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Parathyroid Hormone Assay as a Predictor for Post Operative Hypocalcemia in Patients Undergoing Total Thyroidectomy

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Abstract

Background: Serum parathyroid hormone assay in the immediate post operative period and at 24 hours can be used as a very reliable predictor for identifying patient at risk of developing Clinically symptomatic hypocalcemia. This study was aimed to ascertain if post operative Parathyroid assay can be used to predict patients at risk of developing clinically symptomatic hypocalcemia and thereby selecting patients for early discharge and patients who will benefit from prophylactic calcium supplements.

Patients and Methods: All patients who underwent Total thyroidectomy with or without neck dissection from October 2021 to June 2022 were included in the study. Samples for serum PTH within 1 hour and 24 hours post-thyroidectomy along with Serum calcium on post-operative days 1,3 and 5 were collected for analysis.

Results: Total number of patients in the study group was 25. Only 5% (3/22) had signs of hypocalcemia. Out of 25 patients 9 were operated for carcinoma of thyroid. 2 patients underwent total thyroidectomy with CCND and ipsilateral neck dissection. Female: Male was 3:1. The median age for female and male was 48 and 49 respectively. There was no significant difference in the PTH value measured within 1hr of surgery vs 24hrs post-surgery (p=0.329). The median PTH value for the patient who did not require calcium supplements was 19(8.91-68.3). The median PTH who required calcium supplement (oral/intravenous supplement) was 5.25(3.3-8.39). The mean post-operative stay was 2.25±0.46, and 4.07±1.20 for those patients who had normal and abnormal PTH value.

Conclusion: Hypocalcemia following thyroidectomy is multifaceted in its development. As an outcome, we have found that taking a 1 hour and 24-hour PTH test measurement is a reliable and early indicator of hypocalcemia.

Keywords: Parathyroid Hormone Assay; Hypocalcemia; Thyroidectomy.

INTRODUCTION

In recent years, thyroid surgery has become a highly safe procedure with low morbidity; however, post-operative hypocalcemia continues to be the most frequent complication that determines length of stay [1]. Hypoparathyroidism brought on by devascularization or unintentional parathyroid gland resection is the cause of post-thyroidectomy hypocalcemia [2].

Hypocalcemia can be temporary or chronic, depending on the type of injury and the number of glands affected. Precision, experience, and in-depth understanding of the anatomy of the neck are necessary for the preservation of the parathyroid glands after thyroid resection [3]. The parathyroid glands differ in size, shape, color, quantity, and position (the inferior parathyroid glands are more widely distributed than the superior glands) [4].

Even though the majority of hypocalcemia appears after the third post-operative day, many surgeons prevent these patients from being discharged too soon. Measuring serum calcium in the immediate post-operative period cannot predict early discharge because the calcium fall occurs up to 48 hours later. Ischemic damage to the parathyroid and unintentional parathyroid gland excision are the most frequent causes of hypocalcemia. The treatment of hypocalcemia following surgery is controversial; some surgeons begin prophylactic calcium immediately after surgery, while others wait for hypocalcemia symptoms or a drop in serum calcium of less than 8 mg/dl. Very few surgeons use PTH hormone as a predictor of hypocalcemia. There is no reliable indicator of hypocalcemia in the postoperative phase, and the cause of hypocalcemia is complex. Early preventative calcitriol medication is essential for maintaining eucalcemia in high-risk patients. Therefore, if post-thyroidectomy patients at risk for hypoparathyroidism and hypocalcemia were identified, early calcitriol therapy might be feasible. However, those who are not at high risk of hypocalcemia after thyroidectomy can be regularly released without worrying about hypocalcemia symptoms and can eliminate the need for frequent blood testing. Hence the objective of our study is to measure the PTH level in the immediate post of period within 1 hour of surgery and 24 hours later for predicting the hypocalcemia, categorizes the patient as low and high risk for hypocalcemia and thereby early discharge [4].

PATIENTS AND METHODS

All patients who underwent Total thyroidectomy with or without neck dissection in our hospital from October 2021 to June 2022, 25 patients were operated for total thyroidectomy with or without neck dissection. The sample size was calculated using the following formula.

n = (Z^2 P(1-P))/d^2,were n = Sample size, Z = Z statistic for a level of confidence=1.96, P = Expected prevalence of proportion, (If the expected prevalence is 34%, then P¬ = 0.34), and d = Precision (If the precision is 5%, then d=0.12). The required sample size as per the above-mentioned calculation was 25 subjects. Pre- operative serum calcium, vitamin D, serum albumin, were normal in all the patients. Female: Male was 3:1. The median age for female and male was 48.63 ± 12.44 years and 49.33 ± 10.52 respectively **(Table 1).**

Pre-operative serum calcium, albumin, vitamin D, PTH were measured for all the patients undergoing total thyroidectomy. Pre-operatively TIRADS scoring and The Bethesda System for Reporting Thyroid Cytopathology (TBS) was done for all cases. Intra operatively all the 4 parathyroid glands were meticulously identified and preserved in all the cases. De-vascularized glands were auto transplanted in the ipsilateral Sternocleidomastoid muscle. Serum PTH within 1 hour of specimen removal and 24 hours later, along with Serum calcium on post-operative days 1,3 and 5 were collected for analysis.

