Original Research Article

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Measurement of intact parathormone after one hour of total thyroidectomy: a predictor of symptomatic hypocalcemia

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ABSTRACT

Background: Hypocalcemia is one of the most common complications of thyroidectomy. Hence, parathyroid hormone (PTH) measurement can be used to predict patients at risk for developing significant postoperative hypocalcaemia after thyroidectomy. The present study was conducted with the objective to find out whether there is any correlation between intact PTH value and patients developing symptoms of hypocalcemia after total thyroidectomy and to determine the threshold value of 1 hour post total thyroidectomy (intact PTH level) that can identify those at high risk for developing symptomatic hypocalcemia.

Methods: Study involved determination of serum calcium, creatinine and albumin preoperatively, serum intact PTH, 1 hour after completion of total thyroidectomy (i.e. after the closure of skin incision), and serum calcium levels 6, 24 and 48 hours postoperatively. Clinical findings suggestive of hypocalcaemia were also watched for and recorded. Symptomatic signs and/or symptoms were recorded. The patients were followed up for 3 days post operatively and the lowest recorded serum calcium was taken into account. The results were tabulated and entered in Microsoft excel and analysed with spss 17 statistical software.

Results: 26% of the study population developed hypocalcemia. Intact PTH was found to be lower in patients who developed symptoms of hypocalcemia. There was a statisticantly significant correlation between the two groups. A one-hour Intact PTH value of 14 pg/ml was found to have high sensitivity (92.3%) and specificity (91.9%).

Conclusions: Hypocalcemia is the most common complication after total thyroidectomy. Intact PTH measurement one hour after total thyroidectomy can be used to predict the patients who will develop hypocalcemia after total thyroidectomy. Therefore, patients having low one-hour intact PTH value could be started on calcium supplementation and those having high PTH could be safely discharged early.

Keywords: Hypocalcemia, Parathyroid harmone, Total thyroidectomy

INTRODUCTION

Thyroidectomy is one of the common surgeries performed worldwide. Total thyroidectomy has been established as the preferred operation for a range of thyroid pathologies including thyroid cancer, multinodular goitre (MNG) and Graves' disease. Postoperative hypocalcaemia is the most common complication observed in patients undergoing total

thyroidectomy, with a reported incidence ranging from 1.6% to 50%.⁴⁻⁸ Transient hypocalcaemia occurs in upto 50% of patients and permanent hypocalcaemia in 2%.⁷ Only few of these patients develop symptomatic hypocalcaemia.

Symptoms usually appear 24 to 48 hours after surgery but even as early as 6 hours. It is not easy to predict which patients are prone to develop this complication and will require calcium and/or vitamin D supplementation. In the absence of any consistent prognosticators of clinically related hypocalcaemia after total thyroidectomy, extended hospitalization to monitor serum calcium concentrations has been considered as the standard ofcare. 9-11

Current health care practices require shorter hospitalisations after thyroidectomy to reduce the costs. To minimize postoperative complications and to permit an early and safe discharge, it is important to identify a method to predict patients at high risk of developing significant hypocalcaemia, who are candidates for early treatment, and patients at low risk who are well suited for early discharge, the usual practice of administering calcium supplements to all patients to allow for early discharge may mask the symptoms of hypocalemia. Besides this practice means that a high percentage of patients take unnecessary calcium supplements, which are unpleasant and could, in some cases, increase the risk of constipation, promote the development of calcium kidney stones, and inhibit iron and zinc absorption from food.

The cause of post thyroidectomy hypocalcaemia is multifactorial but mainly due to transient ischemia of the parathyroid glands or their inadvertent removal. Hence, parathyroid hormone (PTH) measurement can be used to predict patients at risk for developing significant postoperative hypocalcaemia after thyroidectomy. ^{1,12}

The aim of this study was to find out whether there is any correlation between intact PTH value and patients developing symptoms of hypocalcemia after total thyroidectomy and to determine the threshold value of 1 hour post total thyroidectomy i.e. intact PTH level that can identify those at elevated risk for developing symptomatic hypocalcemia.

METHODS

This prospective study was conducted with 50 patients who are undergoing total thyroidectomy at Government Medical College Hospital, Kottayam, Kerala between August-November 2011. Inclusion criteria were all patients with benign or malignant thyroid disorders, undergoing total thyroidectomy with or without neck dissection.

Exclusion criteria were co-existing hypo/hyperparathyroidism patients with renal dysfunction and patients with hypoalbuminemia.

