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RESEARCH

THE EFFECT OF THE VITAMIN D DEFICIENCY ON THE HYPOCALCAEMIA AFTER THYROIDECTOMY IN GERIATRIC PATIENTS

ABSTRACT

Introduction: Post-thyroidectomy hypocalcaemia is common and depends on many factors. Vitamin D has critical role in calcium homeostasis. The main purpose of this study was to determine the effect of vitamin D deficiency on hypocalcaemia after thyroidectomy in geriatric patients.

Materials and Method: The study involved 259 patients who had received a total thyroidectomy at Istanbul University, Cerrahpaşa Medical Faculty, Department of General Surgery between 2012 and 2013. Patients' demographics, preliminary diagnosis, preoperative serum Vitamin-D, PTH, calcium, phosphorus, albumin, ALP, fT3, fT4, TSH and postoperative PTH, and calcium levels were recorded prospectively and examined retrospectively. Patients were separated into two groups: 65 years old and over (Group 1) and under 65 (Group 2).

Results: There were 49 patients in Group 1 and 210 patients in Group 2. In total 189 were female (73%) and 70 were male (27%). In 22 Group1 patients and 102 Group 2 patients, the serum vitamin D value was <15ng/ml. Mean vitamin D(g/dl) was 8.08±2.9, preoperative PTH(pg/ml) was 83.92±41.7, postoperative PTH(pg/ml) was 60.22±42.9, and postoperative calcium(mg/dl) was 8.57±0.58 for the 22 Group 1 patients and 8.58±3.2, 62.11±21.5, 38.97±32.3, and 8.45±0.67 for the 102 Group 2 patients, respectively. The only significant difference was for preoperative PTH (p=0.026).

Conclusion: These results show that, even though vitamin D deficiency is common in geriatric patients, it does not have a significantly different effect on post-thyroidectomy hypocalcaemia in geriatric patients than in non-geriatric patients.

Key Words: Hypocalcaemia; Thyroidectomy; Vitamin D Deficiency; Geriatrics; Parathyroid Hormone.

ARAŞTIRMA

GERİATRİK HASTALARDA D VİTAMİNİ EKSİKLİĞİNİN TİROİDEKTOMİ SONRASI HİPOKALSEMİYE ETKİSİ

ÖZ

Giriş: Tiroidektomi sonrası hipokalsemi sık görülmektedir ve birçok faktör ile ilişkilidir. Vitamin D kalsiyum dengesinde önemli role sahiptir. Bu çalışmanın esas amacı geriatrik hastalarda D vitamini eksikliğinin tiroidektomi sonrası hipokalsemiye etkisini saptamaktır.

Gereç ve Yöntem: Çalışma İstanbul Üniversitesi, Cerrahpaşa Tıp Fakültesi, Genel Cerrahi Anabilim Dalında 2012–2013 yılları arasında total tiroidektomi yapılan 259 hastayı kapsamaktadır. Hastaların demografik bilgileri, ön tanıları, ameliyat öncesi serum D vitamini, PTH, kalsiyum, fosfor, albumin, ALP, sT3, sT4, TSH ve ameliyat sonrası PTH ve kalsiyum değerleri prospektif olarak kaydedilip retrospektif olarak incelendi. Hastalar 65 yaş ve üzeri (Grup 1) ve 65 yaş altı (Grup 2) olmak üzere gruplandırıldı.

Bulgular: Grup 1'de 49 ve Grup 2'de 210 hasta vardı. Toplamda 189 (%73) hasta kadın 70 (%27) hasta erkekti. Grup 1'deki 22 ve Grup 2'deki 102 hastanın serum D vitamin değeri <15ng/ml idi. Grup 1'deki 22 hastanın ortalama serum D vitamini 8,08±2,9 g/dl, ameliyat öncesi PTH 83,92±41,7 pg/ml, ameliyat sonrası PTH 60,22±42,9 pg/ml ve kalsiyum 8,57±0,58 mg/dl ve Grup 2'deki 102 hastanın değerleri sırasıyla 8,58±3,2, 62,11±21,5, 38,97±32,3 ve 8,45±0,67 idi. Tek anlamlı farklılık ameliyat öncesi PTH değeriydi (p=0.026).

