

Role of ioPTH Estimation in Thyroid Surgery for Early Prediction of Post-Operative Hypocalcaemia

Anil Suri¹, Deep Jyoti^{2*}, Arti², Sonika Kotwal³

¹Associate Professor, ²Senior Resident, ³PG Resident,
Department of Otolaryngology, Government Medical College, Jammu, Jammu and Kashmir, India.

ABSTRACT

Background: Damage to the parathyroid glands during thyroid surgery can lead to transient or permanent hypocalcaemia. This is a preventable complication if meticulous technique is followed to prevent damage to parathyroid glands during thyroid surgery. In this study we evaluated intraoperative parathyroid hormone levels (ioPTH) to predict the damage to the parathyroid glands during thyroid surgery and to establish ioPTH as an early indicator of postoperative hypocalcaemia.

Methods: The study was undertaken in the department of otorhinolaryngology with approval of institutional ethical committee. 35 patients undergoing thyroid surgery were subjected to intraoperative parathyroid hormone level estimation. These results were compared with the postoperative s. calcium levels and development of symptomatic hypocalcemia.

Results: Mean value of ioPTH in our study was 20.57 ± 10.01 pg/ml. 12 patients had low ioPTH. Mean s. calcium level was 8.54 ± 0.54 mg/dl. 10 patients with low ioPTH had low s. calcium levels on 1st postoperative day. There was a positive correlation between ioPTH and development of postoperative hypocalcaemia with Pearson correlation coefficient = 0.72 and p value < 0.001. Subtotal and Total thyroidectomy was a

significant risk factor for development of postoperative hypocalcaemia ($p < 0.001$).

Conclusion: Intraoperative parathyroid hormone (ioPTH) levels can detect patients at risk of developing postoperative hypocalcaemia. So, ioPTH estimation should be routinely incorporated while performing thyroid surgery especially during total thyroidectomy.

Keywords: Thyroid Surgery, Hypocalcaemia, Parathyroid Hormone, Calcium Supplements.

*Correspondence to:

Dr. Deep Jyoti,
Registrar, ENT (Senior Resident),
Department of Otolaryngology,
Government Medical College, Jammu, J & K, India.

Article History:

Received: 27-09-2018, Revised: 21-10-2018, Accepted: 16-11-2018

Access this article online

Website: www.ijmrp.com	Quick Response code 
DOI: 10.21276/ijmrp.2018.4.6.010	

INTRODUCTION

Thyroidectomy, be it hemithyroidectomy or total thyroidectomy, puts parathyroid glands at risk of damage or accidental resection which in turn result in hypocalcaemia leading to symptoms like numbness and tingling in perioral region and extremities and life threatening conditions like focal/generalised seizures and cardiac arrhythmia. Postoperative hypoparathyroidism is temporary in most of the cases; however a minority of patients develops permanent hypoparathyroidism.

Damage to the parathyroid glands during the thyroid surgery depends on the indication for thyroid surgery, extent of thyroid resection, anatomy of parathyroid glands, relation of parathyroid glands to the thyroid gland and their delicate blood supply.¹

Postoperative hypocalcaemia incidence after thyroid surgery may go up to as high as 68%² and cause of this may be postoperative impaired PTH secretion, haemodilution and calcitonin release. Close postoperative monitoring of serum calcium levels is a standard of care employed routinely after thyroid surgery.

However, the phenomenon of calcium decline within 24 hours is not specific to thyroid surgery only but is also seen in other surgeries of similar magnitude and duration like herniorrhaphy.¹ Investigators have reported the utility of parathyroid hormone assay, as a good indicator of transient hypocalcaemia because of its short half-life.³

An intraoperative parathyroid hormone assay (quick PTH assay) has been increasingly adopted to monitor the success of parathyroid surgery and to facilitate a focussed approach during parathyroidectomy, but it has also been suggested that the quick PTH assay might have a value in monitoring the development of postoperative hypocalcemia due to parathyroid gland damage in thyroid surgery much earlier than serum calcium monitoring. Intraoperative PTH less than normal range is a strong indicator of postoperative hypocalcaemia⁴ and patients with low intraoperative PTH should be put on calcium and vitamin D supplements.

