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Original Research Article

Study of the incidence of hypocalcemia in patients undergoing bilateral thyroid surgery

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ABSTRACT

Background: Thyroid surgery are among the most common operations performed all over the world. Hypocalcemia following total thyroidectomy is a fairly common complication. Occurrence of acute hypocalcemia can be predicted in patients undergoing thyroid surgery, based on serial calcium measurement and this helps in early prediction of hypocalcemia. The aim of present study was to assess the incidence of post thyroidectomy hypocalcemia and factors which might play a role in its occurrence.
Methods: A total 30 patients who underwent bilateral thyroidectomy were analysed. The study period was from June 2017 to March 2019. The incidence of hypocalcemia was analysed with serial calcium estimation in immediate post-operative period, 4 hours and 24 hours after surgery and on 5th post-operative day. The factors analysed included pre-operative and post-operative serum calcium levels, clinical features, the disease type and factors related to surgery. The ethical approval was taken from the ethical committee of the institute. At the end of the study data was collected and analysed by using student t-test and chi square test. A p-value of less than 0.05 was considered significant.
Results: Post-operative transient hypocalcemia developed in 21 patients out of 30 (70%). Of them six patients (28.75%) developed severe hypocalcemia and 15 (71.42%) developed mild to moderate hypocalcemia. Out of six patients, five patients were histopathologically diagnosed as malignant thyroid disease. 15 patients who developed mild to moderate hypocalcemia were diagnosed to be having benign thyroid conditions.
Conclusions: Patients underwent thyroid surgery for malignant conditions showed higher incidence and severity hypocalcemia as compared to cases where surgery was performed for benign thyroid disease. This complication can be prevented with meticulous perioperative dissection, prompt identification of parathyroid glands and frequent postoperative monitoring of serum calcium levels.

Keywords: Hypocalcemia, Incidence, Parathyroid glands, Subtotal thyroidectomy, Total thyroidectomy

INTRODUCTION

Thyroidectomy is a surgical procedure to remove all or part of the thyroid gland and used to treat diseases of the thyroid gland including thyroid cancer, multi-nodular goiter, solitary thyroid nodules and large goiters. Thyroid surgery has been performed for more than a century. Theodore Kocher first described the standard technique of thyroidectomy in 1872, which was later refined by Theodor Billroth, William S. Halsted and many more. Operative mortality from thyroidectomy was as high as 40 percent in last century.[1] But now-a-days mortality due to thyroid surgery has decreased drastically to less than 1%. Though the mortality has decreased significantly still there are many complications of thyroid surgery. One of the serious and early complications of thyroid surgery is post-operative hemorrhage with the potential for tracheal compression, airway compromise and sometimes even

death. Post thyroidectomy hypocalcemia is one of the important morbidities of thyroid surgery. A 3 to 32% incidence of hypocalcemia has been reported after thyroid surgery and it generally present on second to fifth postoperative day.[2-4] The clinical feature includes circumoral paraesthesia, carpopedal spasm and in severe cases it may lead to tetany. Present study was done to see the incidence of hypocalcemia after total/subtotal thyroidectomy and to analyse the factors which might play role in its development.

METHODS

The present prospective study was conducted in department of general surgery at an apex institute of North India. The study period was from June 2017 to March 2019. Thirty patients were enrolled in study who qualified the inclusion criteria i.e. patients more than 12 year of age including both genders admitted and diagnosed as having thyroid swelling requiring thyroid surgery. Patients less than 12 years of age, pervious thyroid operation or irradiation, concomitant parathyroid disease, hypocalcemic patients, patients already on calcium supplementation were excluded from the study. An informed consent was taken from all patients/guardians for inclusion in study. Data was collected from the patients undergoing thyroid surgery by meticulous history taking, careful clinical examination, appropriate radiological, hematological investigations including serum calcium and serum albumin. Duration of operation and detailed operative findings like site and size of goitre, anatomy of parathyroid glands, anatomy of laryngeal nerves and relation of goitre with regional structures like trachea, esophagus etc. were noted. In post-operative period, all the patients were assessed for any symptoms and signs of hypocalcemia. Serial monitoring of serum calcium levels in immediate and early post-operative period i.e., immediately after the surgery, 4 hours after surgery and 24 hours after surgery and on 5th post-operative day was done. All these findings were entered into predesigned patient proforma and results were analysed. The ethical approval was taken from the ethical committee of the institute. At the end of the study data was collected and analysed by using student t-test and chi square test. A p-value of less than 0.05 was considered significant.