Sonuç: Bulgulara göre geriatrik hastalarda D vitamini eksikliği sık olsa da geriatrik hastalarda tiroidektomi sonrası hipokalsemide geriatrik olmayan hastalara göre farklılık yoktur.

Anahtar Sözcükler: Hipokalsemi; Tiroidektomi; D Vitamini Eksikliği; Geriatri; Parathormon.

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Introduction

The principles of safe and effective thyroid surgery were standardized by Emil Theodor Kocher and Theodor Billroth between 1873-1883, and today these principles still maintain their validity (1). Hypocalcaemia is common after thyroidectomy and it is one of the complications that even experienced surgeons cannot overcome, with an incidence ranging from 1.6% to 50% (2).

The cause of hypocalcaemia after thyroidectomy depends on many factors such as: iatrogenic surgical trauma to the parathyroid glands, incidental parathyroidectomy, remaining number of functional parathyroid glands, expanse of the surgical exploration area, surgical experience, hyperthyroidism, retrosternal goiter, neck dissection and thyroid cancer (3). Experience and familiarity with thyroid and parathyroid anatomy is very important in thyroid surgery.

The rate of incidental parathyroidectomy ranges between 5% and 20%. The relationship between intraoperative observation of the parathyroid gland and postoperative hypocalcaemia is variable; some studies have shown that observing fewer than three parathyroid glands during the operation predicts postoperative hypocalcaemia, while other studies have shown no relationship (3-8).

Vitamin D plays a critical role in calcium homeostasis (9). The indicator of vitamin D in the circulatory system is the inactive form 25-(OH)-D_3 (Vit–D) and its half-life is 2-3 weeks. The active form is 1,25-$(OH)_2$-D_3 but it is not appropriate to evaluate this as the circulation level of vitamin D because the half-life of 1,25-$(OH)_2$-D_3 is only 4-6 hours. According to the *Kidney Dialysis Outcomes Quality Initiative* (K-DOQI) guide, a circulating level of Vit–D lower than 5ng/ml is considered to be severe vitamin D deficiency, between 5-15ng/ml is moderate vitamin D deficiency, between 15-29 ng/ml is vitamin D deficiency, higher than 30ng/ml is normal vitamin D level, and a level higher than 150 ng/ml is vitamin D intoxication (10, 11). Hypocalcaemia that is related to insufficient serum concentration of Vit–D causes elevated parathormone levels. Elevated parathormone and low calcium-phosphate levels increase serum calcium level by increasing 1,25-$(OH)_2$-D_3 (12-14).

The definition of "geriatric" by the World Health Organization is age 65 and over . Vitamin D deficiency is quite common in geriatric people, especially in bedridden geriatric patients. Vitamin D deficiency causes hyperparathyroidism, loss of bone mineralization and bone fractures in geriatric patients (15).

The main purpose of this study was to determine the effect of vitamin D deficiency on hypocalcaemia after thyroidectomy in geriatric patients. Secondary purposes of this study were to analyze the effects of vitamin D, parathormone (PTH) and calcium levels before thyroidectomy on the hypocalcaemia level after total thyroidectomy (TT) in geriatric patients, in addition the effects of gender and BMI.

Materials and Method

This study involved 259 patients who received total thyroidectomy for multinodular goiter and thyroid cancer in the Istanbul University Cerrahpaşa Medical Faculty Department of General Surgery, Endocrine Surgery Unit, between 2012 and 2013. Patients who formerly had thyroid surgery for any reason and were admitted with recurrence of the disease, had a diagnosis of primary hyperthyroidism and chronic kidney failure, were receiving calcium and vitamin D oral replacement treatment, or had neck dissection because of thyroid cancer, were excluded from the study. All patients were operated by the same surgical team. Patients' demographic characteristics (age, gender, height, weight, and neck circumference) and preliminary diagnosis before total thyroidectomy were analyzed and recorded. Biochemical data measured on the morning of the day before surgery as serum Vit–D, PTH, calcium, phosphorus, albumin, alkaline phosphatase (ALP), fT3, fT4 and TSH were recorded. PTH and calcium levels measured 12 hours after the operation were recorded as post-operative values. Body Mass Index (BMI) was calculated as weight (kg) / square meter of height (m^2).

