

EFFECT OF IN SITU PRESERVATION OF PARATHYROID GLAND ON CALCIUM LEVEL AFTER TOTAL THYROIDECTOMY

Muhammad Tariq Ghafoor, Syeda Sabahat Haider, Nouren Kousar, Sohail Sabir, Muhammad Tariq, Maria Bashir

Sheikh Zayed Medical College / Hospital, Raheem Yar Khan, Pakistan

ABSTRACT

Objective: Hypocalcemia is the most common complication encountered in patients after total thyroidectomy. The study was aimed to determine the effect of insitu preservation of parathyroid gland on serum calcium levels after total thyroidectomy.

Material and Methods: This was a retrospective study carried out in the surgical department and chemical pathology department of Sheikh Zayed Medical College/Hospital, Rahim Yar Khan. Data of 150 patients was collected retrospectively since 2016 -2019, who underwent total thyroidectomy and recorded their database prospectively. Study subjects were divided into three groups by number of parathyroid gland (one PTG preserved=group1, two PTG preserved=group2 and >2 PTG preserved =group3). The total calcium, magnesium, vitamin D and parathyroid hormone (iPTH) levels were compared among the three groups. Effect of this preservation on the development of transient and permanent hypocalcemia was noted.

Results: There were 28 patients in group 1, 55 in group 2 and 67 in group 3. The average age of the patients was 45.4±11.7 years in group 1, 42.7±10.2 years in group 2 and 44.8±12.5 years in group 3. There were 19 Female and 09 males in group 1, 42 Females and 13 males in group 2 and 49 female and 18 males in group 3. Pre-operative calcium level was 8.1±0.22mg/dl in group 1, 8.6±0.11mg/dl in group 2 and 8.8±0.37mg/dl in group 3. Post-operative calcium level was 7.2±0.09mg/dl in group 1, 8.4±0.21mg/dl in group 2 and 8.6±0.31mg/dl in group 3 with p value <0.05. Transient hypocalcemia was developed in 53.5% patients in group 1, 10.9% in group 2 while none was observed in group 3. Permanent hypocalcemia developed in 7.1% in group 1 while no permanent hypocalcemia was seen in groups 2 and 3.

Conclusion: Incidence of hypocalcemia can be significantly reduced in-situ preservation of atleast two parathyroid glands with intact blood supply during total thyroidectomy. Lesser preservation of parathyroid glands or its auto-transplantation is independent risk factor for the development of postoperative hypocalcemia.

Key Words: Parathyroid gland, Hypocalcemia, Thyroidectomy.

This article can be cited as: Ghafoor MT, Haider SS, Kousar N, Sabir S, Tariq M, Bashir M. Effect of in situ preservation of parathyroid gland on calcium level after total thyroidectomy. Pak J Pathol. 2020; 31(3): 69-73.

INTRODUCTION

Total thyroidectomy is a time tested popular operative procedure for most of the thyroid diseases. But hypocalcemia/hypoparathyroidism is the most common complication after total thyroidectomy. Although thyroidectomy has become a safe procedure in the hand of skilled surgeons but preservation of all the four parathyroid glands along with their intact blood supply is still quite a challenge. The incidence of transient hypocalcemia is reported to be 10-46% after total thyroidectomy whereas permanent hypocalcemia is noted to be as high as 43% in some studies [1]. Development of such complication postoperatively not only prolongs the hospital stay of the patient thus increasing the chances of getting infection but also the cost of medication and frequent biochemical testing is required making the procedure more expensive.

While the use of lifelong calcium supplements and vitamin D is also quite cumbersome for the affected patients. Injury to parathyroid gland's causes hypocalcemia which may result due to ligation of gland vascular supply, accidental removal, careless use of electro-cauterization or destruction of the gland due to hematoma formation [2,3]. Frequency of incidental parathyroidectomy happens to be 5.2% to 21% [4-6] in some studies making it an independent risk factor for the development of postoperative hypocalcemia.

