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Comparative Analysis of Parathyroid Functions among Sub-total Thyroidectomy Patients after Ligation of Inferior Thryoid Artery

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Authors' contributions

This work was carried out in collaboration among all authors. Author AI give the idea of research, Author NMB write the introduction, author MZ write the methodology and author SKJ write the discussion. All authors read and approved the final manuscript.

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ABSTRACT

Background: Thyroid surgery commonly in developing countries. Hyperparathyroidism is major issue after surgery. The objective of study is to compare the occurrence of hyperparathyroidism after sub-total thyroidectomy with truncal ligation versus non-ligation of inferior thyroid artery.
Methods: Study design was randomized clinical trial. Study was conducted in public sector hospital. Surgical patients who were admitted to hospital for thyroid surgery. Participants were divided into two groups through random allocation, thyroid surgery with and without the ligation of inferior thyroid artery Thyroid surgery for group A with ligation and group B without ligation of

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inferior thyroid artery. Serum PTH levels were measured on 3rd post-operative day. The group A and B were compared for level of for the frequency of transient hyperparathyroidism.
Results: Mean age in group A was 40.83 yrs (SD = 9.9) and in group B it was 41.34 yrs (SD=8.73). Transient hyperparathyroidism was observed in 6.10% of patients in group A and 7.32% patients in group B and this difference was found to be statistically significant (*p*=0.02).
Conclusion: Result showed that ligation of artery decreased the risk of transient hyperparathyroidism after sub-total thyroidectomy.

Keywords: Hypocalcaemia; hyperparathyroidism; inferior thyroid artery; multinodular goitre; recurrent laryngeal nerve.

1. BACKGROUND

Calcium homeostasis sustain on two strong pillars, PTH (Parathormone) and vitamin D [1].

If any one of the pillar is strong enough, you can compromise with the other one [1]. But if both are weak, hypocalcemia cannot be avoided. Transient hypocalcemia is the most common complication of thyroid surgery [1]. It is seen in 25% of patients, undergoing thyroidectomy [1]. If associated symptoms are severe, intravenous calcium gluconate is advised [2]. This post-operative hypocalcemia can be due to number of factors, including plasma dilutional factors, iatrogenic ischemia to parathyroid tissue or release of endothelin-1. Endothelin-1 is an intense stage reactant known to stifle PTH creation, and its dimensions have been raised in patients with transient hypoparathyroidism [3-4]. When ischemic insult to parathyroid tissue has led to this hypocalcemia. then serum intact parathyroid hormone (PTH) levels decrease within 3 hours of surgery and by 3rd day these are clearly decreased [4].

This fact lies in understanding the pharmacokinetics of this 84-amino acid peptide. PTH is a very volatile peptide [5]. The rates of PTH absorption and elimination are very rapid [4-5]. Peripheral metabolism of PTH occurs by non-specific enzymatic mechanisms in the liver followed by excretion via the kidneys [5]. If given via subcutaneous injection, PTH harmone level increases to serum concentrations about 30 minutes after subcutaneous injection of a 20-ug dose and decreaed to concentrations within 3 hours [5-6]. Some authors recommend to screen for parathyroid insufficiency in every case of thyroidectomy by measuring serum PTH 1 hr post-operatively while others emphasize intra-operative measurement of PTH for immediate identification of patients at risk for postoperative hypoparathyroidism. Thus in these cases timely parathyroid auto-transplantation is suggested to prevent postoperative hypoparathyroidism [6-7]. Chronic near-normal hypocalcemia of hypoparathyroidism is asymptomatic and thus may go undetected [7]. It causes irreversble cataract formation, basal nuclei calcification, Parkinsonism and personality changes [8]. Careful and effective haemostasis is the key to reduce mortality and morbidity in thyroid surgery. Few studies have compared s. PTH levels as quantitative variable (in terms of mean and SD) but none has compared s. PTH levels as qualitative variable (in terms of decrease, normal and increase). Say lower limit of serum PTH is 1 pmol/L. Mean value of PTH 2.35 or 1.78 will not matter to patients. What will matter to patients is that when they will have decrease value less than 1 pmol/L; then they will start exhibiting their symptoms. This is crux why we prefferred qualitative variable, instead of quantitative variable.

2. MATERIALS AND METHODS

2.1 Study Design

This randomized controlled trial was carried out in department of surgery, public sector hospital.

