

Clinical, Biochemical, Peroperative Factors Predicting Hypocalcemia in Patients Undergoing Total Thyroidectomy-Our Institute Experience

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Abstract: Total thyroidectomy is a common surgical procedure which has well known complications and hypocalcemia is an important complication encountered commonly. Hypocalcemia is one of the serious complication of thyroid surgery especially total thyroidectomy. Incidence of hypocalcemia ranges from 2-30%⁽¹⁾. Occurrence of post thyroidectomy hypocalcemia is commonly seen several days after total thyroidectomy. This delay will challenge many clinician to monitor serum calcium level periodically.

Methods:Patients attending our outpatient surgical clinic with thyroid disorder requiring total thyroidectomy were selected. Total of 52 patients who underwent total thyroidectomy were included in study in whom various factors predicting hypocalcemia in the preoperative, perioperative and postoperative period were assessed, with serial monitoring of postoperative calcium and PTH levels.

Results: In our study the incidence of symptomatic hypocalcemia apparent in the postoperative period was 34.6% i.e. 18 out of 52 patients. All patients had initial fall in serum ionized calcium level in the postoperative period. In all patients the fall in ionized calcium levels was noticed at 12 hours after surgery. Serum calcium continued to fall in 18 patients at 24 hours post operatively who had a fall in serum calcium at 12 hours postoperatively. By serial calcium measurement remaining 34 patients serum calcium level remained normal like

its preoperative levels. At 72 hours those 18 patients who had hypocalcemia continued to show low serum calcium level.

Keywords: Total Thyroidectomy, Hypocalcemia, Calcium, Pth...

Date of Submission: 23-12-2017

Date of acceptance:16-01-2018

I. Introduction

Total thyroidectomy is a common surgical procedure which has well known complications and hypocalcemia is the important complication encountered commonly. The incidence of post total thyroidectomy hypocalcemia has been decreased because of advances in surgical techniques and technology. In the past the mortality rate after total thyroidectomy was as high as 35-40%⁽¹⁶⁾. Now a days the mortality rates after surgery has significantly reduced to 1-2%⁽¹⁶⁾. Significant morbidity after total thyroidectomy is 3%-4%⁽¹⁶⁾. The early complications of total thyroidectomy are haemorrhage with tracheal compression, airway compromise and even death. Incidence of early hemorrhage is 1-2%⁽¹⁸⁾. Respiratory embrocement can occur because of vocal cord paralysis (or) laryngeal edema. Incidence of life threatening respiratory obstruction occurs in about 0.5-1%⁽¹⁹⁾, and it occur in immediate postoperative day. Hypocalcemia is one of the serious complication of total thyroidectomy. Incidence of hypocalcemia ranges from 2-30%⁽¹⁾. In early days the incidence was very high and due to the advancement in surgical technique the incidence has dropped significantly. Occurrence of post thyroidectomy hypocalcemia is commonly several days after total thyroidectomy. This delay will challenge many clinician to monitor serum calcium level periodically.

II. Method of Study

The present study was conducted in the Institute of General Surgery, Madras Medical College, Chennai. The patients were selected among thyroid patients attending outpatient surgical clinic of Madras Medical College requiring total thyroidectomy. Total of 52 Thyroid patients who underwent thyroid surgery for benign or malignant disorders in whom various factors predicting hypocalcemia in preoperative, perioperative, postoperative period were assessed. There were 48 Female and 4 Male Patients aged between (35-65) who were included in the study. The study was conducted between November 2016 - April

2017 Detailed history and clinical examination were performed in all patients taken up for study, related to thyroid disorders. Serum ionized and total calcium levels were assessed. Preoperatively

1. 12 Hours postoperatively
2. 24 Hours postoperatively
3. 48 Hours postoperatively

Parathyroid hormone estimation is done within 24 hours postoperatively. Intraoperative findings such as

1. Blood loss approximately (in ml)/ any need for blood transfusion if present.
2. Recurrent laryngeal nerve identified and preserved
3. Lymph node dissection was done or not
4. Any other major intraoperative event.

