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An early predictor of postoperative hypocalcemia: parathyroid hormone levels 1 hour after thyroidectomy

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ABSTRACT

Background: The present study compares ionized calcium (Ca²⁺) levels with preoperative serum PTH and with those obtained at 1, 6 and 24 hours after total thyroidectomy with an emphasis on the 1-hour PTH (PTH-1) and the subsequent development of hypocalcemia.

Methods: This is a retrospective study which consisted the cases of consecutive patients undergoing total or completion thyroidectomy between August 2010 and January 2012.

Results: In this study, 200 patients were studied, out of which 24 (12%) were males and 176 (88) were females. The median age of patients in the entire cohort was 60 years. 151 (75.5%) patients underwent total thyroidectomy and 49 (24.5%) patients underwent complete thyroidectomy for malignancy of the entire cohort. 160 (80%) patients had been diagnosed of primary thyroid cancer. 40 (20%) were diagnosed of benign cancer. The mean PTH levels showed significantly higher at 24 hours postoperative in eucalcemic patients, but decreased by PTH-24. The r coefficients were compared between PTH-1, PTH-6 and PTH-24 were 0.85 and 0.99 thus reflecting the relative stability of PTH measurements within first 24 hours postoperative. Hypocalcemia (normal range-1.1-1.32 mmol/L) was 8 (4%) at 1 hour, 20 (10%) at 6 hour and 96 (48.2%) at 24 hour respectively. Factor PTH-1 >1.5 pmol/L, the Ca^{+2} <1.1 mmol/L were 8, the Ca^{+2} >1.1 mmol/L were 68, the Ca^{+2} >1.1 mmol/L were 68, the Ca^{+2} >1.1 mmol/L were 0.

Conclusions: Those who are at risk of hypocalcemia 24 hours postoperatively, our results suggest that PTH-1 is an excellent predictor. To avoid hypocalcemia, therapy with calcitriol should be started if PTH-1 is less than 1.5 pmol/L.

Keywords: Hypocalcemia, Parathyroid harmone, Thyroidectomy

INTRODUCTION

After completion of thyroidectomy, is often associated with significant patient morbidity and a long hospital stay. In this case, parathyroid dysfunction leading to hypocalcemia is not uncommon. With surgical specimen, parathyroid tissue is inadvertently resected. Auto transplantation of normal, devitalized glands into the skeletal muscle should be done when recognized

intraoperative. Traumatic injury to the parathyroid results in the observed fall in parathormone (PTH) levels during thyroidectomy leading to either transient ischemia or even frank infarction of the glands. The PTH hyposecretion may be relatively transient (1.6%-68%) or may be permanent (0.4%-33%).^{2,3} The parathyroid glands secretes intact PTH in response to serum ionized calcium levels. Intact PTH is an 84-amino acid protein and extracellular calcium ions directly control the release of

PTH, as mediated through the cell surface calcium receptor of the parathyrocyte.⁴

The intact PTH has a half-life in minutes and can be reliably assayed. It is degraded into several smaller proteins with variable half-lives and biologic activity. The delay in appearance of postoperative hypocalcemia is up to 48 hours depending on the levels of such biologically active peptides as well as the patient's vitamin D and electrolyte status and the presence or absence of "hungry" bone, among other factors. Early pharmacologic support with calcium, magnesium and calcitriol can potentially keep high-risk patients eucalcemic and asymptomatic, thereby avoiding morbidity is because of the lag between the hypo secretion of PTH and the development of symptomatic hypocalcemia. As a fat-soluble vita- min, its pharmacokinetics are such that an increase in serum calcium may take 24-48 hours early prophylactic administration of calcitriol is important in maintaining eucalcemia in high-risk patients.5,6

Thus, the early identification of post-thyroidectomy patients at risk of hyperparathyroidism and hypocalcemia would allow for the early introduction of calcitriol. Patients at low risk of post- thyroidectomy hypocalcemia can be spared the discomfort of excessive blood tests and can reliably be discharged without fear of symptomatic hypocalcemia. The present study compares ionized calcium (Ca²⁺) levels with preoperative serum PTH and with those obtained at 1, 6 and 24 hours after total thyroidectomy with an emphasis on the 1-hour PTH (PTH-1) and the subsequent development of hypocalcemia.

METHODS

This is a retrospective study which consisted the cases of consecutive patients admitted in general surgery department for total or completion thyroidectomy at Rangaraya Medical College, Kakinada between August 2010 and January 2012.