2.2 Inclusion and Exclusion Criteria

Adult patients of ages between 15 and 65 years of both genders having pre-operative serum Thyroid Stimulating Hormone (0.4 to 4.0 µIU/L), serum intact Parathyroid hormone (1-6 ρmol/L) and whole blood ionized calcium (1.15-1.25 µmol/L) within normal range were included.Patients having disturbed calcium metabolism or any disease which can affect calcium metabolism e.g. renal failure, tumours producing parathyroid hormone related peptide, sarcoidosis, alcoholics or patients with history of diuretics used were excluded.

2.3 Sample Size

The sample size was calculated by using WHO sample size calculator taking level of significance

5%; power of test 80%; population proportion p1=48% [5] after explaining all possible complications as a result of the procedure he/she is going to undergo srugery.

2.4 Sample Technique and Rando-maization

Eighty two cases from surgical out-patient department fulfilling the inclusion criteria were included in the study through non-probability convenience sampling and randomly divided into two equal groups of 41 patients each by lottery method.

2.5 Intervention

In intervention Group A the stem of the inferior thyroid artery was recognized, ligated (with vicryl 2/0) and divided. In control Group B the inferior thyroid artery ligation was not performed. Recurrent laryngeal nerve was not separately dissected, as it is considered too dangerous a practice to dissect the nerve, unless the procedure is radical thyroidectomy.

2.6 Outcome

Serum parathyroid hormone (s.PTH) levels were measured on 3rd post-operative day between 9 am to 2 pm, to negate the effects of diurnal variation.

2.7 Statistical Analysis

Data had been analyzed by using SPSS (version-15). Frequency and percentages was presented for qualitative variables i.e. gender, use of calcium/vitamin D supplement and serum intact parathyroid hormone (PTH) categories. Mean and standard deviation (SD) were calculated for quantitative variable. Serum intact parathyroid hormone (PTH) levels was analyzed as Qualitative data (by converting it into 3 categories i.e. Decrease; Normal; Increase). A *p*-value <0.05 was considered significant.

3. RESULTS

Table 1 Two groups of 41 each were included in study. Mean age in group A was 40.83 yrs (SD = 9.9) with min age of 20 years and max age of 58 years and in group B it was 41.34 years (SD = 8.73) with min age of 19 years and max age of 63 years. There were 38 (92.7%) females in group A and 35 (85.4%) females in group B. Patients using oral calcium or vitamin D analogue were 10 (24.4%) in group A and 6 (14.6%) in group B. Groups of patients were compared with respect to age (*p*=0.805), gender (*p*=0.482) and intake of oral calcium or vitamin supplement (*p*=0.403).

On 3rd post-operative day, patients who developed transient hypoparathyroidism were 5 (12.2%) in group A (2 males and 3 females) and were 6 (14.6%) in group B (all were females) (Fig. 1). The difference was statistically insignificant (*p*=0.542). Symptomatic hypoparathyroidism along with hypocalcemia, was seen in 2 (4.9%) patients in group A and in 1 (2.4%) patient in group-B with significant difference (*p*=0.03) (Fig. 2). All 3 patients were females and all were using oral calcium/ vit D analogue. Symptoms of hypocalcaemia were well controlled with intravenous calcium gluconate; then continued on oral calcium and vitamin D analogue.

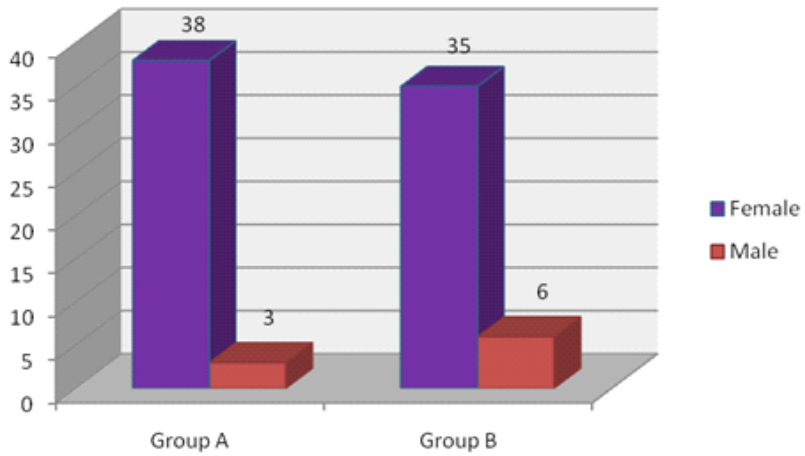

Fig. 1. Figure showing the percentage of patients who developed transient hypoparathyroidism

