AN EARLY PREDICTOR OF POSTOPERATIVE HYPOCALCAEMIA- PARATHYROID HORMONE LEVELS 1 HOUR AFTER THYROIDECTOMY
Dova Subba Rao1, Pagoti Sankara Rao1, Pigilam Syam Prasad2

1Associate Professor, Department of General Surgery, NRI Institute of Medical Sciences, Sangivalasa, Visakhapatnam.
2Senior Resident, Department of General Surgery, NRI Institute of Medical Sciences, Sangivalasa, Visakhapatnam.
3Professor, Department of General Surgery, NRI Institute of Medical Sciences, Sangivalasa, Visakhapatnam.

ABSTRACT

BACKGROUND
The present study compares ionised calcium (Ca\(^{2+}\)) 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 hypocalcaemia.

MATERIALS AND METHODS
This is a retrospective study, which consisted the cases of consecutive patients undergoing total or completion thyroidectomy between August 2012 and January 2016.

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. Hypocalcaemia (normal range 1.1-1.32 mmol/L) was 8 (4%) at 1 hour, 20 (10%) at 6 hours and 96 (48.2%) at 24 hours, 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 124 for factor PTH 1≤1.5 pmol/L, the Ca\(^{2+}\) <1.1 mmol/L were 68, the Ca\(^{2+}\) >1.1 mmol/L were 0.

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

KEYWORDS
Thyroidectomy, Parathyroid Hormone, Hypocalcaemia.

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BACKGROUND
After completion of thyroidectomy is often associated with significant patient morbidity and a long hospital stay. In this case, parathyroid dysfunction leading to hypocalcaemia is not uncommon. With surgical specimen, parathyroid tissue is inadvertently resected. Autotransplantation of normal, devitalised glands into the skeletal muscle should be done when recognised intraoperatively. Traumatic injury to the parathyroids results in the observed fall in Parathormone (PTH) levels during thyroidectomy leading to either transient ischaemia or even frank infarction of the glands. The PTH hyposcretion maybe relatively transient (1.6%-68%) or maybe permanent (0.4%-33%). The parathyroid glands secrete intact PTH in response to serum ionised 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. The intact PTH has a half-life of 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 hypocalcaemia 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 hyposcretion of PTH and the development of symptomatic hypocalcaemia. As a fat-soluble vitamin, its pharmacokinetics are such that
an increase in serum calcium may take 24-48 hours. Early prophylactic administration of calcitriol is important in maintaining eucalcaemia in high-risk patients. Thus, the early identification of post-thyroidectomy patients at risk of hypoparathyroidism and hypocalcaemia would allow for the early introduction of calcitriol. Patients at low risk of post-thyroidectomy hypocalcaemia can be spared the discomfort of excessive blood tests and can reliably be discharged without fear of symptomatic hypocalcaemia. The present study compares ionised calcium (Ca\(^{2+}\)) 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 hypocalcaemia.

**MATERIALS AND METHODS**

This is a retrospective study, which consisted the cases of consecutive patients admitted in General Surgery Department for total or completion thyroidectomy at NRI Institute of Medical Sciences, Sangivalasa, Visakhapatnam, between August 2012 and January 2016.

**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 and type of surgery namely complete or total thyroidectomy. Recording of preoperative serum ionised 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 hypocalcaemia 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 hypocalcaemic. The normal PTH level in our laboratory is 7 to 50 pg/mL. Patients who were suffering from numbness, paraesthesia, a positive Chvostek or Trousseau sign, cardiac arrhythmias or muscle cramps were symptomatic. 0.9 mmol/L or less of calcium was considered as severe hypocalcaemia. Calcium gluconate 10% was administered to patients suffering from severe hypocalcaemia.

Patients Ultimately Fell into 4 Groups-

1. **High-risk, eucalcaemic (adequate replacement).**

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

2. **High risk, hypocalcaemic (inadequate replacement).**

   These patients had 1 hr. PTH level < 12 pg/mL received calcium and calcitriol supplementation, but developed symptoms of hypocalcaemia had documented biochemical hypocalcaemia (corrected calcium ≤1.9 mmol/L) and required increased supplementation.

3. **Low risk, eucalcaemic (true negative prediction of hypocalcaemia).**

   These patients had 1 hr. PTH level ≥ 12 pg/mL and did not develop symptoms of hypocalcaemia, did not have documented biochemical hypocalcaemia and did not require supplementation.

4. **Low risk, hypocalcaemic (false negative prediction of hypocalcaemia).**

   These patients had 1 hr. PTH level ≥ 12 pg/mL, but developed symptoms of hypocalcaemia, had documented biochemical hypocalcaemia and required calcium replacement.

