

Validity of Early Parathyroid Hormone Assay as a Diagnostic Tool for Sub-Total Thyroidectomy Related Hypocalcaemia

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ABSTRACT

Objective: To determine the validity of early (one hour postoperatively) parathyroid hormone (PTH) assay (≤ 10 pg/ml), keeping gold standard as the serum ionic calcium level, for predicting sub-total thyroidectomy-related hypocalcaemia and to calculate the sensitivity and specificity of latent signs of tetany.

Study Design: Cross-sectional validation study.

Place and Duration of Study: Department of General Surgery, Pakistan Institute of Medical Sciences, Islamabad from August 2008 to August 2010.

Methodology: Patients undergoing sub-total thyroidectomy were included by convenience sampling. PTH assay was performed 1 hour post sub-total thyroidectomy. Serum calcium levels were performed at 24 and 48 hours, 5th day and 2 weeks after surgery. Cases that developed hypocalcaemia were followed-up for a period of 6 months with monthly calcium level estimation to identify cases of permanent hypocalcaemia. Symptoms and signs of hypocalcaemia manifesting in our patients were recorded. Data was analyzed through SPSS version 10. 2 x 2 tables were used to calculate sensitivity and specificity of PTH in detecting post-thyroidectomy hypocalcaemia.

Results: Out of a total of 110 patients included in the study, 16.36% (n=18) developed hypocalcaemia including 1.81% (n=2) cases of permanent hypoparathyroidism. The sensitivity of one hour postoperative PTH assay as a predictive tool for post-thyroidectomy related hypocalcaemia was 94.4% while its specificity was 83.6% with 53% positive predictive value and 98.7% negative predictive value.

Conclusion: One hour post sub-total thyroidectomy PTH assay can be helpful in predicting post sub-total thyroidectomy hypocalcaemia. Moreover, it can be useful in safe discharge of day-care thyroidectomy patients.

Key Words: Hypocalcaemia. Parathyroid hormone assay. Sub-total thyroidectomy. Day-care surgery.

INTRODUCTION

Post-thyroidectomy related hypocalcaemia is one of the most important, and potentially life threatening, complications of thyroid related surgeries.^{1,2} Injury and inadvertent removal of the parathyroid glands is considered as the cause of this phenomena which at time can be permanent. The fear of this complication is an important factor in the extended stay of a patient in the hospital, after a procedure on the thyroid.^{3,4}

Serial calcium level monitoring and the subsequent cumbersome and subjective interpretation of its decreasing or increasing levels has been used in the past to predict whether hypocalcaemia will develop or not, but has not been proven to be of much use. Prophylactic calcium supplementation has also been used and yet, this practice is not cost effective and prevents us from recognizing the real candidates for

calcium replacement.⁵ With the advent of the concept of 'day-surgery', thyroidectomy is also considered to be a day-care procedure.⁴ While many of its serious complications are apparent during the first few hours postoperatively, hypocalcaemia is a complication that can prove to be fatal and might not be apparent for several days (upto two weeks) postoperatively.⁶ The short half life of the parathyroid hormone (PTH) and its successful use in parathyroid excision surgery led many researchers including us to evaluate its role in detecting post-thyroidectomy hypocalcaemia. No local study is available on the subject.

Data is required to determine if post-thyroidectomy parathormone assay is sensitive and specific enough to be used in a clinically useful manner in deciding if a patient will or will not develop hypocalcaemia post-operatively with important implications regarding day-care surgery.

The objective of this study was to determine the validity of early (one hour postoperatively) parathyroid hormone (PTH) assay (≤ 10 pg/ml), keeping gold standard as the serum ionic calcium level, for predicting sub-total thyroidectomy-related hypocalcaemia and to calculate the sensitivity and specificity of latent signs of tetany. No local literature is available on this subject.

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METHODOLOGY

This descriptive study was conducted at the Department of General Surgery, Pakistan Institute of Medical Sciences, Islamabad, from August 2008 to August 2010. Patients undergoing sub-total thyroidectomy, for any cause, aged between 15 - 65 years were included in the study. Patients not consenting to be a part of the study and those with already deranged calcium levels due to any reason were excluded from the study. After taking permission from the hospital ethics committee and informed written consent from the patient, data was collected through a Proforma.

Initial assessment was done with adequate history, thorough physical examination and relevant investigations. PTH assay was performed 1 hour post sub-total thyroidectomy. Serum calcium levels, adjusted with albumin, were performed at 24 and 48 hrs, 5th day and 2 weeks after surgery. A follow-up period of 6 months was advised to identify cases of permanent hypocalcaemia and monthly serum calcium estimations were done for those patients who did not settle. Symptoms and signs of hypocalcaemia manifesting in the patients were also recorded. Signs of latent tetany were also elicited and recorded.