Patients have been followed up postoperatively with signs and symptoms of hypocalcemia in immediate postoperative period, 12 hours, 24 hours and 48 hours postoperatively and patient with evidence of clinical and biochemical hypocalcemia have been followed up on outpatient department (OPD) basis with weekly ionized serum calcium levels. Ionized calcium levels are used as follow up marker.

III. Results

In the study 52 patients of thyroid disease were assessed for the occurrence of post thyroidectomy symptomatic hypocalcemia using serial monitoring of pre and postoperative ionized serum calcium levels, Parathormone and Vitamin. Devels. In our study the incidence of symptomatic hypocalcemia apparent in the postoperative period was 34.6% i.e. 18 out of 52 patients. All patients had initial fall in serum ionized calcium level in the postoperative period. In all patients the fall in ionized calcium levels was noticed at 12 hour after surgery. At 24 hours serum calcium continued to fall in 18 patients. By serial calcium measurement remaining 34 patient's serum calcium level remains normal like its preoperative levels. At 72 hours those 18 patients who had hypocalcemia continued to show low serum calcium level. Hence In the present study the incidence of post thyroidectomy symptomatic hypocalcemia was 18%.

3.1 In Relation With Age And Sex Of The Patients:

In present study there were 4 male and 48 female patients, 36 to 65 years of age with overall mean age of 46.5 years.

Age distribution of the subjects (n = 52)

Age	No. of Patients	Hypocalcemia observed	%
35-44	13	-	0
45-54	15	3	20
55-65	24	15	62.5

Sex distribution of the subjects (n= 52)

Sex	No. of Patients	Hypocalcemia	%
Male	4	1	25
Female	48	17	35.4

No patients out of 13 had hypocalcemia in 35-45yrs of age, 3 patients out of 15 had hypocalcemia in 45-54yrs of age, 15 patients out of 24 had hypocalcemia in 55-65 years of age. Hence concluded that old age will have high incidence of hypocalcemia. 1 out of 4 male patients and 17 out of 48 female patients had hypocalcemia. So Female sex had more predilection towards hypocalcemia age and sex had some influence on symptomatic hypocalcemia in our study.

3.2 In Relation With Duration of Surgery

In the present study duration of surgery is classified into 1 hour, 1-2 hour, more than 2 hours, none of the patients was operated in 1 hour, 16% with 1-2 hours and remaining 84% completed total thyroidectomy in more than 2 hours.

Time	No. of patients	Hypocalcemia	%
Short duration (1-2hr)	9	1	11.1
Long duration (>2hrs)	43	17	39.5

In 16% of patients who had short duration of surgery (1-2hrs), 11.1% of the patients developed hypocalcemia. In 84% of patients who had long duration of surgery (>2hrs) 39.5% of patients developed hypocalcemia, and hence concluded that longer duration of surgery indirectly reflects that difficulty in dissection or lymph node dissection may provoke the incidence of post thyroidectomy hypocalcemia.

3.3 Based On Size of Goitre

In this study >6cm size were considered large, 4-6cm as medium and <4cm as small goiter respectively.

3.4 Distribution Based On The Size Of Goiter

Size	No. of patients	Hypocalcemia observed	%
Large	18	13	72.2
Medium	26	4	15.3
Small	8	1	12.5

13 out of 18 pts which is 72.2% with large goiter had hypocalcemia, whereas 4 out of 26 pts(15.3%) with medium size goiter and 1 out of 8 pts(12.5%) with small size goiter had hypocalcemia respectively. Hence concluded that size of goiter has some influence in developing postoperative hypocalcemia probably due to longer duration of surgery and inability to identify parathyroids separately.

