Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jptcp.v31i3.4958

FACTORS DETERMINING HYPOCALCAEMIA AND HYPOMAGNESAEMIA FOLLOWING TOTAL THYROIDECTOMY

Muhammad Tayyab Naeem[1]*, Hafiz Muhammad Sufyan[2], Pashmal Yousaf[3], Hasan Raza Hashmi[4], Hafiz Muhammad Nauman[5], Sameen Nisar Hamdani[6]

[1*,2,3,4,5,6]Department of General Surgery and Surgical Oncology, Shaikh Zayed Hospital, Lahore.

***Corresponding Author:** Muhammad Tayyab Naeem
*Department of General Surgery and Surgical Oncology, Shaikh Zayed Hospital, Lahore.
Email: tayyabmn37@gmail.com

Abstract

Objectives: To find out the factors determining hypocalcaemia and hypomagnesaemia following total thyroidectomy

Materials: In the years 2022–2023, this prospective cross-sectional study comprising of 80 patients was carried out at the Shaikh Zayed Hospital in Lahore. This includes every patient who had a total thyroidectomy. Information was obtained about various factors affecting serum calcium and magnesium after total thyroidectomy.

Results: The patients' average age was 39.21± 5.12 years. In 28.75% of cases, recurrent thyroid disease was discovered. The surgery took an average of 96.12 ±15.31 minutes. The average calcium levels before and after surgery were 7.8 ±3.18 mg/dl and 8.3 ±2.17 mg/dl, respectively. The average magnesium levels after surgery were 1.5 ±2.41 mg/dl. In 23 patients, central lymph node dissection was performed. According to histopathology, 41.25% of patients had malignant disease and 33.75% of patients had benign disease. Recurrent thyroid disease (p 0.001 for hypocalcemia), surgery lasting longer than 130 minutes (p 0.03 for hypocalcemia, p 0.0001 for hypomagnesemia), preoperative hypocalcemia (p 0.001 for hypocalcemia, p 0.0001 for hypomagnesemia), dissection of the central lymph nodes (p 0.03 for hypocalcemia, p 0.0001 for hypomagnesemia), and disease histopathology (p 0.03 for hypocalcaemia, p 0.001 for hypomagnesemia) are the factors that affect postoperative hypocalcaemia and hypomagnesemia.

Conclusion: Postoperative hypocalcaemia and hypomagnesaemia are significantly correlated with preoperative hypocalcaemia, central lymph node dissection, surgery lasting longer than 130 minutes, and malignant thyroid histopathology. Recurrent thyroid disease is positively correlated with postoperative hypocalcemia. Gender and mean age have no impact on postoperative hypocalcaemia and hypomagnesemia. Postoperative hypomagnesaemia was unaffected by recurrent thyroid disease.

Introduction

A thyroidectomy involves little blood or fluid loss and is a clean surgical procedure. For a variety of thyroid pathologies, total thyroidectomy has been determined to be the ideal procedure. Hypocalcaemia is the most frequent side effect following surgery. One of the most common post-operative complications following a total thyroidectomy is hypocalcaemia, which can lead to severe symptoms, anxiety, and longer hospital stays for the affected patients. Short-term hypocalcaemia, which is frequently seen following surgery, usually reacts well to replacement medication in a matter of days or weeks. If, after six months, hypocalcaemia does not return to normal (1.3–3% of cases), it is deemed permanent. [4,5]. Calcium levels have a direct impact on the homeostasis of magnesium ions.[3] The most frequent side effect of total thyroidectomy is temporary hypocalcaemia, which ranges in incidence from 1.6% to over 50% according to published literature [1,2].

Hypocalcaemia resulting from a decline in parathyroid function has been linked to magnesium deficiency. The observed phenomenon could be attributed to various factors such as insufficient PTH production or release, decreased bone response to PTH, increased calcitonin action, reduced bone response to PTH, or a primary alteration in the solubility, growth rate, or dissolution of bone crystals [6]. Magnesium functions as an enzyme cofactor and is an essential component of the human metabolic pathway. It has been suggested that magnesium may influence the amount of calcium by modifying PTH secretion, PTH receptor sensitivity, and renal calcium excretion. It is approved for post-thyroidectomy hypomagnesemia to lower PTH production, PTH receptor affinity, and vitamin D production—all of which can result in hypocalcemia.[7,8,9]. About 10–72% of patients have postoperative hypomagnesemia.[10]. It has been discovered that PTH resistance on organs also develops when magnesium levels drop below a particular threshold.[11]

