Prediction of Hypocalcemia in Postoperative Total Thyroidectomy using Single Measurement of Intra-operative Parathyroid Hormone Level

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Objective: *Many varieties of methods using intra-operative PTH have been applied to predict hypocalcemia after total thyroidectomy. The present study prospectively evaluated the reliability of intra-operative PTH through a single assay to predict hypocalcemia after total thyroidectomy.*

Material and Method: *Intra-operative PTH were performed before and 20 minutes after total thyroidectomy for 30 new patients. The calcium level was measured at 24 and 72 hours after surgery. Patients who had serum calcium < 8.5 mg/dl at 24 or 72 hrs. (hypocalcemia) were compared with normocalcemic patients. The level of intra-operative PTH was determined to predict post operative calcium level.*

Results: *Post operative hypocalcemia developed in 20 of 30 patients. Those hypocalcemic patients showed statistically significant lower intraoperative PTH at 20 minute post total thyroidectomy compared with normocalcemic patients (mean 9.2 vs 24.7, p = 0.006). Sensitivity, specificity, and accuracy for prediction of post total thyroidectomy hypocalcemia were 85%, 80%, and 83.3% respectively. The positive predictive value = 89.5% and negative predictive value = 72.7%. Patients with intra-operative PTH at 20 minute post-total thyroidectomy < 15 pg/ml required close monitoring.*

Conclusion: *Intra-operative PTH at 20 minutes after total thyroidectomy can predict impending post operative hypocalcemia. Based on the result, this can guide which patients will be considered safe, and who can be discharged early. Furthermore, it is used to closely monitor the calcium level and provide early calcium supplementation.*

Keywords: *Intra-operative parathyroid hormone assay, Total thyroidectomy, Hypocalcemia*

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Intra-operative parathyroid hormone (PTH) monitoring has emerged as an indicator of PTH level in parathyroidectomy over the past decade. The application of monitoring PTH in thyroid surgery that potentially affects parathyroid gland function has been reported by many authors[1-8]. The incidences of post operative hypocalcemia range from 1.6 to 50%[2]. Although hypoparathyroidism from thyroid surgery can be monitored by calcium level measurement, the symptom of hypocalcemia may not occur in 24 hours postoperatively and may be delayed to several days. This affects length of stay in hospital for observation. The present study was conducted to determine intra-operative PTH level and calcium level. It was expected that the result of the present study would minimize complication, allow for early discharge and early start calcium, and /or vitamin D supplement. It was also aimed to determine whether a single measurement of PTH level could accurately predict post operative hypocalcemia.

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Material and Method

The present study prospectively evaluated the use of intra-operative PTH level as a predictor of hypocalcemia. Patients undergoing total thyroidectomy at National Cancer Institute Bangkok from November 2002 through January 2005 were studied. Exclusion criteria included previous thyroid surgery. An effort was made to identify and preserve all the parathyroid glands

during total thyroidectomy. Blood was withdrawn from patients at starting of the surgery and 20 minutes after removal of thyroid gland to measure PTH level, and the result was reported within 1 hour after surgery. These patients were then observed for hypocalcemic symptoms. The calcium level was measured at 24 and 72 hours after surgery. All patients had normal albumin level. The author's reference range of total calcium was 8.5-10.5 mg/dl and intra-operative PTH level was 15-65 pg/ml. by the electro-chemiluminescence immunoassay method.

Statistical analysis was performed with commercially available statistic software package. PTH levels from patients who had hypocalcemia were compared with normocalcemic patients at 20 minutes after total thyroidectomy. A probability value of < 0.05 was considered significant. The levels of intraoperative PTH > 15 pg/ml were used to predict postoperative calcium levels and the accuracy, sensitivity, specificity, positive and negative predictive value were determined.

Results

Thirty patients, 23 females and 7 males underwent total thyroidectomy and eleven patients in this group underwent neck dissection. Patients' ages ranged from 18-69 yrs (mean 47.4 yrs). Ten of 30 patients (33.3%) were normocalcemia; and 20 cases (66.7%) were hypocalcemia. Fifteen cases in hypocalcemic group developed hypocalcemia within 24 hrs whereas five cases (25%) developed hypocalcemia within 72 hrs post operation. Table 1 demonstrates intra-operative PTH level of hypocalcemic and normocalcemic patients respectively. The mean of intra-operative PTH level at 20 minutes post total thyroidectomy were 24.7pg/ml in the normocalcemic group and 9.2 pg/ml in the hypocalcemic group. This difference was statistically significant ($p = 0.006$) as shown in Fig. 1. The prediction of post operative calcium level by intra-operative PTH level was shown in Table 2 which showed sensitivity = 85%, specificity = 80% and accuracy = 83.3%, positive predictive value = 89.5%, negative predictive value = 72.7%.

