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Original Article

Post Total Thyroidectomy Hypocalcemia in Toxic MNG and Effect of Post-operative Intravenous Calcium Gluconate in its Incidence

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ABSTRACT

Objective: To see the effects of post-operative intravenous calcium gluconate infusion on post-total thyroidectomy calcium levels in toxic multinodular thyroid patients.

Study Design: Randomized control trial (IRCT20240503061640N1).

Place and Duration of Study: Combined Military Hospital Bahawalpur, Pakistan from Nov 2023 to Jul 2024.

Methodology: Patients with toxic multinodular goiter and having normal calcium levels were included. Baseline parameters, history, and pre-operative calcium levels were measured. Patients were divided into two groups: one interventional group which was given intravenous calcium gluconate infusion, and the other control group was given intravenous normal saline infusion as a placebo. Post-operative measures like calcium level, hospital stay, severe hypocalcemia symptoms, Chvostek sign, Trousseau sign and need for calcium supplements were noted.

Results: Out of seventy-two patients 36 were assigned to each group. Both group shows no significant difference between baseline parameters. The mean value of the post-operative calcium level of the interventional group was 9.472±0.582 mg/dl and the control group was 8.863±0.555 mg/dl with a statistically significant difference (p-value <0.001). The control group shows a significant number of hypocalcemia patients as compared to the interventional group with a p-value of 0.017.

Conclusion: This study concluded that the post-operative use of calcium gluconate reduces the incidence of hypocalcemia in post-thyroidectomy patients with toxic multinodular goiter. Not only does it reduce severe symptoms of hypocalcemia but also reduces the post-operative need for calcium supplements and hospital stay thus ensuring better recovery.

Keywords: Calcium level, Calcium Gluconate, Hypocalcemia, Incidence, Multinodular goiter, Total thyroidectomy, Toxic.

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INTRODUCTION

The most common endocrine gland diseases in the whole world are thyroid disorders and the most common head and neck surgery worldwide is total thyroidectomy.[1,2] After thyroid surgery, complications can occur including decreased calcium levels, recurrent laryngeal nerve injury, hemorrhage, hoarseness of voice, surgical site infection, and airway injuries.[3]

Hypocalcemia is a very common complication after thyroidectomy due to damage or removal of the parathyroid gland, and due to damage to blood vessels of gland during surgery.[4] Temporary hypocalcemia, which resolves within six months of surgery, ranges from 0.3 to 49%, whereas permanent hypocalcemia, persisting beyond six months, occurs at a rate of 0 to 13%.[5] According to most of the studies, serum calcium and parathyroid hormone levels have been used as measures of hypocalcemia or any supplement needed.[6] Latent hypocalcemia is checked by the Chvostek sign and Trousseau sign. Acute and severe hypocalcemia is an emergency and aggressive treatment is often required for post-operative hypocalcemia.[7] Calcium carbonate or calcium citrate is often prescribed. In severe hypocalcemia, intravenous calcium is introduced as a bolus (1 to 2g of calcium gluconate in 50ml of 5% dextrose administered over 20 minutes) or a solution of 11g of calcium gluconate and normal saline or 5% dextrose forming a total volume of 1000 ml at 50ml/hr to maintain low normal range of calcium. The role of postoperative calcium supplementation in preventing post-operative hypocalcemia is still being analyzed.[8] Interventional and national studies have been done on the importance of prophylactic use of intravenous calcium gluconate in preventing post-total thyroidectomy hypocalcemia.[9,10] But, little study has been done on it.

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Post thyroidectomy hypocalcemia is very common complication and it makes patient delay in recovery and prolong hospital stay. So, our study aims to assess the effects of post-operative intravenous calcium gluconate in preventing it.

METHODOLOGY

The research utilized a randomized controlled trial (RCT) methodology (IRCT registered IRCT20240503061640N1) conducted in a single center of Combined Military Hospital Bahawalpur a tertiary health care. The study was conducted from November 2023 to July 2024. The study was conducted under ethical guidelines and approved by the Ethical Committee of Combined Military Hospital Bahawalpur (ERC Ltr No. 1516/EC/01/2023).

