ORIGINAL ARTICLE

POST THYROIDECTOMY HYPOCALCAEMIA

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Aim: *To evaluate the incidence and assess the risk factors of hypocalcaemia and permanent hypoparathyroidism following thyroidectomy.*
Methods: *150 patients operated for thyroidectomy from January 2003 to March 2006 were included in this study the fasting serum calcium and phosphorus levels were measured daily before and after surgery until the day of discharge; parathrome measurement was performed for all hypocalcaemic patients.*
Results: *12 out of 150 patients (8%) developed postoperative hypocalcaemia, 2 of them (16.6%) were considered permanent. Total thyroidectomy was the procedure in 38 patients ,6 from them (15.8%) devoloped hypocalcaemia and the other 6 out of 112 cases(5.4%) were after subtotal thyroidectomy.The hypocalcaemia was 11.4% in toxic goitre (5out of 44 patients),12% were malignant goitre(3 out of 12 patients) and 3.6% were simple multinodular goitre (3.out of 84 patients).*
Conclusions: *When preservation of parathyroid glands and their blood supply is enforced during thyroidectomy, the incidence of postoperative hypocalcaemia and permanent hypoparathyroidism can be consistently deceased.*

Keywords: *Surgical complications, hypoparathyroidism, thyroid carcinoma.*

INTRODUCTION

Chronic hypoparathyrodism is a serious and potentially debilitating disorder that results from a variety of causes. It most commonly occurs as a complication of thyroid surgery, with incidence rates of post thyroidectomy hypoparathyroidism ranging from 0% to 33% depending on the severity of the underlying disease and the extent of the operative procedure.[1]

A postoperative decrease of serum calcium is frequently observed within 2 to 5 days after a total or subtotal thyroidectomy, requiring exogenous replacement therapy to alleviate clinical symptoms.[2] Among the potential factors causing this decrease of serum calcium, heamodilution.[3] calcitonin release.[4] And hungry bone syndrome were implicated in patients with hyperthyroidism and osteodystrophy.[5]

In patients experiencing significant hypocalcaemia, the most probable cause is certainly hypoparathyradism secondary to trauma which usually results from intentional or inadvertent extirpation of the parathyroid glands during thyroidectomy or from interruption of the blood supply to the glands with subsequent infarction.[6] In most cases serum calcium normalize within few months, with subsequent recovery of parathyroid function. In a few patients however, hypoparathyrodism persists after 1 year and must be considered permanent.[7] this dire complication represents a major concern for thyroid

surgeons as the consequences of chronic hypocalcaemia are often insidious and potentially severe.[8] Permanent hypocalcaemia is a common cause of malpractice litigation after endocrine surgery. The risk of permanent hypoparathyroidism following thyroidectomy remains unclear, varying among recent series from zero up to 10 %.[9]

Signs and symptoms of the ensuing hypocalcaemia include perioral or distal extremity parasthesia, muscle cramping, positive Trousseau and Chvostek signs, laryngeal stridor and convulsions, the latter conditions may prove fatal. The long term sequellae of untreated or inadequately treated hypoparathyroidism include premature cataract development, calcification of basal ganglion, recurrent seizures, osteomalacia, and psychiatric symptomatology.[10]

In this study we prospectively evaluate the incidence and assess the risk factors of hypocalcaemia and permanent hypoparathyrodism following thyroidectomy in general surgery department, Assiut University Hospital.

MATERIALS AND METHODS

One hundred and fifty patients (36 males and 114 females) were operated upon for goitre (38 patients were subjected to total thyroidectomy and 112 patients were subjected to subtotal thyroidectomy. Those patients were admitted to the department of general surgery in Assiut University Hospital in the period from January 2003 to March 2006.

This study was approved by the local ethics committee and informed consent was obtained from all participating patients.

Preoperative assessment was done which included full clinical history, physical examination and routine laboratory investigations.

