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Prospective Study of Early Predictive Factors of Hypocalcaemia after Total or Near Total Thyroidectomy in a Tertiary Care Centre

Authors
Preetha S[1], Anilkumar A V[2*]
[1,2] Associate Professor, Department of General Surgery,
Government Medical College, Thiruvananthapuram, Kerala, India
Corresponding Author
Anilkumar A V
Associate Professor, Department Of General Surgery,
Government Medical College, Thiruvananthapuram, Kerala, India . 695011
Email: *anilkumar18avani@gmail.com, phone: 919496173393*

Abstract
Background: *Thyroidectomy though a most common surgical procedure poses two important problems- injury to the recurrent laryngeal nerve and hypoparathyroidism due to its vital anatomical relations. The advances in anesthetic techniques and knowledge of anatomy enabled us to perform thyroidectomies very safely and thus reduce the complications. But problem of hypoparathyroidism still persists especially in patients undergoing total thyroidectomy for neoplasm.*
Methods: *This study is to determine the early predictive factors of hypocalcaemia in post thyroidectomy patients and to study the usefulness of combined serum calcium and serum parathyroid hormone estimation as early predictors of hypocalcaemia after total or near total thyroidectomy.*
Results: *On serial estimation of serum calcium and serum PTH as an early predictor of hypocalcaemia, it was found that all but few showed an initial drop in serum at 6 hrs and progressive drop observed in patients developed clinical hypocalcaemia or likely to develop hypocalcaemia later and in a subset of patients a likelihood of returning to normal was observed after the initial drop, in those are unlikely to develop the same.*
Conclusions: *Serial estimation of serum calcium if done at regular intervals of 6 & 12 hours, the patients who are likely to develop hypocalcaemia can be predicted early.*
Keywords: *thyroidectomy, hypocalcaemia, serial estimation, serum calcium and serum PTH.*

Introduction

Thyroidectomies[1] are one of the most common surgical procedures all over the world. Apart from the usual complications of any surgery such as bleeding, infection and anesthetic accidents, thyroid surgery poses two important problems due to its vital anatomical relations such as injury to the recurrent laryngeal nerve and hypoparathyroidism and related problems due to inadvertent removal of glands or their loss of vascularity. [1, 2]

It was Theodore Kocher [3] who first emphasized the importance of preservation of recurrent laryngeal nerve and glands. The advances in anesthetic techniques and knowledge of anatomy and physiology have enabled us to perform Thyroid surgeries very safely and to reduce the

complications of removing or devascularising the gland. But problem of hypoparathyroidism still persists especially in patients undergoing total thyroidectomy for neoplasm.

The etiology of insufficiency may either due to inadvertent removal of the glands or loss of vascularity by ligation of feeding artery [3] or their thrombosis.[3] Other compounding factors such as the primary thyroid disease like thryrotoxicosis or autoimmune disease also contribute to this. But their roles are inconclusive. The most relevant factor is the surgical technique with preservation of the gland and its vascularity. [4]This study was conducted to find out the usefulness of serum calcium and serum parathyroid hormone in predicting the hypocalcaemia after total or near total thyroidectomy

Materials and Methods

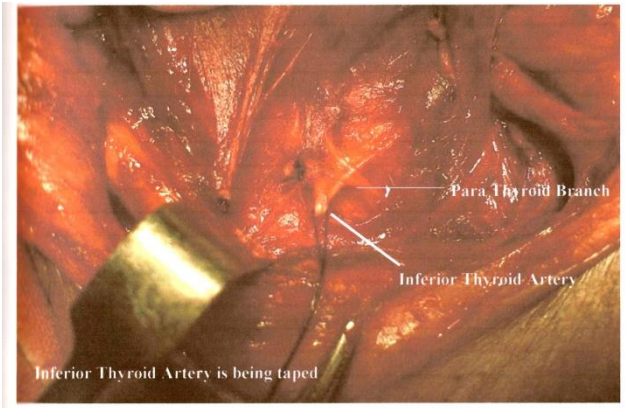
The study group consisted of 110 consecutive thyroidectomies from October 2014 to December 2014, in the Department of Surgery, Medical College Thiruvananthapuram. We conducted this study after obtaining approval from Human Ethical Committee. Of the 110 thyroidectomies, all were evaluated for serum calcium and in 78 patients only we could do serum PTH assay since it is not cost effective. In all patients routine blood and urine examination, blood sugar and urea estimation, X ray of chest and ECG were done. Histopathological diagnosis was obtained by FNAC. The thyroid status was assessed by doing T3, T4 & TSH estimation. The serum calcium level was estimated by drawing blood by venepuncture without manipulation. The normal calcium level ranges from 8-11 mg/dL and values less than 8 mg/dL were considered as hypocalcaemia and the normal range of parathyroid hormone range from 16.6-83.4pg/mL of EDTA sample blood by DRG PTH ELISA technique. iPTH values <15pg/mL is considered below normal. EDTA plasma has been reported to demonstrate improved PTH stability as compared to serum. To assay the specimen in duplicate, 50 microlitre of serum or EDTA plasma is required. The serum or plasma is promptly separated in a refrigerated centrifuge and stored at-20 degree centigrade or lower. Serum or plasma can be stored up to 8 hrs at 2-8 0C and frozen at -20degree are stable up to 4 months.