Table (1): Distribution of age and sex of participants enrolled

Age	
<50 years	15
>50 years	10
Sex (Median Age)	
Male	48.63 ± 12.44
Female	49.33 ± 10.52

PTH assay was done by Electrochemiluminescence Immunoassay (ECLIA) technique and was validated before the use in study. The patients were categorized as low or high risk for hypocalcemia within 3 hours of surgery. We considered serum calcium value between 8 – 10 mg /dl as normal, 7 – 8 mg /dl as mild hypocalcemia, less than 7mg/dl as significant hypocalcemia. and those patients without clinical symptoms and value less than 8 mg/dl as biochemical hypocalcemia. Those patients who had mild hypocalcemia or biochemical hypocalcemia were treated with oral calcium alone or with Vitamin D supplements, and those with significant hypocalcemia were treated with Intravenous calcium.

All the Patients who develop hypocalcemia were discharged only when asymptomatic or serum calcium becomes normal. For those patients who were discharged earlier, Day 3 and Day 5 calcium values were collected through phone calls and advised to review if significantly low. Patients who were operated for thyroid carcinoma were given adjuvant radioactive ablation when indicated and followed every 3 monthly with serum thyroglobulin and Ultrasound neck annually as per our institute protocol.

RESULTS

Between October 2021 to June 2022, A comparable number of patients with each type of thyroid disease like Adenomatous hyperplasia, Multinodular goiter, Hashimoto thyroiditis, Papillary carcinoma and Follicular carcinoma of 25 patients were enrolled. Out of these nine patients were operated for carcinoma of thyroid and out of which 2 patients underwent total thyroidectomy with Central Compartment Neck Dissection (CCND) and ipsilateral neck dissection. Among this, three patients had biochemical hypocalcemia.

There was no significant difference in the PTH value measured within 1hr of surgery vs 24hrs post-surgery(p=0.329). The median PTH value for the patient who did not require calcium supplements was 19 (8.91-68.3). The median PTH who required calcium supplement (oral/intravenous supplement) was 5.25 (3.3-8.39). The lowest PTH (3.3) was recorded in a patient who underwent completion total thyroidectomy. Her pre-operative PTH was at the lower limit of normal 15. Also, patient who underwent neck node (n=2) dissection for carcinoma of thyroid had lower PTH compared to other patients who had hypocalcemia after total thyroidectomy. Patient who was

normocalcemic (n=22) in the immediate post operative period did not require calcium supplements during the follow up. None of the symptomatic patient had PTH >15pg, the median PTH value was 5.25 pg. Those patients who required calcium supplements were tapered slowly with mean time of 15 days. The mean post-operative stay was 2.25±0.46, and 4.07±1 **(Table 2)**.

None of the patient developed permanent hypocalcemia, and those patients who required calcium supplements were tapered slowly within 2 weeks. Sensitivity, or the proportion of true positives, is a test's capacity to accurately identify individuals who have a particular ailment. Sensitivity and specificity can be defined in relation to a "gold standard test" if the actual state of the ailment cannot be determined.The sensitivity of the test was 92.3% specificity was 77.7%, positive predictive value was 85.7%. Negative predictive value was 87.5% (**Figure 1**).

Table (2): Distribution of symptomatic hypocalcemia and length of hospital stay of participants enrolled

Symptomatic hypocalcemia	
Yes	3
No	22
Length of hospital stay	
Patient does not required calcium	21.09 ±0.91
Patient required calcium	2.07±0.93