Patients' data were recorded prospectively and examined retrospectively. Patients were separated into two groups: age 65 and over (Group 1) and under age 65 (Group 2). Pre-operative serum Vit–D concentration under 15ng/ml was accepted as vitamin D deficiency, due to the high prevalence of vitamin D deficiency in Turkey (16). All serum calcium levels were corrected for serum albumin. A post-operative serum calcium concentration under 8 mg/dl was accepted as hypocalcaemia.

This study was approved by Istanbul University Cerrahpaşa Medical Faculty Medical, Clinical Research Ethical Committee, with decision number 83045809/5856, on March, 5 2013.

Biochemical Analysis

Serum calcium, phosphorus, PTH, albumin, ALP, fT3, fT4, and TSH levels were measured by the spectrophotometric and chemiluminescence method via auto-analyzer (Cobas 4000, Roche Diagnostics, Basel, Switzerland). Serum Vit–D levels were measured using the HPLC (High Pressure Liquid Chro-

matography) method via an auto-analyzer (ZİVAK Technologies, Turkey). The normal value for serum calcium was accepted as 8.4-10.2 mg/dl, for Vit–D as 6-46 ng/ml, for phosphorus as 2.7- 4.5 md/dl, for albumin as 3.5-5.2 g/dl, for PTH as 10– 70 pg/ml, for ALP as 30-135 U/L, for fT3 as 1.8-4.2 pg/ml, for fT4 as 0.7-1.9 pg/ml, and for TSH as 0.4- 4.2 mIU/L.

Statistical Evaluation

Data were entered to PASW statistics 18 software and comparison between groups was made using Student's t-Tests and chi-square tests. Continuous variables were denoted as mean ± standard deviation. A two-tailed alpha value of *<0.05* was accepted as statistically significant.

Results

For the total group of 259 cases, mean age was 49.4±13.5 years and the range was 18-84 years. Forty-nine patients were identified as Group 1(? 65 years old), 210 patients as Group 2 (<65). Of the 259 patients involved in the study, 189 were female (73%) and 70 were male (27%). The female/male ratio was 2.7/1. Across all cases, average BMI was 32.2±7.3kg/m^2 and neck circumference was 37.3±4.2 cm. Multinodular goiter (MNG) was detected in 190 patients (73.4%) involved in the study, and malignancy in 69 patients (26.6%). No parathyroid glands were observed on histopathological examination. Comparison of the two groups' gender ratio, BMI, and diagnosis did not reveal statistically significant differences (Table 1).

Average serum levels of all cases before total thyroidectomy were Vit–D 18.5±15.1g/dl, calcium 9.24±0.5mg/dl, PTH 60.1±26.7pg/ml, phosphorus 3.3±0.5mg/dl, albumin 4.31±0.3g/dl, ALP 71.7±24.1U/L, fT3 3.24±0.74pmol/L, fT4 1.19±0.56pmol/L, and TSH 6.01±19.9mlU/L. After total thyroidectomy, the average calcium level was 8.59±0.7mg/dl and serum PTH was 42.01±28.9pg/ml. Average levels for the two groups are shown in Table 2.

Vit–D deficiency (vitamin D <15ng/ml) was detected in 124 patients: for 22 patients in Group 1 and 102 in Group 2, the serum vitamin D value was detected as less than 15 ng/ml. Group values for average Vit–D and PTH before total thyroidectomy, and average PTH and calcium after total thyroidectomy are shown in Table 3.

Table 1— Statistical Comparison of Demographic Characteristics.

Parameter	Group 1	Group 2	p value
Gender F: M	31/18	158/52	0.089
Diagnosis MNG/Malignancy	38/11	152/58	0.461
BMI	32.03±7.1	32.39±0.5	0.760
Neck circumference	38.08±4.3	37.1±4.2	<0.05

Table 2— Statistical Comparison of Biochemical Data.

