Annals of Medicine and Surgery 66 (2021) 102417

Contents lists available at ScienceDirect

Annals of Medicine and Surgery

journal homepage: www.elsevier.com/locate/amsu

Cross-sectional Study

Hypocalcemia following total and subtotal thyroidectomy and associated factors☆

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ARTICLE INFO

Keywords:
Thyroidectomy
Endocrinological
Hypocalcemia
Subtotal
Surgery

ABSTRACT

Background: Thyroidectomy is one of the common endocrinological surgeries for the treatment of thyroid disorders. Hypocalcemia is the potential complication after thyroidectomy, where is persistency can lead to serious systemic effects. The aim of this study is to evaluate the incidence of hypocalcemia in thyroidectomy patients.
Methods: In this cross-sectional study, patients referred to (XXX) for thyroidectomy from 2019 to 2020 were enrolled. Preoperative serum calcium and postoperative 24- and 48-h calcium levels were evaluated in these patients. Demographic data (sex and gender), calcium levels, type of thyroidectomy and duration of surgery was recorded for all the patients. SPSS v22 was used for statistical analysis. $P < 0.05$ was considered as statistically significant.
Results: Of 143 patients included in the study, the mean age was 49.7 ± 10.9 years and 61.5% were females and 38.5% were males. 49% patients had hypocalcemia in the first 24 hours after surgery and 63.6% following 48 hours of the surgery. The difference in calcium levels at three intervals were statistically significant, $p = 0.001$. The incidence of hypocalcemia was significantly more in women at 48 postoperative hours, $p = 0.025$. The age and duration of surgery was not significantly correlated with hypocalcemia, $p > 0.05$, whereas, patients who underwent total thyroidectomy had greater incidence of hypocalcemia 24 hours after the surgery, $p = 0.021$.
Conclusions: The incidence of hypocalcemia is greater in total thyroidectomy and female patients. Our study did not report significant correlation between duration of the surgery and age of the patients.

1. Introduction

Thyroidectomy is one of the most common surgeries with low morbidities [1], which is related to the skill and experience of the surgeon [2]. Because thyroid surgery is performed in an area with a complex anatomy, nerves, glands and surrounding vessels are at risk of damage [3,4]. Complications after thyroidectomy could be anatomic like recurrent laryngeal nerve injury, bilateral recurrent nerve paralysis, cervical hematoma and/or endocrine like hypoparathyroidism, myxedema and hypocalcemia [5,6].

According to British Association of Endocrine and Thyroid Surgeons report, incidence of transient and permanent hypocalcemia after thyroidectomy is 27.4% and 12.1%, respectively [7]. Injury of parathyroid gland or devascularization is known etiology of hypocalcemia after the procedure [8,9]. Persistent hypothyroidism after the surgery is associated with decrease in calcium levels [10]. Hypocalcemia can lead to neuromuscular and psychological dysfunction [11]. Long-term hypocalcemia is associated with cardiac arrythmias and intracranial lesions [12,13]. Symptomatic hypocalcemia is usually seen 24–48 hours after the surgery. In order to prevent hypocalcemia, prolonged hospitalization and further complications, calcium and vitamin D are usually given as supplements preoperatively or postoperatively [14]. In order to avoid the excessive intake of these supplements, prediction of factors that can lead to hypocalcemia is significant [15].

In a recent study conducted at Centers of Al-Zahra and Kashani hospitals in Iran, the incidence of hypocalcemia after thyroidectomy was reported to be 54.4%. It was the most common complication in these patients. Therefore, the aim of this study is to determine the incidence of hypocalcemia among total and subtotal thyroidectomy patients and factors associated with it.

☆ This study was approved by the Research Ethics Board of Lorestan University of Medical Sciences.

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https://doi.org/10.1016/j.amsu.2021.102417
Received 30 April 2021; Received in revised form 15 May 2021; Accepted 16 May 2021
Available online 25 May 2021

2. Methods

In this cross-sectional study, thyroid patients who were referred to (XXX) between 2018 and 2019 were included for whom thyroidectomy was indicated. Serum calcium levels of these patients were obtained after the surgery. Written consent was obtained from all the patients for the participation in the study. Patients with the history of hypercalcemia or hypocalcemia, those undertaking calcium supplements, kidney dysfunction, vitamin D deficiency, orthopedic abnormalities and those who did not consent to participate in the study were excluded from the study.

