The role of perioperative vitamin D measurement after total thyroidectomy as a predictor of hypocalcemia

Original Article

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ABSTRACT

Background: Temporary hypocalcemia, a common occurrence after total thyroidectomy, affects up to 35% of patients, presenting mild to severe symptoms such as paresthesia, tingling, cramps, tetany, and convulsion.

Aim: To discuss the relation between vitamin D and postoperative hypocalcemia in patients undergoing total thyroidectomy and to determine the optimal vitamin D threshold level to reduce hypocalcemia risk, enabling judicious and goal-directed vitamin D replacement.

Patients and Methods: This prospective study was conducted on 200 patients with hypocalcaemia underwent total thyroidectomy in Kasr El-Ainy University Hospitals, Faculty of Medicine, Cairo University from 2023.

Results: Age, female patients, alkaline phosphatase, and hospital stay were significantly higher in patients who developed postoperative Ca less than or equal to 8 mg/dl than those who developed postoperative Ca greater than 8 mg/dl (*P<0.001*). Preoperative and postoperative Ca and preoperative 25-hydroxyvitamin D (OHD) were significantly lower in patients who developed postoperative Ca less than or equal to 8 mg/dl than those who developed postoperative Ca greater than 8 mg/dl (*P<0.001*). Albumin and creatinine were insignificantly different between patients who developed postoperative Ca less than or equal to 8 mg/dl and those who developed postoperative Ca greater than 8 mg/dl.

Conclusion: Patients who developed postoperative hypocalcemia had significantly lower preoperative 25-OHD levels compared to those who did not develop hypocalcemia. Additionally, older age and female sex were identified as risk factors for postoperative hypocalcemia. The study also demonstrated a positive correlation between postoperative calcium levels and preoperative 25-OHD levels, suggesting that adequate vitamin D status may play a protective role against postoperative hypocalcemia.

Key Words: Hypocalcemia, total thyroidectomy, vitamin D.

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INTRODUCTION

Up to 35% of patients may experience temporary hypocalcemia after a complete thyroidectomy; symptoms can range from moderate paresthesia and tingling to more severe cramping, tetany, and convulsions[1].

Following a thyroidectomy, hypocalcemia might result in additional expenses such as an extended hospital stay, more medications, more outpatient appointments, and more blood tests[2].

An increased risk of hypocalcemia is linked to several variables, such as advanced age and Graves' disease. Surgical technique, high surgical volume, and the expertise of the surgeon are more significant factors since they have been demonstrated to reduce the risk. In addition to being proposed as a risk factor for Graves' disease, vitamin D insufficiency has recently been demonstrated to be an independent risk factor for hypocalcemia following complete thyroidectomy for benign goiters[3].

Because vitamin D receptors are found throughout the body, concern about the potential health effects of vitamin D deficiency has grown. Defects in lipid metabolism, diabetes, cancer, heart disease, and bone disease have all been linked to vitamin D insufficiency[4].

If a connection could be shown between low levels of vitamin D and the likelihood of hypocalcemia following surgery for any type of thyroid condition, this would be a low-cost and readily manageable risk factor that could be taken care of prior to surgery[5,6]. In order to provide vitamin D replacement in a prudent, goal-directed manner, the purpose of this work was to investigate the relationship between vitamin D and postoperative hypocalcemia in patients undergoing total thyroidectomy and to identify an appropriate vitamin D threshold level at which the risk of hypocalcemia is increased.

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PATIENTS AND METHODS:

This prospective study was conducted on 200 patients with hypocalcaemia underwent total thyroidectomy in Kasr El-Ainy University Hospitals, Faculty of Medicine, Cairo University from 2023

Inclusion criteria: Primary total thyroidectomy, age from 17 to 70 years and both sexes.

Exclusion criteria: Previous thyroid and parathyroid surgeries, preoperative Hypoparathyroidism and renal impairment.

Confidentiality of data: All study-related information will be stored securely at the study site.

All participant information will be stored in locked file cabinets in areas with limited access.

Participants' study information will not be released outside the study without written permission from participant.

Methods

Following data were collected: Patient demographics including age, sex, type of goiter, associated co-morbidities, null parity, previous surgeries, autoimmune pathology, symptoms and signs of hypocalcemia, investigations was done as s. calcium, vitamin D and [parathyroid hormone (PTH) as exclusion criteria].