MATERIALS AND METHODS

The purpose of our study was to find correlation of ioPTH during thyroid surgery and postoperative hypocalcaemia to establish ioPTH as an early indicator of hypocalcaemia.

The present study was a prospective study and was conducted in the department of Otorhinolaryngology and Head and Neck Surgery, SMGS Hospital, Govt. Medical College. Study was conducted after taking approval from the Institutional Ethical Committee GMC, Jammu. 35 patients were included in our study. All the patients in Department of ENT, undergoing any thyroid surgery like Lobectomy, Hemithyroidectomy, Subtotal, Near-total and Total thyroidectomy with or without Neck dissection and Completion thyroidectomy, were included for the present study. Those patients presenting with thyroid dysfunction were first managed medically to make them euthyroid before being taken up for the surgery. Patients already diagnosed as having parathyroid adenoma or those with preoperative hyperparathyroidism were excluded from our study. Patients with thyroid malignancy involving the parathyroid glands seen during the surgery were also excluded.

A detailed history was taken of the patients and general physical examination followed by the examination of the thyroid swelling was done. Informed and written consent was taken from each patient regarding the procedure. All the patients were taken up for the surgery under general anaesthesia. Extra capsular dissection was performed preserving the RLN and parathyroid glands. Vessels were ligated directly on the surface of the thyroid gland capsule. Parathyroids were peeled away as the dissection proceeded medially.

At the time of skin closure of the thyroid surgery, blood sample for PTH levels was taken and sent for estimation and reference value of serum PTH was taken as (15 - 65) pg/ml. Within 12 to 24 hours (1st postop. day) after surgery, calcium levels were estimated with reference value of 8.5 -10.5 mg/dl. All the patients were also observed for the symptoms of hypocalcaemia like numbness in perioral region and extremities and mental confusion and signs of hypocalcaemia like hyper reflexia, carpopedal spasm (tetany). Chvostek’s sign (tapping of facial nerve at angle of jaw produce momentarily contraction of the ipsilateral facial muscles) and Trousseau’s sign (blood pressure cuff placed around the arm and inflated to a pressure greater than the systolic blood pressure for 3 minutes produce carpopedal spasm) were elicited in latent hypocalcaemia.

After surgery only those patients having low ioPTH levels, signs and symptoms of hypocalcaemia and/or low serum calcium were given calcium supplements.

Patients were evaluated at 1 week after the surgery for symptoms and signs of hypocalcaemia and serum calcium was estimated. Dose adjustment of oral calcium supplements was done in patients still having low serum calcium levels or having symptoms and signs of hypocalcaemia.

At 1 month follow up of the patients, symptoms and signs of hypocalcaemia were observed and serum calcium and serum PTH were again estimated. In patients, who still had low levels of PTH at 1 month or presented with hypocalcaemic features were continued with oral calcium supplements and Vitamin D supplementation was started.

Table 1: Showing patient distribution based on parathyroid hormone levels during surgery (ioPTH) and at 1 month (1M-PTH).

	0-15pg/ml	(15-65) pg/ml	Total
ioPTH	12(34.28%)	23(65.71%)	35
1M-PTH	3(8.57%)	32(91.4%)	35

Table 2: Showing patient distribution of Serum calcium values at different time intervals.

S. calcium	Low (<8.5mg/dl)	Normal (8.5-10.5) mg/dl
1 st POD	10(37.14%)	25(71.42%)
1 week	2(5.7%)	33(94.3%)
1 Month	0	35(100%)

POD- postoperative day

RESULTS

In the present study, all the patients were in the age ranging between 20-63 years. Mean age was 36.17 ± 13.18 years. Maximum number of patients (43%) fell in age group of 31-40 years. This age distribution indicates that the thyroid diseases are more common in middle age group. In the present study, 28(80%) were females (F) and 7(20%) males (M) with female to male ratio (F:M) of 8:1 showing that thyroid disorders are more common in females. The present study included both benign and malignant thyroid swellings. We had 24(71.42%) patients with benign thyroid swelling. Remaining 11(31.43%) patients had malignant thyroid tumors. The results are comparable to Shaha AR.⁵ who reported 88% of the patients in his study as benign and 12% patients with malignant pathology. A total of 12 right (R) and 8 left (L)

hemithyroidectomies, 4 subtotal, 10 total thyroidectomies (including one completion thyroidectomy) and 1 total thyroidectomy with neck dissection were performed.

