FREQUENCY OF HYPOCALCEMIA IN POST THYROIDECTOMY PATIENTS

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ABSTRACT

BACKGROUND: Hypocalcaemia is a common early complication occurring in post thyroidectomy patients. The aim of this study was determine the frequency of hypocalcaemia serum calcium level less than (8.2mg/dl) in patients who were operated upon for goitrier.

OBJECTIVES: The objectives of the study, was to determine the frequency of hypocalcaemia in post-thyroidectomy patients.

PATIENTS AND METHODS: This is a descriptive, prospective study. The study was conducted in the Department Of Surgery, Saidu Group of Teaching Hospital, Saidu Sharif Swat from January 2011 to June 2014. Total of ninety patients were included in the study, these were the patients who underwent total or near total thyroidectomy for any primary disease of thyroid gland like multinodular goiter and carcinoma thyroid gland, irrespective of their ages and gender.

Patients undergoing lobectomy, subtotal or completion thyroidectomy as the risk of developing hypocalcaemia is very low in these procedures, as well as patients having other medical problems causing hypocalcaemia like Chronic Renal Failure ,acid base imbalance and osteomalacia, all of these were excluded from study. Patients were divided into two groups, group A total thyroidectomy and group B near total thyroidectomy. Preoperative serum Ca^{++} level determined in all patients and then repeated on the first post surgery day, and any decrease in serum Ca^{++} level noted in both groups.

RESULTS: Results obtained were tabulated and analyzed. 48 patients(53%) of patients were more than 40 years of age and there was female preponderance. 18 patients (20%)of patients developed hypocalcaemia on the first post-operative day.30 patients(33.4%) of patients had symptoms of hypocalcaemia on first post-operative day.

CONCLUSION: Symptomatically and statistically significant post-operative hypocalcaemia is most common in the first postoperative day but prompt diagnosis is possible to institute treatment.

KEYWORD: Serum calcium levels, Post-operative, Thyroidectomy patients

INTRODUCTION

Hypocalcaemia is a common complication after thyroid surgery with reported incidence of about 39%¹. In the literature, the incidence of temporary hypocalcaemia after thyroid surgery is about 43%, and permanent hypocalcaemia occurs in about 5% of surgeries². Total thyroidectomy, similar to hemithyroidectomy, is followed by a significant reduction in the plasma concentration of Para Thyroid Hormone³, with a parallel reduction in serum calcium levels, evident but transitory in 25% of patients following surgery and permanent in 1% of patients⁴.

The development of postoperative hypocalcaemia is likely to be multifactorial in nature; thyroid lobectomy alone is hardly ever

associated with this complication⁵, which is most common following total thyroidectomy where there is a greater risk of parathyroid injury compared to other forms of thyroid surgery⁵. Hypocalcaemia after thyroidectomy has been most commonly attributed to parathyroid insufficiency related to injury, de-vascularization, or inadvertent excision of the parathyroid glands. Other causative mechanisms that have been implicated in the pathophysiology of post-thyroidectomy hypocalcaemia include calcium uptake by bone in patients with thyrotoxic osteodystrophy, parathyroid suppression from increased calcium restored from the bone of patients with hyperthyroidism, transient preoperative hemodilution with increased renal excretion of

calcium, increased release of calcitonin as a result of thyroid manipulation and autoimmune-related fibrosis of the blood supply to parathyroid glands⁶). Recently there has been interest in identifying factors that can reliably predict the development of postoperative hypocalcaemia after thyroid and parathyroid surgery. The ability to promptly identify those patients who are at risk for developing hypocalcaemia could enable surgeons to select patients who can undergo these procedures on an outpatient or a short-stay basis. Performing these surgical procedures on an outpatient basis could result in a cost reduction of as much as 50% compared with traditional postoperative hospital stays⁷.