To calculate the sample size of the study, using the prevalence of hypocalcemia as 0.03, d = 0.075 and N = 143 in the following formula:

$$n= (Z_{1-}\ \alpha/2)^2 * p(1-p)\ d^2$$

The data required in this study includes the duration of thyroidectomy, calcium levels of patients before the surgery and 24 and 48 hours after surgery and age and sex of patients. Hypocalcemia was not treated until before 48th-hour testing.

At the beginning of the surgery, the duration of the surgery was measured and recorded using a timer from the onset of anesthesia to the patient's recovery. The surgery was performed by the same surgeon in all the cases and serum calcium levels (normal range: 8.6–10.3 mg/dL) were measured using Pars Azmoon kits (Tehran, Iran) as per the protocol provided.

The data obtained were computerized and statistically analyzed using SPSS v22 using descriptive (mean, standard deviation, tables and graphs) and analytical statistics. The calcium levels at three different intervals were analyzed using ANOVA analysis of variance. Due to the lack of sphericity in repeated ANOVA measure, Greenhouse-Geisser was used. The relations of hypocalcemia with dependent) duration of surgery) and independent (gender and age) were evaluated using Chi-square test. P-value<0.05 was considered to statistically significant.

This study was approved by the Research Ethics Board of Lorestan University of (XXX).

The work has been reported in line with the STROCSS criteria [16].

Unique identifying number (UIN) of your study. Researchregistry6776.

3. Results

A total of 143 patients underwent thyroidectomy in this study where the mean age of the patients was 49.7 ± 10.9 years (20–80 years). Of total, 55 were male (38.5%) and 88 were female (61.5%). Other clinical and demographic characteristics of patients are shown in Table 1.

81.1% of thyroid surgeries were total thyroidectomy and 18.9% were subtotal thyroidectomy. Hypocalcemia in the first 24 hours after surgery were seen in 49% of patients and in 63.6% patients following 48 hours of the surgery. The mean preoperative calcium levels were 8.8 ± 0.5 mg/dL whereas serum calcium after 24 and 48 hours of the surgery was 8.5 ± 0.49 mg/dL and 8.3 ± 0.47 mg/dL, respectively. The difference in serum calcium at three intervals were significantly different, p = 0.001 (Fig. 1). Common clinical symptoms among patients presented with hypocalcemia were numbness and tingling in their fingertips, toes, and the perioral region and fatigue. These were seen in 23% patients following 24 hours of the surgery and in 38% patients on 48-postoperative hour.

Table 1
Frequency distribution of demographic and clinical characteristics of the subjects.

	Properties	Number	Percent	cumulative percentage
Age	40 ≥	31	21.7	21.7
	41–60	87	60.8	82.5
	60<	25	17.5	100
Type of surgery	total thyroidectomy	116	81.1	81.1
	subtotal thyroidectomy	27	18.9	100
Hypocalcemia in the first 24 hours after surgery	Positive	70	49	49
	Negative	73	51	100
Hypocalcemia in the first 48 hours after surgery	Positive	91	63.6	63.6
	Negative	52	36.4	100
Total		143	100	

The incidence of hypocalcemia was more in women 24 hours after the surgery, compared to men however the difference was not statistically significant, p = 0.121. At 48 postoperative hours, women were significantly more hypocalcemic compared to men, p = 0.025, Table 2.

Although the incidence of hypocalcemia was higher at the age of 60 years, but no significant relationship was observed between age and the incidence of hypocalcemia at 24 and 48 postoperative hours, p = 0.167 and p = 0.26, respectively. Hypocalcemia was significantly more in total thyroidectomy patients relative to subtotal thyroidectomy patients, 24 hours after the surgery, p = 0.021(Fig. 2). At 48 postoperative hours, this difference was not significantly different, p = 0.37(Fig. 3). The duration of the surgery, less than 120 minutes and more than 120 minutes was not associated significantly with the incidence of hypocalcemia at 24 and 48 postoperative hours, p = 0.41 and p = 0.45, respectively, Table 2.

4. Discussion

The outcomes of the study showed that total thyroidectomy is performed more than subtotal thyroidectomy at our center. The mean calcium levels in patients decreased significantly and 24 hours after the surgery and decreased further at 48 postoperative hours. The incidence of hypocalcemia was significantly more in total thyroidectomy patients. A recent systematic and meta-analysis conducted by Bai et al. [17] 35 studies concluded that total thyroidectomy is one of the significant predictors of hypocalcemia after thyroidectomy.

