Post-thyroidectomy Hypocalcemia and Pre-operative Vitamin D Levels

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Abstract

Background: Post-operative transient hypocalcemia is a common event after total thyroidectomy. It may reveal permanent hypoparathyroidism following total or subtotal thyroidectomy. It has been hypothesized that there is a relationship between underlying vitamin D deficiency and the risk of post-operative hypocalcemia.

Methods: We performed a cross-sectional review on 100 thyroidectomies from 2016 at an academic teaching hospital. Pre-operative vitamin D levels and post-operative calcium level were obtained. The incidence of hypocalcemic symptoms was studied. Biochemical hypocalcemia was defined as any single post-operative corrected calcium level < 8.0 mg/dl (to convert to millimoles per liter, multiply by 0.25).

Results: Post-operative calcemia < 8.0 mg/dl was observed in 19 patients (19%). We found that the patients carried a high risk for post-operative transient biochemical hypocalcemia if the pre-operative serum vitamin D levels < 35 nmol/l. There was a significant differentiation between mean of vitamin D levels in hypocalcemic group and normocalcemic group.

Conclusions: Pre-operative vitamin D levels appear to have a significant effect on the risk of post-thyroidectomy hypocalcemia.

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Introduction

While a variety of improvements in surgical technique are protective of post-operative complications following thyroid surgery, significant and permanent hypoparathyroidism following total or subtotal thyroidectomy is of greater clinical concern. Patients after total thyroidectomy are at risk of post-operative hypocalcemia (affecting 0.3-49% of patients after total thyroidectomy) (1). In the setting of acute transient hypocalcemia, despite the fact that it is self-limiting in most patients, rapid treatment may be necessary. Hypocalcemia can be either temporary (fewer than 6 months). Unfortunately, 0-13% of these patients needs to prolonged hospital stay and close monitoring of serum calcium (s-Ca) levels or treatment with calcium and vitamin D supplements for years after thyroidectomy (1.5-4 percent) (2).

There are no validated criteria that can predict with patients will develop post-thyroidectomy hypocalcemia (3). Monitoring intra- and post-operative parathyroid hormone (PTH) levels is expensive approach and may be using in patients at high risk for severe and prolonged hypocalcemia and cannot be wider clinical use (4).

Short- and long-term post-thyroidectomy parathyroid failure presents as three different metabolic syndromes: (I) Post-operative hypocalcemia is defined as a s-Ca < 8 mg/dl (< 2 mmol/l) within 24 hours after surgery requiring calcium/vitamin D replacement therapy at the time of hospital discharge (which one we studied); (II) protracted hypoparathyroidism as a subnormal intact PTH (iPTH) concentration (< 13 pg/ml) and/or need for calcium/vitamin D replacement at 4-6 weeks; (III) permanent hypoparathyroidism as a subnormal iPTH concentration (< 13 pg/ml) and/or need for calcium/vitamin D replacement 1 year after total thyroidectomy. Each of these syndromes has its own pattern of recovery and should be approached with different therapeutic strategies (5,6).

In Iran at the time of this study, there is no any other research about post-thyroidectomy hypocalcemia and pre-operative vitamin D levels done, but the reported incidence of temporary hypocalcemia following thyroid surgery ranges widely, from 1.6% to 50% (7-10). In this longitudinal study, we checked pre-operative serum vitamin D level < 35 nmol/l and s-Ca < 8 mg/dl (< 2 mmol/l) within 24 hours after surgery to determine the risk factors as well as the prevalence of post-operative hypocalcemia in a sample of thyroidectomies patients.

This study has two major objectives: (i) To estimate the prevalence of post-operative hypocalcemia among patients with total thyroidectomy surgery and (ii) to

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determine what factors are associated with hypocalcemia in this population. The results of this study will provide clinicians with a summary of the current knowledge on whether early (< 24 hours) post-operative s-Ca level, level of pre-operative vitamin D, age or sex is an independent risk factor for transient post-operative hypoparathyroidism. It was hypothesized that the prevalence of post-operative hypocalcemia in patients after thyroidectomy with low serum vitamin D levels would be higher rates than other population, and these patients have special needs.

