ORIGINAL ARTICLE

EFFECT OF VITAMIN D LEVELS ON ASTHMA CONTROL IN ADULTS

Astımlı Hastalarda D Vitamini Düzeyinin Astım Kontrolü Üzerine Etkisi

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ABSTRACT

Objective: The aim of this study is to evaluate the effects of serum vitamin D level and body mass index (BMI) on asthma control and pulmonary functions in asthmatic patients.

Material and Methods: Thirty-five healthy normal controls and 60 patients with asthma were included in the study between December 2016 and February 2017. At initial admission, demographic characteristics and pulmonary function tests (PFT) were recorded and laboratory tests including serum vitamin D, calcium, phosphorus, parathormone and alkaline phosphatase levels were measured. Asthma control test (ACT) was performed to asthmatic patients. Fifty-three patients with asthma and 32 healthy controls with decreased vitamin D level were consulted with Endocrinology Department for vitamin D replacement therapy. ACT and PFT were repeated after therapy at third month in asthmatic patients.

Results: There were totally 95 individuals; 76 females (80%) and 19 males (20%), There were no significant difference between age, gender and demographic characteristics between asthmatics and control group. Smoking status and passive smoking rates were similar. There was no significant difference between daily sun exposure, calcium containing diet and menopausal status. Serum phosphorus, calcium, alkaline phosphatase, parathormone and 25-hydroxyvitamin D levels were similar in both groups. Vitamin levels were low in about 90% of both groups. On the first admission, 71.7% of asthmatic patients were uncontrolled, while the rate of uncontrolled patients decreased to 13.2% after the post-replacement evaluation. There was a significant increase of ACT with respect to vitamin D replacement therapy (22.4 ± 2.7 vs 16 ± 5.4, p=0.001). The mean BMI were high in both groups (≥30 kg/m²). The mean ACT score was lower in obese asthmatics than in non-obese patients, but the difference was not significant (15.3 ± 5.4 vs. 17.5 ± 4.8, p= 0.1). Presence of controlled or uncontrolled disease was similar between the obese and non-obese groups (p = 0.744).

Conclusion: It is suggested that vitamin D replacement therapy had positive effects on asthma control and pulmonary functions but further multicenter, prospective studies with large number of cases are needed to evaluate the effect of vitamin D replacement therapy on these parameters.

Keywords: *Asthma; Vitamin D; Asthma Control Test (ACT); Pulmonary Function Test (PFT)*

ÖZET

Amaç: Çalışmamızın amacı, astımlı hastalarda D vitamini düzeyinin ve vücut kitle indeksinin astım kontrolü ve solunum fonksiyonları üzerine etkilerinin araştırılmasıdır.

Gereç ve Yöntemler: Aralık 2016- Şubat 2017 tarihleri arasında 35 sağlıklı kontrol ve 60 astım tanılı hasta çalışmaya alındı. İlk başvurularında demografik verileri sorgulanan katılımcılara solunum fonksiyon testi (SFT) uygulandı, serum D vitamini, kalsiyum, fosfor, parathormon, alkalen fosfataz düzeyleri ölçüldü. Astım hastalarına astım kontrol testi (AKT) uygulandı. D vitamini düzeyi düşük çıkan 53 astım hastası ve 32 sağlıklı kontrol replasman tedavisi için Endokrinoloji Bölümü ile konsülte edildi. D vitamini replasmanı yapılan 53 astım hastasına üçüncü ayda AKT ve SFT tekrarlandı.