Inclusion Criteria: Patients who were with toxic multinodular goiter visiting Combined Military Hospital Bahawalpur were included. Patients of all ages and genders were included; the patient who underwent total thyroidectomy and with normal pre-operative calcium levels. Patients who did not have any parathyroid disease or disease of calcium levels were included. Only those patients were included who gave consent for study research.

Exclusion Criteria: Patients who were not with toxic multinodular goiter i.e. having diffuse goiter, solitary thyroid nodule, hypothyroidism, thyroid carcinoma and recurrent thyroid swelling were excluded. All the patients whose pre-operative calcium level were deranged, having any parathyroid disease or any kidney diseases causing deranged calcium levels were excluded. Patients who didn't give consent for study research, did not follow properly or took any type of pre-operative calcium supplements were excluded. Patients who underwent lobectomy and isthmusectomy were excluded. Patients having any allergy to calcium gluconate in the past were also excluded.

With the help of WHO sample size calculator with level of significance at 5%, power of test at 90%, Mean±SD serum calcium level in group 1 (received prophylactic calcium gluconate) as 8.9±0.4 mg/dl10 while serum calcium level in group 2 (did not received prophylactic calcium gluconate) as 8.2±0.3 mg/dl10 the minimum sample size was calculated as thirty in each group (interventional and control group) and it was increased for better results. A total of 80 patients underwent total thyroidectomy. Of these 8 were excluded according to the exclusion criteria. Rest 72 patients were randomly assigned by computer-generated software SPSS (Statistical Package for the Social Sciences) into two groups i.e. intervention groups (Group-A) and control group (Group-B). First, group sequences were made with the help of software then patients were assigned into groups as they presented in the hospital according to the sequence. Blinding of participants and operating surgeon was done to reduce bias (Figure).

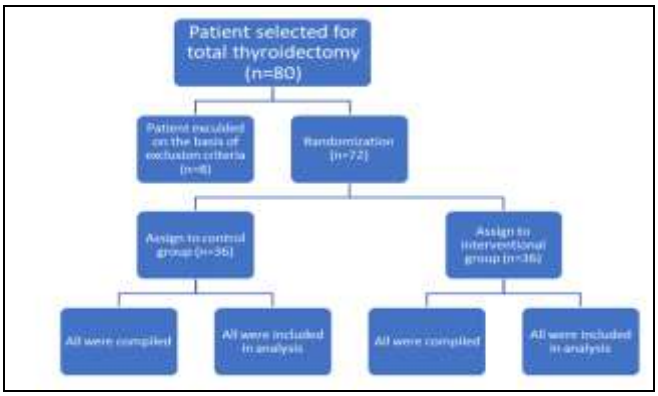

Figure: Flow diagram of randomization of patient

Patients selected were admitted to the hospital. They were counseled about the procedure of the operation and the peri and post-operative complications. Pre-operative calcium was done for all the patients. Same treating surgeon done the surgeries on all patients. Within one-hour post-surgery Group-A (interventional group) was given 1 gram of intravenous calcium gluconate in 100 ml normal saline infusion over 1 hour and Group-B (control group) was given intravenous normal saline 100 ml infusion over 1 hour. Any post-operative complications of hypocalcemia like a neuromuscular spasm or tetany were noted. Post-operative calcium supplements were given to patients who developed such complications. The reference value for hypocalcemia was set at <8.5mg/dl. These primary outcomes (post-operative hypocalcemia) were measured after 12 hours of surgery. Other values like duration of post-operative hypocalcemia, need for any supplementation for hypocalcemia like calcium supplements, Chvostek sign, Trousseau sign, and occurrence of any severe complications like neuromuscular spasm and tetany were included in secondary outcomes. The specimen of the thyroid was sent for histopathology. Data was collected by a trained doctor.

For statistical analysis Statistical Package for Social Sciences (SPSS) version 27 was used. For normal data (age, duration of stay, calcium level) Chi-square

test and independent samples t-test were performed and for non-normal data (time of start of disease) non-parametric test (Mann-Whitney U test) was done to compare the incidence of hypocalcemia between the intervention and control groups and explore potential factors influencing the outcomes. The significant value was set at 0.05.

