Original Article

The use of prophylactic infusion of calcium gluconate compared to placebo in reducing the rate of early hypocalcaemia after total thyroidectomy: a double-blinded, randomized controlled trial

Kah Seng Khoo^, Audrey Yeo, Muhammad Ridwan Bin Mirzan Asfian, Khoon Leong Ng

Department of Surgery, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

Contributions: (I) Conception and design: KS Khoo, MRB Mirzan Asfian, KL Ng; (II) Administrative support: All authors; (III) Provision of study materials or patients: KS Khoo, KL Ng; (IV) Collection and assembly of data: KS Khoo, A Yeo; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Dr. Kah Seng Khoo, MBBS (UM), MRCS (Edinburgh), MS (UM). General Surgeon, Department of Surgery, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia. Email: kahseng901209@gmail.com.

Background: Hypocalcaemia as a common complication after total thyroidectomy [23–40% in University Malaya Medical Centre (UMMC)] and could result in prolonged hospital stay. We compared the early hypocalcaemia rate between prophylactic infusion of calcium and placebo among post total thyroidectomy patients and to establish whether prophylactic intravenous infusion of calcium reduces the rate of hypocalcaemia in the first 48 hours after surgery.

Methods: Patients undergoing elective total thyroidectomy in UMMC between June 2020–May 2022, were recruited and randomized to receive placebo or prophylactic calcium infusion. Both groups of patients received same dosages of post-operative prophylactic vitamin D and oral calcium. Early hypocalcaemia (within 48 hours) rate after surgery was the primary outcome and duration of hospital stay was the secondary outcome. The data collected was analysed using per-protocol analysis.

Results: Thirty-four patients were randomized equally (1:1) into both arms. No differences in the early hypocalcaemia rate between the intervention and placebo arms (0% *vs.* 5.8%, P>0.05). The median serum calcium levels were comparable between the intervention and placebo arms at 6 hours (2.33 *vs.* 2.37 mmol/L, P=0.59) and 48 hours (2.26 *vs.* 2.23 mmol/L, P=0.19) post-surgery. However, the median serum calcium level at 24 hours was statistically significantly higher in the intervention arm than the placebo arm (2.31 *vs.* 2.22 mmol/L, P=0.02). Similar duration of hospital stay between the both groups (2 *vs.* 2 days, P=0.81).

Conclusions: Routine prophylactic calcium infusion with oral calcium and vitamin D does not diminish the rate of early symptomatic hypocalcaemia post total thyroidectomy in a low-risk group. However, its usefulness needs to be further assessed in a large scale randomized controlled trial (RCT) incorporating more bigger population.

Trial Registration: Registered on ClinicalTrials.gov (NCT04491357).

Keywords: Total thyroidectomy; hypocalcaemia; prophylactic calcium infusion; length of stay

Submitted May 23, 2024. Accepted for publication Aug 07, 2024. Published online Aug 28, 2024.
doi: 10.21037/gs-24-190
View this article at: https://dx.doi.org/10.21037/gs-24-190

^ ORCID: 0000-0003-1199-3573.

Introduction

Hypocalcaemia is one of the common complications after total thyroidectomy and reported to occur in 13–49% in a meta-analysis, causing transient and permanent hypocalcaemia (1-3). In the University Malaya Medical Centre (UMMC) Endocrine Surgery (ECS) Unit, the rate of post total thyroidectomy symptomatic hypocalcaemia within 48 hours after surgery in 2018 and 2019 were 40% and 23% respectively. Patients that required rescue doses of intravenous calcium infusion during early post-operative period was 40% and 33% in 2018 and 2019 respectively. The average length of hospital stay was around two days post total thyroidectomy.