Inclusion criteria

Patients undergoing total or completion thyroidectomy

Exclusion criteria

Patients with coexisting parathyroid or renal pathology. The data were generated as part of our adopted thyroidectomy care pathway.

The following information were recorded namely age, sex, indication for surgery either benign or malignant lesion, or type of surgery namely complete or total thyroidectomy. Recording of preoperative serum ionized calcium (Ca) and PTH levels were done and PTH levels at 1,6 and 24 hours were also recorded.

PTH level was measured using the immulite assay immunochemiluminometric test.

Patients who developed symptomatic hypocalcemia were administered oral calcium supplementation with or without calcitriol. Normal range of serum calcium is 1.1-1.32 mmol/L but patients who have less than 1.10 mmol/L are considered as hypocalcemic. The normal PTH level in our laboratory is 7 to 50 pg/mL. Patients who were suffering from numbness, paresthesis, a positive Chyostek or Trousseau sign, cardiac arrhythmias or muscle cramps were symptomatic. 0.9 mmol/L or less of calcium was considered as severe hypocalcemia. Calcium gluconate 10% was administered to patients suffering from severe hypocalcemia.

Patients ultimately fell into 4 groups

High risk, eucalcemic (adequate replacement)

These patients had 1 hour PTH level < 12 pg/ml, received calcium and calcitriol supplementation, did not develop symptoms of hypocalcemia, did not have documented biochemical hypocalcemia (corrected calcium ≤ 1.9 mmol/l), and did not require increased supplementation.

High risk, hypocalcemic (inadequate replacement)

These patients had 1 hour PTH level < 12 pg/ml, received calcium and calcitriol supplementation, but developed symptoms of hypocalcemia, had documented biochemical hypocalcemia (corrected calcium ≤1.9 mmol/l), and required increased supplementation.

Low risk, eucalcemic (true negative prediction of hypocalcemia)

These patients had 1 hour PTH level \geq 12 pg/ml, and did not develop symptoms of hypocalcemia, did not have documented biochemical hypocalcemia, and did not require supplementation.

Low risk, hypocalcemic (false negative prediction of hypocalcemia)

These patients had 1 hour PTH level≥12 pg/ml, but developed symptoms of hypocalcemia, had documented biochemical hypocalcemia, and required calcium replacemen.

RESULTS

In this study, 200 patients were studied, out of which 24 (12%) were males and 176 (88) were females. The median age of patients in the entire cohort was 60 years. 151 (75.5%) patients underwent total thyroidectomy and 49 (24.5%) patients underwent complete thyroidectomy for malignancy of the entire cohort. 160 (80%) patients had been diagnosed of primary thyroid cancer. 40 (20%) were diagnosed of benign cancer.

Table 1: Incidence of hypoparathormonemia at 1, 6 and 24 hours postoperative and it showed a plateau early.

Incidence of hypoparathormonemia and hypocalcemia after total thyroidectomy (n = 200)		
Group %		
Post thyroidectomy	PTH<1.5 pmol/L	Ca ²⁺ <1.1 mmol/L
1 hour	38.7	4
6 hour	42.5	10
24 hour	48.2	48.2

The mean PTH levels in hypocalcemia patients attained an early plateau. The mean PTH levels showed significantly higher at 24 hours postoperative in eucalcemic patients, but decreased by PTH-24. The r coefficients were compared between PTH-1, PTH-6 and PTH-24 were 0.85 and 0.99 thus reflecting the relative stability of PTH measurements within first 24 hours postoperative. Hypocalcemia (normal range-1.1-1.32 mmol/L) was 8 (4%), 20 (10%) and 96 (48.2%) at 1 hour, 6 hour and 24 hour respectively.

Table 2: Sensitivity and specificity analysis of PTH-1 measurement comparing Ca⁺²-24 and hypocalcemia.

Factor	Ca ⁺² <1.1 mmol/L	Ca ⁺² >1.1 mmol/L
PTH-1 >1.5 pmol/l	8	124
PTH-1 ≤1.5 pmol/l	68	0
Total	7 6	124

Table 2 shows for factor PTH-1 >1.5 pmol/L, the Ca^{+2} <1.1 mmol/L were 8, the Ca^{+2} >1.1 mmol/L were 124, for factor PTH-1 \leq 1.5 pmol/L, the Ca^{+2} <1.1 mmol/L were 68, the Ca^{+2} >1.1 mmol/L were 0.

Table 3: Sensitivity, specificity.

Sensitivity	90%
Specificity	100%
NPV	95%
PPV	100%

NPV- negative predictive value; PPV- positive predictive value.

