RESEARCH ARTICLE

The complex role of post-operative magnesium on the long term serum calcium and parathyroid hormone levels in patients undergoing total and near-total thyroidectomy

Sana Viqar,[1] Tasleem Akhtar,[2] Nadeem Ikram,[3] Naeem Zia[4]

Abstract

Objectives: To assess the role of hypomagnesaemia in the development of permanent hypocalcaemia following thyroidectomy.

Method: The prospective cohort study was conducted from April 3, 2017, to January 2, 2020, at Surgical Unit 1, Benazir Bhutto Hospital, Rawalpindi, Pakistan, and comprised of patients of both genders undergoing total and near total thyroidectomy. Post-operative calcium and magnesium levels were noted, and the patients were followed up after 6 months and fasting serum calcium, magnesium and parathyroid hormone levels were checked. Signs and symptoms of hypocalcaemia were noted. Data was analysed using SPSS 22.

Results: Out of the 62 patients followed up, 57 (91.9%) were females and 5 (8.1%) males. The overall mean age was 38.5 ± 12.1 years Post-operative hypomagnesaemia was seen in 6(9.8%) patients and none developed follow-up hypocalcaemia. Post-operative magnesium levels were significantly negatively correlated with follow-up parathyroid hormone level (p=0.006). Fall in magnesium post-operatively and follow-up magnesium were positively correlated with follow-up parathyroid hormone (p<0.05). Permanent hypocalcaemia was seen in 7(11.4%) patients and it was significantly associated with pre-operative and post-operative calcium levels, post-operative symptoms of hypocalcaemia and readmission for hypocalcaemia after discharge (p<0.05). Follow-up hypomagnesaemia was significantly associated with follow-up hypocalcaemia (p=0.024) and follow-up symptoms of hypocalcaemia (p=0.031).

Conclusion: Acute development of mild hypomagnesaemia post-operatively may be beneficial in early positive feedback for parathyroid hormone secretion. Hypomagnesemia 6 months after surgery may be involved in PTH organ resistance. The complex role of hypomagnesemia on PTH levels must be further explored.

Keywords: Magnesium, Calcium, PTH, Thyroidectomy, Post-operative, Follow-up hypomagnesaemia, Permanent hypocalcaemia. (JPMA 72: 2432; 2022) **DOI: https://doi.org/10.47391/JPMA.4681**

Introduction

Hypocalcaemia is a common complication of thyroidectomy. This is as a result of either incidental parathyroidectomy[1] or ischaemia of parathyroid gland due to injury to its vascular supply.[2] In literature, transient and permanent hypocalcaemia have been reported as 43% and 5.5%[3] respectively, while transient and permanent hypoparathyroidism have been reported as 19-24% and 1.2-5% respectively.[4,5]

Magnesium (Mg) is involved in the homeostasis of calcium (Ca) and parathyroid hormone (PTH) in the blood. It has a dual effect on PTH secretion based on its concentration in blood. High Mg level suppresses PTH secretion.[6] Low Mg level, like hypocalcaemia, causes increase in PTH secretion. However, very low Mg level has the opposite effect as it causes inhibition of PTH secretion and increases PTH resistance.[7] This is brought about by the effect of very low Mg on G protein in mimicking the stimulation of Ca-sensing receptors, causing decrease in PTH secretion.[8] There is a growing interest in the role of hypomagnesaemia following thyroidectomy. Studies have reported an association of hypomagnesaemia and hypocalcaemia after thyroidectomy.[9,10] Some have even shown association of hypomagnesaemia with the development of permanent hypocalcaemia.[11]

Permanent hypocalcaemia is a debilitating condition. Recurrent muscle spasms and dependence on Ca supplementation negatively impacts quality of life. Current literature highlights an intriguing role of Mg in post-thyroidectomy patients. If post-operative Mg level can provide prediction of long-term Ca and PTH homeostasis, as suggested by studies, timely correction of both Mg and Ca in the post-operative period may positively impact the homeostasis.

