previous findings [14]. Earlier studies also reported that after thyroid surgery, the serum calcium levels apparently fall to their lowest levels 24 to 48 hours with associated symptoms. However, there are no consistent markers for recognizing patients who are likely to develop symptomatic hypocalcaemia [15,16]. Further a study stated that early post-operatory PTH and calcium are best predictors for the need of oral calcium supplements [17]. In addition the study also stated that postoperative calcium supplementation is effective for avoiding post-thyroidectomy hypocalcaemia. Calcium combine with vitamin D was more effective than calcium alone or no supplements in preventing postoperative hypocalcaemia and diminishing the demand for intravenous calcium supplementation [17]. In cases of hypoparathyroidism calcitriol is preferred [14].

In our study we could not prove the correlation of low vitamin D and hypocalcemia post total thyroidectomy because majority of participants in the cohort had either normal vitamin D or mild deficiency. Furthermore, our study is limited by small sample size which might not powered to explore the correlation between vitamin D level and postoperative hypocalcemia. However, previous studies stated that the overall incidence of post-thyroidectomy hypocalcaemia within 24 hours was 21.4%. The incidence increased from 6 hours (13.8%) to 24 hours post-thyroidectomy (15.8%) and there was indication of both transient and deferredpost-thyroidectomy hypocalcaemia within the first 24 hours. By 6 months post-surgery, 3.6% remained hypocalcaemic and required continual oral supplementation [18]. Hence, we propose herewith assessment of the drop in calcium levels post-operatively compared to the immediate pre-operative levels as a useful and simple predictor of hypocalcemia in patients undergoing total thyroidectomy.

The major limitations of this study include: a relatively small sample size, retrospective in nature, limited– number of risk factors, short duration of follow up postoperatively, limited social, demographic factors examined, surgery performed by 5 different surgeons and the study performed at a single center. More studies on a larger scale are needed to address the limitations indicated in the study. Despite the limitations, the study delivers valuable data for the post-operative hypocalcemia among Saudi patients. Conclusively, the findings of this study evidently illustrated that a significant drop in calcium level after the surgery. Further, well-designed randomized controlled trials with higher sample sizes are essential to validate our findings.

Ethical Approval: The study protocol was approved by the Research and Ethics Committee of Prince Sultan Military Medical City, Riyadh, Saudi Arabia.

Conflict of interest: Authors have no conflict of interests and the work was not supported or funded by any drug company.

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