The fasting serum calcium and serum phosphorus levels were measured daily before and after surgery until the day of hospital discharge, which was usually on the third postoperative day. Hypocalcaemia was defined as a serum calcium level under 8.0 mg/dl on at least two consecutive measurements. When the serum calcium remained under 8.0 mg/dl for more than 2 days[7] or when patients experienced clinical symptoms and signs of hypocalcaemia (paresthesia, carpopedal spasm or positive Chvostek's sign), hypocalcaemia was considered severe and parathyroid hormone (PTH) measurement was performed before starting intravenous or oral calcium supplementation. (Serum levels of PTH were measured with an immunoradiometeric assay. Normal values of serum PTH in our hospital are 7-65 pg/ml) After the relief of clinical symptoms for a 24-hour period, patients were deemed ready for hospital discharge with a prescription of oral calcium substitute (3 g m/day).[7]

After discharge, and within 1 to 3 weeks on calcium supplementation, all patients who experienced severe postoperative hypocalcaemia were evaluated in the out patient clinic to control serum calcium and serum phosphorus levels and to titrate the substitution therapy. All patients were thereafter seen at least once every 3 months in our department. They were followed until normalization of their serum calcium after withdrawal of any substitutive therapy with calcium or vitamin D for more than 1 weak. Permanent hypoparathyroidism was defined by the requirement for vitamin D or calcium supplementation (or both) to maintain eucalcaemia 1 year after thyroidectomy.[7]

Operative Technique: All operations were performed by staff surgeons and consist of subtotal or total thyroidectomy using a standard operative technique[11] in all patients; every effort was made to identify and preserve the recurrent laryngeal nerves and the four parathyroid glands by the naked eye. This was possible in 118 out of 150 patients. In the remaining patients, the parathyroid glands could not identify intraoperatively. In those patients the removed thyroid tissue was examined for an inadvertently removed parathyroid tissue but no evidence of parathyroid tissue could be detected in any case

In 75 out of 150 patients, the inferior thyroid artery was looked for, identified and ligated in continuity. In the remaining 75 patients, the branches of the artery were clamped and ligated on the surface of the gland leaving the main trunk intact

For benign thyroid disease, total resection was conducted intra- capsularly when necessary to preserve the vascularization of the superior parathyroid glands.[12]

Histopathological examination was done for all of the removed glands, which is a routine work after any thyroidectomy

RESULTS

Twelve patients out of 150 developed hypocalcaemia wthin the 3 years period of the study, those patients were operated on in our department by total or subtotal thyroidectomy. Their ages ranged from 15 up to 70 years with a mean of 36.4 years, 36 of them were males and 114 were females.

As regard to pathological diagnosis 84 of them were simple multinodular goitre, 44 patients were toxic goitre, 12 were

malignant goitre and 10 were Hashimoto's thyroditis.

Subtotal thyroidectomy was done for 112 patients, and total thyroidectomy was the procedure for 38 patients.

Twelve patients experienced postoperative hypocalcaemia of whom 10 were considered to have severe hypocalcaemia.

All patients were followed up, 6 of them (50%) became normocalcaemic within 2 weeks, 4 (33%) became normocalcaemic within 2 weeks – 6 months and two patients (16.6%) still required calcium substitution or vitamin D therapy (or both) 1 year after thyroidectomy, hypoparathyroidism was confirmed in those two patients and were considered permanent (parathormone level was 10.6 and 15.3 pg/ml).

As regards the relationship between postoperative hypocalcaemia and type of thyroidectomy. The incidence of hypocalcaemia was higher in total thyroidectomy (6 out of 38 cases) (15.8%) while the incidence was 5.4% (6 out of 112) in subtotal thyroidectomy patients. Moreover the course of hypocalcaemia was most aggressive in patients with total thyroidectomy (all 6 patients) developed carpopedal spasms, 2 of them developed permanent hypocalcaemia and recovery of the other 4 cases were delayed to more than 8 weeks postoperatively.

Also the incidence of postoperative hypocalcaemia was higher in malignant (3 out of 12 cases) (25%) and in toxic goitre 11.4 %(5 out of 44) patients, while in simple multinodular goitre, it was 3.6 %(3 out of 84) patients and only 1 patient out of 10 with Hashimoto thyroiditis (10%).

The main trunk of inferior thyroid artery was ligated in 75 patients, 9 of them (12%) developed hypocalcaemia and 2 of them were permanent hypocalcaemia, while in patients in whom the main trunk of inferior thyroid artery were preserved, only 3 cases (4%) developed post operative hypocalcaemia with less aggressive course (no carpopedal spasm, no permanent hypocalcaemia and recovery within 10 weeks

In 118 patients in whom the parathyroid glands were preserved 6 of them developed post operative hypocalcaemia with 5.4% incidence, which was much lower than the incidence in patients in whom the parathyroid glands could not be identified, which was (18.8%). 6 out of 32 patients.

All clinical, biochemical and operative data for the 12 hypocalcaemic patients were shown in Tables 1,2,3.