All the patients in our study were subjected to the PTH estimation intraoperatively and blood sample was drawn at the time of skin closure. 12 (34.28%) patients had low ioPTH levels with mean of 9.58 ± 0.54 pg/ml. At 1 month, only 3(8.57%) patients still had low PTH levels while in rest of 9 patients PTH levels had improved (Table no.1). Out of these 12 patients, 10 patients had low serum calcium levels estimated on the first postoperative day with mean of 7.85 ± 0.48 mg/dl. At 1 week, only 2 patients had low calcium levels and on follow up at 1 month, the serum calcium levels of all the patients were in normal range (Table no.2).

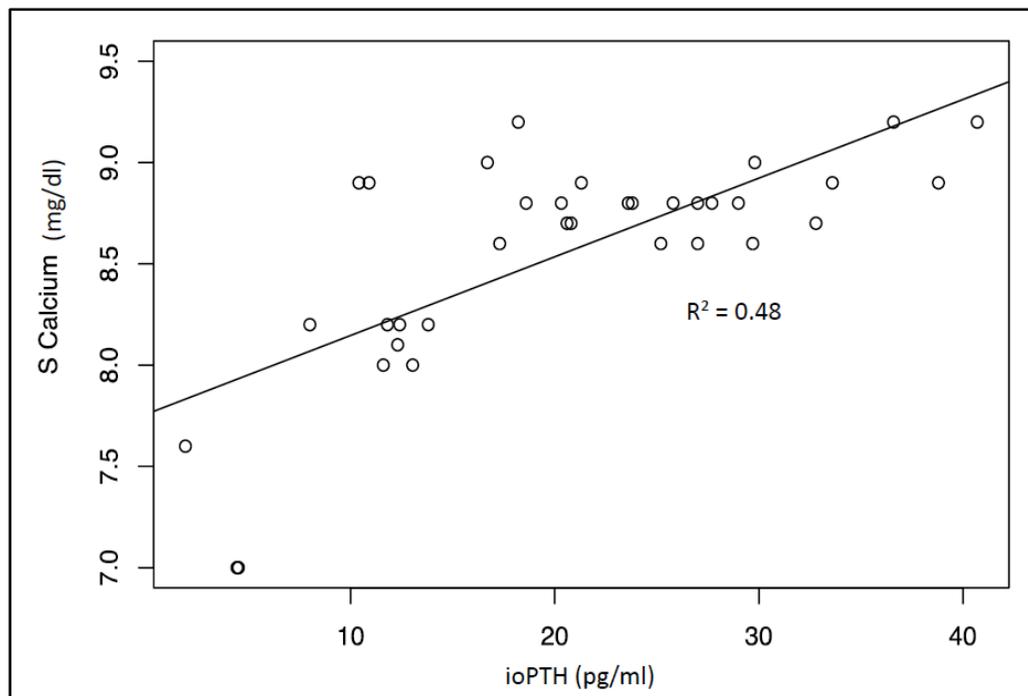


Fig 1: Correlation - scatter diagram between Serum calcium and ioPTH.

Table 3: Showing relation between type of surgery and levels of intraoperative PTH (ioPTH)

Type of surgery	No. of pts. with low ioPTH (< 15pg/ml)	No. of pts. with normal ioPTH(15- 65 pg/ml)
Hemithyroidectomy (n= 20)	1(5%)	19(95%)
Subtotal thyroidectomy(n= 4)	2(50%)	2(50%)
Total thyroidectomy	9(81.82%)	2(18.18%)
Total	12	25

Table 4: Relation of the type of surgery with improvement of PTH value after 1 month.