The current study was planned to find the impact of post-

[1]Department of General Surgery, Pakistan Institute of Medical Sciences, Islamabad, Pakistan, [2]Department of Vascular Surgery, Russells Hall Hospital, Dudley, United Kingdom, [3]Department of Pathology, [4]Department of Surgery, Benazir Bhutto Hospital, Rawalpindi, Pakistan.

Correspondence: Sana Viqar. Email: sana.viqar27@gmail.com

operative hypomagnesaemia on the long-term calcium and PTH levels in patients undergoing total thyroidectomy (TT) or near-total thyroidectomy (NTT).

Patients and Methods

The prospective cohort study was conducted from April 3, 2017, to January 2, 2020, at Surgical Unit 1, Benazir Bhutto Hospital, Rawalpindi, Pakistan. After approval from the research and ethics committee of Rawalpindi Medical University, Rawalpindi, the sample was collected using non-random consecutive sampling technique from among patients of either gender undergoing TT or NTT for any benign or malignant disease of thyroid. All patients undergoing any other thyroidectomy or having known parathyroid disease were excluded. Patients with missing data were also excluded. Pre-operative serum Ca and Mg levels of the patients were noted. Thyroidectomy was performed with extra-capsular technique. Samples were taken 24 hours post-surgery for serum Ca and Mg. No prophylactic Ca was given prior to sampling or symptoms of hypocalcaemia. Signs and symptoms of hypocalcaemia were documented, and, if required, the patients were given 10ml of 10% calcium gluconate diluted in 10 ml normal saline given intravenously over 20 minutes).

Patients were followed up 6 months post-surgery. They were questioned regarding symptoms of hypocalcaemia, frequency of symptoms, calcium supplement intake. Trousseau's and Chvostek's signs were checked. Symptoms included numbness, tingling sensation, muscle cramps or spasm. Fasting serum Ca, Mg and PTH samples were drawn without tourniquet technique and were sent to the laboratory within 30min, and were stored until analysis was done. Samples that reached the laboratory in >30min were not considered for PTH results.

For the purpose of the study, biochemical hypocalcaemia was defined as serum Ca level <8.5mg/dl; biochemical hypomagnesaemia was serum Mg level <1.9mg/dl; symptomatic hypocalcaemia was symptoms of hypocalcaemia with or without laboratory evidence; hypoparathyroidism was defined as PTH <10pg/ml; borderline PTH was 10-14pg/ml; permanent hypocalcaemia was defined as having low Ca and low PTH or low Ca with borderline PTH having either positive signs of hypocalcaemia or the need to continue regular calcium and vitamin D supplements.

Data was analysed using SPSS 22. For categorical variables, chi square test, relative risk (RR) and Fischer's test were applied. To analyse differences in mean values, paired t test and independent student's t test were used. Paired t test was used to compare post-operative and follow-up Ca and Mg levels. Unpaired independent t test was used to compare mean levels of pre-operative, post-operative and follow-up Ca as well as Mg levels with the group developing permanent hypocalcaemia and group not developing permanent hypocalcaemia. Unpaired independent t test was used to compare mean Ca levels in follow-up normomagnesaemic and hypomagnesaemic groups. Follow-up PTH levels were correlated to postoperative Mg, follow-up Mg levels and fall in Mg level post-operatively. Linear regression tests were applied to the above. $P<0.05$ was considered statistically significant.

Results

Of the 75 patients enrolled, 62(82.7%) were followed up; which included 57 (91.9%) females and 5 (8.1%) males. The overall mean age was 38.5 ± 12.1 years. Patients undergoing TT and NTT were 46(79%) and 12(21%) respectively. Post-op hypocalcaemia symptoms were present in 8(13%) (Table-1).

At 6 month follow-up, 31(50.8%) patients had biochemical hypocalcaemia. Mean Ca level was 8.49±0.76. Those having biochemical hypomagnesaemia were 6 (10%), with mean Mg level being 2.08±0.25. All 6(100%) patients with hypomagnesaemia were hypocalcaemic. There was a significant association between follow-up biochemical hypocalcaemia and hypomagnesaemia (p=0.024). Mean Ca levels in follow-up hypomagnesaemic group was 7.88mg/dl ±0.35, while in normomagnesemic group it was 8.54 ± 0.77mg/dl (p=0.043). On follow-up, 48 (94%) patients had PTH in the normal range among which 7(14%) had borderline PTH. Three (5.9%) patients had low PTH. Mean PTH level was 31.64±25.22pg/ml. Overall, 2(3.2%) patients had a very high PTH, and were excluded from the dichotomous PTH status variable. Among the patients followed up, 34(56%) complained of having experienced symptoms of hypocalcaemia.