Post-thyroidectomy hypocalcaemia arises due to either inadvertent parathyroid removal, parathyroid devascularization or gland damage (4,5). There have been multiple reports that administration of prophylaxis oral calcium and vitamin D post-surgery were found to reduce the rate of post-operative hypocalcaemia (6-8). Neck dissection surgery and low postoperative parathyroid hormone (<10 pg/dL) also can predict hypocalcaemia (9-19). However, there is a paucity of literature regarding the role of prophylactic infusion of calcium perioperatively in reducing postoperative early hypocalcaemia.

The primary outcome is to establish whether prophylactic intravenous infusion of calcium reduces the rate of hypocalcaemia in the first 48 hours after surgery. The secondary outcome is to investigate whether prophylactic intravenous infusion of calcium shorten the length of hospital stay. We present this article in accordance with the CONSORT reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-24-190/rc).

Highlight box

Key findings

- Routine prophylactic calcium infusion with oral calcium and vitamin D does not diminish the rate of early symptomatic hypocalcaemia post total thyroidectomy in low-risk group.

What is known and what is new?

- There is little evidence regarding the role of prophylactic infusion of calcium perioperatively in reducing postoperative early hypocalcaemia.
- This study sought to confirm the effective of prophylactic calcium infusion post total thyroidectomy.

What is the implication, and what should change now?

- Our findings suggest that no role of prophylactic calcium infusion on top oral supplements in low-risk group undergoing total thyroidectomy.

Methods

Protocol in UMMC for total thyroidectomy

All patients will be admitted one day prior to surgery and will have their baseline serum calcium and intact parathyroid hormone (i-PTH) levels measured. Subsequently, all patients will have serum calcium levels checked at the 6-, 12-, 24-, 36- and 48-hour mark post-surgery. The i-PTH level will be tested at the 12-hour post-surgery. Oral calcium supplements 2 g a day (calcium carbonate 1 g b.d.) and/or Rocaltrol 0.25 mcg o.d. will be started for all cases once the patients are able to tolerate orally post-surgery. If a patient experiences hypocalcemia symptoms and the corrected serum calcium level is less than 2.0 mmol/L, the patient will be administered a rescue dose of intravenous calcium gluconate (1 g bolus of calcium gluconate over 20 minutes, followed by 3 g of calcium gluconate in 50 mL of normal saline) over 4 hours duration. Afterwards, they will continue with oral calcium supplements either in a similar dosage or increased dosage. On the other hand, if a patient experiences hypocalcaemia symptoms and the corrected serum calcium level is more than 2.0 mmol/L, the patient will be continued on oral supplements either in similar dosage or increased dosage. The usual hospital stay for a total thyroidectomy patient is about 48 hours post-surgery if no issue and will be discharged with outpatient clinic appointment in 2 weeks duration.

Study type and design

This is a single-centre, double-blinded and prospective randomized controlled trial (RCT). The duration of the study was from June 2020 until May 2022. Once recruited, participants will be randomized into intervention group (Group A) and a control group (Group B) in a ratio of 1:1 during admission. Both the treating surgeon and patient are blinded to the randomization and only the primary investigator and assistants are not blinded.

Calcium level being measured are the albumin corrected calcium in this study. Before surgery, baseline serum calcium, magnesium and i-PTH will be obtained. If intra-

operatively, all four parathyroid glands are accidentally removed during the total thyroidectomy, these patients will be excluded from the study. After total thyroidectomy, the intervention group will receive calcium gluconate infusion over 1 hour (1 g of intravenous calcium gluconate, diluted in 100 mL of normal saline) within 4 hours of skin closure. The control group will receive a saline infusion (100 mL of normal saline) infused over 1 hour within 4 hours of skin closure. They will be put on cardiac monitoring during the administration of the intravenous infusion. Post-total thyroidectomy, both groups will receive the same regime of oral calcium carbonate 1 g b.d. and oral Rocaltrol 0.25 mcg o.d. once they are able to tolerate orally. Serum calcium levels will be obtained at the 6-, 12-, 36- and 48-hour mark post-surgery.

