The Egyptian Journal of Hospital Medicine (July 2019) Vol. 76 (2), Page 3419-3424

Effect of Ligation of Inferior Thyroid Artery Main Trunk vs. its Branches on Post Thyroidectomy Hypocalcaemia

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ABSTRACT

Background: more than a century ago, thyroid surgery was a somewhat frightening operation, with a reported mortality rate of 40%. Nowadays, thyroidectomy is one of the most commonly performed surgical procedures. Hypocalcaemia is well recognized phenomenon following thyroidectomy; it has been a matter of interest in the past 100 years**. Objective:** to compare the effect of ligation of inferior thyroid artery main trunk versus its individual branches on postoperative hypocalcaemia. **Patients and Methods:** thirty patients with indication for thyroidectomy were randomly allocated into two groups; 15 patients each. Group A (15 patients) where the main trunk of inferior thyroid artery was ligated, while in group B (15 patients) the individual branches were ligated.

Results: the results of this work showed that the incidence of post thyroidectomy hypocalcaemia, although was statistically significant in some comparisons of calcium and PTH, yet most of the levels were within the normal range, either pre or postoperatively with no clinical effects.

Conclusion: ligation of the main trunk of inferior thyroid artery, although have a statistical significant on the parathyroid function and hypocalcaemia postoperatively, good surgical technique to identify and preserve the parathyroids, is the most important factor which may affect the postoperative hypocalcaemia.

Keywords: Inferior Thyroid Artery, Ligation, Thyroidectomy, Hypocalcaemia

INTRODUCTION

Thyroidectomy is one of the most commonly performed surgical procedures done nowadays. The complications following thyroidectomy are well known, some of them are fatal, others are quite disturbing particularly in their permanent form [(1)]. The most common immediate surgical complication following thyroidectomy is hypocalcaemia with more than 6% of patients experiencing this problem [(2)].

Post thyroidectomy hypocalcaemia may be transient or permanent. There is a great difference in the literatures in reporting the incidence of both. Transient hypocalcaemia ranges from 5.4 to 26%. Such discrepancies are due to differences in the definition of hypocalcaemia and surgical techniques for thyroidectomy [(3)].

The pathogenesis of transient hypocalcaemia is not fully understood. Early post-operative hypocalcaemia in the first post-operative day may be due to perioperative haemodilution. Common causes of temporary hypocalcaemia include: parathyroid vascular event such as ischaemia, oedema or rise of serum calcitonin level as a result of thyroid manipulation [(4)].

Risk factors for post thyroidectomy hypocalcaemia include the extent, exposure of recurrent laryngeal nerves, parathyroid gland identification, reoperation and lack of surgical experience [(1)].

Transient hypocalcaemia may be due to reactive hypoparathyroidism due to reactive hypocalcaemia in thyrotoxic patients and hungry bone syndrome [(5)], release of endothelin 1 which suppress PTH, or hypothermia [(6)].

Permanent hypocalcaemia is usually due to devascularisation or surgical ablation of the parathyroid gland [(6)].

Care of the blood supply of the parathyroid gland during thyroid surgery may reduce the post thyroidectomy hypocalcaemia.

AIM OF THE WORK

It is to compare the effect of ligation of inferior thyroid artery main trunk versus its individual branches on postoperative hypocalcaemia and PTH levels.

PATIENTS AND METHODS

In this prospective study conducted on Sayed Galal University hospital and Police hospital during the period from Dec 2018 to May 2019, where 30 patients with different indications for total thyroidectomy were randomly divided to two groups each was 15 patients.

Group A, submitted for total thyroidectomy with ligation of main trunk of inferior thyroid artery.

Group B, submitted for total thyroidectomy with sparing of the main trunk of inferior thyroid artery.

Methods:

All the patients were submitted to:

I. Preoperative assessment:

A. Clinical:

1. Detailed history: focusing on any history of manifest or latent tetany.
2. Physical examination: General and Local examination.