DISCUSSION

Many studies have been reported for parathyroid hormonal levels after thyroidectomy. Qahtani AA et al they prospectively reviewed the cases of consecutive patients undergoing total or completion thyroidectomy. Ionized calcium (Ca²⁺) and intact PTH levels were measured preoperatively and at 1-, 6- and 24-hour intervals postoperatively. The specificity, sensitivity, negative and positive predictive values of the 1-hour PTH serum levels (PTH-1) in predicting 24 hours post-thyroidectomy hypocalcemia and eucalcemia were

determined. The results were they reviewed the cases of 149 patients. Biochemical hypocalcaemia (Ca^{2+} <1.1 mmol/L) developed in 38 of 149 (25.7%) patients 24 hours after thyroidectomy. The sensitivity, specificity, positive and negative predictive values of a low PTH-1 were 89%, 100%, 97% and 100%, respectively.

They concluded that that PTH-1 levels were predictive of symptomatic hypo-calcemia 24 hours after thyroidectomy. Routine use of this assay should be considered, as it could prompt the early administration of calcitriol in patients at risk of hypocalcemia and allow for the safe and timely discharge of patients expected to remain eucalcemic. Felipe Augusto Brasileiro Vanderlei et al in their study, forty patients who underwent total thyroidectomy were studied prospectively.

Ionized serum calcium and PTH were measured after induction of anesthesia, one hour (PTH1) and one day after surgery (PTH24). Patients were evaluated for symptoms of hypocalcemia and treated with calcium and vitamin D supplementation as necessary. The results were that Symptomatic hypocalcemia developed in 16 patients. Symptomatic patients had significant lower PTH1 and greater drops in PTH levels. The selection of 12.1 ng/L as PTH1 level cutoff level divided patients with and without symptoms with 93.7% sensitivity and 91.6% specificity. The selection of 73.5% as the cutoff value for PTH decrease resulted in 91.6% sensitivity and 87.5% specificity.

This study concluded that PTH1 levels and the drop in PTH levels are reliable predictors of developing symptomatic hypocalcemia after total thyroidectomy. Jeffrey Saad Jumaily, BS et al in their study, individual patient data were obtained from 3 studies (152 patients) that fulfilled our criteria (using PTH assay within hours postthyroidectomy to predict symptomatic hypocalcemia). ¹⁰

The results were that changes in combined PTH and calcium threshold levels checked 1 to 6 hours after thyroidectomy were excellent in predicting postoperative hypocalcemia. A decrease in PTH of 60%, coupled with a simultaneous decrease in calcium of 10%, 5 to 6 hours postoperatively resulted in a sensitivity and specificity of 100%. However, combined PTH and calcium threshold changes were not significantly better than using PTH threshold changes alone. They concluded that threshold changes in serum calcium and PTH, checked hours after surgery, can be used together to accurately predict whether a patient will become hypocalcemic after thyroidectomy. Rio LD et al conducted a study of eightytwo patients who underwent total or completion thyroidectomy from February 2009 to March 2010 were enrolled in this prospective study to determine the best timing and cutoff point of parathyroid hormone to predict hypocalcemia.11

Patients with any condition that could interfere with calcium homeostasis were excluded from the survey. Parathyroid hormone and serum calcium levels were determined preoperatively, immediately after surgery and a number of hours later. The results were that treatment for hypocalcemia was required in 16.7% of patients. A percent of delayed decrease in parathyroid hormone was chosen as the best measurement to predict hypocalcemia. An 80% or higher decrease in delayed parathyroid hormone levels had 100% sensitivity (95% CI: 77.2%-100%) and 8 specificity (95% CI: 77%-93%) for selected patients for early dis- charge. Using this test, 73.2% of the patients could have been discharged 24 hours after surgery.

A 98% decrease in delayed parathyroid hormone levels could select candidates for early calcium replacement with 98.6% specificity (95% CI: 92.2%-99.7%). This study concluded that the decrease in postoperative delayed parathyroid hormone levels is a good predictor of post-thyroidectomy hypocalcemia. A decrease of 80% or more in delayed parathyroid hormone level is a test with excellent sensibility and specificity for selecting candidates for early discharge. The 98% cutoff point has high specificity for selecting patients for early calcium replacement.

CONCLUSION

Those who are at risk of hypocalcemia 24 hours postoperatively, our results suggest that PTH-1 is an excellent predictor. To avoid hypocalcemia, therapy with calcitriol should be started if PTH-1 is less than 1.5 pmol/L.

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