Some studies have recommended to auto-transplant the un-intentionally removed or de-vascularized parathyroid gland in order to decrease the incidence of hypocalcemia [7,8] while others have documented an increased incidence of transient or permanent hypoparathyroidism with parathyroid auto-transplantation [9-11]. There are interestingly few studies which have reported no relationship of total thyroidectomy to this complication [12,13,14]. Hence the effect of auto-transplantation of parathyroid gland on postoperative development of hypoparathyroidism is not fully understood. Moreover, development of

Correspondence: Dr. Muhammad Tariq Ghafoor, Associate Professor of Surgery, Sheikh Zayed Hospital, Raheem Yar Khan Pakistan

Email: tariqghafoor55@gmail.com

Received: 13 May 2020; Revised: 01 Jul 2020; Accepted: 10 Aug 2020

hypoparathyroidism/hypocalcemia in relation with the number of in-situ preserved parathyroid gland still needs to be established. This study was designed to estimate the frequency of hypocalcemia (transient/permanent) in patient with total thyroidectomy and also to evaluate the role of in-situ preservation of one and more than one parathyroid gland in order to prevent transient hypocalcemia in such patients.

MATERIAL AND METHODS

We retrospectively collected the data of 150 patients selected for total thyroidectomy and the study was conducted on a data base. All the surgeries were performed by the author himself or under direct supervision and followed prospectively over the period of six months. We included all the patients selected for total thyroidectomy and the exclusion criteria was malignant tumors of thyroid, preoperative hyper or hypocalcemia, reoperation, chronic kidney disease or incomplete data collection. Preoperative management included the collection of patient demographic data and blood sample for Calcium, Magnesium, Vitamin-D and iPTH levels early on the morning of operation. Calcium and Magnesium levels were analyzed on Backman Coulter 680(USA) in the Department of Chemical Pathology, Sheikh Zayed Medical college/hospital but Vitamin D and iPTH were determined by electrochemilumin-escence technique (USA). Transient hypocalcemia was defined as decreased serum calcium levels (<8 mg/dl) regardless of sign and symptoms and need of calcium after surgery and absence when followed in the first month. And iPTH levels in normal (lower range) while permanent hypocalcemia with low calcium levels along with subnormal or undetectable iPTH four months after the surgery. We used the conventional capsular dissection technique and the parathyroid glands attached to the dorsal surface of thyroid gland were identified and retained in situ with possibly intact vascular supply. We tried to identify and preserve maximum parathyroid glands. The cases with auto-transplanted parathyroid gland in the ipsilateral sternocleidomastoid muscle were excluded in order to reduce the bias. The patients with normocalcemia and clinically no discomfort were discharged on 2nd or 3rd post-operative day and others were given oral or parenteral calcium supplements and vitamin D on case to case basis. Follow up of these study subjects was done rigorously in the OPD with calcium, vitamin D/iPTH (if indicated) every month after discharge until six months. Data was collected and approval of the ethical review board was taken. All the patients were

given written Informed consent for collection of their demographic and clinical data.

Data Analysis: Statistical analysis was done using the SPSS19. Continuous variables were presented as mean \pm SD and the groups were compared by student *t* test. Anova was applied to compare the calcium levels in the three group pre and post operatively. *P* value <0.05 was considered statistically significant.

RESULTS

Based on the inclusion and exclusion criteria, 150 patients were selected Table-1 shows the clinical characteristics of study subjects. We divided the patients in three groups who underwent total thyroidectomy. The group 1 had one parathyroid gland preserved insitu, group 2 patients had two parathyroid glands preserved in situ and group 3 had more than two parathyroid glands preserved in situ. There were 28 patients in group 1, 55 in group 2 and 67 in group 3. The mean age of the patients was 45.4 \pm 11.7 years in group 1, 42.7 \pm 10.2 years in group 2 and 44.8 \pm 12.5 years in group 3. In group 1, there were 68% female and 32% male patients, in group 2 76% female and 24% male while in group 3 there were 73% female and 27 % male patients. Pre-operative calcium level was 8.1 \pm 0.22mg/dl in group 1, 8.6 \pm 0.11mg/dl in group 2 and 8.8 \pm 0.37mg/dl in group 3. In group 1, 15 patients (53.5%) developed transient hypocalcemia and 2 (7.1%) patients suffered from permanent hypocalcemia. In group 2, only 6 (11%) developed transient hypocalcemia while in group 3, none of the patients developed transient or permanent hypocalcemia as shown in table 2. There was significant difference of pre- and post-operative calcium level in group1 patients but in group 2 and 3 patients this difference was found to be statistically insignificant as shown in Table-3.