If a patient exhibited signs of mild symptomatic hypocalcaemia, then immediate serum calcium level will be performed. If the results show serum hypocalcaemia (less than 2.0 mmol/L), a rescue dose of intravenous calcium gluconate (3 g of intravenous calcium gluconate infusion over 4 hours) will be given as per current unit protocol. After completion of the rescue dose of calcium infusion, the serum calcium level will be repeated and further action will be taken based on the result.

However, if the patient developed severe hypocalcaemia symptoms such as carpo-pedal spasm, bronchospasm/laryngospasm or cardiac manifestation, then an immediate serum calcium level will be obtained and an immediate rescue bolus of intravenous calcium gluconate will be administered even before the result are available (1 g of calcium gluconate will be given over 20 minutes). This will be followed by intravenous calcium infusion (3 g of intravenous calcium gluconate infusion over 4 hours) after biochemical confirmation of hypocalcaemia. After completion of the slow calcium bolus and calcium infusion, serum calcium levels will be repeated and further action will be determined based on the post-correction calcium level and patient's symptoms. Both groups of patients will be followed-up until 48 hours post-operation. In the event of an emergency and there is a need to break the code, the clinician can contact the principal investigator immediately to facilitate the rescue process.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This trial has been approved by Medical Research Ethics of UMMC (No. MECID-2020225-8316) and National Medical Research Register (No. NMRR-20-1085-55067). Written informed consent was obtained from all patients.

Inclusion and exclusion criteria

All patients aged 18 till 80 years old who are scheduled for total thyroidectomy between June 2020 till May 2022 were included.

Patients who have their age outside the range of 18–80 years old, comorbid of parathyroid disorders or chronic kidney disease, on calcium or vitamin D supplements prior to surgery, have deranged calcium homeostasis pre-operatively or scheduled for total thyroidectomy plus lymph node dissection (either central or lateral neck dissection) are excluded from the study.

Sample size

An initial pilot study was conducted with a total of 10 patients, 5 patients allocated to the intervention arm and another 5 patients to the control arm in order to calculate the sample size. The mean calcium level in the intervention arm at 24- and 48-hour mark post-surgery are 2.244 and 2.248 mmol/L and the standard deviation are 0.052 and 0.104 respectively. On the other hand, the mean calcium levels in the control arm at 24- and 48-hour mark post-surgery are 2.136 and 2.188 mmol/L and the standard deviation are 0.150 and 0.086 respectively. The calculated effect size, f=0.31. By using alpha: 0.05 and power: 0.80, with G*Power 3.1.9.4 application [analysis of variance (ANOVA): repeated measures, within between interaction], the total sample size required will be 28 participants, including a 10% of dropout rate in this study. *Figure 1* shows the consort diagram for this study.

Statistical analysis

Data analysis was performed using SPSS Statistics version 25 (IBM Corp., Armonk, NY, USA). Categorical descriptive data were expressed as numbers & percentages and continuous descriptive data were expressed as median [interquartile range (IQR)] unless otherwise stated.

Categorical data were analysed using Chi-squared test. All continuous variables were tested for normal distribution by the Shapiro-Wilk test. Normally distributed variables were analysed using Student's *t*-test. Otherwise, continuous variables which were skewed and not normally distributed were analysed using the non-parametric Mann-Whitney *U*-test. A value of $P<0.05$ was considered statistically significant. The data collected were analysed using a per-protocol analysis.