Out of the patients who developed post-operative hypocalcaemia, 21(55.3%) had low calcium, 4(10.5%) had low magnesium and 3(9.4%) had low PTH on follow-up. Of the 7(11.5%) patients who developed post-operative hypomagnesaemia, 2(28.6%) had hypocalcaemia, and none had hypomagnesaemia or hypoparathyroidism.

Table-1: Patient characteristics post-operatively.

Variable	Category	Count (%)
Surgery	TT	46 (79%)
	NTT	12 (21%)
Post-op Calcium	Hypocalcaemia	39 (64%)
Post-op Mg	Hypomagnesaemia	7 (12%)
Post-op Hypocalcaemic symptoms	Present	8 (13%)

TT: Total thyroidectomy, NTT: Near-total thyroidectomy, Post-op: Post-operative.

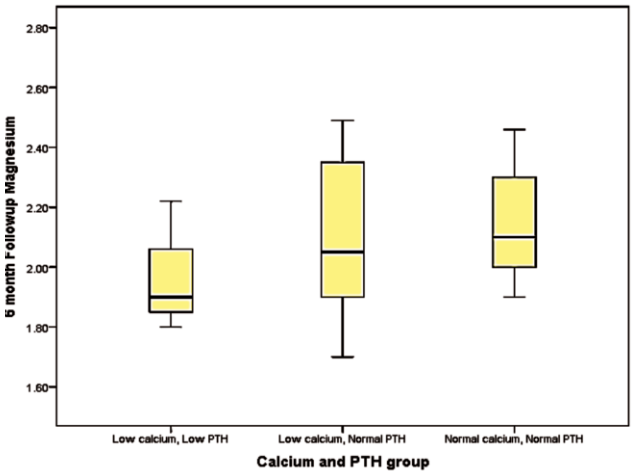

Figure: Boxplot of follow-up magnesium level in follow-up calcium and parathyroid hormone (PTH) groups.

Permanent hypocalcaemia was found in 7(13.5%) patients. Three of the 6 patients with post-operative hypocalcaemia symptoms (50.0%) developed permanent hypocalcaemia symptoms (p=0.006, RR=5.6 times). Permanent hypocalcaemia was significantly associated with post-operative hypocalcaemia (p=0.022), follow-up symptoms of hypocalcaemia (p=0.019) and readmission for hypocalcaemia any time after discharge (p=0.005). RR for post-operative Ca and Mg status could not be calculated due to the small sample size. Permanent hypocalcaemia was compared with other study variables (Table-2). There was a significant difference in mean levels of pre-operative, post-operative and follow-up Ca and PTH in patients who developed permanent hypocalcaemia (Table-3). There was no significant association of permanent hypocalcaemia with post-operative or follow-up Mg level. The patients were divided into 3 groups: normal calcium and PTH, low calcium and normal PTH, and low calcium and low PTH. There were 22(43.1%), 26(51%) and 3(5.9%) patients in the three groups, respectively. Five of the 6 patients having follow-up hypomagnesaemia (83%) fell in the second group (p=0.059). The relationship of these groups with Mg levels was assessed (Figure). Also, 4 of the 5 post-operative hypomagnesaemic patients (80%) had normal calcium and normal PTH on follow-up.

Table-2: Relationship of permanent hypocalcaemia with different variables.