Statistical Package for Social Sciences (SPSS) version 10 was used to report quantitative variables and frequencies with percentages for qualitative data. 2 x 2 tables were constructed to calculate sensitivity and specificity of PTH and signs of latent tetany in detecting post-thyroidectomy hypocalcaemia.

RESULTS

A total of 110 patients were included in the study. Mean age at presentation was 38 ± 13 years; ranging from 17 - 65 years. Eighty seven (79%) patients were females and 21% (n=23) were males.

Eighteen (16.36%) of the patients developed hypocalcaemia, 1.81% (n=2) developed permanent; hypo-

calcaemia while 14.54% (n=16) developed transient hypocalcaemia.

The sensitivity of PTH was found to be 94.4% while specificity was 83.6%. The positive predictive value of PTH assay as a predictor of postoperative hypocalcaemia was found to be 53% while its negative predictive value was 98.7% (Table I).

The sensitivity of the Chvostek's sign was found to be 88.8% while its specificity was 60%. The positive predictive value of Chvostek's sign as a sign of latent tetany was 30% while its negative predictive value was 96.4% (Table I).

Trousseau's sign as a predictor of latent tetany was found to have a sensitivity of 94.4% and a specificity of 93.4%. Its positive predictive value was 74% while its negative predictive value was 98.8% (Table I).

DISCUSSION

Sub-total thyroidectomy is a fairly common procedure and is being carried out quite frequently at the study set-up where cases are received from the endemic goiter belt of the Himalayas as well as plain endemic goiter areas. For better turnover, cost effectiveness and patient satisfaction, there has been a drive in the recent past to convert it into a day care procedure. For an early discharge, patient's safety must never be compromised.⁴ Hematoma, hemorrhage, bilateral recurrent laryngeal nerve palsy and hypocalcaemia are the main life threatening complications of this surgery, the latter also being reported as the most common with an incidence up to 30% in literature.⁷ The conventional method of detecting this complication is serum calcium monitoring in symptomatic patients which requires an extended hospital stay.

Many researchers tried to ascertain the role of postoperative calcium level and its ability to predict post-thyroidectomy hypocalcaemia. However, the applicability of these methods did not translate well into early

Table I: Table for sensitivity / specificity / PPV/NPV of PTH / Chvostek's sign / Trousseau's sign (n=110).

Variable	TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV
Serum PTH (cut off at 10 pg/dl)	17	77	15	1	94.4%	83.6%	53%	98.7%
Chvostek's sign	16	55	37	2	88.8%	60%	30%	96.4%
Trousseau's sign	17	86	6	1	94.4%	93.4%	74%	98.8%

TP = True Positive; TN = True Negative; FP = False Positive; FN = False Negative; PPV = Positive Predictive Value; NPV = Negative Predictive Value. Where: Sensitivity = $TP/TP+FN$; Specificity = $TN/TN+FP$; Positive Predictive Value = $TP/TP+FP \times 100$; Negative Predictive Value = $TN/FN+TN \times 100$.

Table II: Comparison of current study with previous studies.

Researcher	Year	Place	Cut-off level	Sensitivity	Specificity	PPV	NPV
Asari <i>et al.</i> ¹⁹	2008	Austria	15 pg/dl	97.7%	82.66%	65.6%	99.1%
Diez Alonso <i>et al.</i> ²⁰	2009	Madrid, Spain	13 pg/dl	95%	76%	65%	97%
Vescan <i>et al.</i> ¹⁰	2005	Toronto, Canada	10 pg/dl	95%	99%	-	-
Kim ¹³	2011	Seoul, Korea	10 pg/dl (one hour post-op)	72.4%	87.4%	-	-
Palliogianis ¹⁴	2011	Italy	16 pg/dl (one hour post-op)	84.2%	87.1%	90%	80%
Lang ¹²	2012	Hong Kong	1 pmol/L	94.1%	80%	-	-
Current study	2010	Islamabad	10 pg/dl	94%	83%	53%	98.7%

patient discharge and cost effectiveness, as no definite cut off value was found in later studies. Researchers advocated the use of calcium and vitamin D substitute to all or high risk patients.⁸ However, many researchers observed that this practice was not cost effective and also prevented the detection of true candidates for calcium replacement.⁹ For the past two decades, PTH assays have been used to predict post-thyroidectomy hypocalcaemia. Different cut off values have been quoted by different researchers ranging from 8 pg/dl to 15.5 pg/dl.^{10,11} Other researchers sought to find the ideal time to draw blood for the test; from intra-operative PTH, PTH sample drawn at skin closure to several hours postoperatively and found that the results were almost the same (Table II).¹²

