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Original Research Article

Intact PTH measurement 1 hour after total thyroidectomy as a predictor for patients at risk for developing symptomatic hypocalcaemia

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Abstract

Postoperative hypocalcaemia is one of the most common complications observed in patients undergoing total thyroidectomy with a report incidence ranging from 1.6% to 50%. Transient hypocalcaemia occur in up to 50% patients and permanent hypocalcaemia in 2%. Symptoms appear usually between 2nd to 5th postoperative days. In the absence of any reliable predictors of clinically relevant hypocalcaemia after total thyroidectomy, prolonged hospitalization to monitor serum calcium concentrations has been considered the standard of cure. To minimize postoperative complications and to permit an early and safe discharge, it is important to identify various methods to predict patients at high risk of developing significant hypocalcaemia, who are candidates for early treatment and patient at low risk who can be discharged early from hospital. We reviewed our experience in Yenepoya Medical College with 22 total thyroidectomies to determine the threshold value of 1 hour post total thyroidectomy iPTH level that can identify those at high risk for developing symptomatic hypocalcaemia. This is a prospective study done from Sept 2012 to Sept 2013. Based on our observations we concluded that, a 1 hour postoperative serum intact PTH <15pg/l has both sensitivity and specificity >90% for predicting patients at risk for developing post total thyroidectomy symptomatic hypocalcaemia.

Keywords: Parathyroid Hormone; Total thyroidectomy; Hypocalcaemia

1. Introduction

Total thyroidectomy has been established as the preferred operation of various thyroid pathologies. Hypocalcaemia is a common complication of that procedure and a variety of strategies for diagnosing and managing post thyroidectomy hypocalcaemia has been advocated. Symptoms usually appear 24 to 48 hours after surgery but even as early as 6 hours can happen. In the absence of reliable predictors of clinically relevant hypocalcaemia after total thyroidectomy, prolonged hospitalization to monitor serum calcium has been considered the standard of care. To minimize postoperative complications and to permit an early and safe discharge, it is important to identify

other ways to predict patients at high risk of developing significant hypocalcaemia. Use of intact PTH has been utilized to try to predict those patients at risk of developing hypocalcaemia.

2. Materials and Methods

This Study's design is prospective study. The study was conducted for a period of 12 months from September 2012 to September 2013. All patients with benign or malignant thyroid disorders undergoing total thyroidectomy with or without neck dissection in Yenepoya Medical College, Mangalore were allowed to take part in the study. Patients with Coexisting hypo/hyper parathyroidism, renal

dysfunction, Hypoalbuminemia were excluded from the study. But among the patients who were fulfilling the criteria, only 22 were willing to take part in the study.

2.1 Procedure

- Study involved determination of
 - > Serum calcium(preoperatively)
 - > Serum creatinine(preoperatively)
 - > Serum albumin(preoperatively)
 - > Serum iPTH 1 hour after completion of total thyroidectomy
 - > Serum calcium at 6,24 and 48 hours (postop)
- Evaluation of clinical findings suggestive of hypocalcaemia
 - > Perioral numbness
 - > Paraesthesia
 - > Tetany
 - > Chovstek sign
 - > Trousseau's sign
 - > Seizures

Patients with signs and symptoms were recorded as symptomatic. Patients were followed up for 3 days postoperatively and the lowest recorded serum calcium was taken into account

Intact PTH Assay

- The DEMEDITEC Intact PTH ELISA is intended for the quantitative determination of intact PTH in human serum.
- Expected Values

The geometric mean+2 standard deviations of the mean were calculated to be 13.9 to 75.1pg/ml for serum and 16.6 to 83.4 pg/ml for EDTA plasma.

2.3 Statistics

Reported incidence of Postoperative hypocalcaemia in total thyroidectomy patients ranges from 1.6 to 50 %. Transient hypocalcaemia occurs in

up to 50% patients. Permanent hypocalcaemia occurs in 2% of total thyroidectomy patients.

3.Results

3.1 Age

Patients were of varied age group, the youngest being 15 years and the oldest 72 years of age.72.73% of patients were in the age group 31-50 years

Mean age was 42.3years

<30 years = 2patients (9.1%)

31-40years=9 patients (40.91%)

41-50 years=7 patients (31.82%)

>50 years= 4 patients (18.18%)

Total = 22 patients (100%)

The mean age of males was 44 .8 years and for females 41.2 years.

Age did not have any significant correlation with post op hypocalcaemia.

3.2 Sex

There were total 6 males and 16 females in this study. 2 out 6 males and 4 out of 16 females developed post operative hypocalcaemia. There was no statistically significant difference in the occurrence of hypocalcaemia between males and females

3.3 Diagnosis

19 Patients were operated for MNG and 3 were operated for papillary carcinoma thyroid. Central compartment dissection was combined with total thyroidectomy in patients with papillary carcinoma thyroid.2 out of 3 patients with papillary carcinoma thyroid developed symptomatic hypocalcaemia whereas 4 out of 19 patients with MNG had symptomatic hypocalcaemia. Difference was statistically significant with p value of 0.001

Postoperative hypocalcaemia

A total of 7 patients developed hypocalcaemia (biochemical and / or symptomatic).

