

Early prediction of post-thyroidectomy hypocalcemia by early parathyroid hormone measurement



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AIM: Hypoparathyroidism is the most common complication of total thyroidectomy (TT). Postthyroidectomy hypocalcemia occurs 24 to 48 hours after the operation. It prolongs the length of hospital stay, even though transient in most cases. The aim of this study was to predetermine the patients who may develop postthyroidectomy hypocalcemia by using early postoperative serum intact parathormone (iPTH) and calcium (Ca^{2+}) measurements, and to investigate the effects of early initiated oral calcium and vitamin D treatments on the development of transient hypocalcemia.

MATERIAL AND METHODS: Patients who underwent TT after initiation of the early iPTH measurement protocol in January 2013 were included into the study group (Group 1, $n=202$). The control group (Group 2) was composed of 72 patients who underwent TT before the protocol. Prior to the initiation of the protocol, Ca^{2+} was measured instead of iPTH. In the study group, the serum Ca^{2+} and iPTH levels were measured before surgery, and 1 and 24-hours after. A calcium level below 8 mg/dL was accepted as biochemical hypocalcaemia, and a iPTH level under 15pg/mL was accepted as hypoparathyroidism. In the study group, patients with below normal iPTH levels were treated with prophylactic oral calcium and vitamin D.

RESULTS: In Group 1, 15.8% ($n=32$) of the patients had hypoparathyroidism on the 1h and 24 h iPTH measurements. There was no statistically difference with regard to PTH levels measured in the postoperative 1st hour and at the 24th hour ($p= 0.078$). Biochemical hypocalcaemia developed in 16 (7.9%) and 13 (18%) patients in Groups 1 and 2, respectively, 24 hours after thyroidectomy ($p<0.05$). Mean length of hospital stay was 2.17 and 3.26 days in the study and control groups ($p<0.001$).

CONCLUSIONS: We believe that the measurement of iPTH levels one hour after thyroidectomy, when compared to levels at 24 hours after procedure, is a safe, reliable, and adequate method for the effective management of plausible postthyroidectomic hypocalcemia. It yields significantly shorter hospital stay periods.

KEY WORDS: Calcium, Hypoparathyroidism, Postoperative complication, Total thyroidectomy

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Introduction

The close proximity of the parathyroid glands to the thyroid capsule and the recurrent laryngeal nerve, as well as their fragile blood supply makes hypocalcemia the most common complication of thyroid surgery¹⁻³. Recent studies have reported transient hypocalcemia rates as high as 30%, and permanent hypocalcemia rates between 0.5 and 5%⁴⁻⁶.

The measurement of serum calcium levels has been insufficient to predict those patients who will develop post-thyroidectomy hypocalcemia. Thus measurement of the levels of intact parathyroid hormone (iPTH), which has a short half-life and reflects the functions of the parathyroid more rapidly, has been suggested^{7,8}.

The aim of this study was to investigate the efficacy of serum iPTH levels, measured one hour after total thyroidectomy (TT), in the detection of patients who will develop hypocalcemia, and to assess whether iPTH levels measured at 1 hour show any changes in subsequent measurements. The study also aimed, by using iPTH levels, to assess the efficacy of early initiated oral calcium and vitamin D treatments in preventing symptomatic hypocalcemia in patients expected to develop hypocalcemia.

Materials and Methods

The results from 202 patients who underwent TT for nontoxic nodular goitre after the initiation of the clinical protocol, which utilized routine iPTH measurements for the detection of postthyroidectomy hypoparathyroidism, were retrospectively analyzed with respect to the postoperative parathyroid functions (Group 1, study group). Patients with hyperthyroidism, substernal goitre, parathyroid disease together with nodular goitre, and with history of previous thyroid or neck operations were excluded. In addition, those with completion thyroidectomy and neck dissection were also excluded.