Bulgular: Olguların 76'sı (%80) kadın, 19'u (%20) erkekti. Astım ve kontrol grubu arasında yaş, cinsiyet ve demografik verilerde anlamlı farklılık izlenmedi. Aktif ve pasif sigara içiciliği gruplar arasında benzerdi. Her iki grupta günlük güneş ışığı maruziyeti, kalsiyum içerikli beslenme ve menopozal durum açısından fark görülmedi. Her iki grupta fosfor, kalsiyum, alkalen fosfataz, parathormon ve 25-hidroksivitamin D düzeyleri benzerdi. D vitamini seviyeleri her iki grubun yaklaşık %90'ında düşüktü. İlk başvuruda astım hastalarının %71,7'sinde hastalık kontrolsüz iken, replasman sonrası değerlendirmede kontrol altında olmayan hasta oranının %13,2'ye düştüğü görüldü. D vitamini replasmanı sonrası AKT puanında (22,4 ± 2,7), tedavi öncesi AKT puanına (16 ± 5,4) göre anlamlı artış izlendi (p=0,001). Vücut kitle indeksi (VKİ) ortalaması her iki grupta yüksekti (≥30 kg/m2). Ortalama AKT puanının obez astımlılarda obez olmayanlara göre daha düşük olduğu izlendi, ancak aradaki fark anlamlı değildi (15,3 ± 5,4 vs. 17,5 ± 4,8, p= 0,1). Obezite varlığına göre astım kontrolü gruplar arasında benzerdi (p=0,744).

Sonuç: Astım hastalarında D vitamini replasman tedavisinin astım kontrolü ve solunum fonksiyonları üzerine olumlu etkilerinin olduğu, D vitamini replasmanının hastalık kontrolü ve solunum fonksiyonları üzerine uzun dönem etkisini değerlendirecek, geniş olgu sayılı, çok merkezli prospektif çalışmalara ihtiyaç olduğu düşünülmektedir.

Anahtar Kelimeler: *Astım; D Vitamini; Astım Kontrol Testi (AKT); Solunum Fonksiyon Testi (SFT)*

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INTRODUCTION

Asthma is a heterogeneous disease characterized by obstructing expiratory airflow, chronic airway inflammation and commonly accompanied with symptoms such as shortness of breath, coughing and wheezing (1–3). Worldwide about 300 million people are estimated to suffer from asthma (4). Varying from one country to the next, asthma is encountered with a frequency ranging from 1% to 18% of the population, with its prevalence among both adults and children having risen in recent years (5,6).

Recently, with the discovery of the immunomodulatory effect of vitamin D, there has been a surge of interest in the relationship between Vitamin D deficiency and the increase in the prevalence of asthma. The relationship between asthma and Vitamin D has become a popular research topic, leading to an increased number of studies on the subject (7). It is thought that Vitamin D can affect the prognosis of asthma with its anti-inflammatory properties, as well as by promoting pulmonary immunity and reducing steroid resistance (8). Vitamin D has been reported to enhance glucocorticoid response in asthmatics who are glucocorticoid resistant by increasing the secretion of interleukin-10 (IL-10) from cluster of differentiation 4 (CD4) cells, to prevent the narrowing of the airways by exerting direct anti-proliferative effect on human airway smooth muscle cells and to thus assist the prevention and treatment of asthma (9,10).

The aim of this study is to evaluate the effects of serum vitamin D level on asthma control and pulmonary functions in asthmatic patients.

MATERIAL AND METHODS

Sixty patients with asthma who were previously diagnosed according to the Global Initiative for Asthma (GINA) criteria and regularly visited our polyclinic for follow-up were included in the study. As a control group, 35 volunteer healthy individuals that underwent PFT (Pulmonary Function Test) and did not violate the exclusion criteria were enrolled.

Due to the seasonal variability of vitamin D, the study was structured to be completed in a single season and winter months (December 2016- February 2017) were picked as the best fit for the timeline of the study.

There were fewer individuals in the control group than those in the asthmatic patients' group, as the number of volunteers that agreed to join the study and met the criteria for inclusion had not surpassed 35 until the end of winter.

Patients under the age of 18, patients with pregnancy or lactation; alcohol or drugs addiction; diagnosed with chronical bronchitis, emphysema, bronchiectasis, cancer, autoimmune diseases, uncontrolled diabetes, hypertension or gastroesophageal reflux; had a history of malabsorption or were on a diet; suffered an upper airway infection in the previous four-weeks and those that received vitamin D replacement in the past were excluded from this study.