Type of surgery	No. of pts. with ioPTH <15 pg/ml	No. of pts. with 1M-PTH <15pg/ml	No. of pts. improved at 1 M
Hemithyroidectomy	1 (8.35%)	0	1(100%)
Subtotal thyroidectomy	2 (16.68%)	0	2(100%)
Total thyroidectomy	9 (75.02%)	3(25%)	6(66.67%)
Total	12	3	

ioPTH - intraoperative parathyroid hormone 1M - 1 month

Table 5: Showing the s. calcium levels and symptomatic hypocalcaemia in patients with low ioPTH in different types of thyroidectomy.

Type of surgery	Low ioPTH (<15pg/ml)	Low s.calcium (<8.5mg/ml)	Symptomatic hypocalcaemia
Hemithyroidectomy (n=20)	1(8.4%)	1(8.4%)	0
Subtotal thyroidectomy (n=4)	2(16.6%)	1(8.4%)	0
Total thyroidectomy (n=11)	9(75%)	8(66.7%)	4(33.3%)
Total	12(100%)	10(83.3%)	4(33.3%)

Table 6: Showing relation of extent of surgery and levels of ioPTH.

Type of surgery	PTH levels	
	No. of pts. with low ioPTH (< 15pg/ml)	No. of pts. with normal ioPTH (15-65pg/ml)
Total and subtotal thyroidectomy (n = 15)	11 (73.34%)	4 (17.78%)
Hemithyroidectomy (n = 20)	1 (5%)	19 (95%)

9(81.81%) out of 11 patients with total thyroidectomy had low PTH levels. 12 patients had low ioPTH out of which 9(75.02%) had undergone total and 2(16.68%) had undergone subtotal thyroidectomy. One patient who underwent hemithyroidectomy had low ioPTH (Table no.3). 6(66.67%) patients of total thyroidectomy had improved PTH levels at 1 month. All the patients with low ioPTH who improved, had undergone either hemithyroidectomy or subtotal thyroidectomy. Out of 11 patients who had undergone total thyroidectomy, 9 had low ioPTH. 8 (66.67%) patients had low postoperative serum calcium while 4 (33.3%) patients also developed symptoms of hypocalcaemia (Table no. 4,5). Using Fischer exact test p value is 0.00003 which is highly significant ($p < 0.001$) indicating that subtotal and total thyroidectomy are at risk of developing postoperative hypocalcaemia (Table no. 6). This shows that patients undergoing total thyroidectomy at high risk of developing post-operative hypocalcaemia. Serum calcium levels are shown on y- axis and ioPTH levels are shown along the x- axis. Pearson correlation coefficient = 0.72 with $p < 0.001$ which is highly significant. There is positive linear correlation between ioPTH and 1st post-operative day S.calcium indicating that ioPTH can predict the postoperative hypocalcaemia.

DISCUSSION

There are many fragile and physiologically essential structures near the thyroid gland, particularly the parathyroid glands (PGs) and recurrent laryngeal nerve. One of the most common and worrying complications of the thyroid surgery is hypocalcaemia.⁶ Hypocalcaemia results due to injury to the parathyroid glands and their vascularity. Due to the delicate blood vessels, intimate relation with the thyroid and the structural vulnerability, surgical exploration of the thyroid gland puts them in critical position of getting damaged. The preservation of the parathyroid glands has been a constant challenge and a difficult feat to accomplish during total thyroidectomy. To minimize the risk of complications, the operating surgeon should have deep knowledge of the thyroid anatomy and parathyroid glands. A meticulous technique should be employed in order to prevent any inadvertent injury to parathyroid glands.

Incidence of transient hypoparathyroidism is very variable. In present prospective study, we had evaluated the efficacy of intraoperative PTH level in predicting the development of postoperative hypocalcaemia. All the surgeries were performed by adopting capsular technique of the dissection. We used a single PTH measurement to predict the postoperative hypocalcaemia which is supported by Barczynski M et al.⁷ who compared accuracy between PTH at skin closure and at 4 hrs after surgery and found no significant difference between the two. A single PTH measurement taken anytime from 10 minutes to several hours after surgery provide equally accurate predictive results.⁸