Some researchers such as Lang *et al.* also compared the accuracy of PTH at skin closure with that of conventional serial calcium monitoring and found that PTH had a higher specificity than the calcium slope and also that combining the two did not improve the sensitivity and specificity much. Some researchers have also worked on the combined use of PTH and calcium threshold levels. However, a recent study by Jumaily *et al.* concluded that the combined use was not significantly better than using PTH threshold alone.¹²⁻¹⁵

In this study, 10 pg/dl was taken as the cut-off value and the sample was taken in the recovery room, within an hour of the procedure. Serial calcium assays were carried out 1 hour, 24 hours, 48 hours, 5th day and 2 weeks after surgery. Cases of hypocalcaemia were followed for a period of 6 months to identify cases of permanent hypocalcaemia. Sensitivity, specificity, negative predictive value and positive predictive value of PTH as a predictive test were assessed using actual serum calcium level as the gold standard. Similarly, Chvostek's and Trousseau's sign of latent tetany were also assessed as a diagnostic tool for latent tetany for cases of hypocalcaemia. A total of 110 patients were included in this study. The mean age of presentation was 38 ± 13 years. Sixteen point thirty six percent (n=18) patients developed hypocalcaemia out of which 16 had transient hypocalcaemia while 2 (1.81%) had permanent hypocalcaemia. Though permanent hypocalcaemia is not very common with sub-total thyroidectomy, we had 1.81% cases of permanent hypocalcaemia. This is not very different from recent literature where it is reported at 1.2% in a large multicentre cohort study, still others give its incidence from 0.9% to 2%.¹⁶⁻¹⁸

The sensitivity of PTH was found to be 94.4% while specificity was 83.6%. This is comparable to the other studies done where the sensitivities and specificities ranged from 80% to 100%.^{10-15,19,20} The positive predictive (PPV) value of PTH assay as a predictor of postoperative hypocalcaemia was found to be 53% while its negative predictive value (NPV) was 98.7%. A low PPV should not be discouraging in view of its utility

in early discharge in mind. The PTH has a very high NPV which is quite encouraging. A 98.7% NPV translates into a 98.7% surety while discharging a patient that he/she will not develop hypocalcaemia and, therefore, the discharge is safe. A PPV of 53% means that if a100 patients are admitted with the suspicion of possible hypocalcaemia, 47% of them will not develop it and will remain normocalcaemic. However, in day-care surgery, where the safety of patient's discharge is required, this test can be very beneficial in achieving that goal. Hopkins and Steward also appreciated this applicability of PTH assay and named it as one of the 'advances making out-patient thyroid surgery possible'.²¹

Although the cost effectiveness of PTH was not calculated in this study, however, the multiple calcium assays done postoperatively to determine hypo-calcaemia, the extended hospital stay vs. a shorter hospital stay, and a single PTH assay required to predict hypocalcaemia makes it an attractive alternative, probably cost effective and novel innovation in thyroid surgery.

The sensitivity of the Chvostek's sign was found to be 88.8% while its specificity was 60%. The positive predictive value of Chvostek's sign as a sign of latent tetany was 30% while its negative predictive value was 96.4%. This sign was positive in about 30% of the normal patients as well so it was generally not found very useful.

The Trousseau's sign as a predictor of latent tetany was found to have a sensitivity of 94.4% and a specificity of 93.4%. Its positive predictive value was 74% while its negative predictive value was 98.8%. As this sign had better NPV and PPV, it was found beneficial to detect latent tetany.

This study can be taken as a pilot project; this test is useful, applicable, and beneficial and is cost-effective if the hospital has its own machine. In short, though PTH is a very helpful test, yet, there are certain difficulties to it in our setup and until those are dealt with, the practical applicability of this test would be limited.

CONCLUSION

Hypocalcaemia is a well-known complication of sub-total thyroidectomy. One hour post-thyroidectomy PTH assay with a cut-off value of 10 pg/dl has good sensitivity (94.4%) and specificity (83.6%) and is especially helpful in predicting post-thyroidectomy hypocalcaemia due to hypoparathyroidism when sub-thyroidectomy is performed as day-care procedure. Chvostek's sign has low specificity of 60% in detecting latent tetany, however, Trousseau's sign is very helpful with specificity of 93.4% in detecting latent tetany.