Variable	Category	Permanent hypocalcaemia Yes	No	Pvalue
Age category	<40 years	4 (15%)	23 (85%)	1.0
Gender	Female	7 (15%)	41 (85%)	1.0
Symptoms	Hyperthyroidism	4 (25%)	12 (75%)	0.50
	Pressure Symptoms	1 (9%)	10 (91%)	
Surgery	TT	7 (18%)	31 (82%)	0.40
	NTT	0 (0%)	11 (100%)	
Hypocalcaemic symptoms post-op	Present	3 (50%)	3 (50%)	0.028
Post-op Calcium	hypocalcaemia	7 (23%)	24 (77%)	0.034
Post-op Magnesium	Hypomagnesaemia	0 (0%)	6 (100%)	0.579
Histology	Benign	6 (15%)	33 (85%)	0.43
	Malignant	1 (33%)	2 (67%)	
Readmission for hypocalcaemia	Yes	2 (67%)	1 (33%)	0.044
Follow-up Calcium	Hypocalcaemia	7 (25%)	21 (75%)	0.01
Follow-up Magnesium	Hypomagnesaemia	2 (33%)	4 (67%)	0.18
Follow-up Borderline PTH	Yes	3 (43%)	4 (57%)	0.045
Follow-up Hypocalcaemic symptoms	Yes	7 (23%)	24 (77%)	0.033
Frequency of Hypocalcaemic symptoms	Daily	6 (86%)	1 (14%)	<0.001
Taking Calcium Supplements	Daily	4 (24%)	13 (76%)	0.22

Note: (Chi square and Fischer Exact tests were used for the above data). TT: Total thyroidectomy, NTT: Near-total thyroidectomy, Post-op: Post-operative, PTH: Parathyroid hormone.

Table-3: Means of variables in relationship to permanent hypocalcaemia.

	Permanent hypocalcaemia Yes		No		
	Mean	S.D	Mean	S.D	P value
Age of Patient (years)	40	13	40	12	0.95
Duration of Disease (years)	9.40	8.05	6.89	6.62	0.44
Pre-op Ca (mg/dl)	8.36	0.54	8.90	0.52	0.01
Pre-op Mg(mg/dl)	2.24	0.29	2.21	0.19	0.73
Post-op Ca (mg/dl)	7.96	0.36	8.39	0.65	0.02
Post-op Mg (mg/dl)	2.09	0.07	2.11	0.25	0.81
Fall in Ca level	0.40	0.34	0.50	0.70	0.70
Fall in Mg level	0.15	0.27	0.10	0.27	0.64
Follow-up Ca (mg/dl)	7.76	0.62	8.59	0.76	0.008
Follow-up Mg(mg/dl)	1.93	0.14	2.10	0.27	0.11
Follow-up PTH (pg/ml)	12.55	4.86	29.95	12.00	<0.001

SD: Standard deviation, Ca: Calcium, Mg: Magnesium, Pre-op: Pre-operative, Post-op: Post-operative, PTH: Parathyroid hormone.
Note: (Independent Samples T test were used for the above data).

Correlation analysis showed that follow-up Mg levels were significantly correlated with PTH levels with a positive linear relation (p=0.024; R2=0.096). However, post-operative Mg level was also significantly related with follow-up PTH (p=0.006) levels, but with a negative linear correlation. Mean follow-up PTH level in patients developing hypomagnesaemia post-operatively was 53.3 ± 58.1 pg/ml compared to 29.3±17.0 pg/ml with normal post-operative Mg (p=0.03). Fall in Mg level post-surgery was also significantly correlated with follow-up PTH levels (p=0.03) with a positive linear relation.

Linear regression was used to assess the fall in Mg level 24 hours post-surgery in predicting PTH level with a significant regression equation ($F(1,48)=9.503$, $p=0.003$, $R^2=0.165$). With every 1mg/dl increase in the fall of Mg, follow-up PTH increased by 30.965pg/dl. There was no significant correlation between post-operative

and follow-up Ca and Mg levels (p>0.05).