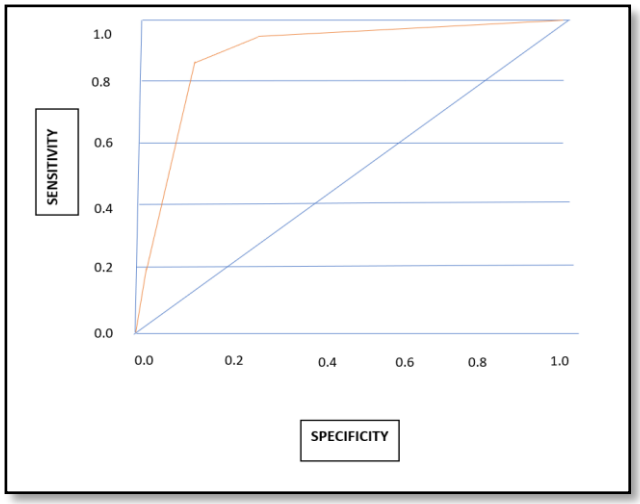

Figure (1): ROC with Area under curve of 92%

DISCUSSION

Globally, thyroid disorders are common [5, 6]. Many disorders are curable with medication. However, a considerable number of people require surgical procedures, including thyroidectomies. Surgery is performed for a variety of reasons, including pressure symptoms, toxicity, retrosternal expansion, malignant goiter, cancer suspicion, and patient requests [7, 8].

Thyroidectomies are generally safe surgeries, and patients are discharged from the hospital 48 hours following the procedure. Hospital stays are prolonged when hypocalcemia or reactive bleeding occurs. Although studies have reported a frequency ranging from 0.36 to 4.3%, reactionary hemorrhage is incredibly rare [9].

Serial monitoring of serum and ionized calcium levels is recommended, along with monitoring for hypocalcemia symptoms (e.g., Trousseau and Chvostek signals) and numbness and paresthesia in the perioral/extremities. Some patients may see a progressive drop in serum calcium levels 5–7 days following surgery. If a good marker for hypocalcemia could be identified, postoperative observation may be limited to 24 hours. Additionally, it might help prevent delayed hypocalcemia.

Although a number of factors have been identified as influencing the likelihood of postoperative hypocalcemia, none of them has been proven to be a reliable indicator of this condition. Numerous studies have used the PTH assay to predict hypocalcemia; however, because of its short half-life, there was no standard time for measurements, thus additional samples were taken from the same patients [10].

We discovered that the PTH test measured at different intervals did not significantly differ from one another, and that measuring PTH within an hour was a more accurate and early predictor of hypocalcemia, which was consistent with previous study [11].

Following surgery, many experts advise patients undergoing a total thyroidectomy to have regular oral calcium and vitamin D supplements [12]. They assert that regular calcium and vitamin D supplementation may prevent hypocalcemia symptoms in patients with false-negative postoperative PTH.

Furthermore, the development of severe hypocalcemia may be less severe in patients who receive frequent supplements than in those who do not, which makes treatment easier to handle. Additionally, following surgery, it would be permissible to skip obtaining recurrent calcium and PTH measurements. However, **Singer et al.** [13] found that 0.7% of their patients needed intravenous calcium to address severe hypocalcemia, while 7.5% of their patients experienced hyper-calcemic symptoms despite taking frequent supplements.

In another studies, 53 patients (37.6%) had a decrease in blood PTH three hours after complete thyroidectomy. Of them, 75.5% experienced hypocalcemia by 24 hours following surgery, and 100% experienced hypocalcemia within 48 hours [14].

In a study done by **Dugani *et al.*,** PTH readings taken four hours after surgery demonstrated a 51% sensitivity, 100% specificity, and a high correlation between the decline in PTH levels and postoperative hypocalcemia [15].

Electrochemiluminescence Immunoassay (ECLIA) method was used to perform the PTH assay. This method was quicker, and within three hours after surgery, patients were classified as either low or high risk for hypocalcemia. Serum calcium values between 8 and 8.5 were regarded as mild hypocalcemia; values below 8 or accompanied by clinical symptoms were regarded as serious hypocalcemia. Vitamin D and calcium supplements were administered orally to individuals with mild hypocalcemia, while intravenous calcium was administered to those with severe hypocalcemia. While age, gender, and the degree of dissection can all predict hypocalcemia, classifying the patient as low or high risk necessitates a precise post-operative study. However, the extent of the surgery corresponded well with the PTH value. The patients who had neck dissection had Low PTH value in the immediate post operate period and required calcium supplements which was more rapid, that

patients could be categorized as low or high risk for hypocalcemia within 3 hours post-surgery.

Conclusion:

After thyroidectomy, hypocalcemia develops in a complex way. Early detection of hypocalcemia after surgery allows for safe and timely discharge, as well as the timely delivery of vitamin D and calcium supplements to prevent symptoms. Therefore, we have concluded that taking a PTH measurement within an hour and 24 hours aids in the early detection of patients who may be at risk of hypocalcemia.

Ethical Statement:

Informed consent of all patients included in the study was obtained. The Ethics Committee approved the study design and methodology.

Conflict of interest: none

Financial Disclosure: None

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