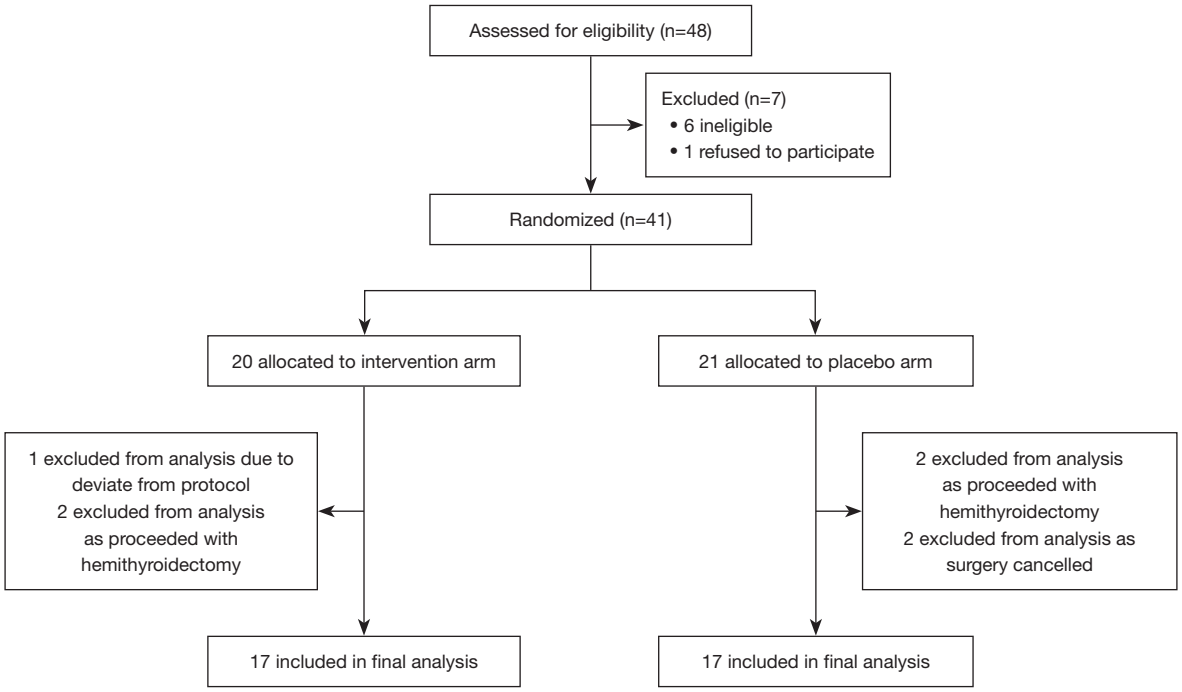

Figure 1 Consort diagram.

Results

A total of 34 patients were included in the final analysis after being assessed for eligibility and exclusion; 17 patients were in the intervention and placebo arms respectively with equal ratio of 1:1. The patients demographics in terms of age, gender, diagnosis, pre-operative serum calcium level and pre-operative serum i-PTH level were shown to be not significant in both arms (placebo and intervention) except for their final specimen weight (*Table 1*). The median (IQR) specimen weight for intervention arm was 113 g (59–177 g) and placebo arm was 66 g (42–117.5 g), the difference which was shown to be statistically significant difference between the two arms with a P value of 0.042.

All patients in both arms were followed up until 48 hours post-surgery. None of the patients in the intervention arm developed complication from calcium infusion. The median serum calcium level at 6 hours post-operatively were comparable between intervention and placebo arms (2.33 *vs.* 2.37 mmol/L, P=0.59). However, for the median serum calcium level at 24 hours post-operatively, the median serum calcium level in the intervention arm was much higher than the placebo arm (2.31 *vs.* 2.22 mmol/L, P=0.02) and this reached statistically significance (*Table 2*). Moving on to the last measurement at 48 hours post-operatively, the median serum calcium levels were comparable between the intervention and placebo arms (2.26 *vs.* 2.23 mmol/L, P=0.19). *Figure 2* illustrates the trends of serum calcium levels of both arms from pre-operative till 48 hours post total thyroidectomy.

Only one of the patients in the whole study (placebo arm) developed symptomatic hypocalcaemia (*Figure 3*) whereby her serum calcium level at 24 hours post-surgery was 1.98 mmol/L and it was associated with mild hypocalcaemia symptoms. She was given rescue intravenous calcium infusion. Finally, the post-operative serum i-PTH levels were comparable between both groups with a P value of 0.13.

The median length of hospital stay was the same between the two groups with a median of 2 days and the P value was 0.81 (*Table 3*).