Procedure

The study involved determination of serum calcium, creatinine and albumin preoperatively, serum intact PTH (iPTH) 1 hour after completion of total thyroidectomy (i.e. after the closure of skin incision), and serum calcium

levels 6, 24 and 48 hours post operatively. Symptomatic hypocalcemia was defined when there was any episode of symptoms or signs of hypocalcemia during the hospital stay; perioral numbness, tingling sense or paresthesia of hands and/or feet, Chvostek sign, Trousseau sign, muscle cramp, or tetany or seizures or ECG changes. Biochemical hypocalcemia was defined when any one of the checked Ca levels dropped below 8.0 mg/dL or when iCa++ level went under 1.05 mmol/L.

The patients were asked to report any postoperative symptoms and signs of hypocalcemia, which were when they admitted to an inpatient ward. The patients were followed up for 3 days post operatively and the lowest recorded serum calcium was taken into account.

Statistical analysis

The results were tabulated and entered in Microsoft Excel and analysed with spss 17 statistical software. Statististical analysis was done using Chi-Square test, Independent t test and paired t test to compare between different variables. Intact PTH value of symptomatic and asymptomatic patients were compared and threshold PTH value was calculated which would predict the patients at risk for developing symptomatic hypocalcemia.

RESULTS

Fifty patients were participated in the study with the age range between 13-66 years and the median age was 41 years. 78% of the study population were females (39 out of 50) as given in Table 1.

Table 1: Demographic characteristics.

Characteristics	No. of patients (n=50)	Percentage
Age (in years)		
<15 years	1	2
years	47	94
>60 years	2	4
Sex		
Females	39	78.0
Males	11	22.0

From Table 2 it was observed that age, sex and diagnostic procedures had no significant statistical correlation with patients developing symptomatic hypocalcemia with p-values 0.754, 0.913 and 0.273 respectively. Out of 50, 13 patients developed symptomatic hypocalcaemia, i.e., signs and/ or symptoms. 3 patients had only signs 5 patients had only symptoms whereas 8 patients had signs and symptoms.

A statistical significant difference was observed in the mean preoperative and postoperative calcium levels as given in Table 3.

Table 2: Relation between age, sex and diagnosis with symptoms.

Variable	Symptoms		The set and leaves	Duolos
Variable	Present No (%)	Absent No (%)	Test values	P value
Age				
<15 years	-	1 (2)		
years	12 (24)	35 (70)	0.315a	0.754
>60 years	1 (2)	1 (2)	0.515a	0.734
Total	13 (26%)	37 (74%)		
Sex				
Females	10 (25.6%)	29 (74.4%)		
Males	3 (27.3%)	8 (72.7%)	1.202b	0.913
Total	13 (26.0%)	37 (74.0%)		
Diagnostic procedures				
MNG	10 (23.3%)	33 (76.7%)	1 2021-	0.272
Carcinoma Thyroid	3 (42.9%)	4 (57.1%)	1.202b	0.273

^a Value calculated by independent t test; b value calculated by Chi-square test.

Table 3: Comparison between pre-op and postoperative calcium.

Calcium levels	Mean	Std. Deviation	Paired t test value	P value
Preoperatively	9.068	0.5044	6.018	< 0.001
Postoperatively	8.216	0.8505		< 0.001

Table 4: Signs and symptoms.

Signs/ Symptoms	Frequency
Perioral numbness	10
Paraesthesia	8
Carpal spasm	4
Laryngeal spasm	NIL
Seizures	NIL
Chvostek's sign	8
Trousseau's sign	2
ECG changes	NIL

Table 4 presents the signs and symptoms noted in the patients with hypocalcaemia after thyroidectomy. The

major symptom observed was perioral numbness followed by paraesthesia, Chvostek's sign, Carpal spasm and Trousseau's sign. A significant difference was observed in the mean PTH values of symptomatic and asymptomatic patients as shown in Table 5. The sensitivity and specificity of iPTH values were noted at different threshold values. Maximum sensitivity (92.3) was observed at with PTH value ≥ 14 and specificity (91.9) at PTH value ≤ 14 with positive predictive value 80% and negative predictive value of 97%. Table 7 presents the relation between symptomatic patients and threshold PTH value. 80% of patients with PTH value ≤ 14 developed symptoms. 2.9% of patients with PTH value ≥ 14 developed symptoms.

Table 5: Comparison between PTH Value of symptomatic and asymptomatic patients.

	No.	Mean PTH	SD	Independent t- test	p value
Symptomatic	13	11.046	3.4099	4.526	< 0.001
Asympomatic	37	32.446	16.8175		

Table 6: Specificity and sensitivity of different threshold PTH values.