RESULTS

Out of seventy-two patients, twenty-three were male and forty-nine were female. Thirty-six patients were assigned to both groups equally. In the interventional group. The mean age group of the patients was 40.56±6.236 years. The median for the time of start of disease was two years for both groups. There was no statistical significance between the primary parameters of both groups. (Table-III).

The mean of the post-operative calcium level showed a significant value as compared to pre-operative calcium level (p<0.001). Only two patients had severe symptoms like tetany and neuromuscular spasm. Out of fourteen patients ten patient required calcium supplements. As shown in Table-II.

Out of seventy-two patient total fourteen patient were hypocalcemia. A significant difference was seen between the interventional and control group when compared with hypocalcemia status as shown in Table-III.

The comparison of postoperative hypocalcemia and normocalcemia shows a p-value<0.05 among ASA grade 1, severe symptoms, need for a calcium

Table-I: Basic parameters of the Study Population (n=72)

Characteristics		Interventional Group (n=36)	Control group (n=36)	Total (n=72)	*p*-value
Age (years), Mean±SD		40.19±6.466	40.94±6.066	40.56±6.236	0.502
Gender	Male, n(%)	10(13.9 %)	13(18.1 %)	23(31.9 %)	0.430
	Female, n (%)	26(36.1 %)	23(31.9 %)	49(68.1 %)	0.349
ASA classification	Grade 1, n (%)	18(25%)	17(23.6%)	35(48.6 %)	0.797
	Grade 2, n (%)	16(22.2%)	16(22.2%)	32(44.4 %)	1.0
	Grade ≥ 3, n (%)	2(2.8 %)	3(4.2 %)	5(6.9 %)	0.640
Time of start of disease (years)	(Median: IQR)	2(3-2)	2(3-2)	2(3-2)	0.638*

ASA, American Society of Anesthesiologists
**p-value by non-parametric test (Mann-Whitney U)*

Table-II: Postoperative parameters of both Groups (n=72)

Measures	Interventional Group (n=36)	Control Group (n=36)	Total(n=72)	*p* - value
Pre-Operative calcium level, mg/dl, Mean ± SD	9.272 ± 0.507	9.408 ± 0.475	9.340 ± 0.492	0.244
Post-Operative calcium level, mg/dl, Mean ± SD	9.472 ± 0.582	8.863 ± 0.555	9.168 ± 0.643	<0.001
Chvostek sign positive n (%)	1 (1.4%)	3 (4.2%)	4 (5.6%)	0.301
Trousseau sign n (%)	3 (4.2 %)	4 (5.6%)	7 (9.7%)	0.688
Severe symptoms, n (%)	0 (0.0 %)	2 (2.8 %)	2 (2.8%)	0.150
Need for post-operative calcium supplements, n (%)	2 (2.8 %)	8 (11.1 %)	10 (13.9 %)	0.041
The average duration of stay (days), Mean ± SD	3.47 ± 0.559	3.77 ± 0.132	3.62 ± 0.700	0.064

Table-I: Frequency distribution of Postoperative Hypocalcemia (n=72)

Hypocalcemia	Interventional Group n (%)	Control Group n (%)	*p*-value
Yes	3 (4.2 %)	11 (15.3 %)	0.017
No	33 (45.8 %)	25 (34.7 %)	
Total	36 (50 %)	36 (50 %)	

Table-II: Postoperative Parameters based on Hypocalcemia (n=72)