Thyroidectomy is commonly performed procedure in our unit, so the rational of our study is to determine the frequency of hypocalcaemia in patients undergoing thyroidectomy. The results of this study will be disseminated to other general surgeons and if the frequency of hypocalcaemia is found to be significant, we will suggest recommendation for modification of the surgical technique of thyroidectomy which will help us to reduce post-op hypocalcaemia and thus reduce costs for medical assistance, shorten hospital stay and safe hospital discharge.

MATERIAL & METHODS

This is a descriptive, prospective study and was set in the Saidu Teaching Hospital Swat, Malakand, KPK, which is a tertiary care and referral hospital. The cases were studied over a period of three and half years. Total of 90 patients of both gender who have undergone total thyroidectomy, 50 patients group, (A) and near total thyroidectomy 40 patients group (B) Those, who satisfied definite inclusion and exclusion criteria were selected.

Intervention: Serum calcium (Ca^{2+}) levels were assessed preoperatively and then on first postoperative day. All patients were already being clinically evaluated for signs and symptoms of hypocalcemia. Patients that

developed tetany were treated with intravenous calcium in addition to oral supplementation. 40(33.3%) Patients who developed symptoms of hypocalcemia were then compared with asymptomatic patients in regard to postoperative Ca^{2+} level. Ethical committee clearance was obtained from the institutional ethical committee of hospital. The observations and data collected were coded and fed into the computer using MS Excel and analyzed using SPSS Version 19 with the assistance of a statistician. Descriptive statistics such as mean, standard deviation and percentage was used. To find association chi square test was used.

RESULTS

Total of 90 patients with unilateral or bilateral thyroid swelling were included in the study. 50 patients were subjected to total thyroidectomy and 40 patients to subtotal thyroidectomy. The total thyroidectomy group was labeled as group (A) while subtotal thyroidectomy group as (B). The total thyroidectomy group (A) consisted of 12 men and 38 women with a mean age of 29 years $\pm$ 10.07. The subtotal thyroidectomy group (B) comprised of 10 men and 30 women with a mean age of 42 years $\pm$ 10.27 (Table No 1, 2).

TABLE NO.1 AGE DISTRIBUTION N=90

Age In Years		Group-A	Group-B
	Min	16	27
	Max	50	67
	Mean	29	42
	Standard deviation	10.07	10.27

TABLE NO.2 GENDER DISTRIBUTION N=90

Gender		Group-A	Group-B	Total
	Male	12(24%)	10(25%)	22(24.4%)
	Female	38(76%)	30(75%)	68(75.6%)
	Total	50	40	90

The indications for surgery were dominated by compressive symptom and or cosmetic reasons. In group (A) most of the patients had compressive symptoms, 25 patients (50%)

followed by cosmetic symptoms 20(40%) patients. 03 patients(6%) had symptoms of thyrotoxicosis while in 02(4%) patient the indications were anxiety and fear.

In group (B), the cosmetic disfigurement dominated the indications for surgery 22(56%) followed by compressive symptoms, 11(27.5%) patients. Fear and anxiety was presentation in 06(15%) while thyrotoxicosis in 01(2.5%) patient only. (Shown in Table No 3)

TABLE NO: 3 INDICATIONS FOR SURGERY

Indication for surgery	Group-A	Group-B	Total
MNG bilateral	n=30(60%)	n=18(45%)	48(40%)
Unilateral thyroid swelling	n=14(28%)	n=16(40%)	58(48.3%)
others	n=6(12%)	n=6(15%)	12(13.4%)
Total	50	40	90

Most of the patients were euthyroid; 45(90%) patients in group (A) and 34(85%) patients in group (B). Three patients (6%) in group (A) and Two patients (5%) in group (B) were hypothyroid while thyrotoxicosis was found in two (4%) and four (10%) patients in group A&B respectively. All the hypo and hyperthyroid patients were made euthyroid prior to surgery with medication.