Table 1. Clinical data of patient with hypocalcaemia.

No.	Sex	Age	Pathology
1	F	43	2 ry toxic G
2	F	26	1 ry toxic G
3	F	42	Simple nodular G
4	F	37	Hashimoto
5	F	48	Simple nodular G
6	M	39	2 ry toxic G
7	F	32	2 ry toxic G
8	F	16	1 ry toxic G
9	F	53	Simple nodular G
10	F	57	Papillary carcinoma
11	M	59	Papillary carcinoma
12	F	43	Follicular carcinoma

Table 2. Laboratory data of hypocalcaemic patient.

No.	Ca^{2+} level mg/dl			PTH level pg/ml	
	Pre	Post 1	Post 3	Pre	Post
1	10.8	8.6	8.0	44.4	40.6
2	9.9	8.9	7.9	23.4	24.3
3	10.3	7.9	8.1	29.3	28.8
4	10.3	7.7	8.0	54.1	40.3
5	11.0	7.5	7.0	48.6	21.2
6	9.7	8.1	7.8	37.6	38.7
7	10.2	7.5	7.1	34.5	17.5
8	9.8	7.6	6.1	67.8	10.6
9	9.1	6.8	6.3	57.7	22.6
10	9.6	8.1	6.6	53.3	23.6
11	10.0	7.8	6.3	64.0	15.3
12	10.3	8.0	6.7	39.2	21.5

Table 3. Surgical data and outcome of hypocalcaemic patient.

No.	Type of thyroidectomy	Parathyroid glands	The main trunk of inferior thyroid artery	Course
1	Subtotal	Preserved	Ligated	Recovery within 2 weeks
2	Subtotal	Preserved	Ligated	Recovery within 2 weeks
3	Subtotal	Preserved	Not	Recovery within 2 weeks
4	Subtotal	Preserved	Not	Recovery within 2 weeks
5	Total	Not	Ligated	Recovery within 18 weeks
6	Subtotal	Preserved	Not	Recovery within 2 weeks
7	Subtotal	Preserved	Ligated	Recovery within 10 weeks
8	Total	Not	Ligated	(Permanent) complete recovery could not be achieved
9	Total	Not	Ligated	Recovery within 2 weeks
10	Total	Not	Ligated	Recovery after 20 weeks
11	Total	Not	Ligated	(Permanent) complete recovery could not be achieved
12	Total	Not	Ligated	Complete recovery after 22 weeks

DISCUSSION

Post operative hypocalcemia is a major concern following thyroid surgery. It often extends the duration of the hospital stay and the need for biochemical tests, when severe, it can lead to serious complications and require intravenous therapy to alleviate the clinical symptoms.[13] Although hypocalcaemia reverses spontaneously in most cases. It can remain permanent when caused by irreversible injury to the parathyroid glands. Life long therapy and follow up are then mandatory to ovoid the subtle but severe and potentially lethal complication of chronic hypocalcaemia.[8] in this prospective study, postoperative hypocalcaemia was observed in (8%) of 150 patients undergoing subtotal or total thyroidectomy. Permanent hypoparthyroidism was found in 2 patients only (1.3%). These figures consistent with previous reports of Tovi et al.[14] and Megherbi et al.[15] (9% & 9.9% respectively). fFollowing thyroid surgery. Postoperative hypocalcaemia is reported to occur in a few to more than 50% of patients. Various factors account for these differences in literature, such as the definition of hypocalcaemia, the type of thyroid disease, and the surgical technique for thyroidectomy. To focus our study on clinically significant hypocalcaemia, we considered as hypocalcaemic only patients with a serum calcium level under 8 mg/dl on two occasions and who in most cases required calcium substitution.[7]

The occurrence of post operative hypocalcaemia depends on the type of operation performed and the underlying thyroid pathology. As regards the type of operation, in this present study the incidence was higher with total thyroidectomy (15.8%) than with subtotal thyroidectomy (5.4%), also the two permanent cases was after total thyroidectomy (5.3%), other surgeons reported an incidence of hypocalcaemia after total thyroidectomy varied from 6.2% with Bhattacharyya et al.[16] up to14.4 % reported by Bron and Obrient,[17] while the incidence after subtotal thyroidectomy ranged from 1.6% as reported by Farrar et al. In 1980[18] to 25.9% as reported by Wilkin et al. In 1977).[4] The incidence of permanent hypocalcaemia after total thyroidectomy varies in different studies from 0.4% with Farrar et al.)[18] up to 3% with Mishra, et al[19] while Karlan et al. (1984).[20] Reported on 0.2% incidence after subtotal thyroidectomy.