Materials and Methods

In the years 2022–2023, this prospective cross-sectional study was carried out at the Shaikh Zayed Hospital in Lahore. This includes every patient who had a total thyroidectomy. Every patient's demographic and pathologic information, along with their serum levels of calcium prior to and following surgery, were documented. Serum magnesium level is also noted following total thyroidectomy. Patients with kidney disease (creatinine above 1.5 mg/dl), chronic liver disease and history of repeated blood transfusions, osteoporosis or any bone pathology affecting serum calcium and magnesium levels were excluded, as well as those with albumin levels less than 3 gm/dl. All patients received sufficient information about the type of surgery they would be having and any potential complications before the procedure. The Ethics Committee of Shaikh Zayed Hospital gave its approval to the study.

Objectives

To find out the factors determining hypocalcaemia and hypomagnesaemia following total thyroidectomy

Keywords

Hypocalcaemia, hypomagnesemia, total thyroidectomy

Results

The patients' average age was 39.21± 5.12 years. In 28.75% of cases, recurrent thyroid disease was discovered. The surgery took an average of 96.12 ±15.31 minutes. The average calcium levels before surgery were 7.8 ±3.18 mg/dl and 8.3 ±2.17 mg/dl, respectively. The average magnesium levels after surgery were 1.5 ±2.41 mg/dl. In 23 patients, central lymph node dissection was performed. According to histopathology, 58.75% of patients had malignant disease and 41.25% of patients had benign disease **(Table 1).**

Mean age	39.21 ± 5.12
Recurrent thyroid disease	23/80 (28.75%)
Mean duration of surgery	96.12 ±15.31 (min)
Mean preoperative calcium levels	7.8 ±3.18 mg/dl
Mean postoperative calcium levels	8.3 ±2.17 mg/dl
Mean postoperative magnesium levels	1.5 ±2.41 mg/dl
Central lymph node dissection	23
Histological nature of disease Benign Malignant	 33/80 (41.25%) 47/80 (58.75%)

Table 1. Demographic and Clinical profile of Patients

Recurrent thyroid disease (p 0.001 for postoperative hypocalcemia), surgery lasting longer than 130 minutes (p 0.03 for postoperative hypocalcemia, p 0.0001 for hypomagnesemia), preoperative hypocalcemia (p 0.001 for hypocalcemia, p 0.0001 for hypomagnesemia), dissection of the central lymph nodes (p 0.03 for hypocalcemia, p 0.0001 for hypomagnesemia), and disease histopathology (p 0.03 for hypocalcemia, p 0.001 for hypomagnesemia) are the factors that affect postoperative hypocalcaemia and hypomagnesemia **(Table 2).**

		Postoperative hypocalcaemia (8.5 mg/dl)	**P value**	**Postoperative hypomagnesaemia (1.7 mg/dl)**	**P value**
Age(years)	20-60				
Gender Male Female	 49 31	 04/49 12/31	 0.5	 3/49 1/31	 0.71
Recurrent Thyroid disease	23	11/23	0.001	4/23	2.178
Duration of surgery >130 min	39	21/39	0.03	17/39	0.0001
Preoperative calcium <8.5 mg	61	49/61	0.001	39/60	0.0001
Central lymph node dissection	23	11/23	0.03	14/23	0.0001
Histopathology Malignant Benign	 47 33	 30/47 0/33	 0.03	 25/47 1/33	 0.001

Table 2. Showing association of different factors to postoperative hypocalcaemia and hypomagnesaemia following total thyroidectomy