Parameter	Group 1	Group 2	p value
Vitamin D (g/dl)	16.3±10.5	19.01±16.04	0.277
Phosphorus (mg/dl)	3.33±0.59	3.32±0.57	0.842
Preoperative calcium (mg/dl)	9.22±0.6	9.25 0.48	
0.758			
Preoperative PTH (pg/ml)	71.3±36.2	57.5±23.3	**0.013***
Postoperative PTH (pg/ml)	47.3 29.8		
36.6±28	0.019		
Postoperative calcium (mg/dl)	8.6 0.7		
8.5±0.7	0.083		
Albumin (gr/dl)	4.13±0.33	4.35±0.33	**<0.001***
ALP (U/L)	78.7±24.3	70.1±23.8	**0.025***
fT3 (pmol/L)	3.24±0.9	3.24±0.6	0.994
fT4 (pmol/L)	1.19±0.2	1.19±0.6	0.975
TSH (mIU/L)	1.81 1.35	6.9±2.19	**0.001***

Table 3— Comparison of Cases Diagnosed With Vit–D Deficiency Before Total Thyroidectomy According to Age Group.

	Group	Number	Serum Level (mean±sd)	p value
Vitamin D (ng/ml)	1	22	8.08±2.9	0.503
	2	102	8.58±3.2	
Preoperative PTH (pg/ml)	1	22	83.92 ±41.7	**0.026***
	2	102	62.11 ±21.5	
Postoperative PTH (pg/ml)	1	22	60.22 ±42.9	0.10
	2	102	38.97 ±32.3	
Postoperative calcium (mg/dl)	1	22	8.57 ±0.58	0.435
	2	102	8.45 ±0.67	

In 56 of the 259 (21.6%) patients involved in the study, serum calcium levels after total thyroidectomy were detected as less than 8 mg/dl. In 6 patients of Group 1 (12.2%) and in 29 patients of Group 2 (13.8%), serum calcium levels after total thyroidectomy were detected as less than 8 mg/dl. In 4 of the 22 (18%) geriatric patients who had Vit–D deficiency, serum calcium levels after total thyroidectomy were detected as less than 8 mg/dl. In 17 of the 102 (16%) non-geriatric patients who had Vit–D deficiency, serum calcium levels after total thyroidectomy were detected as less than 8 mg/dl.

When pre-operative serum Vit–D levels and post-operative serum calcium levels were compared, there was no significant difference between Group 1 and Group 2 (16.39±10.51ng/ml versus 19.01±16.04ng/ml and 8.70±0.75mg/dl versus 8.50±0.70 mg/dl, respectively, p>0.05) (Figure 1-2).

For the 124 patients who had vitamin D deficiency, there was no significant difference in post-operative serum calcium levels between Group 1 and Group 2 (8.57±0.58mg/dl vs. 8.45±0.67mg/dl, p>0.05) (Figure 3 and 4).

Discussion

Thyroid diseases are one of the most common and important endocrine problems today. Hypocalcaemia is one of the frequently encountered complications after thyroidectomy, with an incidence range of 1.6 to 50% (2). It can cause serious complications when it is severe. It increases hospitalization time for the patient and increases the need to run biochemical tests (17).

Vit–D deficiency causes hyperparathyroidism, loss of bone mineralization and bone fractures in geriatric patients (15). Vit–D deficiency is commonly encountered in the geriatric population of Turkey (16). One cause of post-operative hypocalcaemia is *Hungry Bone Syndrome:* postoperative temporary iatrogenic hypoparathyroidism and preoperative low Vit–D