Study outcomes

Primary outcome

Share the results of the multicenter research on the relation between vitamin D level and hypocalcemia after total thyroidectomy.

Secondary outcomes

Identify the potential cause of the hypocalcemia after total thyroidectomy and see if any of the following can predict how long it will take for it to resolve:

RESULTS:

Age ranged from 24 to 65 years with a mean±SD of 45.55±11.54 years. There were 129 (64.5%) males and 71 (35.5%) females (Table 1).

Ca and PTH were significantly lower postoperative than preoperative (*P<0.001*) (Table 2).

Fifty-three (26.5%) patients had postoperative Ca less than or equal to 8 mg/dl while 147 (73.5%) patients had postoperative Ca greater than 8 mg/dl (Table 3).

The length of hospital stay ranged from 1 to 8 days with a mean±SD of 2.57±2 days (Table 4).

Age, female patients, alkaline phosphatase (ALP), and hospital stay were significantly higher in patients who developed postoperative Ca less than or equal to 8 mg/dl than those who developed postoperative Ca greater than 8 mg/dl (*P<0.001*).

Preoperative and postoperative Ca and preoperative 25-hydroxyvitamin D (OHD) were significantly lower in patients who developed postoperative Ca less than or equal to 8 mg/dl than those who developed postoperative Ca greater than 8 mg/dl (*P<0.001*). Albumin and creatinine were insignificantly different between patients who developed postoperative Ca less than or equal to 8 mg/dl and those who developed postoperative Ca greater than 8 mg/dl (Table 5).

Age, female patients, and ALP were significantly higher in patients who had preoperative 25-OHD less than or equal to 15 ng/ml than those who had preoperative 25-OHD greater than 15 ng/ml (*P<0.001*). Postoperative Ca was significantly lower in patients who had preoperative 25-OHD less than or equal to 15 ng/ml than those who had preoperative 25-OHD greater than 15 ng/ml (*P<0.001*). Albumin and creatinine were insignificantly different between patients who had preoperative 25-OHD less than or equal to 15 ng/ml and those who had preoperative 25-OHD greater than 15 ng/ml (Table 6).

There was a significant positive correlation between postoperative Ca and preoperative 25-OHD (r=0.636, *P<0.001*). There was a significant negative correlation between postoperative Ca and Age (r=-0.488, *P<0.001*) and ALP (r=-0.688, *P<0.001*). There was an insignificant correlation between postoperative Ca and albumin and creatinine (Table 7).

Table 1: Demographic data of the studied patients

	n=200
Age (years)	
Mean±SD	45.55±11.54
Range	24–65
Sex, *n* (%)	
Male	129 (64.5)
Female	71 (35.5)

Table 2: Comparison between preoperative and postoperative Ca and PTH

	Preoperative	Postoperative	*P* value
Ca (mg/dl)			
Mean±SD	8.98±0.77	8.43±0.77	<0.001*
Range	7.2–10.3	6.8–9.6	
PTH (pg/ml)			
Mean±SD	37.42±14.98	27.77±14.98	<0.001*
Range	13–65	3–58	

PTH, parathyroid hormone.
*Significant as *P value ≤0.05*.

Table 3: Incidence of hypocalcemia of the studied patients

	Preoperative	Postoperative	*P* value
Ca (mg/dl)			
Mean±SD	8.98±0.77	8.43±0.77	<0.001*
Range	7.2–10.3	6.8–9.6	
PTH (pg/ml)			
Mean±SD	37.42±14.98	27.77±14.98	<0.001*
Range	13–65	3–58	