B. Radiological assessment:

1. Chest x-ray: postero-anterior view.
2. Neck ultrasound.

C. Laboratory assessment:

Blood samples were collected using conventional venipuncture for:

Received:10/4/2019
Accepted:9/5/2019

1. Free T3, T4 and TSH assessment.
2. Total serum calcium.
3. PTH assay.
4. Liver enzymes: serum Aspartate transaminase, Alanine transaminase
5. Kidney functions: serum urea and creatinine.
6. Complete blood count (CBC).
7. Fasting blood sugar

The thyrotoxic patients were prepared before surgery by the following:

- Rest.
- Propranolol (30-60 mg per day).
- Carbimazole (40 mg per day for 2 weeks prior for surgery)

Exclusion criteria:

- Recurrent thyroid swelling.
- Patients with chronic renal failure.
- Thyroid malignancy with U/S and/or clinical cervical lymph node enlargement.
- Patients with preoperative abnormal Ca levels or PTH.
- Patients with chronic liver disease with hypoalbumenia.
- All histopathological results showing any parathyroid tissue in the spacemen.

II. Operative Technique

Preoperative consent:

Was done by explanation of the procedure to all patient and expected complications have been done, **written consent has been obtained from all patients and ethical consent obtained from the Research Ethical Committee of Faculty of Medicine, Al-Azhar University.**

The patients were randomly allocated into two groups of 15 patients each:

I. Group A (Main trunk ligation):

Thirty patients have been oprerated upon for total thyroidectomy by the standard methods. Surgical technique was the same for every operation. After making an incision in the lower anterior neck and after dissecting pretracheal muscles; the thyroid gland was exposed and the thyroid capsule was dissected and the lobe was delivered into the wound after ligation of the middle thyroid vein.

The superior thyroid vessels were dissected, ligated and divided as near as possible to the thyroid gland in order to preserve the external laryngeal nerve.

The recurrent laryngeal nerves were systemically searched for an each attempt and efforts were made to identify and preserve the parathyroid glands on each side of the thyroid gland. The main trunk of the inferior thyroid artery has been ligated in continuity as far as possible from the gland.

II. Group B (Individual branches ligation):

Thirty patients have been managed similar to the first group except that the individual branches of the inferior thyroid artery have been ligated as near as possible to the gland without ligation of the main trunk.

III. Postoperative Management:

The postoperative care was conducted in standard manner as regard antibiotics, analgesic, oral intake, care and removal of the drains.

We used two methods; post-operative assessment of CA and PTH levels by:

- Clinical close observation for symptoms and signs of hypocalcemia.
- Laboratory testing of serum Ca and PTH by:

1. Serum total calcium was estimated for all patients on the 1st, 2nd and 3rd postoperative days.
2. PTH assay was estimated for all patients on the 1st postoperative day, 3rd day and one month postoperative in selected cases with prolonged hypocalcaemia.

Symptoms and Sings of hypocalcemia:

Symptoms were nonspecific, including generalized weakness, circumoral tingling and numbness and cramping in the hand and foot.

The temporary post operative hypocalcaemia is divided into three categories according to the severity of the clinical symptoms, physical findings, biochemical findings and the period of recovery: Mild category: Moderate category and Severe category.

Statistical analysis

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done:

- Independent-samples t-test of significance was used when comparing between two means.
- Chi-square (x^2) test of significance was used in order to compare proportions between two qualitative parameters.
- The confidence interval was set to 95% and the margin of error accepted was set to 5%. The p-value was considered significant as the following:
- Probability (P-value)

- P-value <0.05 was considered significant.
- P-value <0.001 was considered as highly significant.
- P-value >0.05 was considered insignificant.

RESULTS

This study included 30 patients who were planned for thyroidectomy. They were randomly allocated into two equal groups of 15 patients each. In group A, the main trunk of the inferior thyroid artery was ligated, while in group B, its individual branches were ligated.

Table (1): The age, sex and thyroid U/S distributions in all patients (30 patients)

		No. = 30
Age	**Mean±SD**	44.30 ± 9.34
	Range	27 – 59
Sex	**Female**	17 (56.7%)
	Male	13 (43.3%)
Thyroid U/S	**Solitary thyroid nodule**	11 (36.7%)
	Multinodular goiter	13 (43.3%)
	2ry toxic goiter	6 (20%)

Table (2): PTH level change in all patients preoperative and postoperative 3rd day

		PTH
		No. = 30
Preoperative	**Mean±SD**	47.84 ± 17.17
	Range	20.2 – 85.5
3rd day Postoperative	**Mean±SD**	43.75 ± 16.27
	Range	14.2 – 79.2
Paired t-test		**10.594**
P-value		**<0.001 (HS)**

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)

Regarding PTH, postoperative levels showed significant decrease compared to preoperative levels typically after total thyroidectomy.