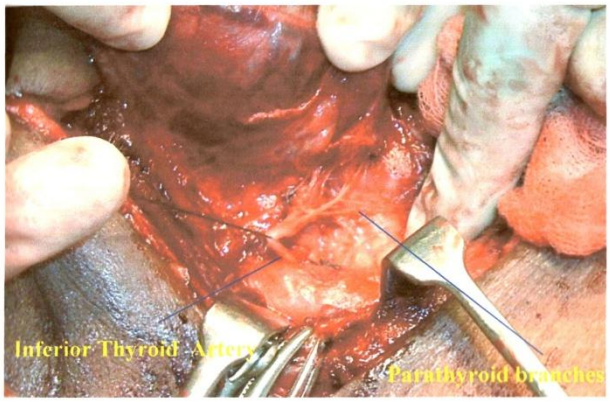
All thyroidectomies were done using a standardized approach. After dissection of middle thyroid veins, medial rotation of the thyroid gland is done, inferior thyroid artery is identified as it emerges behind the common carotid artery gently isolated, dissected by atraumatic fashion and looped with 2.0 vicryl. Using the loop, artery is dissected towards the thyroid, as the dissection proceeds. Most often parathyroid artery is seen as it emerges commonly from the postero inferior aspect of main stem. Occasionally the branches arise from more distal branches of the inferior thyroid artery. As the dissection proceeds, the recurrent laryngeal nerve is encountered at some point which is safe guarded. Inferior thyroid artery is traced in to the thyroid gland and divided and controlled with bi polar cautery at the most distal point. In this way the arterial supply to the parathyroid is safe guarded. Often the parathyroid artery serves as a guide to parathyroid. Superior parathyroid is preserved as usual. But however, the consistent and definite preservation of inferior parathyroid probably accounts for reduction in the incidence of hypocalcaemia in post operative period.

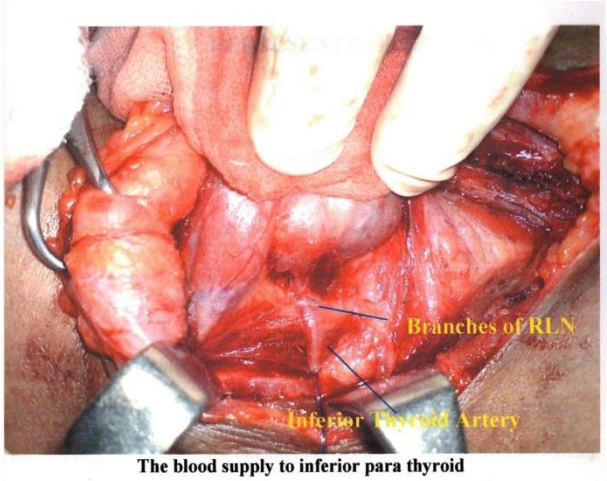
During the postoperative period patients were carefully watched for clinical symptoms and signs of hypocalcaemia. Fatigue, weakness and positive Chovstek's sign and Trousseau's sign [15,16,18,19] were considered as mild hypocalcaemia. Tetany and those with carpopedal spasm, convulsions and laryngeal spasm were considered as advanced hypocalcaemia. Samples were sent for calcium and parathyroid hormone assay 6 and 12 hours post operatively.