RESULTS

In this study, authors followed 30 patients who underwent thyroid surgery for various indications. Demographic profile of all patients i.e., age and sex were studied in all 30 cases as per Table 1.

Table 1 shows age distribution of the study population. Maximum patients were in 41-50 years age group i.e., seven patients and only one patient was in age group of more than 70 years. Mean age of the patients was 47.5±15.02 years with a range of 21-72 years.

Table 1: Demographic profile.

Age (years)	No. of patients	Percentage
≤30	4	13.33
31-40	6	20
41-50	7	23.33
51-60	6	20
61-70	6	20
>70	1	3.33
Mean±SD	47.5±15.02	
Range	21-72	

Table 2: Sex distribution.

Sex	No. of patients	Percentage
Male	7	23.33
Female	23	76.67

Sex distribution of the patients showed that female patients outnumbered male patients by a significant margin. There were 23 (76.67%) females and 7 (23.33%) males.

Table 3: Clinical causes of goitre.

Diagnosis	No. of patients	Percentage
Carcinoma thyroid	13	43.33
Colloid goitre	2	6.66
Multinodular goitre	15	50

A clinical diagnosis was established in all patients after local examination of thyroid. Patients were divided into different groups depending upon their clinical diagnosis as shown in Table 3.

A total of 15 (50%) patients were clinically diagnosed as multinodular goitre followed by 13 (43.33%) patients who had suspected carcinoma thyroid. Only two (6.66%) patients had colloid goitre.

After making clinical diagnosis and USG of the thyroid lesion, all patients underwent FNAC for making the tissue diagnosis. Based on FNAC reports following results were obtained.

Table 4: Distribution of patients according to FNAC report.

FNAC findings	No. of patients	Percentage
Benign follicular cells	2	6.66
Carcinomatous changes	1	3.33
colloid goitre	14	46.66
Papillary carcinoma	6	20
Atypical cells s/o malignancy	7	21

Table 4 depicts distribution of the patients according to FNAC findings. Maximum number of patients had

colloid goitre on FNAC i.e., 14 (46.66%) followed by atypical cells s/o malignancy in 7 (21%) patients. Only one (3.33%) patient had carcinomatous changes which ultimately turned out to be a case of anaplastic carcinoma. Six patients were diagnosed as papillary carcinoma on FNAC findings.

Table 5: Postoperative evaluation of hypocalcemia.

Postoperative progress	No. of patients	Percentage
Paraesthesia	18	60
Carpopedal spasm	0	0
Convulsions	0	0
Chvostek's sign	10	33.33
Trousseau's sign	3	10

After making tissue diagnosis by FNAC and having a complete workup, all patient was subjected to surgical intervention. Subtotal thyroidectomy was carried out only in those patients where there was no evidence of malignancy on FNAC. In 26 (86.67%) patients, total thyroidectomy was performed and in four (13.33%) patients subtotal thyroidectomy was performed.

During surgery, all precautions were taken, to preserve the recurrent laryngeal nerve and parathyroid glands. Recurrent laryngeal nerve was identified in 28 (93.33%) patients on right side and 29 (96.67%) patients on left side.

In postoperative period, all the patients were thoroughly examined and evaluated for signs and symptoms of hypocalcemia like paresthesia's, carpopedal spasm, convulsions, Chvostek's sign and Trousseau's sign.

Postoperative progress of the patients showed that paresthesia was observed in 18 (60.0%) patients, Chvostek's sign in 10 (33.33%) and Trousseau's sign in 3 (10%) patients. In none of the patients, authors found carpopedal spasm and convulsions.