Table 1: Clinical Characteristics of study subjects

Variables	Gp.1 (n=28)	Gp.2 (n=55)	Gp.3 (n=67)
Age(years)	45.4 \pm 11.7	42.7 \pm 10.2	44.8 \pm 12.5
Gender (female/ male)	19/9	42/13	49/18
Diabetes	8	10	2
Hypertension	21	13	1
Graves' disease	10	7	3
Thyroiditis	21	14	5
Nodular goiter	15	13	7
S/Calcium (mg/dl)	8.1 \pm 0.22	8.6 \pm 0.11	8.8 \pm 0.37
S/Mg (mmol/L)	1.7 \pm 0.11	1.9 \pm 0.09	2.1 \pm 0.14
iPTH (pmol/L)	5.49 \pm 1.59	5.54 \pm 2.01	5.82 \pm 1.79
25(OH)D (ng/ml)	47 \pm 1.9	56 \pm 0.88	51 \pm 1.8

Table-2: Incidence of hypocalcaemia (transient/permanent) in the three group (n=150).

Gp	No of insitu preserved parathyroid gland	Total	Transient hypocalcemia (%)	Permanent hypocalcemia (%)
1	1	28	15 (53.5)	2(7.1)
2	2	55	6 (10.9)	0 (0)
3	>2	67	0 (0)	0 (0)

Table-3: In situ preserved Parathyroid gland and calcium level (mg/dl) among groups and the follow up results.

Variable	Preoperative calcium(mg/dl)	Postoperative calcium(mg/dl)	P-value
Group 1	8.3±0.11	7.2±.09	<0.05
Group 2	8.7±1.1	8.4±0.21	NS
Group 3	8.8±0.12	8.6±0.31	NS

DISCUSSION

Since 1980s, thyroidectomy has become a useful surgical treatment for most of the disorders of thyroid gland due to worldwide use of ultrasonographic screening procedures but its postoperative complications are still beleaguering for most of surgeons and physicians. Mostly after thyroid surgery the well-known common complications are injury to the recurrent laryngeal nerve, bleeding and parathyroid insufficiency [15,16,17]. It has been observed that patient age, gender, preoperative calcium level, type and extent of thyroid surgery are usually associated with the development of postoperative hypocalcemia and parathyroid gland failure [18-21]. Currently there are no state-of-the-art guidelines available for the identification or preservation of parathyroid glands and the options studied in the literature are quite divergent. Our findings in this study do verify the results of previous studies but the insitu preservation of parathyroid gland was found to be more promising than other variables. The relationship of the number of Parathyroids preserved and postoperative hypocalcemia has also been studied by Thomusch *et al* and stated it to be at least two, while Pottou *et al* [22,23] claimed it to be minimum three PGs to be visualized and preserved. Some authors have recognized the adverse outcome of active search and dissection as a major cause of devascularization of glands [24-26]. Our study aimed to observe the effect of insitu preservation of parathyroid glands on the development of transient or permanent hypocalcemia in relation with the minimum number of PG saved. The incidence of transient and permanent hypocalcemia in our study was observed to be 53.5 and 7.1% respectively in group one while only transient hypocalcemia was observed in 10.9% cases with atleast two preserved PTG (Table-2 & 3). This frequency is comparable to previous studies of total

thyroidectomy [27-31]. The patients who developed transient hypocalcemia were treated with oral calcium and vitamin D supplements and gradually, normalization of their calcium level was achieved within four weeks. Development of postoperative hypocalcemia is usually seen with parathyroid injury, extensive lymph nodes dissection, parathyroid devascularization and Grave's disease [32-34]. In this study 20 patients with Graves' disease were treated before the total thyroidectomy and the incidence of hypocalcemia was observed to be 18% This finding is also in agreement with the literature as higher incidence of postoperative hypocalcemia is reported to be associated with Graves' disease [35].