As regard the underlying thyroid pathology, higher incidence of hypocalcaemia with malignant (25%) and Toxic goitre (11.4%) than that in simple nodular goitre (3.6%) the high incidence of hypocalcaemia in thyrotoxicosis was noted also by Wingert et al.[21] who reported an incidence of 59% for hypocalcaemia after thyroidectomy for thyrotoxicosis versus 3% incidence after thyroidectomy for simple non toxic goitre. Many theories developed to explain this high incidence of hypocalcaemia after thyroidectomy for thyrotoxicosis. Golding and Krane.[22] Noted that in thyrotoxicosis there is increased bone catabolism and it has been demonstrated that the degree of thyrotoxic osteodystrophy increases proportionally with the severity of thyrotoxicosis. Michie et al. In 1971.[5] postulated that the rapid reversal of osteodystrophy that excisted before surgery that was called Hungary bone syndrome is a possible explanation. Sawers et al.[23] Suggested that the pre operative hypercalcaemia in thyrotoxic patients due to increased bone catabolism is usually associated with a decrease in parathromone level and persistence of this deficiency of parathromone and 1.25 dihydroxy–vitamin D could impair the compensatory responses to hypocalcaemia following thyroidectomy

Hypoparathyroidism after thyroidectomy remains the most widely accepted cause of hypocalcaemia. Edis in 1979.[24] reported that injury, devascularization or inadvertent removal of parathyroid tissue must be the first practical consideration in development of hypocalcaemia. Bourrel et al.[25] found a significant decrease of both PTH and total calcium levels after thyroid surgery proving that functional hypoparathyroidism as an important etiological factor for hypocalcaemia.

This present study supports hypoparathyroidism as a causative factor for hypocalcaemia. The high incidence of hypocalcaemia if parathyroid glands could not be identified and preserved (18.8%) versus the low incidence if the parathyroid glands were identified and preserved (5.4%), in addition to the reduction in the mean postoperative levels of PTH for those patients than their mean preoperative levels support the theory of hypoparathyroidism.

Ligation of the main trunk of inferior thyroid artery lateral in the neck during thyroidectomy gives good haemostasis and avoids injury to recurrent laryngeal nerves, but also it may interfere with the blood supply of parathyroids giving rise to hypoparathyroidism with subsequent hypocalcaemia. Osama, In 1990.[26] found a reduction in the incidence of hypocalcaemia from 52% to 20% when the main trunk of interior thyroid artery was preserved with special reduction of the incidence from 50% to zero percent in the simple nodular variety if the main trunk of inferior thyroid artery was preserved, and this in agree with our results where there was a reduction in the incidence of hypocalcaemia from 12% to 4% when the inferior thyroid arteries were preserved.

Also there was a more reduction in the mean postoperative parathromone levels in patients in whom the inferior thyroid arteries were ligated. However all patients with severe and permanent hypocalcaemia underwent ligation of inferior thyroid arteries during their thyroidectomies. So this present study supports the procedure of ligation of

branches of inferior thyroid artery on the surface of the gland with preservation of the main trunk as it reduce the incidence of postoperative hypocalcaemia and may prevent severe and permanent varieties specially if associated with identification, gentle manipulation and preservation of parathyroid glands.

In Conclusion clinically significant hypocalcaemia following thyroid surgery is secondary to impairment of parathyroid function in most cases. When in situ preservation of parathyroid glands and their blood supply is enforced during thyroidectomy, the incidence of postoperative hypocalcaemia and permanent hypoparathyroidism can be consistently restricted. Also patients with thyrotoxicosis are more liable for post operative hypocalcaemia with high incidence after total thyroidectomy than after more conservative thyroidectomies.

REFERENCES

1. Kahky M, Weber R. Complications of surgery of the thyroid and parathyroid glands. Surg Clin North Am. 1993;73:307-21.

2. Olson JA, DeBenedetti MK, Baumann DS, Wells SA. Parathyroid autotransplantation during thyroidectomy: results of long-term follow-up. Ann. Surg. 1996;223:472.

3. Demeester-Mirkine N, Hooghe L, Van Geertruyden J, de Maertelaer V. Hypocalcaemia after thyroidectomy. Arch. Surg. 1992;127:854.