Preoperative Serum/Ca++ levels revealed, that all the patients in both groups were normocalcemic. In group (A) most of the patients had Serum/ Ca++ level in the range of 9.10-9.50mg% (n=28) followed by range of 8.6 to 9.00mg% (n= 20). The mean level was 9.12mg% $\pm$ 0.42. While in Group (B) it ranged from 8.60 to 9.50mg% (n=38) 95%. In group (B) mean Serum/ Ca++ was 9.0mg% $\pm$ 0.44.

Operation time was analyzed among the two groups, as in group (A) most of the patients 26(52%) were operated in 150 – 180 minutes and mean operating time was 138 $\pm$ 30 min. While in Group (B) most of the patients 22(55%) were operated in 60 – 90 minutes,

mean operating time being 102 $\pm$ 33 min. The difference in operating time was statistically significant (p=0.046).

Histopathological examination of thyroid specimen after surgery revealed incidental thyroid cancer in two (5%) of the patients who underwent subtotal thyroidectomy(B), follicular carcinoma. Thyroid cancer was also found in four (8%) of the patients who were subjected to total thyroidectomy(A). Two patients had follicular carcinoma and the other two had papillary carcinoma.

Complications noted in the study groups were, temporary RLN (recurrent laryngeal nerve) palsy in five (10%) patients in the total thyroidectomy group and three (7.5%) patients in the subtotal thyroidectomy group (B). The difference was statistically non-significant (p=0.641).

Temporary hypoparathyroidism was observed in 10 patients (20%) and 4 (10%) patients underwent total and subtotal thyroidectomy respectively. This difference though apparently greater, was statistically not significant when compared for the two groups (p= 0.278). Only two (4%) patient had permanent hypoparathyroidism in the total thyroidectomy group verses no patient in the subtotal thyroidectomy group (p=0.641).

Majority of the patients were above 40 years of age and there was female preponderance in the study .Most of patients presented with neck swelling (72%) , Out of these around 60% had multinodular goiter. The post- operative Serum /calcium levels were considered low when it was less than 8.2mg%. Only 8{6+2} patients (9%) presented with low post operative calcium levels on the first post-operative day. There is no statistical difference in occurrence of post-operative hypocalcaemia with clinical presentation, regarding the choice of thyroid surgery. Both the gender were equally effected with preponderance in occurrence of hypocalcemia.

TABLE NO: 4 Showing (Post Operative Serum/Calcium Levels)

Post operative Serum/ ca++ Level		Group=A	Group=B	Total
	8.00-8.50	n=6(12%)	n=2(5%)	n=8(8.8%)
	8.60-9.00	n=16(32%)	n=18(45%)	n=34(37.7%)
	9.10-9.50	n=22(44%)	n=16(40%)	n=38(42.2%)
	9.60-10.00	n=6(12%)	n=4(10%)	n=10(11.1%)
Total		n=50	n=40	n=90

DISCUSSION

The ages of the patients in the present study ranged from 16 years to 67 years, showing that a relatively younger age group with greater life expectancy were subjected to total thyroidectomy. Younger patients having greater life expectancy with bilateral MNG (Multi nodular goiter) are currently considered for total thyroidectomy^{1,2}.

In our present study there is female preponderance (table no. 2) which qualifies the widely known fact that thyroid disorders are more common in the females. Most of the patients in our study were euthyroid, 45(90%) patients in group A and 34 (85 %) patients in group B. The rest were made euthyroid with medication.

MNG (multinodular goitre) is an irreversible disease and needs surgical treatment. Current indications for surgery includes compression induced symptoms, suspected malignancy, hyperthyroidism and cosmetic reasons^{1,4}. In our study the indications for surgery were dominated by obstructive and esthetic symptoms. Most of the patients with compressive symptoms, 30 (60%) patients were treated by TT(Total thyroidectomy), while STT(Subtotal thyroidectomy) carried out in 18(45%) patients, showing that patients with huge goitres resulting in tracheo-oesophageal compression and obviously difficult to operate upon were treated with TT. This makes the study considerably biased that patients with larger goiters and difficult surgery, carried greater chances of complications were operated upon TT, yet the results were comparable.