Characteristics		Post operative Hypocalcemic(n=14)	Post operative Normocalcemic (n=58)	p-value
Age (years)	Mean ± SD	41.35 ± 6.890	40.37 ± 6.118	0.602
Gender	Male, n (%)	4 (5.6 %)	19 (26.4 %)	0.762
	Female, n (%)	10 (13.9 %)	39 (54.2 %)	0.762
ASA classification	Grade 1, n (%)	3 (4.2 %)	32 (44.4 %)	0.023
	Grade 2, n (%)	9 (12.5 %)	23 (31.9 %)	0.095
	Grade ≥ 3, n (%)	2 (2.8 %)	3 (4.2 %)	0.228
Time of start of disease (Years)	(Median: IQR)	2 (3-2)	2 (3-2)	0.798*
Severe symptoms	Yes, n (%)	2 (2.8 %)	0 (0 %)	0.004
	No, n (%)	12 (16.7 %)	58 (80.6 %)	
Need for post-operative calcium supplements	Yes, n (%)	10 (13.9 %)	0 (0 %)	<0.001
	No, n (%)	4 (5.6 %)	58 (80.6 %)	
The average duration of stay (days)	Mean ± SD	4.42 ± 0.851	3.43 ± 0.499	<0.001
Chvostek Sign positive	n (%)	4 (5.6 %)	0 (0 %)	< 0.001
Trousseau Sign	n (%)	7 (9.7 %)	0 (0 %)	< 0.001

ASA, American Society of Anesthesiologists
**p-value by non-parametric test (mann-whitney U)*

supplement, and duration of stay Table-VI.

DISCUSSION

Our research influences the effect of post-total thyroidectomy, intravenous Calcium gluconate infusion on calcium levels. Only patients having a history of toxic MNG were selected for this purpose. The mean age of the population was 40.56±6.236 years. Almost the same age group was included in both groups. Females were almost two times more than males showing more prevalence of toxic MNG in this gender. There was no statistical difference between the ASA (American Society of Anesthesiologists classification between the two groups. Most of the patients presented with the symptoms of swelling in front of the neck and difficulty in swallowing. The Median of the time of start of disease was 2 years. However, there were no statistically significant difference between the two groups for time of start of symptoms, age, and gender.

The mean of pre-op calcium levels of both the groups was 9.340±0.492 md/dl showing within the normal limit. After surgery, intervention group patients were given intravenous calcium gluconate infusion under strict measures. The total post-operative calcium mean was merely less than pre-operative calcium levels i.e. 9.168±0.643 mg/dl. This decrease in calcium levels might be due to transient loss of blood supply or removal of one or two parathyroid glands. These similar results can be seen in a study conducted by Miki H *et al.,* which shows that in all types of thyroidectomies, postoperative total calcium levels decreased significantly in comparison to preoperative (p<0.01) and this fall was directly proportional to the extent of surgery.[11] In our study there was a statistically significant difference in post-operative calcium levels between the intervention and control group i.e <0.001. This shows that the use of intravenous calcium gluconate can reduce the chances of hypocalcemia postoperatively. Uruno, T *et al*., study showed similar results. His study consisted of 547 patients who underwent total thyroidectomies. He found a significant difference between the intervention and control group i.e. <0.0001).[9] A study by Arer IM *et al*., showed results similar to our study, but he used oral calcium supplements and found out a significant difference between two groups.[12] Another research by Khaghan BS *et al*., showed results compared to our study with a significant decrease in calcium level in control group. He further seen the effect after one week which still showed significant decrease of calcium levels in the control group.[10] In most cases postoperatively there is a small decrease in calcium levels after a few hours and this decrease is compensated within some time. Sometimes, such a decrease in calcium levels can be symptomatic. This results from damage to the parathyroid glands or often due to devascularization during dissection.[13] Thus, intravenous calcium gluconate postoperatively decreases the chances of such a transient decrease in calcium levels. The Chvostek and Trousseau signs show latent hypocalcemia. In our study the p-value for these signs were more than 0.05. Thus, these were not significant when compared with these two groups. The presence of a Chvostek's sign, is not always reliable, as approximately 25% of healthy individuals exhibit this sign. Furthermore, another study found that nearly 30% of patients with confirmed hypocalcemia did not display a positive Chvostek's sign.[14,15] Only two patients had serious symptoms like tetany postoperatively in the control group. None of the interventional group has severe symptoms or hypocalcemia. This may be explained by the use of intravenous calcium gluconate preoperatively. However, the values were not significant. Also, a significant number of control group patients were given calcium supplements postoperatively due to hypocalcemic symptoms as they were not given intravenous calcium gluconate. This can also be seen in a study by Khaghan BS *et al*.[10] The routine calcium supplements should be used to prevent symptoms of hypocalcemia as demonstrated by Nicholson KJ *et al.,* in his study.16 The average duration of stay for the control group was slightly raised but it seems that intravenous calcium gluconate does not affect the hospital stay in both groups.