All variables were entered into an excel based case report form by residents given training in the data collection procedures. Descriptive statistics were summarized as mean and standard deviation for continuous data and as proportions for the categorical data. Association between variables was assessed with chisquare test. All statistical

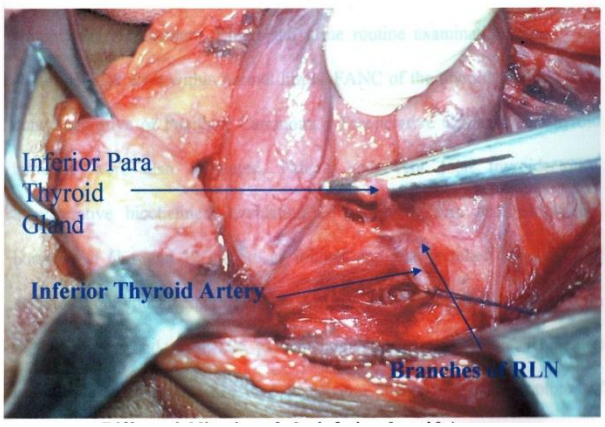
analysis were implemented in spss software







The blood supply to inferior para thyroid



Differential ligation of the inferior thyroid Artery

Observations and Results

Patient Profile Is Given In Table 1

Total thyroidectomy group comprised of 69 patients (62.7%) and near total thyroidectomy of 41 patients (37.3%)

The preoperative diagnosis and mean serum calcium and iPTH in group 1 and group 2 are shown in table 1 and 2 respectively

On serial estimation of serum calcium and serum PTH it was found that overt clinical hypocalcaemia was observed in 6 out of 110 patients (5.45%) and 18(16.36%) patients presented with circumoral numbness and digital paresthesia (total 24 patients) which was correlated with biochemical hypocalcaemia. Of this 24 patients, a total of 17 patients are in group 1(TT) and 7 patients in group 2(NTT), suggesting that the more radical the procedure is, the risk of hypocalcaemia is more. The indications of thyroidectomy are given in (Table 111). The cumulative incidence of hypocalcaemia is 21.8% (table. The usual time of presentation is after 24 hrs ,but in our study 4patients presented with hypocalcaemia before 24 hours and rest of them at variable time within or after 24 hours following NTT/TT, which could be confirmed biochemically early. Majority of the patients in group 1 and 2 received prophylactic oral calcium and vitD3 where there was no clinical evidence of hypocalcaemia but serum calcium and serum PTH showed drop on serial estimation, considering that they are at high risk of developing hypocalcaemia. The positive predictive values for calcium is 96% (p value <.000001) But in about 50 % of cases serum calcium and PTH showed returning to normal levels from an initial drop in serum levels and no clinical hypocalcaemia. They may not require prophylactic calcium and vit D3. Only 6 of the study group presented with carpo pedal spasm, in one such patients the serum level dropped as low as 5.6 mg /dl (representative case 1) and treated with intravenous calcium gluconate and supplemented with oral calcium and vit D3

On serial estimation of serum calcium and serum PTH as an early predictor of hypocalcaemia, it was found that all but few showed an initial drop

in serum at 6 hrs and progressive drop observed in those 24 patients developed clinical hypocalcaemia or likely to develop hypocalcaemia later and in a subset of patients a likelihood of returning to normal was observed after the initial drop, in those are unlikely to develop the same.

Estimation of intact PTH (iPTH) hormone on the contrary showed an equivocal results. In a few cases only s.iPTH showed a corresponding change in the serum levels of iPTH with clinical hypocalcaemia. Serum PTH showed wide range of variations. The lower limit of serum PTH is less than 15 pg /dl and when the PTH levels falls below 1 lpg/dl, clinical hypocalcaemia become evident. P value<.05

Discussion

Hypocalcaemia is a well known complication of thyroid surgeries. It is because of the close approximation of the parathyroid gland to the thyroid and common blood supply from the inferior thyroid artery. The incidence reported by various investigators range from 5 - 20%. The reported frequency of permanent hypocalcaemia has varied from 0% - 3.8% and of transient hypocalcaemia from 0.9% - 25.9%.