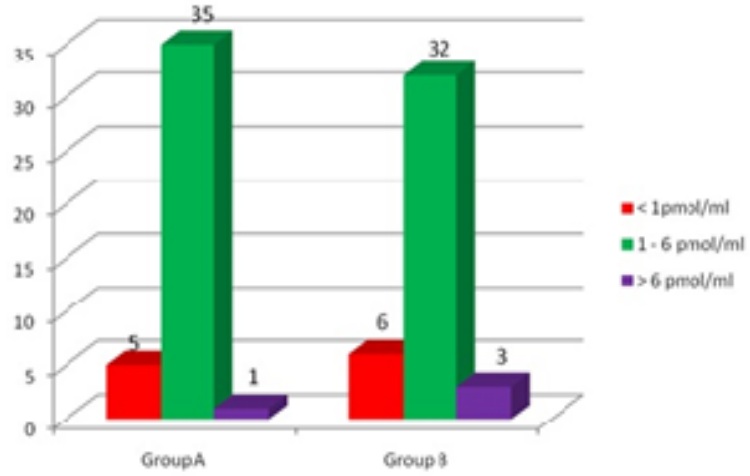

Fig. 2. Comparison of serum intact Parathyroid Hormone (PTH) levels between the group

Table 1. Base line charcteristics for study participantant (n=82)

S. no	Variables	Frequency n-82 (%)		P value
		Intervention group A (n=41)	Control group B (n=41)	
1	**Age (Mean and SD)**	40.83±9.9	41.34±8.73	0.80
2	**Gender**			0.48
	Male	3(7.3)	6(14.6)	
	Female	38(92.7)	35(85.4)	
3	**Oral intake of calcium**			0.40
	Yes	10(24.4)	6(14.6)	
	No	31(75.6)	35(85.4)	

4. DISCUSSION

The study found that there is difference between those patients where infereior thyroid artery ligated and those patients in which inferior thyroid artery not ligate during subtotal thyroidectomy. There is need for larger study to find out the facotrs for trisent hyperparathroidsm during subtoal thyrdodectmy. Our study showed that hypoparathyroidism is seen in an equal extent in all cases regardless of the technique used to ligate the ITA.

Recurrent laryngeal nerve injury is most feared complication of thyroidectomy [9]. The risk to recurrent laryngeal nerves increases if ITA branches are ligated as they are closely related to recurrent laryngeal nerves [10]. So if we can find out with certainty that ligation of inferiro thyroid artery trunk does not increase the risk to parathyroids we can safely ligate it away from the thyroid thus also decreasing the risk of recurrent laryngeal nerve injury [11].

Patients who develop hypoparathyroidism, nearly 1/3 have consequent hypocalcemia; and those who develop hypocalcemia, nearly 1/3 develop consequent symptoms. This was also true in our study, since 77% (10 out of 13) of our hypoparathyroidism patients had no symptoms. Reason behind this myth might be that calcium homeostasis sustains on 2 strong pillars and these patients had well built vitamin D pillar to sustain calcium homeostasis that is why they were not affected by decreased PTH in circulation.

The study [12] was conducted and RCT was done on 100 patients for comparasion of different procedures of bilateral subtotal thyroidectomy for goitre with determien the level of parathyroid harmone postoperativly. One Group (50 patients) experienced ligation of the inferior thyroid artery. Other group (50 patients) some of the branches of arteries were ligated at the thyroid capsule. Serum level of total calcium, ionized calcium and PTH levels were determined before operation, and 6, 24 and 72 h after

surgery. Only ten patients, 5 each required calcium and/or vitamin D supplementation. It was determined that ligation of the total thyroid arterty form trunc during bilateral subtotal thyroidectomy for simple goitre does not cause hypoparathyroidism.

Previous study had studied 84 patients in two groups [13]. The study was performed three times: prior to operative procedure, directly after the operative procedure, and three months after the procedure. It has been shown that there are slight, but statistically significant differences in the concentration of total and dialysable calcium as well as s. PTH in serum. Three months after the operative procedure the mean concentration of s. PTH, total and dialysable calcium was somewhat higher in patients in whom ITA were ligated than in patients in whom the arteries were not ligated. The described changes were of subclinical character.

Araujo-filho VJ et al. [14] studied effect of ligation of ITA on post operative hypoparathyroidism in 48 patients. They were divided into two equal groups with group A undergoing ITA trunk ligation and group B not undergoing sutured of Inferior Thyroid Aartery trunk. Result showed that a significant decrease in serum calcium occurred post operatively in both groups. However when two groups were compared for frequency of hypoparathyroidism the differences were not statistically significant. In this study patients were followed up for six months and parathyroid function was checked using serum total Ca, PTH, urinary Ca and cAMP levels.