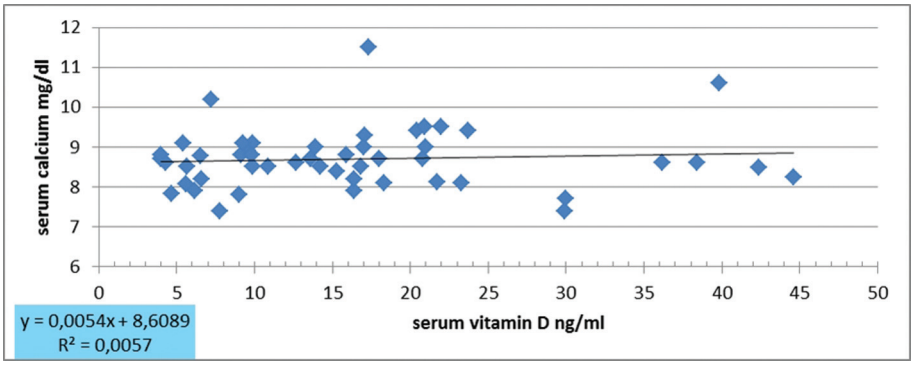

Figure 1— Pre-operative serum vitamin D levels and post-operative serum calcium levels in Group 1.

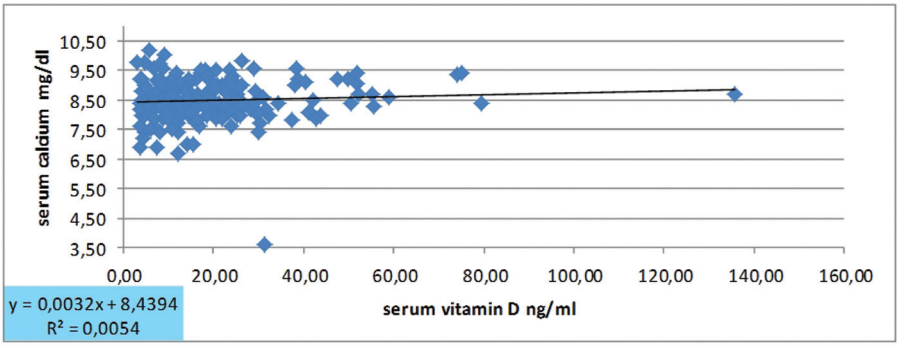

Figure 2— Pre-operative serum vitamin D levels and post-operative serum calcium levels in Group 2.

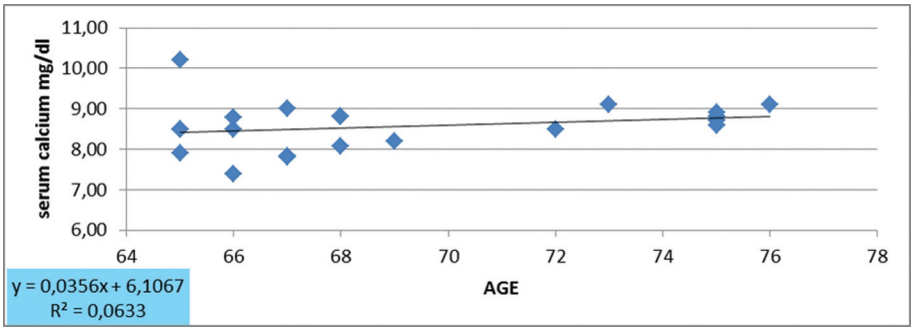

Figure 3— Post-operative serum calcium levels in geriatric patients with vitamin D deficiency.

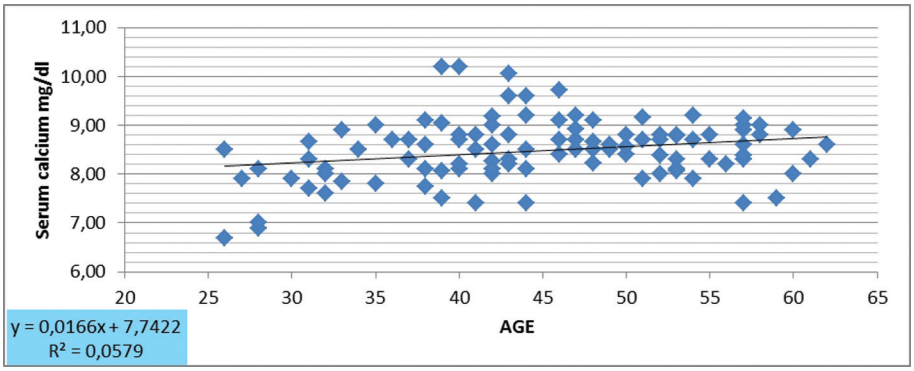

Figure 4— Post-operative serum calcium levels in non-geriatric patients with vitamin D deficiency.