This study was aimed at finding the incidence in our institution, the usefulness of early serum calcium and PTH as early predictors of hypocalcaemia following total or near total thyroidectomy, the effectiveness of management and to compare the incidence with that of other investigators. Various causes are suggested in the development of post thyroidectomy hypocalcaemia. These include the extent of peroperative trauma, ligation of inferior thyroid artery, thyrotoxic osteodystrophy and release of calcitonin during surgery, low preoperative calcium, vitamin D level, serum ALP and vascular spasm that occurs during mobilization of the gland. [22, 23]

Patients underwent Total and Near total thyroidectomies only are randomly selected for the present study and hemi-thyroidectomy /subtotal thyroidectomy are excluded. All patients in our study had serum calcium level within normal limits in the preoperative period. A decrease in serum calcium was noted within the first 6 hours of surgery in almost all patients and in those patients who developed clinical hypocalcaemia, the 12hour calcium also showed a significant drop. Similarly, serum PTH also showed a marked drop in the serum levels at 6 hours and 12hours in patients with overt hypocalcaemia. In a group of patients it was noticed that serum calcium and PTH levels are returning to normal levels from an initial drop and in these patient no symptom in the form of paresthesia and numbness or signs evidence of hypocalcaemia was present. The patients who had clinically overt hypocalcaemia developed within the first postoperative day and within 24 hours were promptly relieved of their symptoms on administration of intravenous calcium gluconate. The calcium level reached within normal range on the third postoperative day. Others who had only paresthesia and progressive drop of serum calcium and serum PTH from the initial levels are supplemented with oral calcium as early as could, so as to prevent the development of transient hypocalcaemia.

In the present study we observed that estimation of serum calcium at 6 hours and 12 hours in post thyroidectomy patients 24 patients developed clinical hypocalcaemia and the biochemical assay also showed hypocalcaemia with a positive predictive value of 94%. PTH also showed similar results but not amount to biochemical hypoparathyroidism. PTH assay is not feasible since it is not cost effective. Independent calcium assay alone is useful in predicting the clinical hypocalcaemia as early as 24 hours and thus early prediction facilitate early discharge of patients after surgery and reduce hospital stay.

Diagnosis & Percentage Table 1

Diagnosis code

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid MNG	58	52.7	52.7	52.7
Pap Ca	11	10.0	10.0	62.7
Fol. Ca	5	4.5	4.5	67.3
Hash	7	6.4	6.4	73.6
Toxic MNG	4	3.6	3.6	77.3
Diff coll	14	12.7	12.7	90.0
Anaplastic Ca	2	1.8	1.8	91.8
MNG It is	6	5.5	5.5	97.3
9.00	3	2.7	2.7	100.0
Total	110	100.0	100.0	

Table II

Procedure code

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid NTT	41	37.3	37.3	37.3
TT	69	62.7	62.7	100.0
Total	110	100.0	100.0	

Diagnosis & Percentage

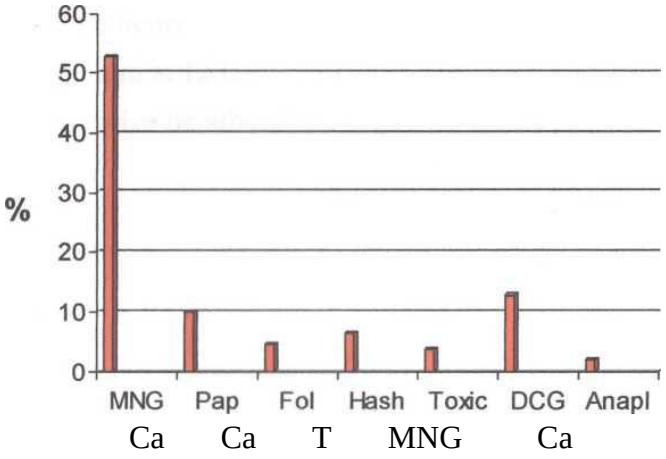


Figure 1

Table III

CAL CAL_6 CAL_12 PTH PTH_6 PTH_12

*Procedure code

Procedure code		CAL	CAL 6	CAL 12	PTH	PTH 6	PTH 12
NTT	Mean	9.524	8.54	8.534	38.7655	38.9607	28.0862
	N	41	41	41	29	28	29
	Std. Deviation	1.030	1.08	1.071	19.4660	60.5707	10.2348
TT	Mean	9.283	8.36	8.139	48.9511	28.4511	25.9404
	N	69	69	69	47	47	47
	Std. Deviation	1.299	.78	.949	78.7485	11.9179	12.8270
Total	Mean	9.373	8.43	8.286	45.0645	32.3747	26.7592
	N	110	110	110	76	75	76
	Std. Deviation	1.206	.90	1.010	63.0060	38.1196	11.8794

CAL = preoperative serum calcium levels
CAL _ 6 = calcium at 6 hours
CAL _12 = calcium at 12 hrs
PTH = preoperative parathyroid hormone