Discussion

The study investigated the role of Mg after thyroidectomy on the development of permanent hypocalcaemia. It is in continuation of a previously published study[12] that investigated the role of Mg in the development of temporary hypocalcaemia. In the said study, post-operative hypomagnesaemia was significantly associated with post-operative hypocalcaemia. The same cohort was included in the current study and the same trend was noted. Follow-up hypomagnesaemia and hypocalcaemia were significantly associated with each other. All patients with hypocalcaemia were also hypomagnesaemic. Such an association has been reported by various studies.[9-11]

In the present study, 31(51%) patients had biochemical hypocalcaemia >6 months post-surgery compared to 20% reported by Garrhy et al.[11] Hypomagnesaemia was seen in only 8(10.7%) post-operative patients compared to 13-70%[9,11,13] reported in literature. Six (10%) follow-up patients had hypomagnesaemia 6 months after thyroidectomy. These 6 patients all had normal Mg levels post-operatively. Only 3(5.6%) patients had low PTH (up to10pg/ml) and 7/51(14%) patients had borderline PTH (10-14pg/ml). Studies have used various cut-off limits for low PTH.[4,5] In the current study population, 7(14%) subjects showed permanent hypocalcaemia, which was higher than what has been the reported by international studies, ranging from 1.2% to 10%[4,5,11,14] as well as local studies, ranging from 0.11% to 1.5%.[15,16] The higher frequency can be accounted for by a number of reasons. Firstly, studies have used permanent hypoparathyroidism and hypocalcaemia interchangeably in which case hypoparathyroidism is inclusive of hypocalcaemia. Some definitions have varied by virtue of the time limit set for permanent hypocalcaemia to occur; for instance, after 6 months or 1 year.[11,14] In the current study the definition was broader as it included not only low Ca and low PTH, but also those with low Ca with borderline PTH having either positive signs of hypocalcaemia or the need to continue regular Ca and vitamin D supplements 6 months following TT or NTT. This was done to include patients with clinical hypocalcaemia having PTH within normal range, a term referred to as relative hypoparathyroidism.[17] Perhaps this explains why in the current study hypomagnesaemia was associated with low Ca levels, but not with permanent hypocalcaemia. The different definitions of permanent hypocalcaemia have nevertheless been a limiting factor for comparison with other studies.

In terms of the role of Post-operative Ca and Mg with permanent hypocalcaemia, 7/31(23%) patients with post-operative hypocalcaemia developed permanent hypocalcaemia. No patient with normal calcium level post-operatively developed permanent hypocalcaemia. This may suggest that post-operative normal Ca level is reassuring for future calcium homeostasis. This relationship between post-operative hypocalcaemia and permanent hypocalcaemia was statistically significant (p=0.02). Similarly, 3/6 (50%) patients who developed symptoms of hypocalcaemia post-operatively also developed permanent hypocalcaemia. This was statistically significant (p= 0.01) with RR of 5.6 times. Patients with post-operative Hypocalcaemic signs or symptoms must be followed up closely to correct electrolyte imbalance in earlier stages. We did not find in literature any documented predictive value of post-operative symptomatic hypocalcaemia with the development of permanent hypocalcaemia.

None of the 6 patients with post-operative hypomagnesaemia developed permanent hypocalcaemia. This was in contrast to a study which reported a significant association between post-operative hypomagnesaemia and permanent hypocalcaemia.[11] Hammerstad et al., likewise, reported a significant correlation between fall in post-operative Mg levels and the development of permanent hypocalcaemia.[14]

Interestingly, in the current study, Mg showed a unique association with PTH levels. Post-operative Mg levels showed a significant negative correlation to follow-up PTH levels. And a fall in Mg level post-surgery had a significant positive correlation with PTH level. A significant negative correlation between Mg and PTH has also been shown by other studies.[18,19] These findings highlight the dual nature of Mg which mimics the function of Ca on calcium-sensing receptors (CaSR), that is, in the presence of lower Mg, there is lesser activation of CaSRs, which in turn promotes the secretion of PTH from parathyroid gland.[20,21] Another study suggested that Mg only suppresses PTH secretion when it falls drastically below a certain level.[22] In the current study, mean post-operative Mg level in hypomagnaesaemic group was 1.6mg/dl, which is considered mild. Therefore, it can be suggested that mild hypomagnesaemia post-operatively is a stimulus for the parathyroid gland activity by positive feedback. Only in 2 patients, Mg levels fell to 1.2mg/dl post-operatively. On 6-month follow-up, one of them had normal PTH level (39pg/ml), while the other was found to have very high levels of PTH (170pg/ml). Despite this, both patients had biochemical hypocalcaemia (7.8 and 7.4mg/dl, respectively) but normal Mg. It may suggest that only severe post-operative hypomagnesaemia could cause PTH target organ resistance as is also suggested by

other studies.[23] But this is a very small sample size to draw substantial conclusion from.