levels are factors that cause high bone destruction, as well as advanced age and hyperthyroidism (5). Some studies report that advanced age is an important risk factor for Vit–D deficiency and causes changes in Vit–D metabolism. It has been found that insufficient serum Vit–D levels cause insufficient calcium reabsorption from intestines, so serum PTH levels increase (18).

According to study of Chailurkit et al. (19) took place in Thailand, a country with wide Vitamin-D insufficiency similar to Turkey, high serum Vit-D levels are related with low serum TSH levels in young individuals (20). Despite study of Chailurkit et al. (19) present study did not reveal such a relation between serum TSH and Vit-D levels.

We suggest that anticipating the risk factors for postoperative hypocalcaemia can be very useful to researchers interested in thyroid surgery.

We propose that Vit–D deficiency in geriatric patients can affect the development of hypocalcaemia after total thyroidectomy because it decreases reabsorption of calcium from the intestines. To our knowledge, there are no published studies that investigate the effect of Vit–D deficiency on hypocalcaemia after total thyroidectomy, comparing patients under age 65 with geriatric patients aged 65 and over. However, this study found that Vit–D deficiency in geriatric patients did not cause hypocalcaemia after total thyroidectomy.

In a retrospective study with 152 patients, Lin et al. (21) found that Vit–D insufficiency (Vit–D<30 ng/ml, n=31) and Vit–D deficiency (Vit–D < 20 ng/ml, s=78) did not cause postoperative hypocalcaemia in patients who had near total thyroidectomy (NTT) and near total thyroidectomy with central lymph node dissection (NTT + CND) . At the same time, they showed that demographic characteristics such as age, gender and preoperative diagnosis did not affect postoperative hypocalcaemia.

Chia et al. (22) could not find a relationship between preoperative serum Vit–D levels and a postoperative decrease in calcium levels. Sam et al. (23) found similar serum calcium levels after thyroidectomy in their studies, in patients both with Vit–D deficiency (Vit–D<25 ng/ml, 37.5%) and without Vit–D deficiency (Vit–D>25 ng/ml, 39.7%).

Some studies in the literature report that Vit–D deficiency before thyroidectomy is a risk factor for postoperative hypocalcaemia development (3, 24-27). In their prospective study of 35 patients, Erbil et al. (24) compared preoperative Vit–D levels and postoperative PTH levels in patients who developed hypocalcaemia after thyroidectomy and in patients who did not. In 13 patients who developed hypocalcaemia after total thyroidectomy, preoperative Vit–D levels and postoperative PTH levels were found to be decreased. However, they found that demographic characteristics such as age and gender did not affect postoperative hypocalcaemia.

Yamashita et al. (25) found low serum calcium levels and high serum PTH levels before thyroidectomy in their study of Graves' disease patients who developed tetany after thyroidectomy. They claimed that decreased serum calcium levels and Vit–D deficiency (Vit–D<25 ng/ml) cause hyperparathyroidism, and tetany occurs due to temporary hypoparathyroidism after thyroidectomy.

In the present study, serum Vit–D levels before total thyroidectomy were found to be similar in both groups. Although preoperative serum PTH and ALP levels were found to be significantly high, postoperative serum PTH levels were found to be significantly low, and no significant difference for postoperative hypocalcaemia was observed.

Kirkby-Bott et al. (27), in their prospective study of 166 patients, separated patients with total thyroidectomy into three groups: patients who had preoperative serum Vit–D <10ng/ml, 10-20ng/ml and >20ng/ml. Patients who had serum Vit–D levels under 10 ng/ml developed postoperative hypocalcaemia more often than patients who had serum Vit–D levels over 20 ng/ml.