3.5 Intra Operative Identification Of Recurrent Laryngeal Nerve:

In the present series, 15 out of 42 (35%) pts where both sides RLN identified had hypocalcemia, 3 out of 9 pts (33%) where one side identified had hypocalcemia, 1 patient where nerve could not be identified didn't develop hypocalcemia. Hence identification of the recurrent laryngeal nerve have not shown any significant effect on the incidence of postoperative symptomatic hypocalcemia.

3.6 Number Of Parathyroid Gland Preserved:

15 out of 15 pts in whom <2 para thyroids preserved had hypocalcemia whereas only 3 out of 37pts in whom >2parathyroids preserved had hypocalcemia.

Parathyroid glands preserved	No. of patients	Hypocalcemia observed	%
Less than 2	15	15	100
2 or more	37	3	8.1

Hence no. of para thyroids preserved has a significant impact in development of postoperative hypocalcemia.

Pth Measurement:

Low PTH concentration after surgery will have increased risk of transient hypocalcemia, which have false, negative value and high negative predictive values. Normal level of PTH excludes permanent hypocalcemia. When the PTH level on 1st Postoperative day is less than 15pg/ml with calcium level less than 1.9mmol/L it has more sensitivity and specificity in prediction of post thyroidectomy hypocalcemia. Hence patient with normal PTH level on first postoperative day can be safely discharged on 2nd postoperative day.

3.7 In Relation With Intraoperative Blood Loss:

In present series mean blood loss when it is significant is 150-200ml. Here out of 8 patients who had blood loss <100ml, 1 patient which is 12.5% had symptom of hypocalcemia. Out of 37 patients in whom blood loss was between 100 and 150 ml, 12 patients which is 32.4% had hypocalcemia. Out of 7 patient's in whom blood loss was >150ml, 5 patients which is 71.4% had symptomatic hypocalcemia.

S. No	Intra operative Blood loss	No. of patient	Hypocalcemia Patient
1	<100ml	8	1 (12.5%)
2	100-150ml	37	12 (32.43%)
3	>150ml	7	5 (71.42%)

So it is concluded that blood loss >150ml put the parathyroid glands at a higher risk for injury during surgery (or) difficulty in the total thyroidectomy

IV. Analysis

In the study 52 patients of thyroid disorder who were taken up for total thyroidectomy were assessed for the occurrence of post thyroidectomy symptomatic hypocalcemia using serial monitoring of pre and postoperative ionized serum calcium levels, PTH and Vitamin. D levels.

4.1 Incidence of Symptomatic Hypocalcemia

In the present study the incidence of post total thyroidectomy symptomatic hypocalcemia was 34.6%. This figure corroborate with that Jacobs et al²⁸ reported that 27.7% of early hypocalcemia patients received calcium supplementation after total thyroidectomy. Wingert et al³⁷ total of 220 patients for malignant as well as benign goiters, they reported 12.5% incidence of symptomatic hypocalcemia. Scanlon et al²¹ported 250 patients undergone total thyroidectomy over a period of 10 years. In which atleast 20% patient required at least one dose of calcium during the immediate postoperative period.

4.2 In Relation With Duration Of Surgery

In our study, duration of surgery is classified into 1 hour, 1-2 hour, more than 2hours, none of the patients was operated in 1 hour, 9 pts operated with 1-2 hours and remaining 43 pts completed total thyroidectomy in more than 2 hours.so 17 out of 43 patients had been operated in longer duration developed hypocalcemia and, 1 out of 9 developed hypocalcemia and hence concluded that longer duration of surgery indirectly reflects that difficulty in dissection or lymph node dissection may provoke the incidence of post thyroidectomy hypocalcemia.

Similar results Wingert et al^[2009] reported an incidence of symptomatic hypocalcemia of 4% for benign disease which increased 20% following total thyroidectomy. Tovi et al^[2008] reported 4 cases of symptomatic hypocalcemia in 100 patients with malignant thyroid problem followed up for 1 year. Lymph node dissection had done in three patients in addition to total thyroidectomy.