Discussion

58.75% of patients in the current study had histopathology-confirmed malignant disease. In malignant disease, the incidence of hypocalcemia and hypomagnesemia was 63.82 % (p 0.03) and 53.19 % (p 0.001), respectively. Since total thyroidectomy offers complete tumor resection and a low recurrence rate, it is the primary treatment for malignant lymphoma and thyroid cancer. However, due to the extensive surgical scope of malignant thyroid disease and the requirement for lymph node dissection, prolonged surgical stimulation increases the release of calcitonin, which lowers blood calcium levels. Furthermore, because the upper parathyroid glands are situated on the posterior and upper sides of the thyroid's upper pole, it is difficult to retain the parathyroid glands during a total thyroidectomy for lymph node dissection. This is especially true of the two pairs of parathyroid glands in the lower pole. The position is easily identifiable and comparatively fixed. Patients' parathyroid gland positions differ significantly from one another.[12,13]. In line with our findings, Li Y-J et al. showed that patients who had a total thyroidectomy had a higher incidence of transient hypocalcemia. [14]. Transient hypocalcemia was more common following total

thyroidectomy than in the group undergoing completion thyroidectomy (26.1% and 13.2%, respectively), while permanent hypocalcemia was more common in the group undergoing completion thyroidectomy than in the total thyroidectomy group (15.8% and 11.7%, respectively). These findings were reported by Bumber, B. et al.[15]. According to research by Randall et al., hypocalcaemia was more common following a total thyroidectomy than a unilateral thyroid lobectomy [16]. In fact, hypomagnesaemia and hypocalcaemia were significantly correlated in a prospective study conducted on a group of fifty patients who had undergone total thyroidectomy, according to Wilson et al[.17.] Due to the extensive surgical scope and the requirement for the removal of neck lymph nodes, pathological type is one of the most significant risk factors. This increases the likelihood that patients with malignant tumors undergoing thyroid surgery alone will experience hypocalcaemia and persistent hypoparathyroidism.[25]

Wilson et al. hypothesized that decreased absorption of magnesium in the kidney and intestine as a result of postoperative hyperparathyroidism and hemodilution brought on by intravenous rehydration could be the cause of postoperative hypomagnesaemia. Following thyroidectomy, patients frequently experience hypocalcemia in addition to hypomagnesemia. After total thyroidectomy, hypomagnesaemia was 19.80% of the time, and it is much more common in hypocalcemic patients. Furthermore, compared to patients with normomagnesemia, those with hypomagnesaemia had a 4.66-fold increased risk of hypocalcaemia [18,19,20].

In this study, preoperative hypocalcemia was significantly correlated with both postoperative hypocalcemia and hypomagnesemia ($p = 0.001$ and $p = 0.000$, respectively). Similar in their chemical makeup, calcium and magnesium ions are regulated by the same homeostasis system, which includes intestinal absorption, renal tubule reabsorption, and excretion[21]. Magnesium ions and calcium ions interact in these regulatory systems[22]. In order to influence the calcium balance in vivo, magnesium ions can participate in the synthesis of 1,25-dihydroxyvitamin D3, which in turn affects the sensitivity of target organs to PTH. They can also regulate the synthesis and/or secretion of PTH[23]. By increasing PTH secretion, controlling PTH receptor sensitivity, and regulating renal calcium excretion, magnesium affects the levels of calcium ions in the blood.[24]

Multiple adhesions to surrounding structures have been associated to recurrent thyroid disease, which may necessitate aggressive manipulations to remove the thyroid gland, potentially damaging numerous structures, including the parathyroid gland and RLN. Patients who undergo multiple thyroid disease surgeries are more likely to experience damage to their parathyroid glands than those who only undergo one procedure.[25,**26,27**]
Central lymph node dissection (LND) is associated with transient hypocalcemia (p 0.03) and hypomagnesemia (0.001). According to Moley and de Benedetti, proper dissection of the central node is typically linked to anatomical and/or blood supply problems for the parathyroid glands, particularly the inferior parathyroids[**28**]

The risk of both temporary and permanent postoperative hypoparathyroidism is significantly increased by central lymph node dissection, and more specifically by bilateral CLND. Patients with LND had a higher rate of transient hypoparathyroidism than patients without LND ($p < 0.001$) [**29**]. Postoperative hypoparathyroidism is the primary cause of hypocalcemia, and patients with PTC who have had TT + central lymph node dissection are more likely to experience hypoparathyroidism and hypocalcemia following surgery.[**30**]
According to the current study, a mean surgery duration longer than 130 minutes is linked to a higher risk of hypocalcemia (p 0.03). A study by Sonne-Holm et al. aims to illustrate the relationship between the length of surgery and the hypoparathyroidism risk. Subgroups of patients were created according to how long the surgery lasted: <60, 60–120, 120–180, 180–240, or >240 minutes. Hypoparathyroidism was found in 33, 31, 41, 51, and 62% of cases, respectively [**31.**] A longer than 120-minute surgery most likely results in ischemic changes to the parathyroid glands

because of reduced blood flow. Thus, the conclusion that a lengthy surgical stay is a predictor of persistent hypoparathyroidism is consistent with the aforementioned Kim et al. The current study shows that low parathyroid hormone subsequently causes a decrease in serum levels of magnesium and calcium.[32]