All participants provided written informed consent prior to enrolment in the study. Approval was obtained from the local ethics committee (Approval Project no. KÜ GOKAEK 2016/310).

The demographic characteristics (sex, age, BMI [weight (kg)/height squared (m^2)]), nutritional habits, conditions that could affect vitamin D level (menopause, sun exposure, daily calcium intake, turban use) were asked. Smoking history and the passive smoke exposure were recorded. Smoking intensity [cigarettes smoked in a day (packs) x duration of smoking (years)] was calculated. Their respiratory systems were examined. Serum 25-hydroxyvitamin D levels, as well as the levels of calcium (Ca), phosphorous (P), alkaline phosphatase (ALP) and parathormone that can influence the vitamin D levels were checked. Pulmonary function test results of both asthmatics and control group were recorded.

Asthma Control Test (ACT) were performed to patients with asthma. Patients were categorized according to their ACT score, as uncontrolled for 19 or below and controlled for 20 or above. No alterations were made to the ongoing asthma treatments of the patients, who were recommended to continue with their routine clinical controls. Regarding vitamin D levels, while 30 ng/ml and above was taken to be normal, levels below 30 ng/ml was considered vitamin D deficiency. Of all the participants of the study, those with low vitamin D levels were referred to the Endocrinology Department, where they were treated with vitamin D replacement therapy in daily doses of cholecalciferol oral drops amounting to a total of 50000 IU/week, for a duration of 6 to 8 weeks. Once their serum 25-hydoxy vitamin D levels reached the targeted level of 30 ng/ml or above,

patients continued to receive a maintenance dose of 1000 IU/day. At the follow-up control after 3 months of vitamin D replacement therapy, PFT and ACT were repeated for asthmatic patients.

In this study, pulmonary function test was done with a Koko Legend brand (Ferraris Med. Co., USA) portable pulmonary function testing device, in accordance with the criteria of the American Thoracic Society. Prior to the test, each participant was informed of how the test was performed. Two, or three participants were tested each day. At a minimum 3 tests were done with the participant in a sitting position and having rested for 15 minutes. In order to obtain 3 acceptable maneuvers [less than 200 mL variation between both the best two forced vital capacity (FVC) and the best two forced expiratory volume in one second (FEV1) measurements] the test was repeated at most 8 times. If, in spite of this, no acceptable maneuver could be obtained or if the patient got tired testing was ended. FVC, FEV1, FEV1/FVC and peak expiratory flow (PEF) parameters were evaluated with the pulmonary function test. Spirometer was calibrated daily with a 3-L syringe.

A Roche Cobas® c702 2 (Roche Diagnostics, Basel, Switzerland), device was used with a colorimetric method to measure alkaline phosphatase and with a photometric method to measure calcium and phosphorous; while a chemiluminescent method was used with Beckman Coulter UniCel™ DxI 600 Access® Immunoassay System to measure parathormone and with an IDS Immunodiagnostics Systems device to measure 25-hydroxyvitamin D.

Statistical Analysis

Statistical analysis was made with the packaged software IBM SPSS 20.0 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.). G*Power® version 3.1.9.2 (Dusseldorf University, Kiel, Germany) packaged software was used to determine the power of the study/sample size. Power analysis based on the study "Vitamin D deficiency and level of asthma control in women from north of Jordan: A case control study (Samrah, S., et al., J Asthma, 2014; 51(8): 832-8)" computed n=53 for power=0.90 with α=0.05 and β=0.20 (11). Kolmogorov-Smirnov Test was used to assess normality. Numerical variables were given as mean ± standard deviation and frequency (percentages). Variations between the groups were compared with the student's t test when assessing numerical variables with normal distribution. When assessing differences between measurements, t test was used for paired and continuous variables with normal distribution, while McNemar chi-square test was used for categorical variables and to assess the difference between the first and final results of the asthma control test. For categorical variables, differences between the groups were assessed with Fisher's Exact chi-square test, Yates' chi-square test and Monte Carlo chi-square test. For two-tailed tests $p<0.05$ was taken to be statistically significant.

