The Serum 25(OH) Vitamin D, Calcium, and Parathyroid Hormone Levels of The Patients with The Obstructive Sleep Apnea Syndrome

Sıdıka Deniz Yalım[1], Selçuk Matyar[2], Hakan Yalım[3]

1 Department of Otorhinolaryngology, University of Health Sciences Adana City Training and Research Hospital, Adana, Türkiye
2 Department of Biochemistry, University of Health Sciences Adana City Training and Research Hospital, Adana, Türkiye
3 Department of Anesthesia and Reanimation, University of Health Sciences Adana City Training and Research Hospital, Adana, Türkiye

Abstract

Aim: Although there is evidence linking vitamin D to many neurochemical processes involved in sleep, the association between the obstructive sleep apnea and vitamin D, calcium and parathyroid hormone is still unknown, as clinical research have shown inconsistent findings. In this study we aimed to examine the hypothesis that if there is any relationship between obstructive sleep apnea and serum vitamin D, calcium and parathyroid hormone levels in order to manage treatment.

Methods: 56 patients (32 male, 24 female) admitted to the University of Health Sciences Adana City Training and Research Hospital otorhinolaryngology clinic between January 1st, 2022 and January 1st 2023 without any acute and chronic disease were included in the study. The range of participants was 18-70. In this study we examined the serum vitamin D, calcium and parathyroid hormone levels of 32 obstructive sleep apnea patients and compared their serum vitamin D, calcium and parathyroid hormone levels with the serum vitamin D, calcium and parathyroid hormone levels of 24 normal patients in the control group.

Results: When the serum vitamin D, calcium and parathyroid hormone levels of obstructive sleep apnea patients and serum vitamin D, calcium and parathyroid hormone levels of normal patients were compared we did not find a statistically significant difference which may be due to our patient density.

Conclusions: Vitamin D, calcium and parathyroid hormone levels are not likely related to the presence or absence of obstructive sleep apnea. More intervention studies are needed to better clarify the relation between the obstructive sleep apnea and vitamin D, calcium and parathyroid hormone

Keywords: *Sleep, apnea, vitamin D, calcium, parathyroid hormone*

1. Introduction

Obstructive Sleep Apnea Syndrome (OSAS) is diagnosed when the Apnea-Hypopnea Index (AHI) is above 5 as determined by polysomnography, accompanied by excessive daytime sleepiness, witnessed apnea symptoms, and cardiac disorders. Recent studies have reported vitamin D deficiency in patients with OSAS. Studies independent of geography and season suggest factors other than sunlight may be influential. Additionally, vitamin D deficiency has been associated with sleep apnea, restless sleep, night sweats, and restless legs syndrome.[1] Vitamin D is a fat-soluble vitamin stored in adipose tissue. It plays a role in the skeletal system and calcium and phosphorus metabolism and balance. The term vitamin D includes cholecalciferol (D2) and ergocalciferol (D3). D2 is obtained from the diet, while D3 is synthesized in the skin via ultraviolet rays from sunlight. Hydroxylation in the liver produces 25-hydroxy (OH) vitamin D (calciferol). Further hydroxylation in the kidney results in 1,25-dihydroxy D3. The synthesis of 1,25 OH D is balanced by parathyroid hormone (PTH), serum calcium, and phosphorus levels.

Vitamin D's effects on the skeletal system are critical for bone health and development, but it also impacts the musculoskeletal system, immune system, cardiovascular system, metabolic, neurological, and psychiatric functions. Measuring vitamin D levels in the blood is done by assessing the most stable form, serum 25 OHD. It has a half-life of three weeks. Serum 25 OHD levels below 10 ng/ml are considered deficient, and levels below 20 ng/ml indicate insufficiency. Ideal levels are considered to be 30 ng/ml. With the widespread measurement of 25 OHD levels, vitamin D deficiency can be diagnosed without disease symptoms.[2]

There are varying results in the literature regarding the relationship between obstructive sleep apnea and vitamin D levels, and

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there is no consensus on the mechanisms involved. This study aims to shed light on the relationship between OSAS and levels of 25 (OH) vitamin D, calcium, and parathyroid hormone.

2. Materials and methods

The approval was obtained from the Ethics Committee of the University of Health Sciences Adana City Training and Research Hospital for this study (Ethic no: 30.05.2024/29). Written consent was obtained from the patients. Between January 1, 2018, and January 1, 2023, 56 adult patients (aged 18-65 years) who presented to the ENT outpatient clinic of University of Health Sciences Adana City Training and Research Hospital were retrospectively examined for serum 25 OH vitamin D, calcium, and parathyroid hormone levels, age, body mass index (BMI), AHI, oxygen desaturation index (ODI), mean oxygen saturation, minimum oxygen saturation, the time below 90% oxygen (TSAT90), and heart rate. Patients with chronic diseases, those using medication, those who did not agree to the tests, and those with incomplete records were excluded.