Table 4: Hospital stay of the studied patients

	n=200
Hospital stay (days)	
Mean±SD	2.57±2
Range	1–8

Table 5: Patients' data according to postoperative hypocalcemia

	Ca ≤8 mg/dl (*n*=53)	Ca >8 mg/dl (*n*=147)	*P* value
Age (years)			
Mean±SD	56.92±6.06	41.45±10.22	<0.001*
Range	45–65	24–60	
Sex, *n* (%)			
Male	14 (26.42)	115 (78.23)	<0.001*
Female	39 (73.58)	32 (21.77)	
Albumin (g/dl)			
Mean±SD	4.43±0.41	4.3±0.47	0.091
Range	3.5–5.1	3.5–5.1	
Creatinine (mg/dl)			
Mean±SD	0.9±0.16	0.91±0.15	0.558
Range	0.7–1.1	0.7–1.1	
ALP (U/l)			
Mean±SD	276.17±57.78	134.51±36.25	<0.001*
Range	185–370	71–200	
Preoperative Ca (mg/dl)			
Mean±SD	7.95±0.4	9.36±0.47	<0.001*
Range	7.2–8.8	8.4–10.3	
25-OHD (ng/ml)			
Mean±SD	10.21±6.97	35.11±10.68	<0.001*
Range	1–23.8	15.7–53	
25-OHD, *n* (%)			
≤15 ng/ml	40 (75.47)	0	<0.001*
>15 ng/ml	13 (24.53)	147 (100)	
Postoperative Ca (mg/dl)			
Mean±SD	7.37±0.36	8.81±0.45	<0.001*
Range	6.8–8	8.1–9.6	
Hospital stay (days)			
Mean±SD	5.3±2.06	1.59±0.49	<0.001*
Range	2–8	1–2	

ALP, alkaline phosphatase; OHD, hydroxyvitamin D.
*Significant as *P value ≤0.05*.

Table 6: Patients' data according to preoperative serum 25-OHD level

	25-OHD ≤15 ng/ml (*n*=40)	25-OHD >15 ng/ml (*n*=160)	*P* value
Age (years)			
Mean±SD	56.7±5.95	42.76±10.9	<0.001*
Range	45–65	24-64	
Sex, *n* (%)			
Male	9 (22.5)	120 (75)	<0.001*
Female	31 (77.5)	40 (25)	
Albumin (g/dl)			
Mean±SD	4.42±0.42	4.32±0.46	0.188
Range	3.5–5.1	3.5–5.1	
Creatinine (mg/dl)			
Mean±SD	0.88±0.16	0.92±0.15	0.193
Range	0.7–1.1	0.7–1.1	
ALP (U/l)			
Mean±SD	282±60.22	144.56±50.24	<0.001*
Range	188–370	71–323	
Postoperative Ca (mg/dl)			
Mean±SD	7.41±0.34	8.69±0.62	<0.001*
Range	6.8–8	6.8–9.6	
Postoperative Ca, *n* (%)			
≤8 mg/dl	40 (100)	13 (8.13)	<0.001*
>8 mg/dl	0	147 (91.88)	

ALP, alkaline phosphatase; OHD, hydroxyvitamin D.
*Significant as *P value ≤0.05*.

Table 7: Correlation between postoperative Ca and other data of the studied patients (n=200)

	Postoperative Ca (mg/dl)	
	r	*P* value
Age (years)	–0.488	<0.001*
Albumin (g/dl)	–0.077	0.279
Creatinine (mg/dl)	0.067	0.347
ALP (U/l)	–0.688	<0.001*
25-OHD (ng/ml)	0.636	<0.001*

ALP, alkaline phosphatase; OHD, hydroxyvitamin D; r, correlation coefficient.
*Significant as *P value ≤0.05*.

DISCUSSION

In this study, age of the studied patients ranged from 24 to 65 years with a mean±SD of 45.55±11.54 years. There were 129 (64.5%) males and 71 (35.5%) females. Age was significantly higher in patients who developed postoperative Ca less than or equal to 8 mg/dl than those who developed postoperative Ca greater than 8 mg/dl (*P<0.001*).

This is in line with the findings of Erbil *et al*.[7], who looked at the age prediction value for postoperative hypocalcemia following complete and nearly total thyroidectomies. They discovered that postoperative hypocalcemia was substantially correlated with advanced age.

This is at odds with the findings of Rubin *et al*.[8], who demonstrated that in this group, age is a significant predictor of postoperative hypocalcemia, with younger patients having a higher risk of postoperative hypocalcemia than older patients (41.2 6 14.0 vs. 47.9 6 14.1 years, *P=0.01*). These contradictory results can be the result of variations in the surgical techniques or research populations.

This is also at odds with a study by Baldassarre *et al*.[9] that used a nationwide inpatient sample

(n=119 567 patients) and included patients undergoing thyroidectomies between 1998 and 2008. The study showed that patients older than 45 years old had a significantly lower risk of postoperative hypocalcemia than younger people.

In our study, female patients were significantly higher in patients who developed postoperative Ca less than or equal to 8 mg/dl than those who developed postoperative Ca greater than 8 mg/dl (*P<0.001*).