Preservation of parathyroid gland could not be achieved due to different reasons for example they are located within or anterior to thyroid gland. On the other hand, if the removed parathyroid gland was placed intentionally into the muscle also resulted in failure of parathyroid gland. Our observation in the study were same as auto transplantation of the parathyroid gland was associated with immediate postoperative fall in calcium levels and these findings are in agreement with Hallgirimson *et al* [36] and Kihara *et al* [37]. Though mostly available data on auto transplantation of parathyroid gland has somehow overestimated its effect and under estimated the impact of insitu preservation of parathyroid gland on its function [38-41]. So, in our study, we did not observe any significant difference in the iPTH levels among the three groups by the end of six month follow up but we did observe that the recovery rate of the patients in group 2 and 3 were far noticeable than group-1 and those with unintentional parathyroidectomy (72.1%/71.9% vs 63%). There are two studies which have reported that if all the identified parathyroid gland are auto-transplanted, it can significantly lower the risk of failure of parathyroid gland [42,43] but these findings are subjective to many confounding variables like variety of thyroid disorder, number of preserved or auto-transplanted parathyroid glands, number and types of neck surgeries. Preservation of atleast two functional parathyroid glands was found to be necessary to avoid postoperative hypocalcemia as stated by Attie and Kahafif [29] and it was also suggested by Wingert *et al* [28] that there is increased risk of hypocalcemia if more than two PGs are resected. These findings have strengthened our results in which no permanent hypocalcemia was found in group where atleast two parathyroid were preserved insitu.

CONCLUSION

The most important factor for development of permanent hypocalcemia is the number of preserved parathyroid glands. Preservation of atleast two parathyroid glands insitu is a better strategy not only to avoid postoperative hypocalcemia but also ensures rapid recovery. Further prospective studies are required to observe and document the long-term effect on follow up and to confirm these findings