The peripheral venous blood samples were collected under standard conditions in anticoagulant-free (plain tube) vacuum biochemical tubes from fasting patients in the morning at the blood collection unit of University of Health Sciences University Adana City Training and Research Hospital. After allowing the samples to clot at room temperature for 15-20 minutes, they were centrifuged at 3000 rpm for 10 minutes. Total calcium, parathyroid hormone (PTH), and 25 (OH) vitamin D were immediately tested from the obtained serum samples. Serum 25(OH) vitamin D and PTH levels were measured using chemiluminescence with Beckman Coulter kits (CA) on a UniCel DXI 800 (Beckman Coulter Inc., CA, USA) automated immunoassay analyzer. The reference range for 25 OH Vitamin D Concentration (Vitamin D Status ng/mL) is 11.5-84.5. The reference range for PTH in individuals aged 19–67 is 12–88 pg/mL.

The serum total calcium levels were measured using Beckman Coulter kits (CA) on a Beckman UniCel DXC 5800 Synchron (Beckman Coulter Inc., CA, USA) automated analyzer via the colorimetric method. The reference range for total calcium levels in adults is 8.8 – 10.6 mg/dL.

The polysomnography tests were performed using Comet Grass (Astro-Med, Inc., West Warwick, Rhode Island, United States) devices and scored according to the American Academy of Sleep Medicine (AASM) guidelines. According to AASM 1999 criteria, an AHI below 5 is considered normal, 5-15 indicates mild OSAS, 15-30 indicates moderate OSAS, and above 30 indicates severe OSAS.

2.1. Statistical Analysis

The statistical analysis was performed using SPSS version 27.0 software (SPSS Inc., Chicago, Illinois, United States). The mean values of the study and control groups were compared using the Student t-test, and descriptive statistics were presented as mean ± standard deviation. The relationship between vitamin D and age, BMI, AHI, ODI, mean and minimum oxygen saturation, TSAT90 and heart rate was analyzed using Pearson correlation analysis. A p-value of <0.05 was considered significant.

3. Results

There were 32 obstructive sleep apnea study group (24 male, 8 female) patients and 24 normal control group (8 male, 16 female) patients.

There was no statistically significant difference in 25 (OH) vitamin D levels between OSAS patients and the control group (p=0.112). There was no significant difference in serum total calcium and parathyroid hormone levels between OSAS patients and the control group (r=0.437 and p=0.244, respectively).

A negative but not statistically significant relationship was found between 25 OHD levels and age in OSAS patients (r=-0.230, p=0.206).

A significant negative relationship was found between 25 OHD levels and BMI in OSAS patients (r=-0.379, p=0.032).

No significant relationship was found between 25 OHD levels and AHI values (r=0.186, p=0.307), ODI values (r=-0.017, p=0.927), mean oxygen saturation values (r=-0.237, p=0.192), TSAT90 levels (r=0.278, p=0.124), minimum oxygen saturation values (r=-0.296, p=1.0), or heart rate values (r=0.129, p=0.482).

No significant relationship was found between serum calcium levels and age (r=-0.214, p=0.239), BMI (r=0.056, p=0.761), AHI values (r=0.446, p=0.11), ODI values (r=0.311, p=0.083), mean oxygen saturation values (r=-0.261, p=0.149), minimum oxygen saturation values (r=-0.266, p=0.188), TSAT90 values (r=0.121, p=0.509), or heart rate (r=0.253, p=0.163) in OSAS patients.

No significant relationship was found between serum parathyroid levels and age (r=0.176, p=0.335), BMI (r=0.182, p=0.319), AHI values (r=0.42, p=0.017), ODI values (r=0.585, p=0), mean oxygen saturation values (r=-0.585, p=0.001), minimum oxygen saturation values (r=-0.169, p=0.623), TSAT90 values (r=0.403, p=0.22), or heart rate (r=0.291, p=0.106) in OSAS patients. (Table 1)

Table 1

The correlation between the parameters of the obstructive sleep apnea and the control group.