Materials and Methods

Population: This longitudinal, cross-sectional study included patients with total thyroidectomy between 2015 and 2016 at Emam-Ali Hospital, a University Hospital affiliated to Zahedan University in Zahedan, Iran. The study protocol was approved by Zahedan University of Medical Science's Committee of Ethics. The procedure was explained completely to the guardians, and written informed consents were obtained before their participation. Typical diagnoses of patients in this hospital include retrosternal goiter, multinodular goiter, thyroids cancers, and/or other severe thyroidal illness. A total of 110 patients were admitted to the hospital for thyroidectomy during the 12-month study period. 100 patients met eligibility criteria and enrolled.

We used pre-operative serum vitamin D level and early (< 24 hours) post-operative measurements of s-Ca levels. s-Ca < 8 mg/dl (< 2 mmol/l) 24 hours after surgery were considered post-operative hypocalcemia. During hospitalization days, s-Ca and hypocalcemic symptoms (parastesy, tetany, showestoc, and terusu) were checked. Due to the fact that these symptoms may correspond to other reasons else hypocalcemia that is prone to remit within few days after surgery assessment for s-Ca was done on discharge. The threshold of 8 for s-Ca was selected according to the results of many studies in western and eastern countries.

Other sociodemographic parameters were collected separately with an additional questionnaire. Age, sex, and fetal medical problems were asked.

S-Ca before operation was measured. Based on s-Ca, 24 hours after surgery prevalence of post-thyroidectomy hypocalcemia was measured. The potential risk factors for post-thyroidectomy hypocalcemia were investigated and compared between the two groups (before operation and after operation) using Pearson's chi-squared test (corrected by Fisher Exact for small samples). The level of significance was set throughout the study at $P \leq 0.050$. A multivariate stepwise regression was performed using all the predictive variables selected in our study. Only the variables with a $P \leq 0.050$ were retained in our final model. Data entry was carried out on Microsoft Excel. Data analysis was performed using the software SPSS (version 19; SPSS Inc., Chicago, IL., USA).

Results

At the first assessment at admission, 100 patients were included in our sample. 14 patients were man and 86 patients were woman. In case of s-Ca, two groups created; one group had s-Ca ≥8 [no hypocalcemic group = 100 (100)] and one group had s-Ca < 8 [hypocalcemic group = 0 (0)] and the average s-Ca was 8.62 [standard deviation (SD) = 0.59]. At 24 hours after surgery 81 (81), patient had s-Ca ≥8 and 19 (19) persons had s-Ca < 8 and the average s-Ca was 8.24 (SD = 0.53). Three mans (21.4% of men's) and 16 woman (18.6% of woman) had post-thyroidectomy hypocalcemia.

Mean of patients duration of hospitalization was 1.24 days (SD = 0.53). Mean age of the patient was 38.14 years (SD = 7.65) which men was 39.21 years (SD = 7.74) and women was 37.97 years (SD = 7.67). Mean pre-operative vitamin D level was reported 33.49 nmol/l (SD = 13.9). Its fewer than 35 in 41 (41) and normal in 59 (59). Six patients with pre-operative vitamin D deficiency were men (42.9% of men) and 35 patient was women (40.7% of women).

There is no significant differentiation between men and women who had hypocalcemia (P = 0.520) and who had pre-operative vitamin D deficiency (P = 0.550).

The group of patient suffering from early post-operative hypocalcemia (s-Ca < 8) 24 hours after surgery was compared to the group of normal participants (Table 1). There is only significant differentiation between s-Ca and vitamin D level (P = 0.001) (mean post-operative s-Ca in vitamin D deficient group was 7.84 ± 0.51 and in normal vitamin D group was 8.52 ± 0.33). Vitamin D deficiency significantly related with s-Ca < 8 (P = 0.001).

Table 1. Comparison of the characteristics of patient between the two groups 24 hours after surgery

Parameters	s-Ca ≥ 8 (%)	s-Ca < 8 (%)	P-value*
N	81 (81)	19 (19)	
Mean age	38.36 ± 8.18	37.21 ± 4.91	0.559
Sex			
Male	11 (13.6)	3 (15.8)	0.805
Female	70 (86.4)	16 (84.2)	
Vitamin D deficiency			
No	59 (72.8)	0 (0)	< 0.001*
Yes	22 (27.2)	19 (100)	

s-Ca: Serum calcium

There is a significant correlation between s-Ca level on admission and 24 hours after surgery (P = 0.001). Table 2 shows a significant difference in the mean of vitamin D level at admission between the group of patient with s-Ca < 8 and the other group (P = 0.001). All patients who s-Ca was fewer than 8 on 24 hours