Our study showed that age is not associated with incidence of post-thyroidectomy hypocalcemia. greater than 60 is associated with greater incidence of hypocalcemia following thyroidectomy. A prospective study by Sousa et al. [15] including 333 patient reported that age greater 50 years is a significant predictor of hypocalcemia after thyroidectomy, along with total thyroidectomy and increased operation time. Our study did not report a significant correlation between the operation time and hypocalcemia in these patients. Ambe et al. [18] conducted single center study on 305 thyroidectomy patients also reported that prolonged surgery, greater than 120 minutes, is not associated with hypocalcemia and other complications after thyroidectomy. Baldassarre et al. [19] evaluated the predictors of hypocalcemia after thyroidectomy in 6,605 patients from the nationwide inpatient sample databases. The study indicated that female gender, thyroid neoplasm and total thyroidectomy were significant risk factors. Our study showed that at female gender was associated greater incidence of hypocalcemia at 48 hours at the surgery. In a retrospective study conducted on 304 patients, Noureldine, et al. [20] also reported that female gender is a significant predictor of postoperative hypocalcemia. This could be because the risk of vitamin D and calcium deficiency is more in females [21,22].

Our study did not distinguish between mild and significant hypocalcemia (long term requirement of calcium supplements in patients to stay normocalcemic). Additionally, type of thyroid disease, transient or permanent hypocalcemia and other biochemical parameters like vitamin D, serum magnesium and parathyroid hormone were not evaluated in the study.

During the study, patients had difficulty in addressing the symptoms of hypocalcemia like tingling, muscle spasm and fatigue. A detailed explanation was provided by the researchers to overcome this challenge.

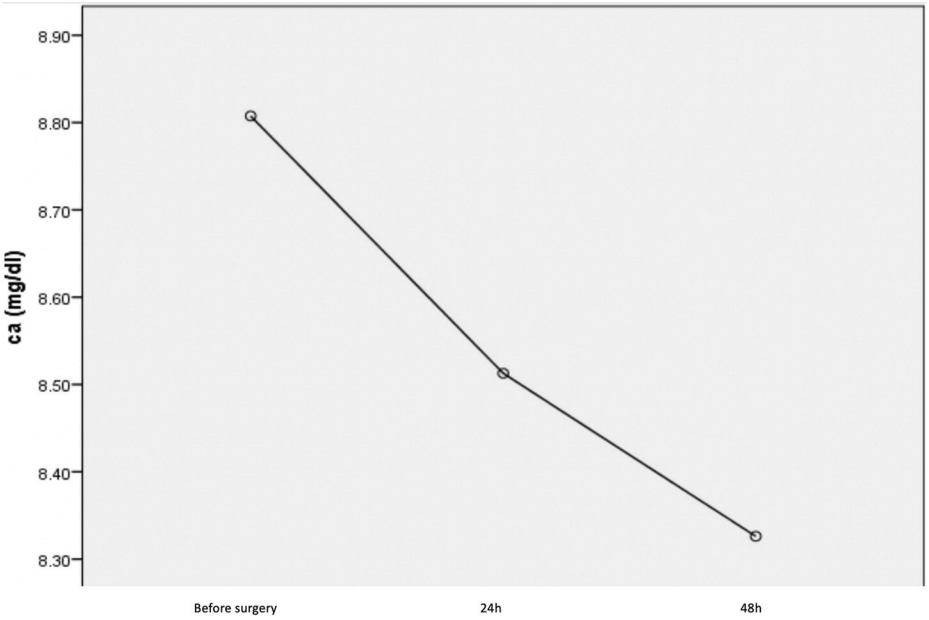

Fig. 1. Comparison of mean calcium at three distinct times.

Table 2
Investigating the relationship between variables.

Properties		Hypocalcemia in the first 24 hours after surgery		p-value	Hypocalcemia in the first 48 hours after surgery		p-value
		Positive	Negative	0.121	Positive	Negative	0.025
Sex	Male	23(41.8%)	32(58.2)		29(52.7%)	26(47.3%)	
	Female	47(53.4%)	41(46.6%)		62(70.5%)	26(29.5%)	
Age	40 ≥	12(38.7%)	19(61.3%)	0.167	17(54.8%)	14(45.2%)	0.26
	41–60	42(48.3%)	45(51.7%)		55(63.2%)	32(36.8%)	
	60<	16(64%)	9(36%)		19(76%)	6(24%)	
Type of surgery	total thyroidectomy	62(53.4%)	54(46.6%)	0.021	75(64.7%)	41(35.3%)	0.37
	Near-total thyroidectomy	8(29.6%)	19(70.4%)		16(59.3%)	11(40.7%)	
Duration of surgery	120min>	5(41.7%)	7(58.3%)	0.41	7(58.3%)	5(41.7%)	0.45
	120min<	65(49.6%)	66(50.4)		84(64.1%)	47(35.9%)	