In their prospective study of 200 patients with TT and NTT, Erbil et al. (3) compared preoperative age, serum Vit–D and ALP levels with postoperative serum calcium levels. They divided the cases into two groups: cases that developed hypocalcaemia after TT (n=49; serum Ca^{++} <8 mg/dl) and those that did not develop hypocalcaemia (n=151). No significant differences were observed in serum calcium and albumin levels before TT between the two groups. Preoperative serum Vit–D levels and postoperative serum calcium levels were found to be lower in patients who developed hypocalcaemia after TT than in patients who did not.

In the same study, cases were also compared according to preoperative serum Vit–D levels. In 33 patients who had preoperative serum Vit–D levels <15 ng/ml, postoperative serum calcium levels were detected to be significantly lower than those for the 167 patients who had preoperative serum Vit–D levels >15 ng/ml. At the same time, in 33 patients who had preoperative serum Vit–D levels <15 ng/ml, preoperative ALP levels were higher than those for the 167 patients who had preoperative serum Vit–D levels over 15 ng/ml. Incidental parathyroidectomy was not found to be statistically significant for hypocalcaemia development after total thyroidectomy.

The mean age of patients who had preoperative serum Vit–D levels <15ng/ml and developed postoperative hypocalcaemia was found to be high. Serum Vit–D levels before TT were lower in female patients than in male patients, and the effect of serum Vit–D levels on postoperative hypocalcaemia was statistically significant.

In the present study, even though there was a significant difference in postoperative serum PTH levels between patients under 65 year old and over 65 year old who had Vit–D deficiency, postoperative serum calcium levels were not significantly different. Similar to the study of Erbil et al. (3), there was no significant difference between the 2 age groups for serum albumin and calcium levels before TT. Of the 259 patients involved in the study, the F:M ratio was 2.7:1; there were no significant differences between males and females in terms of serum Vit–D levels before thyroidectomy, and postoperative serum calcium levels.

In conclusion, this study found that even though Vit–D deficiency is common in geriatric patients, it does not have a significant effect on post-thyroidectomy hypocalcaemia in geriatric patients compared to non-geriatric patients.

Conflict of Interest

All authors of this study declare no conflict of interest.

References

1. Tan SY, Shigaki D. Emil Theodor Kocher (1841-1917): Thyroid surgeon and Nobel laureate. Singapore Med J 2008;49(9):662-3. (PMID:18830536).
2. Kamer E, Unalp HR, Erbil Y, et al. Early prediction of hypocalcemia after thyroidectomy by parathormone measurement in surgical site irrigation fluid. Int J Surg 2009;7(5):466-71. (PMID:19619679).
3. Erbil Y, Barbaros U, Temel B, et al. The impact of age, vitamin D(3) level, and incidental parathyroidectomy on postoperative hypocalcemia after total or near total thyroidectomy. Am J Surg 2009;197(4):439-46. (PMID:19324110).
4. Thomusch O, Machens A, Sekulla C, et al. Multivariate analysis of risk factors for postoperative complications in benign goiter surgery: prospective multicenter study in Germany. World J Surg 2000;24(11):1335-41. (PMID:11038203).