	25 OHD	Calcium	Parathyroid hormone
Age	r=-0.230 p=0.206	r=-0.214 p=0.239	r=0.176 p=0.335
Body Mass Index	r=-0.379 p=0.032	r=0.056 p=0.761	r=0.182 p=0.319
AHI	r=0.186 p=0.307	r=0.446 p=0.11	r=0.420 p=0.017
ODI	r=-0.017 p=0.927	r=0.311 p=0.083	r=0.585 p=0.000
Mean Oxygen Saturation	r=-0.237 p=0.192	r=-0.261 p=0.149	r=-0.585 p=0.001
Tsat90	r=0.278 p=0.124	r=-0.266 p=0.188	r=-0.169 p=0.623
Minimum Oxygen Saturation	r=-0.296 p=1.0	r=0.121 p=0.509	r=0.403 p=0.220
Heart Rate	r=0.129 p=0.482	r=0.253 p=0.163	r=0.291 p=0.106

4. Discussion

In our study, no relationship was found between vitamin D levels and the severity of OSA or AHI values. A negative relationship was found between vitamin D and BMI. Since vitamin D is fat-soluble, it is stored in adipose tissue, leading to lower serum vitamin D levels. This explains the negative correlation between vitamin D levels and BMI. No relationship was found between vitamin D and ODI, mean and minimum oxygen saturation levels, TSAT90, or heart rate. Vitamin D levels were not related to OSA regardless of geography and season. The study was conducted in a region with a sunny and warm climate all year round.

In the literature, Erden[3] and Bozkurt[4] et al.'s studies also found an inverse relationship between vitamin D levels and BMI. However, Erden reported that vitamin D levels were lower in OSA patients. Similar to our study, Bozkurt et al. found that vitamin D levels were not different between OSA patients and normal subjects. Salepci[5] et

al. reported no relationship between vitamin D levels and the severity of OSA or AHI values and BMI. Mete et al.[6] found no difference in vitamin D levels between OSA patients and normal subjects. Pazarlı et al.[7] also found no relationship between vitamin D and OSA.

Kerley et al.[8] reported lower 25-OHD levels in OSA patients and found that vitamin D levels were related to AHI. Vitamin D levels were inversely related to AHI, BMI, and heart rate. Piovezan et al.[9] found a relationship between low 25 OHD levels and moderate to severe OSAS and short sleep duration. Archontogeorgis et al.[10] reported that serum 25 OHD levels were low and negatively associated with AHI, ODI, TSAT90, and positively associated with mean oxygen saturation levels.

Goswami et al.[11] reported that low 25 OHD levels were associated with OSA severity and hypoxemia duration. Despite conflicting results in the literature, vitamin D and OSAS studies mostly agree that lower vitamin D levels are present in OSA patients, regardless of geography and season. Therefore, it may be beneficial to routinely measure vitamin D levels in OSA patients.

Toujani et al. found that vitamin D levels were positively associated with both mean and minimum oxygen saturation levels in patients with obstructive sleep apnea syndrome (OSAS) . While the exact mechanisms linking vitamin D to OSAS are not fully understood, several theories have been proposed, including inflammation, hypoxia, immunological responses, muscle dysfunction, and vitamin D receptor gene polymorphisms .

Neighbors et al., in their meta-analysis, reported that serum 25-hydroxyvitamin D (25 OHD) levels were significantly lower in patients with OSAS and that these levels correlated with the severity of OSAS. They also noted that the relationship between vitamin D levels and OSAS was influenced by body mass index (BMI) . Given that both untreated OSAS and vitamin D deficiency can increase cardiovascular morbidity and mortality, early diagnosis and treatment are crucial .

The limitations of our study include the small sample size of 59 patients, the lack of nationwide representation despite patients coming from various cities in the region, and the limited insight provided into the mechanisms behind the relationship between vitamin D and OSAS.

In the literature, no significant relationship was found between serum calcium levels and OSAS. However, calcium levels were within the reference range and not indicative of calcium metabolism disturbances. Our study also did not find a relationship between calcium levels and OSAS or its severity.

Parathyroid levels, though not generally reported in OSA studies, were examined in our study. No significant relationship was found between parathyroid levels and OSAS, AHI, or BMI. PTH is expected to increase in cases of vitamin D deficiency due to the role of vitamin D in calcium absorption. However, our study did not find such an association.

5. Conclusion

The relationship between vitamin D deficiency and OSAS remains inconclusive. Routine evaluation of vitamin D, calcium, and PTH levels in OSAS patients could be beneficial, but further studies are needed to clarify the underlying mechanisms and establish definitive guidelines for the management of these patients.

Statement of ethics

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki and was approved *Health Sciences University Adana City Training and Research Hospital for this study (Ethic no: 30.05.2024/29)*

Conflict of interest statement

The authors declare that they have no financial conflict of interest with regard to the content of this report.

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Author Contributions

All authors reviewed the results and approved the final version of the manuscript.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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