RESULTS

Of the participants 76 (80%) were women, while 19 (20%) were men. Mean age was 54.9 ± 12.9 years (min: 26, max: 91) and mean BMI was 32.52 ± 7.33 kg/m² (min:19.2, max:56.6).

The demographic characteristics of the asthmatics and control group were similar except atopy history (Table 1). There was no statistically significant difference in respect to conditions that could affect the vitamin D level (nutrition, menopause, sun exposure, daily calcium intake and turban use) between the groups (Table 1). Also, vitamin D levels and laboratory findings related with vitamin D (P, Ca, ALP, Parathormone, vitamin D) were similar (Table 1).

Our study has identified a large majority (~90%) of both the asthmatic and control groups to have vitamin D insufficiency (Table 2). The mean vitamin D level was 16.1 ± 10.8 ng/ml in asthmatics and 17.1 ± 10.9 ng/ml in control group, and the difference was not significant (p=0.637). When asthmatics were categorized according to the severity of their asthma, vitamin D levels of different groups were found to be similar (p>0.05).

Initial assessment of chronic asthma severity in asthmatics revealed that 12 patients (20%) were intermittent, 10 patients (16.7%) mild persistent, 24 patients (40%) moderate persistent and 14 patients (22.3%) severe persistent (Figure 1). Regarding patients' treatment, it was found that 85.3% used a combination of inhaled corticosteroids and long-acting beta-2 agonists (ICS+LABA). While a single individual

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Table 1. Demographic characteristics, Conditions associated with vitamin D level, Laboratory results of the groups

		Asthma %	Control %	p
Gender	Female	80	80	
	Male	20	20	
Marital status	Single	1.7	8.6	
	Married	88.3	85.7	
	Divorced	10	5.7	
Education level	Primary school	45	51.4	
	Middle school	8.3	5.7	
	High school	11.7	11.4	
	University	6.7	11.4	
Smoking history	Current smoker	11.7	17.2	
	Ex-smoker	25	22.8	
	Nonsmoker	63.3	60	
Passive smoking	(+)	51.7	37.1	
Atopy	(+)	66.7	17.1	
Comorbidities	Hypertension	43.3	28.6	
	Coronary Artery	15	2.9	
	Disease	5	0	
	Peptic Ulcer & GER	25	20	
	Diabetes Mellitus	30	20	
	Others			
Menopausal status	Pre-menopausal	25	35.7	
	Menopausal	4.2	7.1	0.499
	Postmenopausal	70.8	57.1	
Sun exposure	<1 hour	73.3	74.3	
	1-2 hours	23.3	25.7	0.682
	3-5 hours	3.4	0	
Nutritional properties	Vegetable origin	21.7	8.6	
	Animal origin	8.3	2.9	0.12
	Balanced diet	70	88.6	
Daily calcium consumption	(At least two portion)	53.3	48.6	0.814
Turban use	(+)	72.9	85.7	0.314
Phosphorus mg/dL		3.3 ± 0.5	3.5 ± 0.6	0.061
Calcium mg/dL		9.5 ± 0.6	9.5 ± 0.5	0.811
Alkaline Phosphatase U/L		72.7 ± 21.7	69.6 ± 27.2	0.552
Parathormone pg/ml		86.8 ± 49.7	85 ± 43.1	0.855
25(OH) Vit D ng/ml		16.1 ± 10.8	17.1 ± 10.9	0.637

GER: Gastroesophageal reflux **mg:** milligram, **dL:** deciliter, **U:** unit, **L:** liter, **pg:** picogram, **ml:** milliliter, **25(OH) Vit D:** 25-hydroxy vitamin D