Table (3): PTH level in each preoperative and postoperative group on the 3rd day showing highly significant change

PTH		**Main trunk ligation**	**lective branches ligation**	**est value**	**P-value**	**ig.**
		No. = 15	**No. = 15**			
Preoperative	Mean±SD	48.11 ± 18.09	47.57 ± 16.84	0.086•	0.932	NS
	Range	20.2 – 73.7	23.3 – 85.5			
day preoperative	Mean±SD	42.55 ± 17.29	44.95 ± 15.70	-0.398•	0.694	NS
	Range	14.2 – 68.1	15.3 – 79.2			
% change	Mean±SD	-12.61 ± 4.01	-5.44 ± 1.64	-4.542‡	0.000	HS
	Range	-20.57 – -6.93	-7.58 – -2.62			
Paired t-test		**13.454**	**7.074**			
P-value		**0.000 (HS)**	**0.000 (HS)**			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
•: Independent t-test; ‡: Mann Whitney test

In group (A) patients, the postoperative serum calcium was significantly reduced on day 1, on postoperative days, the serum calcium levels changed as showing in table 3.

Table (4): Preoperative and postoperative Ca levels in all patients (30 patients)

		Ca
		No. = 30
Pre	Mean±SD	9.73 ± 0.48
	Range	9.1 – 10.6
1st Day	Mean±SD	9.26 ± 0.64
	Range	7.6 – 10.1
2nd Day	Mean±SD	9.23 ± 0.62
	Range	7.6 – 10
3rd Day	Mean±SD	9.29 ± 0.59
	Range	7.7 – 10.2
Repeated Measure ANOVA test		**183.281**
P-value		**<0.001 (HS)**

Table (5): Calcium levels in each group preoperative, 1st, 2nd and 3rd day postoperative

Ca		Main trunk ligation	Selective branches ligation	Test value•	P-value	Sig.
		No. = 15	No. = 15			
Pre	Mean±SD Range	9.71 ± 0.35 9.1 – 10.5	9.75 ± 0.32 9.2 – 10.6	0.086•	0.836	NS
1st	Mean±SD Range	9.15 ± 0.34 7.6– 9.7	9.37 ± 0.51 7.9 – 10.1	-5.810•	0.000	HS
2nd	Mean±SD Range	9.13 ± 0.29 7.6 – 9.5	9.32 ± 0.54 8.1 – 10	-5.586•	0.000	HS
3rd	Mean±SD Range	9.18 ± 0.26 7.7 – 9.9	9.39 ± 0.49 8.5 – 10.2	-6.203•	0.000	HS
% change	Mean±SD Range	-10.75 ± 2.04 -13.54 – -6.67	-8.09 ± 2.41 -10.56 – -2.91	-2.470ǂ	0.012	S
Repeated measure ANOVA test		**141.278**	**67.451**			
P-value		**0.000 (HS)**	**0.000 (HS)**			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
•: Independent t-test; ‡: Mann Whitney test

In our study there were 4 patients with mild to moderate symptoms and sings of hypocalcaemia in the form of tingling and numbness sensation of the face and latent tetany discovered during routine examination of vital signs.

Laboratory examination of those patients shows significant decrease in serum Ca and PTH levels in 1st day postoperative but return to normal level in day 3 postoperative. 3 of the 4 patients were belonged to group A and all 4 patients were thyrotoxic before surgery. There were subclinical laboratory changes in serum PTH in 10% (3 patients) in group A, and 3% (1 patient) in group B but serum Ca level not below 8.6 gm/dl.

Comparative analysis between the two groups:

Both groups were comparable as regard, number of patients, age, sex and indication for thyroidectomy. They were also comparable as regard their postoperative serum Calcium and PTH levels.Postoperative reduction of serum calcium level was higher in group A than group B patients after thyroidectomy (table 5).PTH levels were more reduced in group A than group B after thyroidectomy (table **3**).

DISCUSSION

Only few patients (0.1% - 3%) develop postoperative permanent hypocalcaemia [(7)]**.** Incidence of permanent hypocalcaemia reported in different studies are 0.7% [(8)], 5% [(9)], 5.4% [(10)], 7.7% [(11)]**.** In the present work, no cases of permanent hypocalcaemia were reported, which were followed up to 3 months postoperatively.