To add to the unique and complex role of Mg, follow-up Mg had a significant positive correlation to follow-up PTH. This could explain PTH's role in the maintenance of Mg levels in the body by mediating renal reabsorption.[24] If such positive correlation exists, then there must be an explanation why majority patients (5/6) with follow-up hypomagnesaemia fell in the category that had low Ca and normal PTH. Perhaps there is an ongoing positive feedback by Mg which helps to maintain normal PTH. The failure of PTH to maintain optimum Ca levels could suggest a degree of suppression of PTH action on target organs. So while acute post-operative hypomagnesaemia provided a stimulus for PTH secretion and normal target organ sensitivity (as 4/5 post-operative hypomagnesaemic patients had normal Ca and normal PTH on follow-up), hypomagnesaemia 6 months post-surgery may not be able to have positive impact on Ca levels in spite of normal PTH. To strengthen this idea, all 6(100%) follow-up hypomagnesaemic patients had biochemical hypocalcaemia (p=0.024) even though 5/6(83%) had normal PTH levels. Furthermore, all follow-up hypomagnesaemic patients significantly complained of hypocalcaemia symptoms (p=0.031), an association similar to the results of Wilson et al.[25] It is of no surprise to see conflicting results of the relationship of Mg with regards to PTH in literature. This is due to the complex and paradoxical role of Mg. The possibility of chronic hypomagnesaemia having an impact on PTH resistance rather than secretion must be investigated. For such a purpose, serial testing of Mg levels must take place to understand the trend and its impact.

A statistically significant association was seen between permanent hypocalcaemia and pre-operative hypocalcaemia. Patients developing permanent hypocalcaemia had significantly lower mean pre-operative calcium level compared to those not developing it (8.3 mg/dl vs 8.9mg/dl, RR=1.6times) Similar association was seen by Hammerstad et al.[14] Another significant association noted was between re-admission to hospital for hypocalcaemia with the development of permanent hypocalcaemia with RR 6.5 times. This suggests that patients having a hospital re-admission for hypocalcaemia symptoms any time after discharge following thyroidectomy must be followed up regularly to ensure electrolyte imbalance is corrected and PTH secretion and organ sensitivity are not negatively impacted.

The current study has its limitations. The sample size was small, particularly the number of patients who developed hypomagnesaemia post-operatively was very small. This limited the statistical tests that could be applied, especially with regard to RR for hypocalcaemia and hypomagnesaemia. A few post-operative patients were lost to follow-up and some laboratory samples had missing values. Definitions for hypocalcaemia, hypomagnesaemia and hypoparathyroidism have varied across literature. Our cut-off for hypomagnesaemia was 1.9mg/dl, according to local laboratory range, was slightly higher than the cut-off limit in most studies which have been 1.7 or 1.8mg/dl.[11,13,14] One study used two cut-off values for hypomagnesemia (1.7 and 1.9 mg/dl) and found that both groups had significant association with symptomatic hypocalcemia.[26] Serum PTH is an unstable hormone and can give false levels. We followed strict instructions in taking the sample without the tourniquet, sending the sample to the main laboratory for storage within half-an-hour. Nonetheless, these accounted for logistical limitations. Post-operative PTH, serial testing of electrolytes and vitamin D insufficiency were not taken into account which could have added to our understanding of follow-up electrolyte balance.

The strengths of the current study include its prospective cohort nature. Patients were strictly followed up at 6 months after undergoing TT and NTT. On follow-up, fasting blood levels for Ca, Mg and PTH were taken from the same site to ensure uniformity. To the best of our knowledge this is the first study in Pakistan to investigate the role of Mg in the long-term Ca and PTH homeostasis in patients undergoing thyroidectomy.