Discussion

Postoperative symptomatic hypocalcaemia is an important issue as this subset of patient will require a prolonged hospital stay to monitor their serum calcium level to ensure that they can be discharged safely and to reduce the readmission rate. In an audit done in the UMMC, symptomatic hypocalcaemia rates after total thyroidectomy

Table 1 Baseline participants demographics of both arms

Variables	Participants (n=34)		P value
	Intervention (n=17)	Placebo (n=17)	
Age (years)	64 [49.5–68.5]	59 [39–67]	0.31
Gender			0.69
Female	12 [70.6]	14 [82.4]	
Male	5 [29.4]	3 [17.6]	
Diagnosis			0.62
Toxic multinodular goitre	5 [29]	7 [41]	
Euthyroid multinodular goitre	7 [41]	4 [24]	
Graves' disease	1 [6]	1 [6]	
Hashimoto thyroiditis	1 [6]	0	
Thyroid malignancy	3 [18]	5 [29]	
Pre-operative serum calcium level (mmol/L)	2.36 [2.33–2.44]	2.39 [2.36–2.44]	0.32
Pre-operative serum i-PTH (pmol/L)	4.9 [3.6–6.75]	5 [3.7–6.45]	0.76
Specimen weight (g)	113 [59–177]	66 [42–117.5]	0.042

For continuous factors, the Mann-Whitney test was used whereas categorical factors were analysed using the Chi-squared test. Data are presented as median [IQR] or n [%]. i-PTH, intact parathyroid hormone; IQR, interquartile range.

Table 2 Result of the pre- and post-operative serum calcium levels, i-PTH levels and symptomatic hypocalcaemia

Primary objective	Participants (n=34)		P value
	Intervention (n=17)	Placebo (n=17)	
Serum calcium at 6 h (mmol/L)	2.33 (2.27–2.43)	2.37 (2.27–2.41)	0.59
Serum calcium at 24 h (mmol/L)	2.31 (2.25–2.38)	2.22 (2.16–2.31)	0.02
Serum calcium at 48 h (mmol/L)	2.26 (2.20–2.34)	2.23 (2.11–2.28)	0.19
Early hypocalcaemia			>0.99
No	17 (100.0)	16 (94.2)	
Yes	0	1 (5.8)	
Rescue intravenous calcium gluconate			>0.99
No	16 (100.0)	15 (93.8)	
Yes	0	1 (6.3)	
Post-operative serum i-PTH (pmol/L)	1.8 (0.5–3.6)	0.5 (0.5–2.55)	0.13

All the continuous variables were measured using the Mann-Whitney test. Categorical variables were measured using the Chi-squared test. Data are presented as median (IQR) or n (%). i-PTH, intact parathyroid hormone; IQR, interquartile range.

were 40% and 23%, in 2018 and 2019 respectively. With that, it raised our concern and interest to study more in the role of prophylactic intravenous calcium infusion on top of our usual practice of daily prophylactic oral calcium or vitamin D supplementation. This study was formulated by including the low-risk group of patients as they constitute the majority of cases in our centre and worldwide.

This is the first randomized controlled study to evaluate

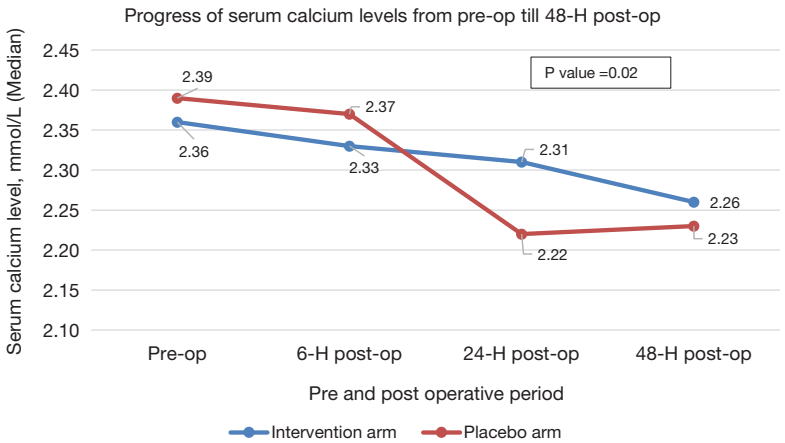

Figure 2 Illustrates the trends of serum calcium levels of both intervention and placebo arms from pre-operative till 48 hours post total thyroidectomy.