This is in line with the findings of Bove *et al*.[10], who said that the distribution of women across the two groups is one of the other important statistics that came out of their investigation. The proportion of hypocalcemic women has significantly increased (*P<0.05*) as compared to the remaining normocalcemic women. Despite the fact that the result was not statistically significant (*P>0.05*), their logistic regression analysis revealed that having a female partner raised the chance of postoperative hypocalcemia by five times.

In this study, Ca and PTH were significantly lower postoperative than preoperative (*P<0.001*).

In accordance, Metere *et al*.[11] who aimed to investigate serum PTH values 3 h after thyroidectomy as a predictor of hypocalcemia. They reported that, within 24 h after total thyroidectomy, 53 patients (37.6%) showed a reduction in serum PTH (*P<0.001*).

In contrast, Seo *et al*.[12] who aimed to evaluate early predictive factors and long-term changes in intact parathyroid hormone (iPTH) levels in patients with transient and permanent hypocalcemia after total thyroidectomy. They found no difference in serum Ca levels 1 month after surgery between patients with transient and permanent hypocalcemia. This implies that calcium levels did not differ significantly between these two groups at 1 month postoperatively.

According to our study, postoperative Ca was significantly lower ≤8 mg/dl in patients who had preoperative 25-OHD less than or equal to 15 ng/ml than those who had preoperative 25-OHD greater than 15 ng/ml (*P<0.001*). There was a significant positive correlation between postoperative Ca and preoperative 25-OHD (r=0.636, *P<0.001*). There was a significant negative correlation between postoperative Ca and Age (r=-0.488, *P<0.001*) and ALP (r=-0.688, *P<0.001*). There was an insignificant correlation between postoperative Ca and albumin and creatinine.

In accordance, Erbil *et al*.[7] showed that there were negative connections between the blood calcium level and age and the serum alkaline phosphatase level, whereas a positive association was discovered between the serum calcium level and the serum 25-OHD level.

This is consistent with the findings of Rubin *et al*.[8], who demonstrated a strong correlation between postoperative hypocalcemia (12.0 ng/ml) and low perioperative 25(OH)D levels in comparison to normocalcemia (27.5 ng/ml).

This also agrees with Bove *et al*.[10] who reported that, found that serum preoperative vitamin D levels were significantly lower in the group of patients who developed hypocalcemia (19.57 [(7.10–24.84) ng/ml] compared to normocalcemic patients [28.7 (23.5–40.5) ng/ml] (*P=0.012*).

In our study, hospital stay (from 3 to 8 days) was significantly higher in patients who developed postoperative Ca less than or equal to 8 mg/dl than those who developed postoperative Ca greater than 8 mg/dl (*P<0.001*).

This agrees with Rubin *et al*.[8] who reported that, subjects who were hypocalcemic experienced a significantly longer hospital stay (2.9±2.5 vs. 1.4±1.1 days, *P<0.01*). They also suggested that perioperative treatment of low vitamin D status may lead to decreased incidence of transient post thyroidectomy hypocalcemia, resulting in decreased hospital length of stay and ultimately reducing the financial burden on health care entities.

In our study, age was significantly higher in patients who had preoperative 25-OHD less than or equal to 15 ng/ml than those who had preoperative 25-OHD greater than 15 ng/ml (*P<0.001*).

Erbil *et al*.[7] found that aging was a significant risk factor for vitamin D insufficiency. Changes in vitamin D metabolism are linked to aging. Research has shown that (1) the activity of renal 1-hydroxylase and intestinal calcium absorption diminish with age, and (2) the amount of 7-dehydrocholesterol that accumulates on the skin decreases with age. This cholesterol is transformed into previtamin-D3 by solar UV radiation.

CONCLUSION

Patients who developed postoperative hypocalcemia had significantly lower preoperative 25-OHD levels compared to those who did not develop hypocalcemia. Additionally, older age and female sex were identified as risk factors for postoperative hypocalcemia. The study also demonstrated a positive correlation between postoperative calcium levels and preoperative 25-OHD levels, suggesting that adequate vitamin D status may play a protective role against postoperative hypocalcemia. Furthermore, the results indicate that a preoperative 25-OHD level of 15 ng/ml or lower was associated with an increased risk of postoperative hypocalcemia and longer hospital stay.

CONFLICT OF INTEREST

There are no conflicts of interest.

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