The control group consisted of 73 patients who had undergone TT within the 12 months period prior to the initiation of the study protocol and who did not have the exclusion criteria, as well. Total calcium levels in the venous blood samples taken preoperatively and on postoperative days 1 and 2. The clinical signs of symptomatic hypocalcemia were compared with the study group. Hypocalcemic patients in this group underwent twice-daily assessment of serum calcium levels until discharge.

In the study group (Group 1, n=202), a venous blood sample was obtained before, one hour and one day after the operation, and iPTH level was measured. Normal

iPTH level was accepted as 15-88 pg/ml. Patients with iPTH levels under 15 mg/dl at the postoperative first hour blood sample received prophylactic treatment with oral calcium (3 g/day), and vitamin D (1µg / day). Serum total calcium levels were determined from the venous blood samples drawn before the operation, and 1 and 2 days after the operation.

A serum total calcium level below 8 mg/ml was defined as hypocalcemia. The presence of laboratory findings alone was defined as asymptomatic hypocalcemia. The presence of paresthesia, muscle spasm, Chvostek or Trousseau signs along with laboratory findings was defined as symptomatic hypocalcemia. In hypocalcemic patients, serum calcium levels were measured twice a day until the patients were discharged.

Total thyroidectomy was performed with extracapsular dissection. In all patients, the recurrent laryngeal nerve was seen and preserved during surgery. Additional dissection for exposing the parathyroid glands was not performed, however, the presence of adequate perfusion was confirmed in parathyroid glands, which were seen during the operation. The thyroidectomy specimen was macroscopically examined in the operating room in regard to accidentally removed parathyroid glands.

To analyze the data, the results obtained from the two groups were evaluated using Fischer's exact test, and Pearson Chi-Square test for comparisons between categorical variables. Student t-test was used for numerical variables with normal distribution and Mann-Whitney U test was applied, when distribution was not normal. We considered a p value < 0.05 was considered to be statistically significant.

Results

The study group (group 1) included 202 patients with a mean age of 45.6 years (range: 17-69). The control group (group 2) consisted of 73 patients with a mean age of 43.4 years (range: 19-67). Two groups were similar considering demographic features (Table 1). Preoperative calcium levels did not show a statistically significant difference. Patients in both groups underwent TT, and there were no accidentally removed parathyroid

TABLE I - Demographics and postoperative data of patients

	Group 1 (study group; n=202)	Group 2 control group; n=73)	p value
Age (mean ±SD)	45.6± 14	43.4± 12	0.177
Gender (M/F)	38 / 164	11 / 62	0.592
Asymptomatic hypocalcemia, n, %	16 (7.92 %)	13 (18%)	0.025
Symptomatic hypocalcemia, n, %	8 (3.96 %)	9 (12 %)	0.019
Hypoparathyroidism, n, %	32 (15.84 %)	13 (18%)	0.701
Mean hospital stay, days	2.17±0.5	3.26±1	<0.01

glands detected in either the intraoperative specimens examinations or postoperative histopathological studies. In 32 of the 202 patients in the study group (15.8%), the serum PTH levels measured on the postoperative 1st hour and 1st day were below normal levels. In these 32 patients, comparison of the mean serum PTH levels between postoperative 1st hour versus 1 day did not show any statistical significance ($p=0.078$). In the remaining 170 patients in this group, whose PTH levels were within normal limits in the 1st hour measurements, the serum PTH levels on the postoperative day one were also within normal limits. Comparison of the serum PTH levels in these patients between the 1st hour versus 1st day did not also reveal any statistical significance ($p=0.089$).

Postoperative hypoparathyroidism was similar between Group 1 and 2 (15.8% vs. 18%, respectively, $p=0.701$). Serum calcium levels measured 24 hours after the operation were below 8 mg/dl in 16 patients (7.9%) in the study group, and 13 (18%) in the control group ($p=0.025$). Symptomatic hypocalcemia developed in 8 patients (3.9%) in the study group, and 9 (12.5%) in the control group, the difference between the two groups was statistically significant ($p=0.019$). Mean length of stay in the hospital was 2.17 days in the study group, and 3.26 days in the control group, the difference was statistically significant ($p<0.001$).