In the light of the findings, it is suggested that pre-operative Ca level test must be conducted in patients undergoing thyroidectomy and treating it, if necessary, well before the surgery. The complex role of acute and chronic hypomagnesaemia on serum PTH levels in patients undergoing thyroidectomy must be further explored.

Conclusion

A fall in Mg and acute development of mild hypomagnesaemia post-operatively was correlated with higher PTH levels at 6-month follow-up, suggesting a beneficial role of early positive feedback to parathyroid glands to secrete PTH. On follow-up, Mg and PTH were positively correlated, suggesting hypomagnesaemia 6 months post-surgery did not provide the desired feedback. As the follow-up hypomagnesaemic patients had low Ca but normal PTH, it may highlight a degree of PTH resistance in prolonged hypomagnesaemia. Permanent hypocalcaemia was also significantly associated with pre-operative and post-operative calcium levels, positive post-operative hypocalcaemic symptoms and re-admission to hospital for hypocalcaemia. The complex role of acute and prolonged, mild and severe hypomagnesemia on PTH levels must be further explored.

Disclaimer: The study is the continuation of our previously published study. The same post-operative sample population was followed up after 6 months for the present study.

Conflict of Interest: None.

Source of Funding: None.

References

1. Bai B, Chen Z, Chen W. Risk factors and outcomes of incidental parathyroidectomy in thyroidectomy: A systematic review and meta-analysis. PLoS One 2018;13:e0207088. doi: 10.1371/journal.pone.0207088.
2. Ji YB, Song CM, Sung ES, Jeong JH, Lee CB, Tae K. Postoperative Hypoparathyroidism and the Viability of the Parathyroid Glands During Thyroidectomy. Clin Exp Otorhinolaryngol 2017;10:265-71. doi: 10.21053/ceo.2016.00724..
3. Pfleiderer AG, Ahmad N, Draper MR, Vrotsou K, Smith WK. The timing of calcium measurements in helping to predict temporary and permanent hypocalcaemia in patients having completion and total thyroidectomies. Ann R Coll Surg Engl 2009;91:140-6. doi: 10.1308/003588409X359349.
4. Coimbra C, Monteiro F, Oliveira P, Ribeiro L, de Almeida MG, Condé A. Hypoparathyroidism following thyroidectomy: Predictive factors. Acta Otorrinolaringol Esp 2017;68:106-11. English, Spanish. doi: 10.1016/j.otorri.2016.06.008.
5. Asari R, Passler C, Kaczirek K, Scheuba C, Niederle B. Hypoparathyroidism after total thyroidectomy: a prospective study. Arch Surg 2008;143:132-7; discussion 138. doi: 10.1001/archsurg.2007.55.
6. Rodríguez-Ortiz ME, Canalejo A, Herencia C, Martínez-Moreno JM, Peralta-Ramírez A, Perez-Martinez P, et al. Magnesium modulates parathyroid hormone secretion and upregulates parathyroid receptor expression at moderately low calcium concentration. Nephrol Dial Transplant 2014;29:282-9. doi: 10.1093/ndt/gft400.
7. Vetter T, Lohse MJ. Magnesium and the parathyroid. Curr Opin Nephrol Hypertens 2002;11:403-10. doi: 10.1097/00041552-200207000-00006
8. Meng C, Xie J, Wang W, Xia F, Li X. Hypomagnesemia and post-thyroidectomy hypocalcemia: molecular mechanisms and clinical potential. Int J Clin Exp Med 2018;11:11554-66.
9. Chincholikar SP, Ambiger S. Association of Hypomagnesemia with Hypocalcemia after Thyroidectomy. Indian J Endocrinol Metab 2018;22:656-60. doi: 10.4103/ijem.IJEM_599_17.