REFERENCES

1. Fong J, Khan A. Hypocalcaemia: updates in diagnosis and management for primary care. *Can Fam Physician* 2012; **58**: 158-62.

2. Prowse SJ, Sethi N, Ghosh S. Temporary hypocalcaemia is one of the most common complications of total thyroidectomy. *Ann Otol Rhinol Laryngol* 2012; **121**:827.
3. Sousa Ade A, Salles JM, Soares JM, Moraes GM, Carvalho JR, Savassi-Rocha PR. Predictors factors for post-thyroidectomy hypocalcaemia. *Rev Col Bras Cir* 2012; **39**:476-82.
4. Houlton JJ, Pechter W, Steward DL. PACU PTH facilitates safe outpatient total thyroidectomy. *Otolaryngol Head Neck Surg* 2011; **144**:43-7.
5. Lo CY, Luk JM, Tam SC. Applicability of intra-operative parathyroid hormone assay during thyroidectomy. *Ann Surg* 2002; **236**:564-9.
6. Krukowski ZH. The thyroid and parathyroid glands. In: Williams NS, Bulstrode CJK, O'Connell PR, editors. Bailey and Love's short practice of surgery. 26th ed. Florida: CRC Press; 2013.p.778-97.
7. Trottier DC, Barron P, Moonje V, Tadros S. Outpatient thyroid surgery: should patients be discharged on the day of their procedure? *Can J Surg* 2009; **52**:182-6.
8. Lewandowics M, Kuzdac K, Pasioka Z. Intraoperative parathyroid hormone measurement in thyroidectomized patients: preliminary report. *Endocr Regulat* 2007; **41**:29-34.
9. Huang SM. Do we overtreat post-thyroidectomy hypocalcaemia? *World J Surg* 2012; **36**:1503-8.
10. Vescan A, Witterick I, Freeman J. Parathyroid hormone as a predictor of hypocalcaemia after thyroidectomy. *Laryngoscope* 2005; **115**:1362-6.
11. Chia SH, Weisman RA, Tieu D, Kelly C, Dillmann WH, Orloff LA. prospective study of perioperative factors predicting hypocalcaemia after thyroid and parathyroid surgery. *Arch Otolaryngol Head Neck Surg* 2006; **132**:41-5.
12. Lang BH, Yih PC, Ng KK. A prospective evaluation of quick intraoperative parathyroid hormone assay at the time of skin closure in predicting clinically relevant hypocalcaemia after thyroidectomy. *World J Surg* 2012; **36**:1300-6.
13. Kim JH, Chung MK, Son YI. Reliable early prediction for different types of post-thyroidectomy hypocalcaemia. *Clin Exp Otorhinolaryngol* 2011; **4**:95-100.
14. Paliogiannis P, Attene F, Torre C, Denti S, Trignano E, Scognamillo F, et al. IPTH dosage as a prognosis predictor of postoperative hypocalcaemia in patients submitted to total thyroidectomy. *Ann Ital Chir* 2011; **82**:111-5.
15. Jumaily JS. Prediction of hypocalcaemia after using 1 to 6 hours postoperative parathyroid hormone and calcium levels: an analysis of pooled individual patient data from 3 observational studies. *Head Neck* 2010; **32**:427-34.
16. Vaiman M, Nagibin A, Hagag P, Buyankin A, Olevson J, Shlamkovich N. Sub-total and near total versus total thyroidectomy for the management of multinodular goiter. *World J Surg* 2008; **32**:1546-51.
17. Järhult J, Andersson PO, Duncker L. Alternating from sub-total thyroid resection to total thyroidectomy in the treatment of Graves' disease prevents recurrences but increases the frequency of permanent hypoparathyroidism. *Langenbecks Arch Surg* 2012; **397**:407-12.
18. Riju R, Jadhav S, Kanthaswamy R, Jacob P, Nair CG. Is total thyroidectomy justified in multinodular goitre? *J Indian Med Assoc* 2009; **107**:223-5.
19. Asari. Hypoparathyroidism after total thyroidectomy: a prospective study. *Arch Surg* 2008; **143**:132-7.
20. Díez Alonso M. Serum PTH levels as a predictive factor of hypocalcaemia after total thyroidectomy. *Cir Esp* 2009; **85**: 96-102.
21. Hopkins B, Steward D. Outpatient thyroid surgery and the advances making it possible. *Curr Opin Otolaryngol Head Neck Surg* 2009; **17**:95-9.