Discussion

The popularity of ambulatory procedures in endocrine surgery has increased in recent years. However, TT is associated with high rates of transient hypocalcemia, which can be detected at least 24-48 hours later. This condition both prolongs the length of stay and negatively affects patient comfort. In addition, some of the patients may be discharged with normal calcium levels 48 hours after the operation, yet they may require readmission due to signs of hypocalcemia in the late period (postoperative 5-7 days)⁹.

Previous studies have advocated routine prescription of oral calcium after the operation to prevent postthyroidectomy hypocalcemia, and thus enable earlier discharge from the hospital^{10,11}. However, this protocol may lead to unnecessary treatment in some patients and occasionally to hypercalcemia¹².

Measurement of iPTH is routinely performed during parathyroid surgery, as the half-life of iPTH is very short (3.5-5 minutes)¹³⁻¹⁵. In the last decade, it has been suggested that ischemia of parathyroid gland is one of the most important reasons for hypoparathyroidism and iPTH measurement can also be beneficial for predicting postoperative hypocalcemia in patients undergoing TT¹⁶⁻¹⁸. However, timing of blood sampling for PTH still remains unclear. This time period ranges from ten-minutes after thyroidectomy to postoperative 48h¹⁹⁻²². In

our clinical practice, for patient undergoing TT, we initiated a new protocol for PTH measurement to predict postoperative hypocalcemia. Based on the clinical protocol we constructed 3 years ago, iPTH was measured 1 and 24 hours after the operation. The aim of the 1st hour measurement was to provide an early detection of patients who would develop hypocalcemia, and the aim of 24th hour measurement was to control if there were any significant changes in iPTH levels. In the study group, both postoperative 1st hour and 24th hour measurements revealed no significant differences between those patients with normal iPTH levels and those with hypoparathyroidism. Also, none of the patients with normal iPTH levels showed a significant decrease to below normal levels on the first postoperative day. Our results were comparable with the literature^{17,18}. We believe that this outcome is associated with the short half-life of iPTH. Intraoperative ischemia of the parathyroid glands causes immediate emergence of symptoms that do not show any changes up to 24 hours.

In our study, the absence of any statistically significant differences between mean serum iPTH levels at the postoperative 1st and 24th hours suggested that measuring iPTH levels on the postoperative 1st hour was effective and reliable in the prediction of postoperative hypoparathyroidism. Thus, patients who had normal iPTH levels at the 1st hour could be safely discharged from the hospital.

During the study period, the patients, who were diagnosed with hypoparathyroidism in the postoperative 1st hour, received prophylactic calcium and vitamin D, before the emergence of signs of hypocalcemia. In the study group, hypocalcemia developed in half of the patients with postoperative hypoparathyroidism. And, only 8 of these patients with biochemical hypocalcemia had hypocalcemia symptoms. With regard to hypocalcemia, comparison of the results between two groups showed a statistically significant difference. Therefore, we suggest that diagnosis of the patients having hypoparathyroidism on the postoperative 1st hour, and administration of prophylactic calcium and vitamin D can decrease the development of both symptomatic and asymptomatic hypocalcemia. Likewise, several studies have provided the efficacy of prophylactic calcium and vitamin D on prevention of the development of symptomatic hypocalcemia in patients with hypoparathyroidism detected in the postoperative 1st hour²⁵⁻²⁷.

It has been advocated that ambulatory thyroid surgery can be safely performed when postoperative hypocalcemia is prevented²⁸⁻³⁰. Considering the results of our clinical protocol, prophylactic calcium and vitamin D supplementations based on 1st hour iPTH measurement significantly decreased the length of hospital stay. We believe that early discharge of patients with normal iPTH levels, as well as the prevention or immediate correction of hypocalcemia by the prophylactic administration of calcium and vitamin D, did affect this outcome.

Conclusions

It is effective and adequate method to perform an iPTH measurement in the 1st postoperative hour following thyroidectomy in the detection and management of post-thyroidectomy hypocalcemia. In addition, it provides the additional benefit of shorter hospital stay.

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