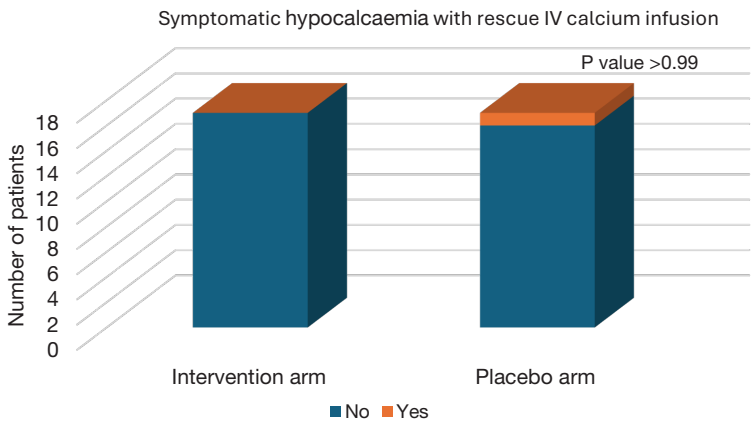

Figure 3 Illustrates the number of symptomatic hypocalcaemia with rescue IV calcium infusion for both intervention and placebo arm. IV, intravenous.

Table 3 Length of hospital stays after total thyroidectomy

Secondary objective	Participants (n=34)		P value
	Intervention (n=17)	Placebo (n=17)	
Length of hospital stay (days)	2 [2–3]	2 [2–3.5]	0.81

Continuous variables measured using the Mann-Whitney test. Data are presented as median [IQR]. IQR, interquartile range.

the role of prophylactic calcium infusion on top of routine oral calcium and vitamin D supplementation in reducing the rate of early symptomatic hypocalcaemia post total thyroidectomy. There were limited evidences on the role of prophylactic calcium infusion previously and limitations were observed in those studies. Hence, we designed this randomized controlled study to identify and remove the possible bias in which were present in the previous studies in order to improve the quality of results.

In comparison to the previous audit in the UMMC mentioned previously, the symptomatic hypocalcaemia rate in this study was only 2.9% only (1 out of 34 recruited participants) combining both groups. Multiple confounding factors were identified in the previous study such as multiple surgeons involved, study cohort included all patients who underwent elective and semi-elective total thyroidectomy cases (including high-risk cases such as neck dissection and patients with calcium or vitamin D supplementation as well), non-standardisation of post-operative oral calcium

and vitamin D supplementation, etc. However, in this present randomized controlled study, these confounding factors were identified during the phase of study proposal and reduced by excluded those high risk of hypocalcaemia patient.

For the primary outcome, the serum calcium level at post-operative 6 hours was not statistically significant between the two arms. However, for the serum calcium level at 24 hours post-operative, the intervention arm showed a much higher median serum calcium level as compared to the placebo arm and this reached statistical significance. For the serum calcium levels 48 hours post-operatively, the median level was also higher in the intervention arm as compared to the placebo arm. This could be explained by the fact that the prophylactic calcium infusion on top of the prescribed oral calcium and vitamin D supplements helped to maintain the serum calcium level higher than the placebo group, and hence theoretically prevented early hypocalcaemia postoperatively. We did not report the 12- and 36-hour postoperative serum calcium levels in this study as there were some missing data for this two particular time points of monitoring. This is due to the treating physician deciding to skip these two monitoring points in certain patients who showed persistently high normal serum calcium levels and with the anticipation that they will not develop hypocalcaemia within a short period of time.