Conclusion

Postoperative hypocalcemia and hypomagnesaemia are significantly correlated with preoperative hypocalcemia, central lymph node dissection, surgery lasting longer than 130 minutes, and malignant thyroid histopathology. Recurrent thyroid disease is positively correlated with postoperative hypocalcemia. Gender and mean age have no impact on postoperative hypocalcemia and hypomagnesemia. Postoperative hypomagnesemia was unaffected by recurrent thyroid disease.

References

1. Pattou F, Combemale F, Fabre S, et al. Hypocalcemia following thyroid surgery: incidence and prediction of outcome. World J Surg. 1998;22(7):718-724. doi:10.1007/s002689900459
2. Puzziello A, Rosato L, Innaro N, et al. Hypocalcemia following thyroid surgery: incidence and risk factors: a longitudinal multicenter study comprising 2,631 patients. Endocrine. 2014;47(2): 537-542.
3. Andrade A, Salles J, Soares J, Moraes J, Carvalho J, Rocha P. Evolution of blood magnesium and phosphorus ion levels following thyroidectomy and correlation with total calcium values. Sao Paulo Med J. 2010; 128:268–71
4. Bentrem DJ, Rademaker A, Angelos P. Evaluation of serum calcium levels in predicting hypoparathyroidism after total/ near-total thyroidectomy or parathyroidectomy. Am Surg. 2001; 67:249–251.
5. Abboud B, Sargi Z, Akkam M, et al. Risk factors for post thyroidectomy hypocalcemia. J Am Surg. 2002; 195:456–461.
6. Cherian AJ, Gowri M, Ramakant P, Paul TV, Abraham DT, Paul MJ. The Role of Magnesium in Post-thyroidectomy Hypocalcemia. World J Surg. 2016;40(4):881-8. https://doi. org/10.1007/s00268-015-3347-3 PMID:26578317
7. Gums JG. Magnesium in cardiovascular and other disorders. American journal of health-system pharmacy: AJHP: official journal of the American Society of Health-System Pharmacists. 2004; 61:1569–76.
8. Allgrove J, Adami S, Fraher L, Reuben A, O'Riordan JL. Hypomagnesaemia: studies of parathyroid hormone secretion and function. Clin Endocrinol. 1984; 21:435–49.
9. Fatemi S, Ryzen E, Flores J, Endres DB, Rude RK. Effect of experimental human magnesium depletion on parathyroid hormone secretion and 1,25-dihydroxyvitamin D metabolism. J Clin Endocrinol Metab. 1991; 73:1067–72.
10. Luo H, Yang H, Zhao W, et al. Hypomagnesemia predicts postoperative biochemical hypocalcemia after thyroidectomy. BMC Surg. 2017;17(1). doi:10.1186/s12893-017-0258-2
11. Walker HK, Hall WD, Hurst JW, editors. Clinical Methods: The history, physical, and laboratory examinations. 3rd edition. Boston: Butterworths 1990; Chapter 143.
12. Bellantone R, Lombardi CP, Bossola M, et al. Total thyroidectomy for management of benign thyroid disease: review of 526 cases. World J Surg 2002; 26:1468–1471. doi: 10.1007/s00268-002-6426-1
13. Del Rio P, Rossini M, Montana CM, et al. Postoperative hypocalcemia: analysis of factors influencing early hypocalcemia development following thyroid surgery. BMC Surg 2019; 18: 25. doi: 10.1186/s12893-019-0483-y.
14. Li Y-J, Wang Y-Z, Yi Z-B, Chen L-L, Zhou X-D. Comparison of Completion Thyroidectomy and Primary Total Surgery for Differentiated Thyroid Cancer: A Meta-Analysis. Oncol Res Treat. 2015;38(10):528–31. 10.1159/000440690