Table 2. Comparison of the mean of vitamin D level between two groups

Parameters	s-Ca		P-value*	OR (95% CI)
	≥ 8	< 8		
N	81	19		
Mean of vitamin D level	38.34 ± 10.26	12.78 ± 6.0	0.001	1.86 (1.40-2.47)

* Significance threshold P ≤ 0.050. OR: Odds ratio; CI: Confidence interval

after surgery suffered from vitamin D deficiency. Those patients were 1.86 times more likely to develop hypocalcemia (95% confidence interval 1.40-2.47). A positive correlation was noted between s-Ca on admission and length of hospitalization (r = 0.5, P = 0.001) (Table 3).

Table 3. Comparison of the prevalence of PPD at D 42

Parameters	s-Ca		P-value*
	≥ 8	< 8	
N	81	19	
Length of hospitalization	1.0 ± 0.0	2.26 ± 0.45	0.001

* Significance threshold P ≤ 0.050, PPD: Prevalence of postpartum depression; s-Ca: Serum calcium

Discussion

Screening, intervention, and prevention efforts for post-thyroidectomy hypocalcemia are currently reimbursable by insurance because these efforts are important. For post-operative hypocalcemia screening and intervention programs to become customary and sustainable, researchers must demonstrate a reduction in health-care utilization and decreased hospital costs resulting from those efforts. List of risk factors by implementing regular screenings for post-operative hypocalcemia can targets patients who need intervention earlier and reduce their chances of developing post-thyroidectomy hypocalcemia symptomatology.

As hypothesized, pre-operative vitamin D deficiency was associated with the post-thyroidectomy hypocalcemia in other studies was 0-43.8% (3) suggest the importance of screening for this variable, but in concordance with many other studies (11-13), factors related to the age and gender of the patient were not associated with post-thyroidectomy hypocalcemia. Other personal factors may be having a role in post-thyroidectomy hypocalcemia then further research is needed to better understand the individual contributions of these factors. Post-operative hypocalcemia was highly correlated with vitamin D deficiency in admission.

This study also evaluation of the rates of post-operative hypocalcemia in patients. The prevalence of hypocalcemia after total thyroidectomy was 0.3-49 percent (14), nearly one-fifth of patients in this study met criteria for post-thyroidectomy hypocalcemia diagnosis.

There was no association between age and post-operative hypocalcemia that converges with some studies (15). Conversely, other studies showed that female gender was more frequently observed among post-operative hypocalcemic patient (13).

In our study, the risk of longer hospitalization was increased in hypocalcemic state patient, contrarily to the findings of other studies where showed no relationship (16). In many other studies, a positive lower vitamin D levels has been confirmed to be a risk factor for longer hospitalization (1), and then we included them from our study.

In our study, the prevalence of pre-operative vitamin D deficiency is around 41% which is considered close to the prevalence found in the sample of the study done by Griffin et al. (2).

The multivariate stepwise regression showed that the two factors significantly associated with post-operative hypocalcemia are pre-operative vitamin D deficiency (1.86 times) and pre-operative s-Ca (2.63 times) higher risk of developing post-operative hypocalcemia. Therefore, we can speculate that patients who have vitamin D deficiency are candidates for a close follow-up because of their higher risk for post-operative hypocalcemia.

However, post-operative hypocalcemic symptoms that arrived from low level of s-Ca around the time of post operation abated within the first days after operation, admission serum vitamin D level < 35 seems to be predictive of a risk of post-operative hypocalcemia (r = 0.51) that was similar to founding by Griffin et al. (2) and Glinoer et al. (15). Our study included Emam-ali Hospital admitted patients. The high rate of vitamin D deficiency in our sample can be justified by the fact that high prevalence of vitamin D deficiencies in Zahedan that was matched with some studies (17). In our study, the diagnosis of post-thyroidectomy hypocalcemia was based on s-Ca < 8 mg/dl (< 2 mmol/l) 24 hours after surgery.

In conclusion, this study demonstrates that an admission vitamin D level < 35 benefits for evaluation potential risk of developing post-operative hypocalcemia in a sample of total thyroidectomies patients. Patient with lower vitamin D levels should benefit from a screening for post-operative hypocalcemia.

Conflict of Interests

Authors have no conflict of interests.

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