In this study, only one patient in the placebo arm developed symptomatic hypocalcaemia and the patient required rescue intravenous calcium infusion too. None of the patients in the intervention arm developed symptomatic hypocalcaemia and none of them required rescue intravenous calcium infusion as well, but this did not reach statistically significance between the two groups. We conclude that prophylactic calcium infusion in a low-risk group of patients undergoing total thyroidectomy makes no difference in the rate of early hypocalcaemia when the surgery is in experienced hands.

Length of hospital stay can be indirectly affected by a few factors such as complications of surgery, comorbidities which require pre- and post-operative optimisation, logistic reason and of course the presence of early hypocalcaemia post total thyroidectomy. Hence, we decided to set the secondary objective as the length of hospital stay. No difference in the length of hospital stay after surgery was observed between both arms but this was already anticipated as the rate of symptomatic hypocalcaemia was similar in the two groups.

There are a few possibilities for the outcomes observed in terms of the primary and secondary objectives in this RCT. The main reasons may be because we excluded high-risk groups of patients, involvement of a single experienced endocrine surgeon and standardization of the post-operative oral calcium and vitamin D regime. Therefore, providing prophylactic oral calcium and vitamin D supplements may be adequate to prevent early hypocalcaemia rate in low-risk group of patients going for total thyroidectomy without neck dissection.

Regarding the limitation of this study, this is a single-centre study performed in a tertiary centre with an endocrine surgeon and hence, the surgical experiences and technique may not be directly extrapolated to other centres. However, this being randomized controlled study with only a single endocrine surgeon being involved, may have reduced the bias of inter-surgeon technique and experiences.

Secondly, if the recruited patient was admitted to the intensive care unit due to various reasons (underlying medical comorbid or serious postoperative complications), we are unable to follow the study protocol as the decision to monitor and correct the calcium level will be managed by the intensivist team. In addition, if hemithyroidectomy was being performed instead of total thyroidectomy because of recurrent laryngeal nerve injury, we will exclude the patient from the study and therefore unable to collect the data for analysis. Hence, it will lead to a deviation of protocol and the patient will need to be excluded from data analysis.

Conclusions

Routine prophylactic calcium infusion with oral calcium and vitamin D supplements have no role in reducing the rate of early symptomatic hypocalcaemia post total thyroidectomy in low-risk group. However, its usefulness needs to be further assessed in a larger scale multi-centre RCT incorporating bigger population.

Acknowledgments

The abstract of this study was presented in "The 18th Congress of the Asian Association of Endocrine Surgeons—AsAES 2023" as oral presentation.
Funding: None.

Footnote

Reporting Checklist: The authors have completed the

CONSORT reporting checklist. Available at https://gs.amegroups.com/article/view/10.21037/gs-24-190/rc

Trial Protocol: Available at https://gs.amegroups.com/article/view/10.21037/gs-24-190/tp

Data Sharing Statement: Available at https://gs.amegroups.com/article/view/10.21037/gs-24-190/dss

Peer Review File: Available at https://gs.amegroups.com/article/view/10.21037/gs-24-190/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-24-190/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are 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. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This trial has been approved by Medical Research Ethics of University Malaya Medical Centre (No. MECID-2020225-8316) and National Medical Research Register (No. NMRR-20-1085-55067). Written informed consent was obtained from all patients.