15. Bumber, B., Potroško, V., Vugrinec, O., Ferenčaković, M., & Gršić, K. (2020). Hypocalcemia After Completion Thyroidectomy for Papillary Thyroid Carcinoma. Acta clinica Croatica, 59(Suppl 1), 136–145.
16. Baldassarre RL, Chang DC, Brumund KT, Bouvet M. Predictors of hypocalcemia after thyroidectomy: Results from the nationwide inpatient sample. ISRN Surg 2012. 2012:838614
17. Wilson RB, Erskine C, Crowe PJ. Hypomagnesemia and hypocalcemia after thyroidectomy: prospective study. World J Surg. 2000; 24:722–6.
18. Wilson RB, Erskine C, Crowe PJ. Hypomagnesemia and hypocalcemia after thyroidectomy: prospective study. World J Surg. 2000;24(6):722–726. doi: 10.1007/s002689910116
19. Hodgkinson A, Marshall DH, Nordin BE. Vitamin D and magnesium absorption in man. Clin Sci (Lond). 1979;57(1):121–123.
20. Ramakant AJCM, Paul TVPD. The role of magnesium in post-thyroidectomy hypocalcemia. World J Surg. 2016;40(4):881–888. doi: 10.1007/s00268-015-3347-3
21. Law PH, Sun Y, Bhattacharya SK, et al. Calcium and magnesium homeostasis in aldosteronism: response to diuretics. Journal of Investigative Medicine 2005; 53: S266.
22. Chattopadhyay N, Mithal A, Brown EM. The calcium-sensing receptor: a window into the physiology and pathophysiology of mineral ion metabolism. Endocr Rev 1996; 17: 289–307.
23. Rodríguez-Ortiz ME, Canalejo A, Herencia C, et al. Magnesium modulates parathyroid hormone secretion and upregulates parathyroid receptor expression at moderately low calcium concentration. Nephrol Dial Transplant 2014; 29: 282–289.
24. Rodelo-Haad C, Pendón-Ruiz de Mier MV, Díaz-Tocados JM, et al. The Role of Disturbed Mg Homeostasis in Chronic Kidney Disease Comorbidities. Front Cell Dev Biol 2020; 8: 543099.
25. 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. Ann Surg 2007; 245: 604–610.
26. Lefevre, J. H., Tresallet, C., Leenhardt, L., Jublanc, C., Chigot, J. P., & Menegaux, F. (2007). Reoperative surgery for thyroid disease. Langenbeck's archives of surgery, 392(6), 685–691.
27. Menegaux, F., Turpin, G., Dahman, M., Leenhardt, L., Chadarevian, R., Aurengo, A., du Pasquier, L., & Chigot, J. P. (1999). Secondary thyroidectomy in patients with prior thyroid surgery for benign disease: a study of 203 cases. Surgery, 126(3), 479–483.
28. Moley JF, De Benedetti MK. Patterns of nodal metastases in palpable medullary thyroid carcinoma: recommendations for extent of node dissection. Ann Surg (1999) 229:880–7. doi: 10.1097/00000658-199906000-00016
29. Baud, G., Jannin, A., Marciniak, C., Chevalier, B., Do Cao, C., Leteurtre, E., Beron, A., Lion, G., Boury, S., Aubert, S., Bouchindhomme, B., Vantyghem, M. C., Caiazzo, R., & Pattou, F. (2022). Impact of Lymph Node Dissection on Postoperative Complications of Total Thyroidectomy in Patients with Thyroid Carcinoma. Cancers, 14(21), 5462.
30. Caulley L, Johnson-Obaseki S, Luo L, et al. Risk factors for postoperative complications in total thyroidectomy: A retrospective, risk-adjusted analysis from the National Surgical Quality Improvement Program. Medicine (Baltimore) 2017; 96: e5752
31. Sonne-Holm, E., & Holst Hahn, C. (2017). Prolonged Duration of Surgery Predicts Postoperative Hypoparathyroidism among Patients Undergoing Total Thyroidectomy in a Tertiary Referral Centre. European thyroid journal, 6(5), 255–262.
32. Kim SM, Kim HK, Kim KJ, Chang HJ, Kim BW, Lee YS, Chang HS, Park CS. Recovery from permanent hypoparathyroidism after total thyroidectomy. Thyroid. 2015; 25:830–833.