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Comparison of Vitamin D Levels in Allergic Patients with and Without Asthma

Astım Tanısı Olan ve Olmayan Allerjik Hastalarda Vitamin D Seviyelerinin Karşılaştırılması

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Abstract

Objective: To determine whether serum vitamin D levels had a relationship with pulmonary function test (PFT) results and serum immunoglobulin E (IgE) levels in allergic patients with and without asthma.

Method: The study group was comprised of patients who had positive allergy skin tests with and without asthma (n=31, n=28, respectively) and healthy controls (n=31). The skin allergy test (prick test) and PFT were performed on all of the study groups. Also, the patients' serum vitamin D and IgE levels were determined. Comparisons among these groups and also subgroups of the patients were investigated in addition to correlation analyses for vitamin D, IgE and PFT results.

Results: Seventy percent of the asthma group was found to have abnormal PFT results, while all healthy controls and non-asthmatic patients had normal PFT results (p<0.001). IgE levels were significantly higher in asthma and non-asthma groups compared to the control group (p=0.024). Asthma and non-asthma groups were similar regarding the frequency of multiple allergic factors (p=1.000). In terms of vitamin D levels, the asthma group and the non-asthma group were similar, while the healthy control group was found to have a significantly higher mean vitamin D level than both groups.

Conclusion: The results of our study indicate that vitamin D levels are lowered in patients with allergies; however, no association with asthma was determined. Additionally, we found no correlations between vitamin D, IgE and PFT results. The literature on this topic is highly conflicted and there is a requirement for future studies that evaluate vitamin D levels according to covariates.

Keywords: Vitamin D, asthma, allergy

Öz

Amaç: Astım tanısı olan ve olmayan alerjik hastalarda D vitamini düzeylerinin solunum fonksiyon testi (SFT) sonuçları ve serum immünoglobulin E (IgE) düzeyleri ile ilişkisinin belirlenmesi amaçlandı.

Yöntem: Çalışma grubu, alerjik cilt testi pozitif olan astımı olan ve olmayan hastalardan (sırasıyla n=31, n=28) ve sağlıklı kontrollerden (n=31) oluşuyordu. Tüm çalışma grubuna cilt alerji testi (prick testi) ve SFT uygulandı. Ayrıca, hastaların serum vitamin D ve IgE seviyeleri belirlendi. Vitamin D, IgE ve SFT sonuçları arasındaki korelasyon analizlerine ek olarak bu gruplar ve hasta alt grupları arasında karşılaştırmalar yapıldı.

Bulgular: Astım grubunun %70'inde anormal SFT sonuçları saptanırken, tüm sağlıklı kontroller ve astımlı olmayan hastalar normal SFT sonuçlarına sahipti (p<0,001). IgE düzeyleri astım ve astım olmayan gruplarda kontrol grubuna göre anlamlı derecede yüksekti (p=0,024). Astım ve astım olmayan gruplar, çoklu alerjik faktörlerin sıklığı açısından benzerdi (p=1,000). Vitamin D düzeyleri açısından, astım grubu ve astım olmayan grup benzerdi, sağlıklı kontrol grubunun her iki gruptan anlamlı seviyede yüksek ortalama vitamin D seviyesine sahip olduğu bulundu.

Sonuç: Çalışmamızın sonuçları alerjisi olan hastalarda vitamin D seviyelerinin düştüğünü göstermektedir; ancak, astım ile ilişki tespit edilememiştir. Ek olarak, vitamin D, IgE ve SFT sonuçları arasında korelasyon saptanamamıştır. Bu konuyla ilgili literatür oldukça çelişkilidir ve vitamin D seviyelerini karıştırıcı faktölere göre değerlendiren daha ileri çalışmalara ihtiyaç vardır.

Anahtar kelimeler: D vitamini, astım, allerji

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Introduction

Asthma is a respiratory condition which manifests with episodes of spasms in the bronchi. It is a rather complex disease which originates from a variety of genetic changes and has been associated with various environmental triggers; including allergens, microorganisms and irritants (1). In recent years, the prevalence of asthma has been increasing in parallel with the increase in atopic sensitization, in developed and developing countries alike (2).

Many cell types have been associated with asthma pathogenesis and asthma attacks (3) and some relatively recent studies have associated vitamin D levels with asthma incidence and allergic rhinitis (4,5). Indeed, Vitamin D has some properties which can be associated with the immune system, such as regulation of T-cells, production of cytokines, and decrease in the production of IgE (6,7). Furthermore, some studies have shown that lower 25(OH)D levels are associated with various characteristics of the condition, including worsened disease control, attack frequency and respiratory function in terms of clinical findings; and elevation of inflammatory parameters and decrease in T-cell ratio (Th1/Th2) in terms of laboratory findings (8,9,10,11,12). Vitamin D has been shown to promote the production of the anti-inflammatory cytokine, IL-10; while its biologically active form [1.25(OH)D] is suggested to have anti-inflammatory properties in various tissues, including the lung (11,13). Vitamin D receptors have also been found to be abundant in the epithelium and smooth muscle of the respiratory system (14).