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Table 2. Vitamin D levels of the groups, n (%)

	25(OH) Vit D		
	Low (< 30 ng/ml)	Normal (30-100 ng/ml)	High (>100 ng/ml)
Asthma (n=60)	53 (88.3%)	7 (11.7%)	0
Control (n=35)	32 (91.4%)	3 (8.6%)	0

25(OH) Vit D: 25-hydroxy vitamin D, **ng:** nanogram, **ml:** milliliter

Figure 1. Severity of asthma, %

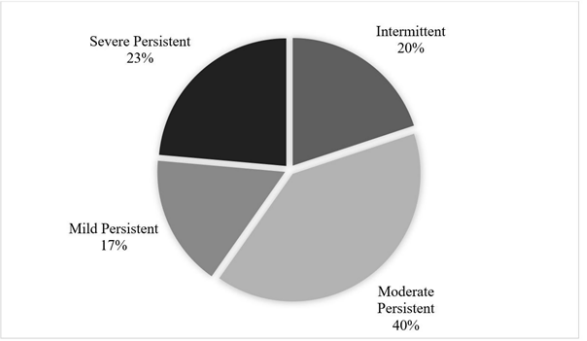
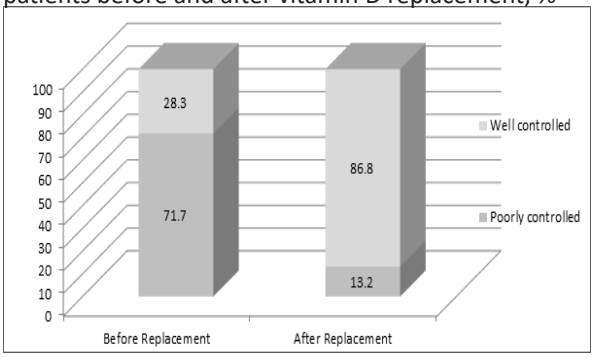


Figure 2. Asthma control test comparison of asthma patients before and after vitamin D replacement, %



(1.7%) used an inhaled corticosteroid only, 4 patients (6.7%) used a combination of inhaled corticosteroids and a leukotriene receptor antagonist (ICS+LTRA).

Initial assessment of the asthma control test of asthmatics revealed that 43 (71.7%) patients had uncontrolled asthma (ACT≤19) while 17 (28.3%) patients' asthma was under control (ACT≥20). Although long-acting beta 2 agonist (LABA) and LTRA usages were higher in the uncontrolled asthma group in comparison to the controlled asthma group as per ACT results, the differences were not statistically significant (p=0.05 and p=0.07). Moreover, no statistically significant difference was found between the controlled and uncontrolled groups, in terms of the distribution of other drugs.

In all 53 patients with low vitamin D levels, following the replacement therapy vitamin D levels were elevated to the normal range. Following the vitamin D replacement therapy, ACT was repeated and compared with the baseline ACT. There was no intervention in the patients' asthma treatment during this entire process.

The post replacement evaluation found that 7 (13.2%) patients' asthma was uncontrolled, while 46 (86.8%) patients' asthma was under control (Figure 2). The difference observed between the asthma control test results of the patients prior to and following vitamin D replacement was statistically significant (p=0.001).

Of the patients whose asthma was under control prior to the vitamin D replacement, none was observed to have uncontrolled asthma following replacement. On the other hand, of the 38 uncontrolled asthmatics, 31's asthma had gotten under control after the replacement therapy (Table 3). The success of the vitamin D replacement therapy was evaluated with McNemar test, and the difference was found to be statistically significant (p=0.001).

Regarding the parameters of the pulmonary function test before and after vitamin D replacement therapy, statistically significant increases were observed in the values of FVC (L), FVC (%) and FEV1/FVC (p=0.007; p=0.014 and p=0.008, respectively) (Table 4).