The pathogenesis of the permanent form is invariably the parathyroid ablation or devascularization[(12)]**.** Four commonly cited possibilities of postoperative parathyroid insufficiency in literature were discussed. They were; accidental devascularization of one or several parathyroid gland, infarction during manipulation, inadvertent removal of the parathyroids with the thyroid lobes or release of calcitonin due to manipulation during surgery [(13)]**.**

Thus some surgeons become reluctant to perform total thyroidectomy because of the risk of permanent damage of the parathyroid glands and such incomplete thyroid surgery may compromise patient management [(14)]**.**

In thyroid surgery it has been reported to occur more commonly after total thyroidectomy with reported incidence ranging from 6.9% to 25% [(14)] or 6.9%-30%[(5)]**.**

Iqbal *et al.*[(15)] noticed that patients undergoing total thyroidectomy developed asymptomatic hypocalcaemia in 18.8%, and transient symptomatic hypocalcaemia needing calcium supplements in 5.54% of the patients. None of the patients in this study had permanent hypocalcaemia.

The reported incidence of permanent hypoparathyroidism after total thyroidectomy remains high, varying from 2 to 33% in different cases of total thyroidectomy in the treatment of patients with thyroid carcinoma[(15)]**).** In our study, 4 cases with postoperative temporary hypoparathyroidism were reported which improved in the first month postoperatively.

Nies *et al.*[(16)] and **Kovacs *et al.*[(10)]** observed that transient mild hypocalcaemia may not be due to parathyroid insufficiency. It can also be observed after another operations accompanied by blood loss or development of hypoalbuminemia. They are of the opinion that fluid shifts and dilutional effects can cause temporary hypoalbuminemia; calcium binding capacity is thereby reduced causing a decrease in total serum calcium concentrations. Ionized calcium levels are not influenced by this effect. It may also be a cause of the asymptomatic hypocalcaemia in the immediate postoperative period. However, the presence of post thyroidectomy lower levels of PTH in this study in

comparison with hypocalcaemia may be against this hypothesis.

The level of PTH is an important parameter of parathyroid function [17]. In the study conducted by **Araujo *et al.*** [18], they noticed that all of the hypocalcaemic patients had low levels of PTH. On the other hand, 10.7% of the levels were low in normal calcaemic patients.

In our study, PTH was measured in both groups, preoperatively and on day 3 postoperatively, and showed significant reduction postoperative.

The main source of blood supply to the parathyroid glands is the inferior thyroid artery. About 80% - 86% of upper and 90% - 95% of lower parathyroid arteries originate from the inferior thyroid artery [9].

Schmauss *et al.* [19] claimed reduction in incidence of hypocalcaemia after non ligation of inferior thyroid artery in their study.

Thomusch *et al.* [20] recommended that ligation of inferior thyroid artery at thyroid capsule is a better technique and having less incidence of hypocalcaemia.

Our study showed that the incidence of post thyroidectomy reduction in the calcium level was more after truncal ligation of the inferior thyroid artery, than after ligation of its individual branches sparing that for the parathyroid glands. This difference was statistically significant, but most of patient's level of calcium or PTH were within normal range either pre or postoperatively, so this clinically insignificant.

Regarding the hypothesis of devascularization of the parathyroid gland, there is a rich anastomotic network of the capillaries in the neck that if the arterial supply of the parathyroids is even compromised, still these should regenerate and revascularize in the much natural way as opposed to the auto-transplanted glands when accidentally or willingly removed [21]. This may be an explanation to the difference of post thyroidectomy hypocalcaemia in the two groups.

In our study, the postoperative hypocalcaemia which was transient in all of the patients those manifested by hypocalcaemia in both groups improved by the first month postoperatively.

CONCLUSION

- Post-thyroidectomy complications are much less common nowadays with reported mortality rate less than 1%.
- Incidence of post-thyroidectomy hypocalcaemia is more common with ligation of the inferior thyroid artery main trunk than with ligation if its individual branches.
- PTH although a sensitive test as a measure of post-thyroidectomy hypoparathyroidism, but is too nonspecific.
- The results of this work showed that the incidence of post thyroidectomy hypocalcaemia, although was statistically significant in some comparisons of calcium and PTH, yet most of the levels were within the normal range, either pre or postoperatively with no clinical effects.
- Only 4 patients manifested mild hypocalcaemia and hypoparathyroidism, 3 of them were truncal ligation and one of them was selected braches ligation, all of these 4 patients were improved in the first month post-operative.
- Ligation of the main trunk of inferior thyroid artery, although have a statistical significant on the parathyroid function and hypocalcaemia postoperatively yet, good surgical technique to identify and preserve the parathyroids, is the most important factor which may affect the postoperative hypocalcaemia.