AUTHORS CONTRIBUTION

Muhammad Tariq Ghafoor: Concept, study design& final approval

Syeda Sabahat Haider: Data collection, drafting and data analysis

Nouren Kousar: Data interpretation and work design

Sohail Sabir: Questionnaire design, revision and finalization of results

Muhammad Tariq: Literature search and acquisition

Maria Bashir: Data collection

REFERENCES

- Sidhic KA, Hisham Y, Nabeel TP, Abid KPA. The number of parathyroid glands preserved during thyroidectomy and relationship between hypoparathyroidism. *Int Surg J*. 2017; 4(9): 2898-902.
- Bliss RD, Gauger PG, Delbridge LW. Surgeon's approach to the thyroid gland: surgical anatomy and the importance of technique. *World J Surg*. 2000; 24: 891-7.
- Shaha AR, Burnett C, Jaffe BM. Parathyroid auto-transplantation during thyroid surgery. *J Surg Oncol*. 1991; 46: 21-24.
- Gourgiotis P, Moustafellos N, Dimopoulos G, Papaxoinis S, Hadjiyannakis E. Inadvertent parathyroidectomy during thyroid surgery: the incidence of a complication of thyroidectomy. *Langenbeck's Archives Surg*. 2006; 391(6): 557-60.
- Page C, Strunski V. Parathyroid risk in total thyroidectomy for bilateral, benign, multinodular goitre: report of 351 surgical cases. *J Laryngol & Otol*. 2007; 121(03): 237-41.
- Applewhite MK, White MG, Xiong Metal. Incidence, risk factors, and clinical outcomes of incidental parathyroidectomy during thyroid surgery. *Annals of Surg Oncol*. 2016; 23(13): 4310-15.
- Wei T, Li Z, Jinetal J. Auto-transplantation of inferior parathyroid glands during central neck dissection for papillary thyroid carcinoma: a retrospective cohort study. *Int J Surg*. 2014; 12(12): 1286-90.
- Song CM, Jung JH, Ji YB, Min HJ, Ahn YH, Tae K. Relationship between hypoparathyroidism and the number of parathyroid glands preserved during thyroidectomy. *World J Surg Oncol*. 2014; 12(1): 200-4.
- Lorente-Poch L, Sancho JJ, Ruiz S, Sitges-Serra A. Importance of in situ preservation of parathyroid glands during total thyroidectomy. *British J Surg*. 2015; 102: 359-67.
- Kihara M, Miyauchi A, Kontani K, Yamauchi A, Yokomise H. Recovery of parathyroid function after total thyroidectomy: Long term follow-up study. *ANZ J Surg*. 2005; 75: 532-6.
- Kirdak T, Dundar HZ, Uysal E, Ocakoglu G, Korun N. Outcomes of parathyroid auto-transplantation during total thyroidectomy: A comparison with age and sex-matched controls. *J Investigative Surg*. 2017; 30: 201-9.
- Ondik MP, McGinn J, Ruggiero F, Goldenberg D. Unintentional parathyroidectomy and hypoparathyroidism in secondary central compartment surgery for thyroid cancer. *Head and Neck*. 2010; 32: 462-6.
- Rix TE, Sinha P. Inadvertent parathyroid excision during thyroid surgery. *Surg*. 2006; 4: 339-42.
- Lin DT, Patel SG, Shaha AR, Singh B, Shah JP. Incidence of inadvertent parathyroid removal during thyroidectomy. *Laryngoscope*. 2002; 112: 608-11.
- Shaha AR, Jaffe BM. Practical management of post-thyroidectomy hematoma. *J Surg Oncol*. 1994; 57: 235-8.
- Cheah WK, Arici C, Ituarte PH, Siperstein AE, Duh QY, Clark OH. Complications of neck dissection for thyroid cancer. *World J Surg*. 2002; 26: 1013-16.
- Kark AE, Kissin MW, Auerbach R, Meikle M. Voice changes after thyroidectomy: role of the external laryngeal nerve. *Br Med J (Clin Res Ed)*. 1984; 289: 1412-15.
- Erbil Y, Barbaros U, Temel B, Turkoglu U, İşsever H, Bozboru A, *et al*. The impact of age, vitamin D3 level and incidental parathyroidectomy on postoperative hypocalcemia after total or near total thyroidectomy. *Am J Surg*. 2009; 197(4): 439-46.
- Sands NB, Payne RJ, CôtéV, Hier MP, Black MJ, Tamilia M. Female gender as a risk factor for transient post-thyroidectomy hypocalcemia. *Otolaryngology-Head and Neck Sur*. 2011; 145(4): 561-4.
- Sitges-Serra A, Ruiz S, Girvent M, Manjón H, Dueñas JP, Sancho JJ. Outcome of protracted hypoparathyroidism after total thyroidectomy. *Bri J Surg*. 2010; 97(11): 1687-95.
- Thomusch O, Machens A, Sekulla C, Ukkat J, Lippert H, Gastinger I, *et al*. Multivariate analysis of risk factors for postoperative complications in benign goiter surgery; prospective multicentre study in Germany. *World J Surg*. 2014; 24(11): 1335-41.
- Thomusch O, Machens A, Sekulla C, Ukkat J, Brauckhoff M, Dralle H. The impact of surgical technique on postoperative hypoparathyroidism in bilateral thyroid surgery: a multivariate analysis of 5846 consecutive patients. *Surg*. 2003; 133: 180-5
- Palazzo FF, Sywak MS, Sidhu SB, Barraclough BH, Delbridge LW. Parathyroid auto-transplantation during total thyroidectomy: does the number of glands transplanted affect outcome? *World J Surg*. 2005; 29: 629-31
- Lappas D, Noussios G, Anagnostis P, Adamidou F, Chatzigeorgiou A, Skandalakis P. Location, number and morphology of parathyroid glands: results from a large anatomical series. *Anatomical Science International* 2012; 87(3): 160-4.
- Paek SH, LeeYM, Min SY, Kim SW, Chung KW, Youn YK. Risk factors of hypoparathyroidism following total thyroidectomy for thyroid cancer. *World J Surg*. 2013; 37(1): 94-101.
- Roh JL, Park JY, Park CI. Total thyroidectomy plus neck dissection in differentiated papillary thyroid carcinoma patients: pattern of nodal metastasis, morbidity, recurrence, and postoperative levels of serum parathyroid hormone. *Annals of Surg*. 2007; 245(4): 604-10.
- McHenry CR, Speroff T, Wentworth D, Murphy T. Risk factors for post-thyroidectomy hypocalcemia. *Surg*. 1994; 116: 641-7.
- Wingert DJ, Friesen SR, Iliopoulos JI, Pierce GE, Thomas JH, Hermreck AS. Post-thyroidectomy hypocalcemia. Incidence and risk factors. *Am J Surg* 1986; 152: 606-10.
- Attie JN, Khafif RA. Preservation of parathyroid glands during total thyroidectomy. Improved technic utilizing microsurgery. *Am J Surg*. 1975; 130: 399-404
- Farrar WB, Cooperman M, James AG. Surgical management of papillary and follicular carcinoma of the thyroid. *Ann Surg*. 1980; 192: 701-4.
- Lal G, Ituarte P, Kebebew E, Siperstein A, Duh QY, Clark OH. Should total thyroidectomy become the preferred procedure for surgical management of Graves' disease? *Thyroid*. 2005; 15: 569-74.