4.3 Intra Operative Identification Of Recurrent Laryngeal Nerve:

In the present series, the identification of the recurrent laryngeal nerve have not shown any effect on the incidence of postoperative symptomatic hypocalcemia. Wade et al^[1998] referred that 50 patients undergoing thyroidectomy routine identification of the recurrent laryngeal nerve does not increase the risk of postoperative hypocalcemia. Harris et al⁽¹⁹⁹²⁾ reported that series of 95 thyroidectomy patients no case hypoparathyroidism relation with recurrent laryngeal nerve identification. Rao et al^[2006] presented a series in which 29 patients underwent total thyroidectomy, no case of permanent hypo parathyroidism in this series. In all recurrent laryngeal nerve were identified. In our study out of 42 bilateral recurrent laryngeal nerve identified patients, 15 developed hypocalcemia. Out of 9 unilateral identification of RLN patients, 3 developed hypocalcemia. Serial monitoring also did not show any fall in calcium and PTH level. Hence it can be derived that identification of nerve doesn't place parathyroid gland at a risk of surgery.

4.5 Pth Measurement

OEdafe et al ^[2014] defined that single PTH measurement within 24 hours after surgery especially 12 hours after total thyroidectomy was more accurate in predicting transient hypocalcemia. Low PTH concentration after surgery will have increased risk of transient hypocalcemia, which have low false negative value and high negative predictive values. Normal level of PTH excludes permanent hypocalcemia: Reza Asan et al^[1995] concluded in his study that combined measurement level of parathyroid hormone and serum calcium level helpful in predicting postoperative hypocalcemia which has minimal laboratory effort and low cost. Identification of parathyroid gland during thyroidectomy: In multivariable analysis found that fewer than 2 parathyroid glands associated with transient and permanent hypocalcemia.

V. Conclusion

In this study, the incidence of post thyroidectomy symptomatic hypocalcemia was 34.6%, however all patients had initial fall in ionized calcium levels in immediate postoperative period, most of them stay among symptomatic hypocalcemia group and ionized calcium level comes to preoperative value early in postoperative period.

1. 7 out of 8 patients with symptomatic hypocalcemia had undergone total thyroidectomy with functional neck dissection for thyroid malignancy.
 - a. 1 patient undergone total thyroidectomy for Grave's disease and 43 patients underwent total thyroidectomy for multi nodular goiter.
 - b. Hence it can be concluded the greater the extent of surgery more is the chance of developing symptomatic hypocalcemia, or we can say that the malignant goiters have a much higher incidence of symptomatic hypocalcemia than benign goiter by virtue of extent of surgery.

2. The age and sex of patients have influence on incidence of post total thyroidectomy symptomatic hypocalcemia. Thus older age and female sex have more chances of developing hypocalcemia.
 3. Preservation of less than two parathyroid glands will have more risk of developing hypocalcemia.
 4. The intra operative identification of the recurrent laryngeal nerve did not affect the incidence of postoperative symptomatic hypocalcemia.
 5. The intra operative blood loss is directly correlated with increased incidence of postoperative symptomatic hypocalcemia.
1. Result of our study suggested that early serial ionized calcium, PTH level monitoring in postoperative period can predict whether the patient will have postoperative symptomatic hypocalcemia or not. Thus the study concludes that normal levels of postoperative calcium values based on two early ionized calcium values and parathyroid hormone level within 24 hours after total thyroidectomy are strongly predictive of a stable postoperative calcium level. These patients thus can have an early and safe discharge from the hospital. Patients with decreased calcium and parathyroid hormone values in the postoperative period are at a higher risk of developing symptomatic hypocalcemia and require careful follow up and monitoring. So these predictors will influence the occurrence of hypocalcemia after total thyroidectomy, and to be prevented whenever possible....

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Dr.G.Muthukumaran. Clinical, Biochemical, Peroperative Factors Predicting Hypocalcemia in Patients Undergoing Total Thyroidectomy-Our Institute Experience" *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, vol. 17, no. 1, 2018, pp. 62-66.