It has been observed in our study that post-operative hypocalcemia was significantly more in control group as compared to the interventional group as the p-value was 0.017. Thus, our study strongly supports the use of intravenous calcium gluconate to avoid hypocalcemia in post-operative patients. Also, it reduces the occurrence of severe symptoms (neuromuscular disorders, seizures, and tetany), and decreases the use of post-operative calcium supplements in post-operative patients. There were no statistically significant differences between the mean of age, gender, and time of start of disease between post-operative normocalcemic and hypocalcemic patients.

ASA classification grade 1 has a decreased rate of post-operative hypocalcemia with a significant value of 0.023 as compared to post-operative normocalcemia. Hypocalcemic patients have a prolonged stay at the hospital because of the ongoing treatment of hypocalcemic symptoms. These results are in accordance with the study done by Ghafouri *et al.*, in which there was an increase in mean hospital stay in hypocalcemic patients as compared to normocalcemic with the *p*-value 0f 0.006.[17] Calcium level disturbances after total thyroid removal can lead to prolonged hospital stays and an increased risk of readmission due to parathyroid gland complications.[18] Sometimes, the severe symptoms may take 3 to 4 weeks to get settled. Chvostek and Trousseau sign both showed significant value in the identification of hypocalcemic patients.

Thus, our study emphasizes the benefit of post-operative intravenous calcium gluconate in the incidence of hypocalcemia. Our study adds valuable study material for the new researchers and the existing knowledge. By using calcium gluconate, it can decrease the incidence of postoperative hypocalcemic symptoms, use of calcium supplements, hospital stay, and transient hypocalcemia. In this way, it will reduce the cost-effectiveness of the hospital.

LIMITATIONS OF STUDY

Our study only included patients with toxic multinodular goiter. The sample size was small, more is needed for better results. The thyroid surgery is operative dependent and the result depends on surgeon efficacy. The per-operative findings also affect the parathyroid gland functioning like vascularity of the gland, variability on the position, and adhesions. Also, the nutritional status and diet of the patient of the patient might affect the calcium status.

CONCLUSION

This study concluded that the post-operative use of calcium gluconate reduces the incidence of hypocalcemia in post-thyroidectomy patients with toxic MNG. Not only does it reduce severe symptoms of hypocalcemia but also reduces the post-operative need for calcium supplements and hospital stay thus ensuring better recovery.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MAM & MSA: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

MHA & SAA: Data acquisition, data analysis, approval of the final version to be published.

KA & FA: Critical review, concept, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCE

1. Alqahtani SM, Alatawi AS, Alalawi YS. Post-thyroidectomy hypocalcemia: a single-center experience.Cureus 2021; 13(11) e20006. http://doi.org/10.7759/cureus.20006
2. Layegh P, Sajjadi ZS, Mostaan LV, Mohebbi M, Kabiri M, Yaghoubi MA et al. Preoperative Vitamin. D Status and Post-Total Thyroidectomy Hypocalcemia. Iranian J Otorhinolaryngol 2024; 36(1): 343.
3. Alqahtani SM, Almussallam B, Alatawi AS, Alsuhaimi NA, Albalawi A, Albalawi NS, et al. Post-thyroidectomy complications and risk factors in Tabuk, Saudi Arabia: a retrospective cohort study. Cureus. 2020; 12(10). e10852. https://doi.org/10.7759%2Fcureus.10852
4. Sharifi A, Rousta F. Hypocalcemia: Why does this happen after thyroidectomy?. Eurasian J Chem Med Petroleum Res 2023; 2(4): 329-339. https://doi.org/EJCMPR/20231215
5. Sittitrai P, Ruenmarkkaew D, Klibngern H, Ariyanon T, Hanprasertpong N, Boonyaprapa S, et al. Perioperative versus postoperative calcium and vitamin D supplementation to prevent symptomatic hypocalcemia after total thyroidectomy: a randomized placebo controlled trial. Int J Surgery 2023; 109(1): 13-20. https://doi.org/DOI:10.1097/JS9.0000000000000192
6. Soares CS, Oliveira CC, Koga KH, Moriguchi SM, Terra SA, Tagliarini JV, et al. Postoperative serum magnesium levels as a predictor for the need for calcium replacement after total thyroidectomy: a prospective study. Arch Endocrinol Metabol 2023; 67(3): 355-360. https://doi.org/10.20945/2359-3997000000581
7. Pepe J, Colangelo L, Biamonte F, Sonato C, Danese VC, Cecchetti V, et al. Diagnosis and management of hypocalcemia. Endocrine 2020; 69: 485-495. https://doi.org/10.1007/s12020-020-02324-2
8. Stack Jr BC, Bimston DN, Bodenner DL, Brett EM, Dralle H, Orloff LA, et al. American association of clinical endocrinologists and American college of endocrinology disease state clinical review: postoperative hypoparathyroidism-definitions and management. Endocrine Pract 2015; 21(6): 674-685. https://doi.org/10.4158/ep14462.dsc
9. Uruno T, Miyauchi A, Shimizu K, Tomoda C, Takamura Y, Ito Y, et al. A prophylactic infusion of calcium solution reduces the risk of symptomatic hypocalcemia in patients after total thyroidectomy. World J Surg 2006; 30(3): 304-308. https://doi.org/10.1007/s00268-005-0374-5
10. Khaghan BS, Junaid F, Hussain SA, Noor AI, Iqbal T, Maham M et al. Role of Prophylactic Administration of Calcium Gluconate in the Early Post Operative Period after Total Thyroidectomy at Surgical department Ayub Teaching Hospital Abbottabad. Med Forum Month 2023; 34(9). 169-172.
11. Miki H, Inoue H, Kitaichi M, Masuda E, Komaki K, Monden Y et al. Estimation of free calcium levels after thyroidectomy. Journal of Med Invest 1997; 44 (1-2): 83-88.

12. Arer IM, Kus M, Akkapulu N, Aytac HO, Yabanoglu H, Caliskan K, et al. Prophylactic oral calcium supplementation therapy to prevent early post thyroidectomy hypocalcemia and evaluation of postoperative parathyroid hormone levels to detect hypocalcemia: a prospective randomized study. Int J Surg 2017; 38(1): 9-14. https://doi.org/10.1016/j.ijsu.2016.12.041
13. Pãduraru DN, Ion D, Carsote M, Andronic O, Bolocan A. Post-thyroidectomy hypocalcemia-risk factors and management. Chirurgia 2019; 114(5): 564-570. http://doi.org/10.21614/chirurgia.114.5.564
14. Hoffman E. The Chvostek sign: a clinical study. Am J Surg 1958; 96(1): 33-37. https://doi.org/10.1016/0002-9610(58)90868-7
15. Fonseca OA, Calverley JR. Neurological manifestations of hypoparathyroidism. Arch Int Med 1967; 120(2): 202-206. https://doi.org/10.1001/archinte.1967.00300020074009
16. Nicholson KJ, Smith KJ, McCoy KL, Carty SE, Yip L. A comparative cost-utility analysis of postoperative calcium supplementation strategies used in the current management of hypocalcemia. Surgery 2020; 167(1): 137-143. https://doi.org/doi:10.1016/j.surg.2019.05.077
17. Ghafouri A, Shirangi S, Mohseni S, Shojaiefard A, Khorgami Z, Hedayat A et al. Prophylactic oral calcium reduces symptomatic hypocalcemia in patients undergoing total or subtotal thyroidectomy: a randomized controlled trial. Acad J Surg 2014; 1(3-4): 40-44.
18. McHenry CR. Same-day thyroid surgery: An analysis of safety, cost savings, and outcome. Am Surg 1997; 63(7): 586.