4. Wilkin JT, Paterson CR, Isles TE, Crooks J, Beck JS. Post-thyroidectomy hypocalcaemia: a feature of the operation or the thyroid disorders. Lancet. 1977;1:62-623.

5. Michie W, Duncan T, Hamer-Hogdges DW, Bewsher PD, Stowers JM, Pegg CAS, et al. Mechanism of hypocalcaemia after thyroidectomy for thyrotoxicosis. Lancet. 1971;1:508.

6. Foster R. Thyroid gland. In: Davis J, Sheldon G, eds. Surgery: A Problem-Solving Approach. St. Louis, Mo: Mosby-Yearbook. 1995;2185-247

7. Patto F , Combemale F, Faper S, Carnaille B, Decoulx M,Wemeau JL, et.al. Hypocalcaemia following thyroid surgery : incidence and prediction of outcome . World J. Surg. 1998;22:718-24.

8. Bellamy RJ, Kendall-Taylor P. Unrecognized hypocalcaemia diagnosed 36 years after thyroidectomy. J. R. Soc. Med. 1995;88:690.

9. Al-Suliman NN, Ryttov NF, Qvist N, Blichert-Toft M, Graversen HA. Experience in a specialist thyroid surgery unit: a demographic study, surgical complications, and outcome. Eur. J. Surg. 1997;163:13.

10. Fonseca O, Calverley J. Neurological manifestations of hypoparathyroidism Arch Intern Med. 1967;120:202-6.

11. Reeve TS. Right subtotal thyroid lobectomy. In Malt RA, ed. Surgical Techniques Illustrated. Boston : Little Brown and Co. 1977; 61-70.

12. Delbridge L.,Total thyroidectomy: the evolution of surgical technique . ANZ J. Surg. 2003;73:761–8.

13. Reber PM, Heath H: Hypocalcemic emergencies. Md. Clin. North Am. 1995;79:93.

14. Tovi F, Noyek AM, Chapnik JS, Freeman JL. Safety of total thyroidectomy: review of 100 consecutive cases. Laryngoscope. 1989;99:1233.

15. Megherbi MT, Graba A, Oulmane D, Saidini M, Benabadji R. Complications of séquelles de la chirurgie thyroïdienne bénigne [Complications of benign thyroid surgery] (in French). J. Chir. (Paris). 1992;129:41.

16. Bhattacharyya N, Fried MP. Assessment of the morbidity and complications of total thyroidectomy. Arch otolaryngeol Head Neck Surg. 2002;128:553-4.

17. Bron LP, Obrien CJ, Total thyroidectomy for clinically benign disease of the thyroid gland. Br.J.Surg. 2004;91:569-74.

18. Farrar WB, Cooperman M, James AG. Surgical management of papillary and follicular carcinoma of the thyroid. Ann Surg. 1980;192:701-4.

19. Mishra A, Agarwal A,Agarwal G,Mishra SK, Total thyroidectomy for benign thyroid disorders in endemic region. Word J. Surg. 2001;25:307-10.

20. Karlan MS, Catz B, Dunkelman D, Uyeda RY, Gleischman S. A safe technique for thyroidectomy with complete nerve dissection and parathyroid preservation. Head Neck Surg. 1984;6:1014-9.

21. Wingert DJ, Friesen SR, Iliopoulos JI, Pierce GE, Thomas JH, Her Merck AS. Post-thyroidectomy hypocalcaemia. Incidence and risk factors. Am J Surg. 1986;152:606-610.

22. Golding SR, Krane SM. Organ system manifestations of thyrotoxicosis: the skeletal system. In: Ingbar SH, Braverman LE, eds. The Thyroid. Philadelphia, Pennsylvania: JB Lippincott. 1986;558-615.

23. Sawyers JL, Martin CE, Byrd BF, Rosenfeld L. Thyroidectomy for hyperthyroidism. Ann Surg. 1972;175:939-47.

24. Edis AJ. Prevention and management of complications associated with thyroid and parathyroid surgery. Sur Clin North Am. 1979;59:83-92.

25. Bourrel C, Uzzan B, Tison P, Despreaux G, Frachet B, Modigliani E, Perret G. Transient hypocalcemia after thyroidectomy. Ann Otol Rhinol Laryngol. 1993;102:496-501.

26. Osama OB. Post-thyroidectomy calcium level with special. Emphasis on the effect of ligation of the inferior thyroid artery. Ms Thesis, Assiut Egypt. 1990.