Intact PTH	Sensitivity	Specificity
13	84.61	91.9
14	92.3	91.9
15	92.3	91.9
16	92.3	85.29

DISCUSSION

Thyroidectomy is one of the common surgeries performed worldwide. Postoperative hypocalcaemia was the most common complication observed in patients undergoing total thyroidectomy. To minimize postoperative complications and to permit an early and safe discharge, it is important to identify a method to

predict patients at high risk of developing significant hypocalcaemia, who are candidates for early treatment, and patients at low risk who are well suited for early discharge. Many studies have been conducted all over the world to determine the methods that would predict the development of post thyroidectomy hypocalcaemia.

			Symptoms		Total
			Present	Absent	
Threshold		Count	12	3	15
PTH	≤14	% within threshold PTH	80.0%	20.0%	100.0%
		% within symptoms	92.3%	8.1%	30.0%
	≥14	Count	1	34	35
		% within threshold PTH	2.9%	97.1%	100.0%
	_	% within symptoms	7.7%	91.9%	70.0%
Total		Count	13	37	50

Table 7: Relation between symptomatic patients and threshold PTH value.

Studies conducted by Tredici et al and Wong et al showed the utility of serial measurement of calcium levels preoperatively and postoperatively immediately after thyroidectomy. ^{13,14} In both these studies sensitivity of serum calcium measurement as a predictor of hypocalcaemia is too low to be used as a reliable screening test.

Estimation of preoperative serum ALP levels was another procedure to note the calcium levels after thyroidectomy. In a study conducted by Demeester-Mirkine et al it was observed that there was a slight correlation between the preoperative serum alkaline phosphatase level and the minimal postoperative serum calcium level. It was concluded that post-thyroidectomy hypocalcaemia is a multifactorial phenomenon. It was due, at least in part, to hemodilution. A temporary parathyroid insufficiency after subtotal and total thyroidectomy, and an avidity of the skeleton for calcium in hyperthyroid patients, may aggravate the hypocalcaemia.

Serial measurement of serum PTH, preoperatively—baseline (BL), at the end of surgery—skin closure (SC), and at 4 h postoperatively (4H) was also considered as specific factor for predicting post thyroidectomy hypocalcaemia. In a study accompanied by Marcin Barczynski et al concluded that the criterion of iPTH serum level less than 10 pg/ml at 4 h postoperatively had the highest accuracy in predicting serum calcium level below 2.0 mmol/1 after total thyroidectomy when compared with the other criteria. ¹⁶

The high cost of serum iPTH measurement makes its serial measurement less feasible. Hence it would be desirable if a single iPTH measurement predicts the development of post thyroidectomy hypocalcaemia. Several studies were conducted measuring the sensitivity of iPTH done intraoperatively, immediate post operatively and in the morning after thyroidectomy. A study was done by Lombard et al in which iPTH was

measured preoperatively, at the end of the surgical procedure, and at 2, 4, 6, 24, and 48 hours after the operation. It was concluded that a single iPTH levels below the normal range (<10 pg/mL) between 4 and 6 hours after the operation correctly predicted postoperative hypocalcaemia (sensitivity 94% and specificity 100%).¹⁷ Another study was done by Graff et al 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.¹⁸ Patients can develop symptoms of hypocalcaemia as early as 6 hours after thyroidectomy. Serum intact PTH measurement 1 hour after thyroidectomy may be clinically a useful parameter. Hence it would be desirable to identify at risk patients very early in the postoperative period (within 2 hours) so that early supplementation of oral/ parenteral calcium is possible to prevent the development of symptoms. In a study conducted by Valerie Cote et al, intact PTH measured at 1 hour post operatively had a sensitivity of 96% in predicting patients developing hypocalcaemia after thyroidectomy.¹⁹ In the present study, a 1 hour postoperative serum intact PTH value of <14.45 pg/m1 has a sensitivity of 92.3% and a specificity of 91.9% for predicting patients at risk for developing post total thyroidectomy symptomatic hypocalcaemia.

Limitations of the study

- Study population belongs to the group of patients presented to one medical college; can be generalised only after conducting the study on a larger population.
- Patients were followed up only for a few days till they were discharged. Ideally patients should be followed up for 6 months to detect patients developing permanent hypocalcemia.

CONCLUSION

For predicting patients at risk for developing post thyroidectomy symptomatic hypocalcemia, a 1 hour post-operative serum intact PTH value of \leq 14.45 had a sensitivity of 92.3% and specificity of 91.9%. So it can be used as a screening test after total thyroidectomy to identify patients at risk for developing hypocalcemia.

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institutional ethics committee

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