Table 6: Preoperative and postoperative serum calcium levels (immediate to subsequent follow ups).

Mean serum calcium (pre-operative)	Immediate (post-operative)	4 hours post-operative	24 hours after surgery	Day 5 after surgery	Statistical analysis			
					Immediate	**4 hours**	**24 hours**	**Day 5**
8.81±0.24	8.38±0.26	7.90±0.46	7.76±0.58	7.86±0.58	<0.001	<0.001	<0.001	<0.001

Table 7: Histopathological findings.

Histopathological findings	No. of patients	Percentage
Anaplastic carcinoma thyroid	1	3.33
Colloid goitre	12	40
Multinodular goitre	4	13.33
Papillary carcinoma thyroid	13	43.33

Table 8: Incidence of hypocalcemia in different thyroid conditions.

Severity of hypocalcemia	No. of patients	Final diagnosis	Incidence (%)
Severe	6	Papillary carcinoma=4 Anaplastic=1 Multinodular=1	20
Mild to moderate	15	Colloid goitre=4 Multinodular=2 Papillary carcinoma=9	50
Normocalcemic	9	Colloid goiter=8 Multinodular=1	30

In postoperative period, serial monitoring of serum calcium was done in all patient and it was compared with preoperative serum calcium levels as per Table 6.

Mean serum calcium preoperatively was 8.81±0.24 and when it was compared with serum calcium level in immediate postoperative, 4 hours after surgery, 24 hours after surgery and 5 days after surgery, it showed a significant difference ($p<0.001$). The maximum level of hypocalcemia was noted at 24 hours after surgery.

After the completion of desired procedure, excised thyroid gland specimen was sent for histopathological examination and following observations were made.

Histopathological findings of the study population showed that majority of patients had papillary carcinoma thyroid i.e., 13 (43.33%) followed by colloid goitre 12 (40%). Four patients had multinodular goitre and only one patient had anaplastic carcinoma thyroid.

In the end, the comparison of severity of hypocalcemia was made with histopathological nature of disease as shown in Table 7.

Table 8 shows incidence of hypocalcemia in different thyroid conditions. In the present study, authors observed total incidence of hypocalcemia as 70% that means 21 patients out of 30 developed hypocalcemia. Out of these 21 patients, six patients (28.57%), developed severe hypocalcemia and five of them were due to malignancy of thyroid. 15 patients out of 21 (71.42%) developed mild to moderate hypocalcemia and majority of them were having benign thyroid diseases as shown in Table 8.

DISCUSSION

In the present era mortality after thyroid surgery has decreased drastically because of expertise of surgeons and better surgical techniques. But post-operative complications specially hypocalcemia remains a fairly prevalent complication in patients undergoing total thyroidectomy and central lymph node dissection. Decreased serum calcium, secondary to hypoparathyroidism, may present clinically with muscle cramps, perioral and peripheral paresthesia's, tetany and confusion.[5] Large volume goiter, total thyroidectomy, recurrent goiter, retrosternal extension, advanced cancer, hyperthyroidism and experience of the surgeons were found as risk factors predisposing to post thyroidectomy hypocalcemia. Depending on the extent of parathyroid gland damage, hypocalcemia may be transient resolving within few months or permanent, requiring lifelong oral calcium and vitamin D supplementation.[5]

Authors carried out a prospective study on thyroid disease undergoing total/subtotal thyroidectomy to see the incidence of hypocalcemia in this study population and also the possible risk factors for its development.