Cakmakli S et al. [15] carried out a prospective study on 80 patients, to assess the possible role of truncal ligation of ITA on post-thyroidectomy hypocalcemia. Bilateral subtotal thyroidectomy was performed for non-toxic nodular goiter in two groups. ITA were ligated bilaterally in 50 patients but not ligated in 30 patients. In both groups mean serum calcium levels on the first and second postoperative days were found to be significantly lower than preoperative levels. However these falls were similar in both groups.

Chaudhery et al. [16] recently conducted a study locally. The objective of this study to determine the prevalence of hypocalcaemia in 310 patients after ligation and non-ligation of the inferior thyroid artery during thyroid surgery. Study participants were divided into two groups at random. One Group had ligated the ITA and other group without liagated during surgery. Mostly the study participants were female (97.10%). Brief hypocalcaemia was find in 4.29% patients in Group I and 3.4% patients in Group II. Only few (1.84% in group 1 and 1.36% in group 2) study participants was observed that permanent hypocalcemia. Results were statistically insignificant (p-value >0.5%).

Pellizo MR et al. [17] prospectively analyzed two homogeneous groups of 10 study participants, surgery with or without ligation of ITA and compared the postoperatively serum calcium level. A decrease in mean calcium levels was observed only in the first postoperative day. Hypocalcemia was noted paradoxically to occur more frequently in G-2 patients, out of which one developed a permanent hypoparathyroidism.

Maralcan et al. [18] did a prospective randomized trial on 98 patients. Study participants were divided into groups and ITA trunk was ligated in group 1 while ITA terminal branches were ligated in group 2. Difference for serum level were no statistically significant between groups on postoperative days 1, 2, 3, and 30 (p > 0.05). Hypocalcemia was noted on postoperative days 1, 2, and 3 in 9 (9.2%), 15 (15.3%), and 2 (2.0%) patients, respectively. By day 5 of surgery all patients had recovered from hypocalcaemia.

Jahangir et al. [19] prospectively analyzed 100 patients, compared the level of serum calcium postoperatively between two groups. The result of study showed that the significant difference occurred between groups in calcium level of serum [more in Group A (48%) as compared to Group B (22%)]. This difference was statistically significant shown by the p value <0.5 on the 1st postoperative day in patients with ligation of inferior thyroid artery. It was concluded that ligated the inferior thyroid artery which lead to hypocalcaemia. Nawrot et al. [25] studied 37 patients in two groups. ITA trunk was ligated in group 1 while ITA terminal branches were ligated in group 2. Based on pre operative and postoperative total calcium and PTH level they concluded that there was no statistically significant difference between the two groups. Klammer et al. [20] studied 279 patients suffering from benign nodular goiter. They have concluded that by ligating the ITA trunk the incidence of recurrent laryngeal nerve damage is reduced to 0.4% and permanent hypocalcaemia to 0.3%. Thomusch et al. [21] did a multivariate analysis of 5846 patients for various risk factors leading to postoperative hypocalcaemia. It was a multicenter study involving 45 hospitals. The

overall incidence of transient and permanent hypoparathyroidism was 7.3% and 1.5%, respectively. Dolapci et al. [22] did a prospective non-randomised study studied on 216 patients. They ligated the inferior thyroid artery during thyroidectomy in study partcipants who had bilateral subtotal thyroidectomy for non-toxic nodular goiter.

A study was conducted in Pakistan by Khan et al. [23] total 100 patients were included in the study to determine the level of serum of CA between two groups, one for ligated the ITA and other group not ligated. Result of study showed that there is statiscally different between two group of serum calcium level on postperatevily. In this study frequency of temporary hypoparathyroidism after subtotal thyroidectomy was 13.41%. In international literature, frequency of hypo-parathyroidism after subtotal thyroidectomy has been quoted in different studies as 23% [24], 15.6% [25], 22.22% [26], 24.1% [27], 18% [28], 30% [29], 24.11% [30]. Limitation of this study was that patients with symptomatic hypoparathyroidism were not followed up for permanent hypoparathyroidism. There are many further research avenues which can be covered in further studies. Studies could be carried on efficacy of intra-operative PTH levels or 1-hour assay for the early prediction of hypoparathyroidism after thyroidectomy. Further studies are needed to clearly establish frequency of postoperative hypoparathyroidism patients who develop hypocalcemia, and thereon how much frequency develop symptoms.

5. CONCLUSION

It is proved that truncal ligation of ITA in subtotal thyroidectomy may be the one of the factor which caused hypo-parathyroidism in immediate post operative period. There is need for further studies to explore the other factors which contribute the hypo-parathyroidism.

CONSENT AND ETHICAL APPROVAL

Research involving human participants: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed written consent was obtained from each participant.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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