5. Khairy GA, Al-Saif A. Incidental parathyroidectomy during thyroid resection: incidence, risk factors, and outcome. Ann Saudi Med 2011;31(3):274-8. (PMID:21623057).
6. Gourgiotis S, Moustafellos P, Dimopoulos N, et al. Inadvertent parathyroidectomy during thyroid surgery: the incidence of a complication of thyroidectomy. Langenbecks Arch Surg 2006;391(6):557-60. (PMID:16951969).
7. Sasson AR, Pingpank JF, Jr., Wetherington RW, Hanlon AL, Ridge JA. Incidental parathyroidectomy during thyroid surgery does not cause transient symptomatic hypocalcemia. Arch Otolaryngol Head Neck Surg 2001;127(3):304-8. (PMID:11255476).
8. Pattou F, Combemale F, Fabre S, et al. Hypocalcemia following thyroid surgery: Incidence and prediction of outcome. World J Surg 1998;22(7):718-24. (PMID:9606288).
9. Hickey L, Gordon CM. Vitamin D deficiency: new perspectives on an old disease. Current Opinion in Endocrinology, Diabetes and Obesity 2004;11(1):18-25.
10. Block GA, Port FK. Re-evaluation of risks associated with hyperphosphatemia and hyperparathyroidism in dialysis patients: recommendations for a change in management. Am J Kidney Dis 2000;35(6):1226-37. (PMID:10845841).
11. Grant WB, Holick MF. Benefits and requirements of vitamin D for optimal health: A review. Altern Med Rev 2005;10(2):94-111. (PMID:15989379).
12. Lieben L, Carmeliet G, Masuyama R. Calcemic actions of vitamin D: effects on the intestine, kidney and bone. Best Pract Res Clin Endocrinol Metab 2011;25(4):561-72. (PMID:21872798).
13. Bouillon R, Carmeliet G, Boonen S. Ageing and calcium metabolism. Baillieres Clin Endocrinol Metab 1997;11(2):341-65. (PMID:9403126).
14. Lips P. Vitamin D physiology. Prog Biophys Mol Biol 2006;92(1):4-8. (PMID:16563471).
15. Lips P. Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications. Endocr Rev 2001;22(4):477-501. (PMID:11493580).
16. Atli T, Gullu S, Uysal AR, Erdogan G. The prevalence of vitamin D deficiency and effects of ultraviolet light on Vitamin D levels in elderly Turkish population. Arch Gerontol Geriatr 2005;40(1):53-60. (PMID:15531023).
17. Reber PM, Heath H, 3rd. Hypocalcemic emergencies. Med Clin North Am 1995;79(1):93-106. (PMID:7808098).
18. Heaney RP, Weaver CM. Calcium and vitamin D. Endocrinol Metab Clin North Am 2003;32(1):181-94, vii-viii. Review. (PMID:12699298).
19. Chailurkit LO, Aekplakorn W, Ongphiphadhanakul B. High vitamin D status in younger individuals is associated with low circulating thyrotropin. Thyroid 2013;23(1):25-30. (PMID:22931506).
20. Cigerli O, Parildar H, Unal AD, et al. Vitamin D deficiency is a problem for adult out-patients? A university hospital sample in Istanbul, Turkey. Public Health Nutr 2013;16(7):1306-13. (PMID:22877974).
21. Lin Y, Ross HL, Raeburn CD, et al. Vitamin D deficiency does not increase the rate of postoperative hypocalcemia after thyroidectomy. Am J Surg 2012;204(6):888-93; discussion 93-4. (PMID:23231931).
22. Chia SH, Weisman RA, Tieu D, et al. Prospective study of perioperative factors predicting hypocalcemia after thyroid and parathyroid surgery. Arch Otolaryngol Head Neck Surg 2006;132(1):41-5. (PMID:16415428).
23. Sam AH, Dhillo WS, Donaldson M, et al. Serum phosphate predicts temporary hypocalcaemia following thyroidectomy. Clin Endocrinol (Oxf) 2011;74(3):388-93. (PMID:21143616).
24. Erbil Y, Ozbey NC, Sari S, et al. Determinants of postoperative hypocalcemia in vitamin D-deficient Graves' patients after total thyroidectomy. Am J Surg 2011;201(5):685-91. (PMID:21545922).
25. Yamashita H, Murakami T, Noguchi S, et al. Postoperative tetany in Graves disease: important role of vitamin D metabolites. Ann Surg 1999;229(2):237-45. (PMID:10024106).
26. Yamashita H, Noguchi S, Murakami T, et al. Calcium and its regulating hormones in patients with graves disease: sex differences and relation to postoperative tetany. Eur J Surg 2000;166(12):924-8. (PMID:11152251).
27. Kirkby-Bott J, Markogiannakis H, Skandarajah A, et al. Preoperative vitamin D deficiency predicts postoperative hypocalcemia after total thyroidectomy. World J Surg 2011;35(2):324-30. (PMID:21153820).