Discussion

Post operative hypocalcemia after total thyroidectomy has been reported to range from 1.3% to 50%[2,8,9]. Parathyroid function can be easily compromised in thyroid surgery because of their sensitivity to surgical manipulation. Kuhel and Carew[10] studied

Table 1. Demonstration of intraoperative PTH level at start (PTHs) and at 20 minute (PTH 20) post total thyroidectomy of normocalcemic and hypocalcemic patients

Normocalcemic patients			Hypocalcemic patients		
Pt. No.	PTHs (pg/ml)	PTH20 (pg/ml)	Pt. No.	PTHs (pg/ml)	PTH20 (pg/ml)
13	39.72	7.75	1	98.45	2.69
17	32.70	10.11	2	16.71	3.05
20	42.46	15.25	3	50.13	4.15
21	59.89	17.80	4	20.49	4.17
23	41.35	18.78	5	41.67	4.93
24	34.67	18.85	6	30.21	5.07
27	61.18	33.31	7	62.00	5.47
28	91.91	40.25	8	40.12	5.52
29	30.05	42.04	9	99.76	6.34
30	55.39	43.26	10	66.93	6.63
			11	42.74	6.66
			12	29.55	7.36
			14	39.87	9.53
			15	76.94	9.71
			16	90.16	9.87
			18	34.69	12.31
			19	33.23	12.66
			22	60.15	17.82
			25	35.30	24.15
			26	40.57	26.62

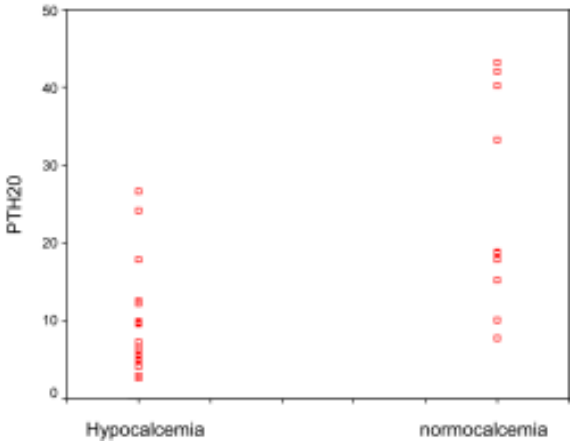

Fig. 1 Diagram demonstrate PTH level at 20 minute after total thyroidectomy in normocalcemic and hypocalcemic patients

Table 2. Number of normocalcemic and hypocalcemic patients correlation with normal and hypoparathyroid hormone level at 20 minutes post thyroidectomy

	Calcium < 8.5	Calcium ≥ 8.5	Total
PTH20 < 15	17	2	19
PTH20 ≥ 15	3	8	11
Total	20	10	30

(PTH 20 = parathyroid hormone level at 20 minuts post total thyroidectomy)
Sensitivity = 17/17+3 = 85%
Positive Predictive value = 17/17+2 = 89.5%
Specificity = 8/8+2 = 80%
Negative Predictive value = 8/8+3 = 72.7%
Accuracy = 17+8/30 = 83.3%

the reliability of parathyroid gland color as a mean of assessing parathyroid gland function and concluded that the absence of discoloration was not a reliable way to determine whether the parathyroid blood supply is intact.

In 1995, the introduction of rapid parathyroid hormone assays allowed for intra-operative measurement of hormone level, which was initially used in hyperparathyroidism. After that, there are many reports demonstrating that the intra-operative PTH assay could predict the group at high risk for hypocalcemia after thyroid surgery. Cohen JI et al[7] reported that normal intra-operative PTH at 10 minutes after total or completion thyroidectomy indicates a low risk of postoperative hypocalcemia. Lo et al[11] examined 100 patients and 20 control subjects using intra-operative PTH to monitor PTH level, they found that a normal PTH or less than 75% of decline in PTH level after thyroidectomy accurately identified normocalcemia patients post operatively. Urken et al[5] reported that 64% of patients, who required post operation, calcium supplementation, had a change in PTH level of greater than 75% from baseline and the most predictive value was the change at 20 minutes after removing the thyroid. In the present study, blood was drawn intra-operatively at post induction, 5 min, 10 min, and 20 min after excision of thyroid gland. This required the collection of several samples during the operation and used five assays. Bellantone et al[2] reported early prediction of post thyroidectomy hypocalcemia by single intra-operative PTH measurement and found that measurement at 4 hours after operation could represent the earliest and most accurate predictor with 98% accuracy. Lam and Kerr[12] reported that serum intra-operative PTH level below the normal range 1 hour after operation was 100% specific and sensitive in prediction symptomatic hypocalcemia after total thyroidectomy.