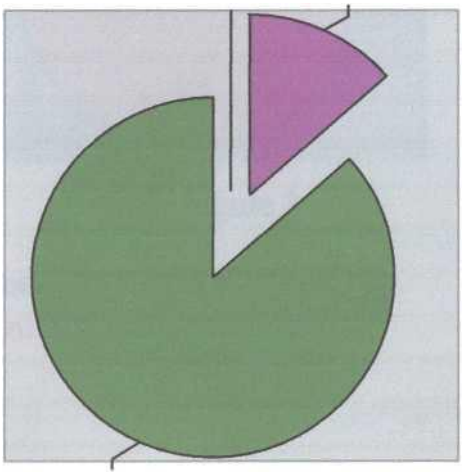
Conclusion

CAL CAL 6 CAL 12 PTH PTH 6 PTH 12

*** Age Code**

AGE CODE		CAL	CAL 6	CAL 12	PTH	PTH 6	PTH _12
15-34	Mean	9.549	8.55	8.364	36.9393	29.1630	29.3929
	N	39	39	39	28	27	28
	Std. Deviation	1.335	.94	1.085	14.2184	11.1647	11.4971
35-54	Mean	9.310	8.31	8.200	40.1300	35.0950	24.2675
	N	61	61	61	40	+ 40	40
	Std. Deviation	1.144	.83	.978	22.5960	51.4019	12.7027
55+	Mean	9.070	8.64	8.510	98.1750	29.6125	30.0000
	N	10	10	10	8	8	8
	Std. Deviation	1.052	1.12	.935	187.8343	9.3296	5.2858
Total	Mean	9.373	8.43	8.286	45.0645	32.3747	26.7592
	N	110	110	110	76	75	76
	Std. Deviation	1.206	.90	1.010	63.0060	38.1196	11.8794

13.6



86.4

Figure 2

Sex incidence

Male

Female

Table IV

Hypocalcaemia code

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid Yes	24	21.8	21.8	21.8
No	86	78.2	78.2	100.0
Total	110	100.0	100.0	

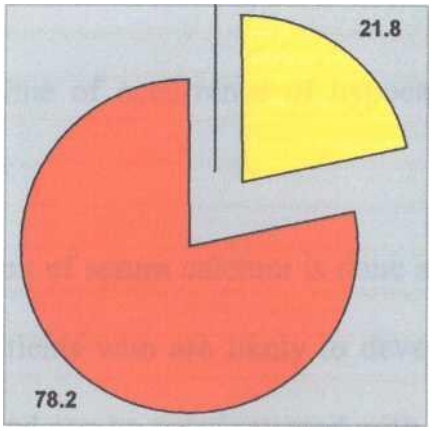


Figure 3

Percentage of hypocalcaemia

• No hypocalcaemia (78.2%)

*……

Age group

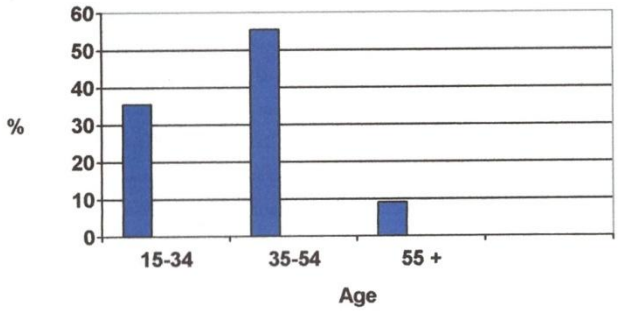


Figure 4

Transient biochemical hypocalcaemia occur in all forms of thyroid surgery in the immediate post operative period. Incidence of clinical hypocalc-aemia is maximum in total or near total thyroidectomy. Most common time of occurrence of hypocalcaemia is in the first 48 hours of surgery. If serial estimation of serum calcium is done at regular intervals of 6 & 12 hours, the patients who are likely to develop hypocalcaemia can be predicted early and can be supplemented with prophylactic oral calcium or intravenous calcium gluconate if overt hypocalcaemia present or develops. The incidence of clinical hypocalcaemia in total thyroidectomy is approximately 5.4%. Patients with serum calcium level that drop at 6 & 12 hours from the preoperative level of calcium after total or near total thyroidectomy without clinical evidence of hypocalcaemia, may be considered are safe to discharge with oral calcium and vitamin D3 with or without one or two days more of observation. Serum calcium assay even though it is useful in early prediction of hypocalcaemia it is not very useful as an early predictor because of cost factor.

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