32. Demeester-Mirkine N, Hooghe L, Van Geertruyden J, De Maertelaer V. Hypocalcemia after thyroidectomy. *Arch Surg.* 1992; 127: 854-8.
33. Pesce CE, Shiue Z, Tsai HL, Umbricht CB, Tufano RP, Dackiw AP *et al.* Postoperative hypocalcemia after thyroidectomy for Graves' disease. *Thyroid.* 2010; 20: 1279-83.
34. Hermann M, Alk G, Roka R, Glaser K, Freissmuth M. Laryngeal recurrent nerve injury in surgery for benign thyroid diseases: effect of nerve dissection and impact of individual surgeon in more than 27,000 nerves at risk. *Ann Surg.* 2002; 235(2): 261-8.
35. Sheahan P, Mehanna R, Basheeth N, Murphy MS. Is systematic identification of all four parathyroid glands necessary during total thyroidectomy? A prospective study. *Laryngoscope.* 2013; 123(9): 2324-8.
36. Hallgrímsson P, Nordenstrom E, Almquist M, Bergenfelz AO. Risk factors for medically treated hypocalcemia after surgery for Graves' disease: a Swedish multicenter study of 1,157 patients. *World J Surg.* 2012; 36(8): 1933-42.
37. Sitges-Serra A, Ruiz S, Girvent M, Manjón H, Dueñas JP, and Sancho JJ. Outcome of protracted hypoparathyroidism after total thyroidectomy. *British J Surg.* 2010; 97(11): 1687-95.
38. Zedenius J, Wadstrom C, Delbridge L. Routine auto-transplantation of at least one parathyroid gland during total thyroidectomy may reduce permanent hypoparathyroidism to zero. *Australian & New Zealand J Surg.* 1999; 69: 794-7.
39. Ahmed N, Aurangzeb M, Muslim M, Zarin M. Routine parathyroid auto-transplantation during total thyroidectomy: A procedure with predictable outcome. *J Pak Med Assoc.* 2013; 63: 190-3.
40. Mann B, Buhr HJ. Lymph node dissection in patients with differentiated thyroid carcinoma--who benefits? *Langenbeck's Archives of Surg.* 1998; 383: 355-8.
41. Lo CY, Lam KY. Postoperative hypocalcemia in patients who did or did not undergo parathyroid auto-transplantation during thyroidectomy: a comparative study. *Surg.* 1998; 124: 1081-6.
42. Funahashi H, Satoh Y, Imai T, Ohno M, Narita T, Katoh M, *et al.* Our technique of parathyroid auto-transplantation in operation for papillary thyroid carcinoma. *Surg.* 1993; 114: 92-6.
43. Kikumori T, Imai T, Tanaka Y, Oiwa M, Mase T, Funahashi H. Parathyroid auto-transplantation with total thyroidectomy for thyroid carcinoma: long-term follow-up of grafted parathyroid function. *Surg.* 1999; 125: 5048.