In the present study, the authors analyzed the PTH level at 20 minutes after total thyroidectomy and the result demonstrated that this was potentially used in prediction of post operative hypocalcemia with accuracy, sensitivity and specificity more than 80%.In contrast to other studies, the result of prediction can demonstrate by one assay of intra-operative PTH at 20 minutes after total thyroidectomy which will decrease the expense of the institute. The symptoms of hypocalcemia make patients meet unwanted situations. These symptoms can occur later as shown in the result, so the patients have to stay in hospital for observation of calcium level after the symptoms occur. However all hypocalcemia patients did not develop any symptoms and all patients with a PTH level at 20 minutes more than 15 pg/ml did not develop symptoms of hypocalcemia and did not need calcium supplementation at all.

In conclusion, the present data showed that one assay of intra-operative PTH level at 20 minutes after total thyroidectomy can predict post operative hypocalcemia. Based on the result, this can guide which patients will be considered safe or be discharged early as well as closely monitor calcium level and early calcium supplementation

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การพยากรณ์ภาวะระดับแคลเซียมต่ำภายหลังการผ่าตัดต่อมไทรอยด์ออกทั้งหมดโดยการตรวจพาราไทรอยด์ฮอร์โมนในห้องผ่าตัดครั้งเดียว

สมจินต์ จินดาวิจักษณ์

วัตถุประสงค์: *เนื่องจากมีรายงานการตรวจพาราไทรอยด์ฮอร์โมนในห้องผ่าตัดเพื่อพยากรณ์ภาวะระดับแคลเซียมต่ำหลังการผ่าตัดต่อมไทรอยด์ออกทั้งหมดหลายวิธี ในการศึกษานี้เพื่อประเมินความน่าเชื่อถือของการตรวจ พาราไทรอยด์ฮอร์โมนในห้องผ่าตัดครั้งเดียวสำหรับการพยากรณ์ภาวะระดับแคลเซียมต่ำหลังการผ่าตัด ต่อมไทรอยด์ออกทั้งหมด*

วัสดุและวิธีการ: *ทำการตรวจพาราไทรอยด์ฮอร์โมนในห้องผ่าตัดก่อนการผ่าตัด และหลังการผ่าตัดต่อมไทรอยด์ออกทั้งหมด 20 นาที ในผู้ป่วยใหม่ 30 ราย หลังจากการผ่าตัดทำการวัดระดับแคลเซียมที่เวลา 24 และ 72 ชั่วโมง เปรียบเทียบผู้ป่วยที่มีระดับแคลเซียมน้อยกว่า 8.5 pg/dl ที่เวลา 24 หรือ 72 ชั่วโมง (ภาวะแคลเซียมต่ำ) กับผู้ป่วยที่มีระดับแคลเซียมปกติ หลังจากนั้นตรวจสอบการตรวจพาราไทรอยด์ฮอร์โมนในห้องผ่าตัด ในการพยากรณ์ภาวะระดับแคลเซียมต่ำหลังการผ่าตัดต่อมไทรอยด์ออกทั้งหมด*

ผลการศึกษา: *ภาวะแคลเซียมต่ำหลังการผ่าตัดต่อมไทรอยด์ออกทั้งหมดเกิดขึ้นกับผู้ป่วย 20 ใน 30 ราย ผู้ป่วยที่มีภาวะแคลเซียมต่ำพบว่ามีระดับพาราไทรอยด์ฮอร์โมนที่เวลา 20 นาทีหลังการผ่าตัดต่ำกว่าผู้ป่วยที่มีภาวะแคลเซียมปกติอย่างมีนัยสำคัญ ($p = 0.006$) จากการศึกษาความน่าเชื่อถือพบว่า การตรวจมีความไว = 85% ความจำเพาะ = 80% ความถูกต้องของการตรวจ = 83.3% โอกาสที่ผลการตรวจพบ PTH < 15 pg/ml จะมีผลการตรวจค่าแคลเซียมต่ำ = 89.5% และโอกาสที่ผลการตรวจพบ PTH > 15 จะมีผลการตรวจไม่พบค่าแคลเซียมต่ำ = 72.7% ผู้ป่วยที่มีค่าพาราไทรอยด์ฮอร์โมนที่เวลา 20 นาทีหลังการผ่าตัดต่อมไทรอยด์ออกทั้งหมดน้อยกว่า 15 pg/ml ควรต้องได้รับการสังเกตอาการแคลเซียมต่ำอย่างใกล้ชิด*

สรุป: *การตรวจพาราไทรอยด์ฮอร์โมนที่ 20 นาทีหลังการผ่าตัดต่อมไทรอยด์ออกทั้งหมด สามารถพยากรณ์ภาวะแคลเซียมต่ำหลังการผ่าตัด และจากผลการศึกษานี้จะสามารถใช้เป็นแนวทางในการดูแลผู้ป่วยว่าผู้ป่วยคนใดจะสามารถออกจากโรงพยาบาลได้อย่างปลอดภัยหรือผู้ป่วยรายใดควรได้รับการสังเกตอาการแคลเซียมต่ำอย่างใกล้ชิด และต้องได้รับแคลเซียมทดแทน*