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Table 3. Distribution of patients according to ACT scores before and after vitamin D replacement, n

		After vitamin D replacement		Total
		Poorly Controlled (ACT ≤19)	Well Controlled (ACT ≥20)	
Before vitamin D replacement	Poorly Controlled (ACT ≤19)	7	31	38
	Well Controlled (ACT ≥20)	0	15	15
Total		7	46	53

ACT: Asthma Control Test

Table 4. PFT, ACT values before and after vitamin D replacement

Asthma (n=53)	Before vitamin D replacement	After vitamin D replacement	p
25(OH) Vit D, ng/ml	12.9 ± 5.4	41.1 ± 15.3	**0.001**
FVC, L	2.35 ± 0.75	2.47 ± 0.8	**0.007**
FVC, %	77.9 ± 19.5	81.4 ± 19.1	**0.014**
FEV_1, L	1.8 ± 0.7	1.84 ± 0.7	0.169
FEV_1, %	72.3 ± 23.1	73.4 ± 21.2	0.399
FEV_1/FVC	76.4 ± 12.4	74.6 ± 11.8	**0.008**
PEF, L	4.9 ± 1.5	5.03 ± 1.5	0.342
PEF, %	76.4 ± 22.1	77.7 ± 21.7	0.471
ACT	16 ± 5.4	22.4 ± 2.7	**0.001**

PFT: Pulmonary Function Test, **ACT:** Asthma Control Test, **25(OH) Vit D:** 25-hydroxy vitamin D, **ng:** nanogram, **ml:** milliliter, **FVC:** Forced vital capacity, **L:** liter, **FEV1:** Forced expiratory volume in one second, **PEF:** Peak expiratory flow

DISCUSSION

It was found that vitamin D deficiency prevalence was extremely high (~90%) in our study population and ACT and PFT scores were significantly improved after vitamin D replacement in asthmatics. At initial admission 71.7% of the patients had uncontrolled asthma, but this rate declined to 13.2% after vitamin D replacement.

In a study conducted in Turkey mean level of 25-hydroxyvitamin D in the overall population was 17.4 ± 11.5 ng/ml while insufficiency and deficiency were evident in 24% and 66% of patients, respectively. Similarly, vitamin D deficiency was quite common in our study (12).

Although numerous studies have examined the relationship between serum vitamin D and asthma, their findings are contradictory. The effects of vitamin D on the pulmonary function parameters, particularly on FEV1 has been widely studied. A study of Chinese adults found a significant association between FEV1, FEV1/FVC and vitamin D (13). In another study, after adjusting for age, sex, height, BMI, ethnicity and history of smoking, a strong relationship was found between vitamin D and FEV1 and FVC (14).

A prospective study of Danish adults found no association between serum vitamin D levels and asthma or the prevalence of atopy, while reporting meaningful association between low levels of vitamin D and low FEV1 percentage, as well as no meaningful association between vitamin D and FEV1/FVC (15). In another study that compared smoking, vitamin D and lung functions, it was stated that vitamin D had no significant effect on lung functions (16). A study with 30 severe uncontrolled asthma patients also failed to show an association between vitamin D and FEV1 (17). Disparities in the findings of these studies are thought to emerge from the differences in sample sizes and study populations.

A study investigating the association of vitamin D with asthma control and severity that included 70 asthmatic patients and 20 healthy controls found strong correlation between vitamin D and asthma severity and control. By taking into account the severity of their symptoms and FEV1 levels, asthmatic patients were divided into four groups as intermittent, mild, moderate and severe in the said study, which found vitamin D levels to decrease markedly as the severity of asthma increased (18). Since a large majority (~90%) of both the asthma and the control groups were identified with vitamin D deficiency in our study, the correlation between FEV1 and vitamin D could not be evaluated. When asthmatic patients were categorized according to the severity of their asthma, different groups were found to have similar vitamin D levels.