References

1. Chadwick D, Kinsman R, Walton P. Fifth national audit report of the British Association of Endocrine and Thyroid Surgeons. Henley-on-Thames, UK: Dendrite Clinical Systems Ltd., 2017:28-106.
2. Uruno T, Miyauchi A, Shimizu K, et al. A prophylactic infusion of calcium solution reduces the risk of symptomatic hypocalcemia in patients after total thyroidectomy. World J Surg 2006;30:304-8.
3. Xing T, Hu Y, Wang B, et al. Role of oral calcium supplementation alone or with vitamin D in preventing post-thyroidectomy hypocalcaemia: A meta-analysis. Medicine (Baltimore) 2019;98:e14455.
4. Hafez AT, El-Shakhs SAR, El-Najjar MM, et al. The role of intraoperative calcium injection for prevention of postoperative hypocalcaemia after total thyroidectomy. Menoufia Med J 2014;27:629-31.
5. 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.
6. Jaan S, Sehgal A, Wani RA, et al. Usefulness of pre- and post-operative calcium and Vitamin D supplementation in prevention of hypocalcemia after total thyroidectomy: A randomized controlled trial. Indian J Endocrinol Metab 2017;21:51-5.
7. Maxwell AK, Shonka DC Jr, Robinson DJ, et al. Association of Preoperative Calcium and Calcitriol Therapy With Postoperative Hypocalcemia After Total Thyroidectomy. JAMA Otolaryngol Head Neck Surg 2017;143:679-84.
8. Roh JL, Park JY, Park CI. Prevention of postoperative hypocalcemia with routine oral calcium and vitamin D supplements in patients with differentiated papillary thyroid carcinoma undergoing total thyroidectomy plus central neck dissection. Cancer 2009;115:251-8.
9. Edafe O, Prasad P, Harrison BJ, et al. Incidence and predictors of post-thyroidectomy hypocalcaemia in a tertiary endocrine surgical unit. Ann R Coll Surg Engl 2014;96:219-23.
10. Noureldine SI, Genther DJ, Lopez M, et al. Early predictors of hypocalcemia after total thyroidectomy: an analysis of 304 patients using a short-stay monitoring protocol. JAMA Otolaryngol Head Neck Surg 2014;140:1006-13.
11. Chen Z, Zhao Q, Du J, et al. Risk factors for postoperative hypocalcaemia after thyroidectomy: A systematic review and meta-analysis. J Int Med Res 2021;49:300060521996911.
12. Nair CG, Babu MJ, Menon R, et al. Hypocalcaemia following total thyroidectomy: An analysis of 806 patients. Indian J Endocrinol Metab 2013;17:298-303.
13. Wilson RB, Erskine C, Crowe PJ. Hypomagnesemia and hypocalcemia after thyroidectomy: prospective study. World J Surg 2000;24:722-6.
14. Besic N, Zagar S, Pilko G, et al. Influence of magnesium sulphate infusion before total thyroidectomy on transient

hypocalcemia – a randomised study. Radiol Oncol 2008;42:143-50.
15. Antakia R, Edafe O, Uttley L, et al. Effectiveness of preventative and other surgical measures on hypocalcemia following bilateral thyroid surgery: a systematic review and meta-analysis. Thyroid 2015;25:95-106.
16. Kwon YH, Lee KE, Kwon JY, et al. Preoperative parathyroid hormone level as a predictive factor for post-thyroidectomy hypoparathyroidism. Korean J Clin Oncol 2013;9:28-32.
17. Amir A, Sands NB, Tamilia M, et al. Preoperative serum calcium levels as an indicator of postthyroidectomy hypocalcemia. J Otolaryngol Head Neck Surg 2010;39:654-8.
18. Carvalho GB, Giraldo LR, Lira RB, et al. Preoperative vitamin D deficiency is a risk factor for postoperative hypocalcemia in patients undergoing total thyroidectomy: retrospective cohort study. Sao Paulo Med J 2019;137:241-7.
19. Jan BS, Alamri AH, Alkaff HH, et al. Risk factors for postoperative hypocalcemia following total thyroidectomy: a retrospective study. Ann Saudi Med 2024;44:39-47.

Cite this article as: Khoo KS, Yeo A, Mirzan Asfian MRB, Ng KL. The use of prophylactic infusion of calcium gluconate compared to placebo in reducing the rate of early hypocalcaemia after total thyroidectomy: a double-blinded, randomized controlled trial. Gland Surg 2024;13(8):1378-1386. doi: 10.21037/gs-24-190