**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.

| Incidence of Hypoprothrombinemia and Hypocalcaemia after Total Thyroidectomy (n=200) Group Percentage |
|--------------------------------------------------|--------------------------------------------------|
| Post Thyroidectomy PTH<1.5 pmol/L Ca\(^{2+}\) <1.1 mmol/L |  |
| 1 hour | 38.7 | 4 |
| 6 hours | 42.5 | 10 |
| 24 hours | 48.2 | 48.2 |

**Table 1. Shows incidence of Hypoprothrombinemia at 1, 6 and 24 hours Postoperative and it Showed a Plateau Early**

The mean PTH levels in hypocalcaemia patients attained an early plateau. The mean PTH levels showed significantly higher at 24 hours postoperative in eucalcaemic 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. Hypocalcaemia (normal range - 1.1-1.32 mmol/L) was 8 (4%), 20 (10%) and 96 (48.2%) at 1 hour, 6 hours and 24 hours, respectively.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Ca(^{2+}) &lt;1.1 mmol/L</th>
<th>Ca(^{2+}) &gt;1.1 mmol/L</th>
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</thead>
<tbody>
<tr>
<td>PTH-1 &gt;1.5 pmol/L</td>
<td>8</td>
<td>124</td>
</tr>
<tr>
<td>PTH-1 ≤1.5 pmol/L</td>
<td>68</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>76</td>
<td>124</td>
</tr>
</tbody>
</table>

**Table 2. Shows Sensitivity and Specificity Analysis of PTH-1 Measurement Comparing Ca\(^{2+}\)-24 and Hypocalcaemia**
Table 2 shows for factor PTH-1 >1.5 pmol/L, the Ca\textsuperscript{2+} <1.1 mmol/L were 8, the Ca\textsuperscript{2+} >1.1 mmol/L were 124, for factor PTH-1 ≤1.5 pmol/L, the Ca\textsuperscript{2+} <1.1 mmol/L were 68, the Ca\textsuperscript{2+} >1.1 mmol/L were 0.

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>90%</th>
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<tbody>
<tr>
<td>Specificity</td>
<td>100%</td>
</tr>
<tr>
<td>NPV</td>
<td>95%</td>
</tr>
<tr>
<td>PPV</td>
<td>100%</td>
</tr>
</tbody>
</table>

Table 3. Shows Sensitivity, Specificity

NPV - Negative predictive value, PPV - Positive predictive value.

DISCUSSION

Many studies have been reported for parathyroid hormonal levels after thyroidectomy. Awad Al Qahtani et al,\textsuperscript{1} they prospectively reviewed the cases of consecutive patients undergoing total or completion thyroidectomy. Ionised calcium (Ca\textsuperscript{2+}) and intact PTH levels were measured preoperatively and at 1-, 6- and 24-hour intervals postoperatively. The sensitivity, specificity, positive and negative predictive values of the 1-hour PTH serum levels (PTH-1) in predicting 24-hour post-thyroidectomy hypocalcaemia and eucalcaemia were determined. The results were, they reviewed the cases of 149 patients. Biochemical hypocalcaemia (Ca\textsuperscript{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 hypocalcaemia 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 hypocalcaemia and allow for the safe and timely discharge of patients expected to remain eucalcaemic. Felipe Augusto Brasileiro Vanderlei et al\textsuperscript{9} in their study, 40 patients who underwent total thyroidectomy were studied prospectively. Ionised serum calcium and PTH were measured after induction of anaesthesia, one-hour (PTH1) and one day after surgery (PTH24). Patients were evaluated for symptoms of hypocalcaemia and treated with calcium and vitamin D supplementation as necessary. The results were that symptomatic hypocalcaemia 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 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 hypocalcaemia after total thyroidectomy. Jeffrey Saad Jumaily, BS et al\textsuperscript{10} in their study, individual patient data were obtained from 3 studies (152 patients) that fulfilled our criteria (using PTH assay within hours post-thyroidectomy to predict symptomatic hypocalcaemia). The results were that changes in combined PTH and calcium threshold levels checked 1 to 6 hours after thyroidectomy were excellent in predicting postoperative hypocalcaemia. 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 hypocalcaemic after thyroidectomy. Laura Del Rio et al\textsuperscript{11} conducted a study of 82 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 hypocalcaemia. 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 hypocalcaemia was required in 16.7% of patients. A percent of delayed decrease in parathyroid hormone was chosen as the best measurement to predict hypocalcaemia. An 80% or higher decrease in delayed parathyroid hormone levels had 100% sensitivity (95%, CI: 77.2%-100%) and 87% specificity (95%, CI: 77%-93%) for selecting patients for early discharge. Using this test, 73.2% of the patients could have been discharged 24 hrs. 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 hypocalcaemia. 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 at risk of hypocalcaemia 24 hours postoperatively, our results suggest that PTH-1 is an excellent predictor. To avoid hypocalcaemia, therapy with calcitriol should be started if PTH-1 is less than 1.5 pmol/L.

REFERENCES

[4]