REFERENCES

1. **Bergamaschi R, Becouarn G, Ronceray J *et al.* (1998):** Morbidity of thyroid surgery. The American Journal of Surgery, 176(1):71-5.
2. **Battachary N and Marivin MP (2002):** Assessment of the morbidity and complications following total thyroidectomy. Arch Otolaryngeal Head and Neck Surg., 176(1):71-5.
3. **Fahmy FF, Gillette D, Lolen Y*et al.* (2004):** Management of serum calcium level in post thyroidectomy patients. Clinic Otolaryngology, 114:168-74
4. **Cakmakli S, Aydintug S and Erdem E (1992):** Post thyroidectomy hypocalcaemia: Does arterial ligation play a significant role?.Int Surg., 77(4):428-6.
5. **See SC and Soo KC (1997):** Hypocalcaemia following thyroidectomy for thyrotoxicosis. BrJSurg., 84(1):95-7.
6. **Rubin AD and Sharma PK (2001):** Complication of thyroid surgery. E Medicine J., 2(9):1-15.
7. **Schulte KM andRocher HD (2001):** Complications in thyroid surgery of benign thyroid disease. ActaChirurgicaAustriaca, 33 (4): 164-72.
8. **Pisanu A, Piu S, CoisA*et al.* (2005):** Hypocalcaemia following total thyroidectomy, early factors predicting long term outcome. G Chir., 26(4):131-4.
9. **Anjum MN, Malik A andHaq A (2003):** Postoperative hypocalcaemia after thyroidectomy: analysis of risk factors. Pak Postgrad Med J., 13(3):112-5.
10. **Kovacs L, Goth MI, Voros A*et al.* (2000):** Changes of serum calcium level following thyroid surgery-reasons and clinical implications. Exp Clin Endocrinal Diabetes, 108(5):364-8.
11. **Wilson RB, Erskin C and Crowe PJ (2000):**Hypomagnesemia and hypocalcaemia after thyroidectomy. World J Surg., 24 (6):722-6
12. **Watson CC, Steed DL, Robinson AC *et al.* (1981):** The role of calcitonin and parathyroid hormone in the pathogenesis of post thyroidectomy hypocalcaemia. Metabolism, 30:588-589.
13. **Bashir EA, Khan FA and Javeed M (1995):** Ligation of inferior thyroid arteries in subtotal thyroidectomy and postoperative parathyroid functions, J CollPhyscSurg Pak., 8(1):17-9.
14. **Bourrel C, Uzzan B, Tison P*et al.* (1993):** Transient hypocalcaemia after thyroidectomy. Ann OtolRhinolLaryngol., 102(7):496-501
15. **Iqbal J, Ali B and Pasha HK (1997):** Total thyroidectomy: a study of 85 cases. J CollPhyscSurg Pak., 7 (1):20-1.

16. **Nies C, Sitter H, Zielke A *et al.* (1994):** Parathyroid function following ligation of the inferior thyroid arteries during bilateral subtotal thyroidectomy. B.M.J., 81: 1757-1759.
17. **Hamada N, Mimura T, Suzuki A *et al.* (1986):** Serum parathyroid hormone concentration measured by highly sensitive assay in post-thyroidectomy hypocalcaemia of patients with Grave's disease. Endocrinal Japon., 36:281-8
18. **Araujo F, Silva FG, Brandao LG *et al.* (2000):** The importance of ligation of inferior thyroid artery in parathyroid function after subtotal thyroidectomy, Rev HospClinFac Med Sao Paulo, 55(4):113-20.
19. **Schmauss AK and Zech U (1981):** Das Verhalten der Serrumkalzium und SerumphosphatwertenachEingriffienan der SchilddruseohneLjgatur der Aa. Thyroideaemeferiores. ZentralblChir., 106:1063-73 .
20. **Thomusch O, Machens A, Sekulla C*et al.* (2003):** The impact of surgical technique on post operativehypoparathyroidism in bilateral thyroid surgery: a multivariate analysis of 5846 patients. Surgery, 133(2):180-5.
21. **Chen H, Civelek AC, Westra WH*et al.* (2000):** Use of Tc 99mSestamibi scintigraphy for recurrent tertiary hyperparathyroidism from a parathyroid forearm graft. South Med J., 93(2):215-7.