Table 1: Patients who developed postoperative hypocalcaemia

Hypocalcaemia	Number	Preoperative calcium - Mean (mg/dl)	Postoperative calcium-Mean (mg/dl)	1 Hour postoperative intact PTH-Mean (pg/ml)
YES	7	9.01	7.42	12.16
NO	15	9.089	8.66	36.56

There was no significant difference in the preoperative serum calcium levels in 2 groups (p=0.26). Mean postoperative serum calcium in hypocalcaemic patients was 7.42 mg/dl with a standard deviation of 0.58. Whereas the mean postoperative serum calcium in patients without hypocalcaemia was 8.66mg/dl with a standard deviation of 0.37. The difference was statistically

significant with a p value of 0.001. The mean 1 hour post operative serum intact PTH in hypocalcaemic patients was 12.16 pg/ml with a SD of 4.54. Where as in patients without hypocalcaemia intact PTH was 36.56 with a SD of 19.82. The difference was statistically significant with a p value of 0.001. 6 patients developed symptomatic hypocalcaemia and 6 patients had biochemical hypocalcaemia.

Symptomatic Hypocalcaemia

Table 2: Incidence of Symptomatic Hypocalcaemia

Symptoms	Frequency	Percentage
Yes	6	27.27
No	16	72.72

A total of 6 patients of 22 patients developed symptomatic hypocalcaemia. i.e. signs and/or symptoms. 2 patients had only signs whereas 4 patients had signs and symptoms.

Signs /Symptoms	Frequency
Perioral numbness	4
Paraesthesia	3
Carpal spasm	1
Laryngeal spasm	NIL
Seizures	NIL
Chovstek's sign	6
Trousseau's sign	NIL
ECG changes	NIL

Table 3: Mean, Standard Deviation and P Value

Symptoms		N	Mean	SD	T Test (P Value)
Preop Calcium (mg/dl)	Yes	6	9.250	0.759	0.082
	No	16	8.953	0.351	
Postop Calcium (mg/dl)	Yes	6	7.433	0.588	0.000
	No	16	8.688	0.392	
1Hour Intact PTH (pg/l)	Yes	6	11.67	03.34	0.000
	No	16	34.44	20.10	

The mean postoperative calcium was 7.433 mg/dl in symptomatic group whereas it was 8.688 mg/dl in asymptomatic group. The difference was statistically significant.

The mean 1 hour postoperative serum intact PTH was 11.67 pg/ml with a SD of 3.34 in

symptomatic group whereas it was 34.44 pg/ml with a SD of 20.20 in asymptomatic group. This was also statistically significant. By taking mean + 1SD as the cutoff value, a 1 hour postoperative serum intact PTH of <15.0pg/l would predict the patients at risk for developing symptomatic hypocalcaemia.

Table 4: Sensitivity, specificity, positive Predictive Value and Negative Predictive Value for 1 Hour postoperative Intact PTH

	Sensitivity	Specificity	Positive predictive value	Negative predictive value
1 Hour postop Intact PTH	91.66%	93.75%	84.62%	96.77%

For predicting patients at risk for developing post total thyroidectomy symptomatic hypocalcaemia, a 1 hour postoperative serum intact PTH value of <15 pg/l has a sensitivity of 91.66% and a specificity of 93.75%. There were 8.33% false negatives and 6.25% false positives.

4. Discussion

Various studies have been done all over the world to determine the methods that would predict development of post thyroidectomy hypocalcaemia. Study conducted in 2006 by Marcin *et al*[2], in which 3 blood samples for iPTH were taken in each patient preoperatively –baseline, at end of surgery-skin closure, and at 4 hour post operatively for predicting post thyroidectomy hypocalcaemia. It was concluded that iPTH serum level less than 10 pg/ml at 4 hour postoperative had the highest accuracy in predicting

serum calcium level below 2 mmol/l after total thyroidectomy.

Study conducted by Celestino *et al*[5] in which iPTH was measured preoperatively, at end of surgical procedure and at 2,4,6,24, and 48 hours after the surgery. It was concluded that a single iPTH level below the normal range (<10pg/ml) between 4 and 6 hours after the operation correctly predicted postoperative hypocalcaemia (sensitivity 94% and specificity 100%).

Another study was done by Graff *et al*[6], in which a single early postoperative intact PTH measurement 6-18 hours after surgery was found to be the most cost effective screening tool for hypocalcaemia. But even greater specificity can be achieved by combining those findings with a serum calcium measurement taken 6 hours postoperatively.

Roderick *et al*[10] did a study where iPTH was measured intraoperatively after the removal of

both lobes of thyroid. Its sensitivity for predicting post thyroidectomy hypocalcaemia was found to be 78.57%.

Since patients can develop symptoms of hypocalcaemia as early as 6 hours after thyroidectomy, it would be desirable to identify at risk patients very clearly in the postoperative period (within 2 hours) so that early supplementation of oral/parenteral calcium is possible to prevent the development of symptoms. Intraoperative I PTH has a low sensitivity (75-80%). Valerie *et al*[13] conducted a study where intact PTH measured at 1 hour postoperatively had a sensitivity of 96% in predicting patients developing hypocalcaemia after thyroidectomy.

In the present study a 1 hour postoperative serum intact PTH value of <15 pg/l has a sensitivity of 91.65% and sensitivity of 93.76% for predicting patients at risk for developing post total thyroidectomy symptomatic hypocalcaemia.

5. Summary

31.82% of patients in this study developed post total thyroidectomy hypocalcaemia. 27.3% of patients developed symptomatic hypocalcaemia. Malignancy with central compartment dissection was associated with high incidence of symptomatic hypocalcaemia. For predicting patients at risk for developing post total thyroidectomy symptomatic hypocalcaemia, a 1 hour post operative serum intact PTH value of <15 pg/ml had a sensitivity of 91.66%, so it can be used as an effective screening test to identify at risk patients.

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