In a study examining vitamin D's association with steroid requirement in asthma, which included both asthmatics and a healthy control group, it was reported that more than 75% of the patients used inhaled corticosteroids and 47.6% had vitamin D deficiency; however, details pertaining to the severity of patients' asthma and the year they were diagnosed were not shared. In that study, while no association was found between vitamin D and ICS dose among adult asthma patients, such a relationship was observed in the pediatric group (19). A similar study reported that 54% of the 54 persistent asthma patients used ICS or a combination of ICS+LABA and suggested that vitamin D supplementation should be considered in patients with reduced steroid response (20). In our study, more than 60% of the asthmatic patients were diagnosed more than ten years ago. An assessment of the severity of their chronic disease revealed that a large majority was in the moderate persistent group and that 85.3% used a combination of an inhaled corticosteroid and a long-acting beta 2 agonist. In spite of using ICS+LABA, most of the patients (71.7%) were observed to have poor asthma control. Of the asthma patients 53 were identified with vitamin D deficiency, with just 7 patients having normal levels of vitamin D. This fact suggests that asthma control is hampered by vitamin D deficiency and underlines the importance of assessing comorbidities in addition to medical treatment in asthma control.

Although various studies that assess the relationship between vitamin D replacement and asthma do exist, their findings are inconclusive. In a double-blind, randomized, placebo-controlled study of the relationship between upper respiratory tract infections, asthma exacerbation and vitamin D replacement, 250 adults with asthma were given placebo or oral cholecalciferol drops for over a year and once the vitamin D levels were normalized no significant difference was observed in the annual rate of upper respiratory infections, the ACT score or FEV1 level versus those for the placebo (21). In another multi-center, double-blind, randomized, placebo-controlled study that enrolled patients with symptomatic asthma and vitamin D deficiency, after a 28-week treatment with cholecalciferol or placebo the findings revealed that vitamin D replacement had no significant effect on the treatment or exacerbation of asthma (22). In a similar vein, according to a meta-analysis of seven studies, vitamin D replacement had no significant effect on the ACT and FEV1 and was ineffective in reducing asthma exacerbation; however, it was also stated in this study that not all patients' vitamin D levels had reached the levels released by the Endocrine Society (23). On the other hand, in their study Babar et al. have shown an 8-week long vitamin D replacement to improve FEV1 level (24). Black et al.'s study has also found significant improvements in asthma symptoms, as well as FEV1 and FVC values after vitamin D replacement (14). In a randomized, double-blind study by Majak et al., the risk of asthma exacerbation was found to be lower among kids that received 500 IUs of vitamin D (25). Similarly, another study conducted with asthmatic school age

kids in Japan has found improved asthma control in the group that received vitamin D as opposed to the placebo group (26).

Having been conducted at a single center, the low number of patients enrolled and the lack of information on the long-term results due to the short follow-up period are the limitations of our study. There were very few asthma patients with normal vitamin D levels at initial admission, preventing the formation of an asthmatic control group and this is, arguably, the most significant limitation of our study. Even though the asthma treatment and follow-up of the patients were not interfered with in our study, this circumstance may have increased the adherence to the asthma medication and the ACT score as the patients reached the follow-up for the control for vitamin D. This could be considered as one of the study's limitations. On the other hand, the existence of a healthy control group; the similarities between the asthmatic and control groups in terms of characteristics like age, sex and BMI, as well as factors such as dietary habits, daily calcium intake and menopausal status; and the fact that in all cases vitamin D levels had reached the normal range following vitamin D replacement are the strengths of our study.

CONCLUSION

It was found that 71.7% of the patients had uncontrolled asthma at initial admission, but the rate of patients with uncontrolled asthma declined to 13.2% after vitamin D replacement. Statistically significant improvements were observed in the scores of asthma control tests and pulmonary function tests done before and after vitamin D replacement. It is suggested that vitamin D replacement therapy had positive effects on asthma control and pulmonary functions. This raises the question of whether vitamin D levels should be examined in patients with uncontrolled asthma in the future, and if insufficiency is detected, replacement should be added to the treatment plan.

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