10. Wang W, Meng C, Ouyang Q, Xie J, Li X. Magnesemia: an independent risk factor of hypocalcemia after thyroidectomy. Cancer Manag Res 2019;11:8135-44. doi: 10.2147/CMAR.S218179.
11. Garrahy A, Murphy MS, Sheahan P. Impact of postoperative magnesium levels on early hypocalcemia and permanent hypoparathyroidism after thyroidectomy. Head Neck 2016;38:613-9. doi: 10.1002/hed.23937.
12. Viqar S, Akhtar T, Ikram N, Zia N. Frequency of Hypomagnesaemia following Total and Near-total Thyroidectomy and its relationship with Hypocalcaemia. J Coll Physicians Surg Pak 2021;30:571-5. doi: 10.29271/jcpsp.2021.05.571.
13. Cherian AJ, Gowri M, Ramakant P, Paul TV, Abraham DT, Paul MJ. The Role of Magnesium in Post-thyroidectomy Hypocalcemia. World J Surg 2016;40:881-8. doi: 10.1007/s00268-015-3347-3.
14. Hammerstad SS, Norheim I, Paulsen T, Amlie LM, Eriksen EF. Excessive decrease in serum magnesium after total thyroidectomy for Graves' disease is related to development of permanent hypocalcemia. World J Surg 2013;37:369-75. doi: 10.1007/s00268-012-1843-2.
15. Baloch N, Taj S, Anwer M, Naseem M. Frequency of Hypocalcaemia following Total Thyroidectomy. Pak J Med Sci 2019;35:262-5. doi: 10.12669/pjms.35.1.93.
16. Saaiq M, Shah SA, Zubair M. Clinical audit of the presentation and outcome of benign thyroid disorders in a tertiary care setting in Pakistan. J Pak Med Assoc 2013;63:1172-5.
17. Orloff LA, Wiseman SM, Bernet VJ, Fahey TJ 3rd, Shaha AR, Shindo ML, et al. American Thyroid Association Statement on Postoperative Hypoparathyroidism: Diagnosis, Prevention, and Management in Adults. Thyroid 2018;28:830-41. doi: 10.1089/thy.2017.0309.
18. Pironi L, Malucelli E, Guidetti M, Lanzoni E, Farruggia G, Pinna AD, et al. The complex relationship between magnesium and serum parathyroid hormone: a study in patients with chronic intestinal failure. Magnes Res 2009;22:37-43.
19. Navarro JF, Mora C, Jiménez A, Torres A, Macía M, García J. Relationship between serum magnesium and parathyroid hormone levels in hemodialysis patients. Am J Kidney Dis 1999;34:43-8. doi: 10.1016/s0272-6386(99)70106-x.
20. Ferrè S, Hoenderop JG, Bindels RJ. Sensing mechanisms involved in Ca2+ and Mg2+ homeostasis. Kidney Int 2012;82:1157-66. doi: 10.1038/ki.2012.179.
21. Inaba M, Okuno S, Imanishi Y, Nishizawa Y, Morii H. Magnesium deficiency enhances secretion of parathyroid hormone in normal and 5/6-nephrectomized uremic rats. J Endocrinol Invest 1992;15(9 Suppl 6):135-42.
22. Mutnuri S, Fernandez I, Kochar T. Suppression of Parathyroid Hormone in a Patient with Severe Magnesium Depletion. Case Rep Nephrol 2016;2016:2608538. doi: 10.1155/2016/2608538.
23. Rude RK, Oldham SB, Singer FR. Functional hypoparathyroidism and parathyroid hormone end-organ resistance in human magnesium deficiency. Clin Endocrinol (Oxf) 1976;5:209-24. doi: 10.1111/j.1365-2265.1976.tb01947.x.
24. Blaine J, Chonchol M, Levi M. Renal control of calcium, phosphate, and magnesium homeostasis. Clin J Am Soc Nephrol 2015;10:1257-72. doi: 10.2215/CJN.09750913.
25. Wilson RB, Erskine C, Crowe PJ. Hypomagnesemia and hypocalcemia after thyroidectomy: prospective study. World J Surg 2000;24:722-6. doi: 10.1007/s002689910116.
26. Brophy C, Woods R, Murphy MS, Sheahan P. Perioperative magnesium levels in total thyroidectomy and relationship to hypocalcemia. Head Neck 2019;41:1713-18. doi: 10.1002/hed.25644.