Surgical options include STT, NTT (near total thyroidectomy) and TT, but the role of TT for benign MNG has been a controversial issue due to its greater extent of resection and presumed increased risk of complications besides the need for hormone replacement. However with the recognition of the pit-falls associated with incomplete excision of the gland, it is now being increasingly accepted surgery of choice in many centers for the management of most of the thyroid diseases that involve the entire gland⁸. In Australia and New Zealand, 90% of benign bilateral MNGs are currently treated by TT as the primary operative procedure of choice⁹. However, in Pakistan, due to presumed higher rates of complications associated with TT the standard surgical procedure for treating MNG is still STT despite the fact that most of our patients present with huge, neglected goitre virtually having no normal thyroid tissue.

Worldwide, the popularity of STT is decreasing with time. The reason is that in some patients with a huge goiter it is difficult to leave healthy tissue intact because the nodular alternation reaches the dorsal capsule. It is accepted that when the entire gland is diseased in patients with multinodular goiter, a subtotal thyroidectomy, although reducing the bulk of the diseased tissue, is not an optimal treatment¹⁰. In the surgical management of multinodular goiter, surgeons should aim to remove all nodular structures without increasing morbidity, because remaining nodular tissue can be regarded as the main cause of recurrent disease. Recurrence rates as high as 45%, that are uninfluenced by thyroxine therapy have been reported^{11,12}. Recurrence has been found to be highest in patients belonging to iodine deficient regions. Frequency of recurrences are inversely proportional to the extent of surgery, and the average interval to recurrence is just over 10 years^{9,11,12,13,14}. In general about one half of patients with recurrence undergo secondary thyroidectomy; this carries a ten folds increased risk of permanent complications^{11,12,13,15}. In endemic regions in particular when both sides

have been previously operated upon, secondary thyroidectomy is feared of distressing complications. The increased risks of secondary thyroidectomy overweighs any potential advantages in terms of lower complication rate which may be achieved by less extensive initial surgery.

TT obviates the need for secondary thyroidectomy as the incidence of recurrent goitre is practically eliminated. Thyroxin suppressive therapy was once regarded as a valuable method for preventing recurrence after STT. Failure of thyroxin therapy to prevent recurrence has been observed by some authors^{16,17}. Several authors have pointed out the possibility of autonomous behavior of the thyroid gland remnant¹⁸. This process may occasionally result in the development of superimposed hyper-thyroidism or neoplasia¹⁹. Thyro-suppressive therapy is only likely to be successful if the residual gland is normal or the disease is in early stages. An observation made by others with which we agree is that it is difficult to find any appreciable normal tissue during operations in long-standing large MNGs especially in the endemic regions²⁰.

One potential reason for performing STT is the maintenance of euthyroid status without thyroxin replacement. However, leaving a remnant of thyroid tissue in situ does not prevent the occurrence of hypothyroidism; a fact which is well documented^{11,21,22}. Koyuncu et al, in their study found that levothyroxine supplementation was required in 52.1% patients who were subjected to STT²³. Sedar et al, reported thyroxine requirement in 100% of all the patients who underwent STT²⁴.

Thus, a remnant of thyroid tissue left in STT and which is often diseased does not safe guard one against thyroxine requirement. Another pitfall of STT is unrecognized malignancy in MNG in which case it represents an inadequate surgery. The current evidence suggests that the incidence of occult malignancy ranges from 3% to 16.6%^{23,25,26}. In the present study, the

incidence of occult carcinoma was 5 % (n=2) in STT group and 8% (n=4) in TT group, with overall incidence of 6.67%. Out of these six patients four had follicular carcinomas and two papillary carcinoma. These findings are comparable with the observations made by Cuello, that follicular carcinomas are more common in MNG in iodine deficient areas²⁷. Under these circumstances, TT offers complete initial treatment, taking care of multi-centricity and future transformation into undifferentiated carcinoma, eliminates the need for completion thyroidectomy, while STT would represent inadequate surgery, will need completion thyroidectomy which steeply increases the morbidity by fifteen folds^{15,28}.