In our study, 12 (34.28%) patients had low ioPTH ($< 15\text{pg/ml}$). Calcium supplements were started in these patients. Another sample was drawn at 1st postoperative day (approx. 24hrs) for serum calcium levels. Serum calcium was low ($< 8.5\text{mg/dl}$) in 10 cases. All these patients also had low ioPTH. Those patients with low calcium levels were followed by continuous calcium monitoring till calcium levels were stabilised. All the patients were again followed at 1 week and 1 month for S. calcium and symptoms and signs of hypocalcaemia. At 1 month, PTH level

was again estimated. At 1 month, only 3(8.87%) patients had low PTH while S. calcium levels were in normal range in all the patients. No patient showed any symptom of hypocalcaemia. It indicated that 9 out of 12 patients with low ioPTH had improved after 1 month of surgery probably because there was temporary injury to the parathyroids during the thyroid surgery. Supplements were continued and vitamin D was started in these 3 patients while in rest of the 9 patients, further supplements were not required. Incidence of postoperative biochemical hypocalcaemia was 37.14%. Sheahan P⁹, reported postoperative hypocalcaemia in 22.2%. Results of postoperative symptomatic hypocalcaemia in our study (11.42%). Cavicchi O et al.¹⁰ (2008), Sheahan P (2013)⁹ reported the biochemical hypocalcaemia in 14.19% and 10.3% of patients in their respective studies.

Incidence of low ioPTH in our study was 34.28% (12 patients). Majority (83%) patients with low ioPTH in our study also had low S. calcium as estimated on 1st postoperative day. 4(33.3%) patients with low ioPTH developed symptomatic hypocalcaemia. None of the patients, with normal ioPTH developed symptoms of hypocalcaemia.

ioPTH levels and 1st postop day s. calcium showed significant ($p < 0.001$) positive linear correlation using a scatter diagram indicating that ioPTH is an efficient indicator of postoperative hypocalcaemia. PTH levels provide more accurate reflection of parathyroid gland function than s.calcium levels. Half life of PTH is 2- 4 min and thus indicate true status of parathyroid gland function whereas s. calcium levels may not fall until 48- 72 hrs after the surgery. Usefulness of adopting ioPTH depends on its ability to influence the decision to categorise the patients who need calcium and Vitamin D supplements before the symptoms of hypocalcaemia develop. Parathyroid insufficiency is the main contributor for severe and symptomatic hypocalcaemia.¹¹ In the present study we evaluated the single postoperative PTH measurement to classify the patients who were at risk of developing postoperative hypocalcaemia.

In the present study maximum patients (9) with low ioPTH had undergone total thyroidectomy. 2 patients had subtotal thyroidectomy and 1 patient had hemithyroidectomy. Low s. calcium levels were observed in 10(83%) patients. All of them were in low ioPTH group. Symptoms of hypocalcaemia developed in 4 patients of total thyroidectomy. Result of our study indicate that patients undergoing total thyroidectomy are at greater risk of developing postoperative hypocalcaemia which is significant using fischer exact test ($p < 0.001$)

CONCLUSION

It is concluded from the present study that ioPTH is first indicator of showing the risk of developing postoperative hypocalcaemia. Hence, ioPTH estimation can be incorporated in thyroid surgery. With only single preoperative ioPTH estimation, need of doing serial calcium monitoring can be avoided. Calcium supplements can be started in the patients having low ioPTH levels. This also decreases patient's morbidity and can facilitate early discharge of patients who are not at risk of postoperative hypocalcaemia. At 1 month, 9 out of 12 patients had normal PTH and calcium levels, showing that ioPTH can be due to transient insult to the parathyroid glands. Calcium supplement should be continued in patients still having hypocalcaemia/ low PTH levels and vitamin D supplements also be added.

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Source of Support: Nil. **Conflict of Interest:** None Declared.

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Cite this article as: Anil Suri, Deep Jyoti, Arti, Sonika Kotwal. Role of ioPTH Estimation in Thyroid Surgery for Early Prediction of Post-Operative Hypocalcaemia. *Int J Med Res Prof.* 2018 Nov; 4(6):56-60. DOI:10.21276/ijmrp.2018.4.6.010