Demographic profile

Demographic profile of all patients was studied as shown in Table 1 which shows that maximum number of patients were from middle age i.e., age ranging from 31 to 50 years. This finding is consistent with the other study available in literature.[5,6]

Regarding sex distribution

Thyroid diseases were more prevalent in females which is also reported in the various studies in the literature.[5-7] Morganti et al in their study concluded that aging has been proposed to represent a trigger for the development of autoimmune phenomena resulting in the production of both organ and non-organ-specific antibodies.[8] They reported that studies on the relationship between sex and thyroid autoimmunity in elderly subjects have shown that the age-related prevalence of antithyroid autoantibodies is greater in women >60 years of age. They concluded that an increased prevalence of hypothyroidism has been demonstrated in the elderly populaion.[8]

Distribution of patients according to their clinical diagnosis

In the present study, multinodular goitre was the most common clinical diagnosis after examination. A total of 15 patients (50%) were suffering from multinodular goitre followed by 13 patients (43.33%) who were clinical diagnosed as cases of carcinoma thyroid. The results are comparable with other studies.[9,10]

Recurrent laryngeal nerve and parathyroid gland identification

In the present study, recurrent laryngeal nerve (RLN) was tried to identify in all the patients. In 28 patients (93.33%) it was identified on right side and in 29 patients (96.67%) it was identified on left side. Zakaria et al in their study identified recurrent laryngeal nerve in 67.35% patients.[11] The identification of recurrent laryngeal nerve by the surgeon during the surgery minimizes the risk of damage to the nerve during surgical dissection. Recurrent laryngeal nerve injury after thyroidectomy can jeopardize the quality of life. In addition to the hoarseness of voice that occurs with unilateral recurrent laryngeal nerve injury, bilateral nerve injury leads to dyspnea and often life-threatening glottal obstruction. In this study authors could identify all parathyroid glands in 46.6% patients, three parathyroid glands in 23.3% patients, two parathyroid glands in 23.3% patients and one parathyroid gland in 6.8% patients. Nair et al in their study could identify all parathyroid gland in 80.14% patients and three parathyroid glands in 19.8% patients.[9] Eismontas et al in their study identified all parathyroid glands in 21.3% patients, three parathyroid in 52% patients, two parathyroid in 24.2% and single parathyroid gland in only 2% patients.[7] The greater the number of PGs found during the surgery, lower the chance of hypocalcemia. The study by Thomusch et al determined that permanent post-operative hypocalcemia was more likely to developed if less than two PGs were found during surgery.[12] On other hand, some studies have found that more PGs found during the surgery may be associated with temporary hypocalcemia.

Postoperative evaluation

Paresthesia's was the most commonly seen clinical symptom after hypocalcemia in this study. In the present study, paresthesia was seen in 18 patients (60%). Chvostek's sign was seen in 10 patients (33.33) and Trousseau's sign seen in three patients (10%). It was comparable to the results of the study of Eismontas et al

who in their study reported paresthesia in 22.6% patients, Chvostek's sign in 5.4% patients and Trousseau's sign in 3.6% patients.[7]

Correlation of histopathological findings with hypocalcemia

In the present study, out of 16 benign goitre patient's hypocalcemia was seen in seven patients (43.75%). Out of 14 carcinoma patients, hypocalcemia was seen in all the 14 patients (100%). Incidence of hypocalcemia was found higher in carcinoma patients. The results are comparable to the results of the study done by various other authors reported in the literature. The higher incidence of hypocalcemia in malignant condition is because of excessive dissection required for resection of thyroid and clearance of lymph nodes. This can lead to compromise of vascular supply of parathyroid gland despite their safe preservation.

The literature demonstrates a wide range of reported hypocalcemia rates following thyroidectomy (0.33%-83%).[13-15] The incidence of hypocalcemia was higher in this study as compared to other studies probably due to more number of carcinoma patients in this study as compared to other studies.[9,10] The reason for having more no of malignant goitre in this study is because of fact that surgical oncology unit in study institute is part of general surgery department. Another reason for having higher incidence of hypocalcemia in this study is that authors had included the cases of total and subtotal thyroidectomy in this study while other studies also included other procedures of lobectomy and hemithyroidectomy also.

CONCLUSION

Incidence of hypocalcemia is more in cases who are operated for malignant thyroid conditions and also the incidence of severe hypocalcemia is again more common with malignant thyroid conditions as compared to benign goitres. The estimation of serial serum calcium levels is fairly predictable and cost-effective method for diagnosis of early post-operative hypocalcemia and prediction of patients who are at higher risk of developing long-term hypocalcemia after thyroid surgery.

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