Another principle advantage of TT, is the ability to use I¹³¹ for the detection (surveillance) and ablation of metastasis, and the utility of thyroglobulin as a tumor marker becomes extremely useful. Moreover, malignant transformation in the thyroid remnant after subtotal resection ranges from 4% to 17%¹⁶.

Potential benefits of TT include adequate removal of the disease tissue, prevention of recurrence and the avoidance of completion surgery in the presence of occult malignancy^{9,29}. The only real argument against TT is its potential for increased risk of complications including, the crucial major complications of permanent hypoparathyroidism and permanent RLN palsy.

A review of recent literatures, however demonstrate that this is in fact a myth and the incidence of permanent complication after total thyroidectomy in experienced hands is acceptably low. Koyuncu et al and Giles et al reported no incidence of permanent nerve palsy and hypoparathyroidism in their studies^{30,31}. Mishra et al reported an incidence of 0.8% nerve injury and 1.6% hypoparathyroidism²⁰. Muller et al. revealed an incidence of 0.9% for both nerve injury and hypoparathyroidism. The acceptable rate of these crucial complications in expert hands is 1 to 2%³².

In the present study, the total thyroidectomy group showed permanent RLN palsy and hypoparathyroidism in none (0%) and two (4%) patients respectively. These complications were not observed in any patient with subtotal thyroidectomy. Though 4% value for permanent HPT in TT group in our study is higher than acceptable range i.e 1% to 2%, but is still comparable with the results of other studies reporting the rate of permanent HPT in TT from 0.7-3.5%^{1,9,22}. The difference for permanent HPT between the two procedures was statistically not significant (0.641), and that total thyroidectomy can be performed with a morbidity rate comparable to that of lesser procedures.

Previous studies have reported that the incidence of temporary hypoparathyroidism ranges from 1.6-22% after subtotal thyroidectomy and from 24- 35% after total thyroidectomy^{11,20}. In the present study, the proportion of temporary hypoparathyroidism was 6(15%) and 12(24%) in subtotal and total thyroidectomy, respectively. These results for temporary HPT are within the afore mentioned reported ranges and the difference between the two groups, though apparently large, but statistically not significant ($p=0.278$). Transient hypocalcemia or HPT after TT, however, is seen more as a sequel rather than a complication. Delbridge et al state that transient hypothyroidism should be an acceptable outcome of bilateral thyroid surgery rather a complication⁹. Moore has recommended that all patients having TT should have routine calcium supplements prior to discharge from the hospital³³.

CONCLUSION & RECOMMENDATIONS

Total thyroidectomy is a safe and effective procedure for benign multinodular goiter, which completely removes abnormal thyroid tissue and eliminates the possibility of future recurrence, the necessity for secondary thyroidectomy and also offers an optimal treatment for unsuspected malignancy thus obviates the need for

completion thyroidectomy with acceptably low risk of permanent complications.

While on the other hand, Subtotal thyroidectomy is associated with significant recurrence of goiter, inadequately treated incidentally detected thyroid cancers with increased risks of secondary or completion thyroidectomy and provides little significant advantage of being safer procedure compared to total thyroidectomy.

As in our this study, we observed that only (4%) patients developed hypoparathyroidism in total thyroidectomy group in comparison, subtotal had (0%). The difference for permanent hypoparathyroidism between the two procedures was statistically not significant (0.641), and that total thyroidectomy can be performed with a morbidity rate comparable to that of lesser procedures.

So we recommend Total thyroidectomy in general for all patients with bilateral benign multinodular goiter and particularly for those who are younger, having longer life expectancy and greater chances of recurrences.

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