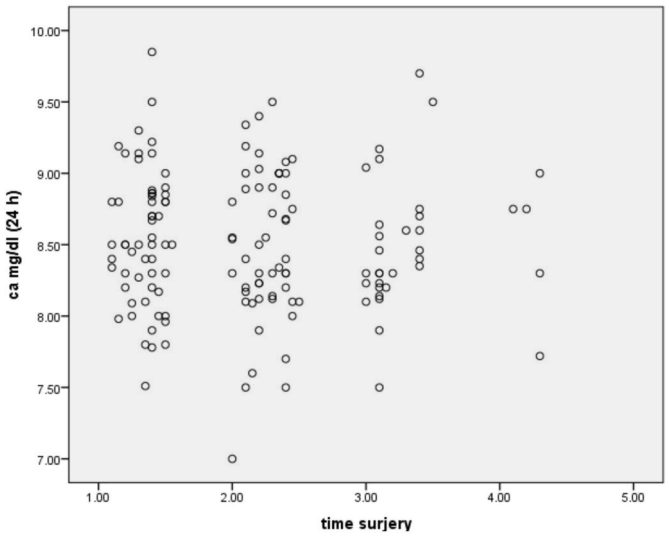

Fig. 2. Distribution chart of the relationship between calcium and duration of surgery in the first 24 hours after surgery.

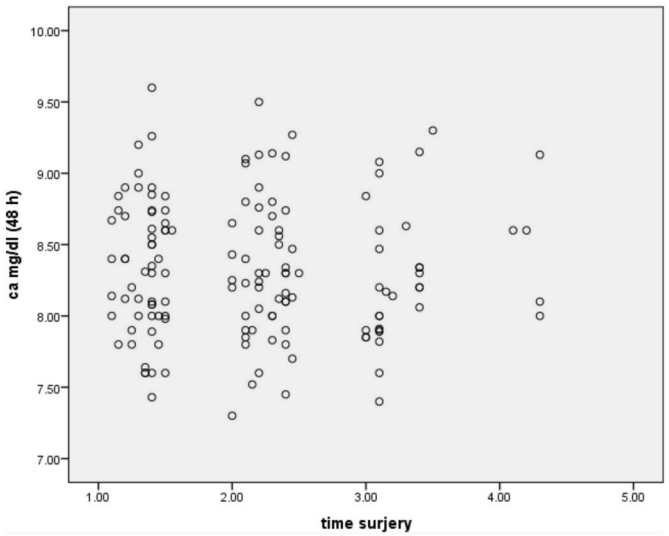

Fig. 3. Distribution chart of the relationship between calcium and the duration of surgery in the first 48 hours after surgery.

5. Conclusion

The results of our study showed that duration of the surgery and age might not be significant to predict the incidence of hypocalcemia after thyroidectomy however, female gender, and total thyroidectomy is likely to increase the risk of hypocalcemia in these patients. These factors should be considered in deciding postoperative prevention and/or management of hypocalcemia. Further studies are suggested in this domain to include these parameters with greater sample size, biochemical analysis and obtaining data from multiple centers. We recommend that female patients undergoing total thyroidectomy should be considered for hypocalcemia testing.

Availability of data and material

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Funding source

No funding was secured for this study.

Ethical approval

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Sources of funding

No funding was secured for this study.

Contributors' statement page

Dr.Morteza Azadbakht: conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. Dr. Saleh Azadbakht: Designed the data collection instruments, collected data, carried out the initial analyses, and reviewed and revised the manuscript. Dr.Seyed Mostafa Emadi-jamali: Coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content.

Consent

Not applicable.

Registration of Research Studies

Name of the Registry: Lorestan University of Medical Sciences.

Unique Identifying number or registration ID: IR.LUMS.REC.1397.084.

Hyperlink to the registration (must be publicly accessible): https://ethics.research.ac.ir/ProposalCertificateEn.php?id=27119&Print=true&NoPrintHeader=true&NoPrintFooter=true&NoPrintPageBorder=true&LetterPrint=true.

Guarantor

Morteza Azadbakht.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Declaration of competing interest

The authors deny any conflict of interest in any terms or by any means during the study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2021.102417.

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