Therefore, Vitamin D levels may have an important role in the respiratory system and the body's allergic response. However, to date there has been no definite association between asthma and parameters of pulmonary function and allergy; largely due to differences in disease mechanism and the allergy levels of patients. To address this problem, we comprised our study group from patients who were confirmed to have allergies by prick test. Our aim was to determine the relationship between serum vitamin D levels and the results of pulmonary function test (PFT) and serum immunoglobulin E (IgE) levels in allergic patients with and without asthma, and to compare results with healthy controls.

Material and Methods

A total of 59 patients who had positive allergy skin tests in our clinic from December 2017 to February 2018, and 31 healthy controls were included in the study. The lowest number of individuals required to complete the study with 95% confidence level (alpha=0.05) and 90% power (beta=0.10) was calculated as 48 for each group. One patient group was comprised of those who were positive for both allergy skin test and asthma [asthma group, n=31 (52.5%)], while the other patient group was comprised of patients who were positive for allergy skin test but did not have asthma [non-asthma group, n=28 (47.5%)]. The control group was comprised of 31 healthy individuals.

The criteria for patient inclusion were as follows: 1) being aged between 18-50, 2) having a medical history and physical examination compatible with allergy, 3) having a positive allergy skin test result, and–for those who were included in the asthma group–having stable asthma without any attacks in the prior month. Exclusion criteria were as follows: 1) Acute or chronic respiratory disease, 2) gestation, 3) having any type of autoimmune disease, 4) having any type of oncologic disease. The control group was comprised of health volunteers.

Patients who accepted to participate the study were included in the study after they completed the questionnaire in full. Ethical approval was obtained from the local Clinical Research Ethical Committee (approval no: 25.12.2017/052). All steps of the study complied with the Helsinki Declaration.

Measurements

1-The skin allergy test (prick test) contained the most common allergens such as house dust, mushrooms and pollens. The negative control solution was serum physiologic and the positive control solution was histamine (Albio skin prick test). The application was made on the inside of the forearm and was interpreted after 20 minutes of waiting. A wheal larger than 3 millimeters in diameter was accepted to show a positive result. Patients were told not to use antihistamines and paracetamol during the 10 days before the test.

2-Pulmonary function test was performed with spirometry (Custo Med, Germany) and the patient was told not to use short-acting beta two agonist medications 8 hours before the test. The measurement was performed by closing the nose with the nasal plug while the patient was in the sitting position. Forced expiratory volume (FEV1) and forced vital capacity (FVC) were measured, from which the FEV1/FVC ratio was calculated.

3-Serum Vitamin D concentrations were measured by ELISA (Enzyme-linked Immunosorbent Assay). It was noted that

the patients had not received vitamin D supplementation in the past year. A result between 30-150 ng/mL was considered normal, 10-30 ng/mL was considered to show insufficiency, and 0-10 ng/mL was defined as deficiency (DIA source 25OH Vitamin D Total Elisa kit lowain-L NEUVE).

4-Serum IgE level was measured by ELISA (Bio-Clin-Inc., USA).

Statistical Analysis

All analyses were performed on SPSS version 21. For the normality check of continuous variables, the Shapiro-Wilk test was used. Data were given as mean ± standard deviation for normally distributed data and median (minimum-maximum) for non-normally distributed data. Categorical variables were given as frequency (percentage). The independent samples t-test and the Mann-Whitney U test were used to compare continuous variables in regard to normality of distribution. Categorical variables were evaluated by the chi-square test with continuity correction. For continuous variables, either the Pearson or the Spearman Correlation Coefficients were calculated according to normality of distribution. Comparison of Vitamin D levels were made by using the Analysis of Covariances (ANCOVA) with age as a covariate because of significant correlation between age and Vitamin D levels. For continuous variables, either the Pearson or the Spearman correlation coefficients were calculated according to normality of distribution. We created subgroups for patients and controls regarding the presence of single or multiple allergic factors and comparison of our subgroups were made by two-way Analysis of Variances (ANOVA). P≤ 0.05 values were accepted as statistically significant.

Results

We included 90 individuals into our study, mean age was 33.51±15.92. Mean age was significantly higher in the healthy group than in the other groups (p<0.001) and male frequency was significantly lower in the healthy group than in the other groups (p=0.048). Seventy percent of the patients with asthma were found to have abnormal PFT results while all individuals in the other groups had normal PFT results (p<0.001). IgE levels were significantly higher in the healthy group than in the other groups (p<0.001). We also evaluated a number of allergic factors and found that there were no significant differences between allergic patients with asthma and without asthma regarding the frequency of single factor or multiple factor allergies (p=1.000).

Vitamin D levels were significantly higher in the females (p=0.027; 21.87±13.57 vs 16.54±8.75) and also individuals with normal PFT results (p=0.002; 21.13±12.31 vs 13.90±7.53). There was a significant negative correlation between IgE and Vitamin D levels (r=-0.286; p=0.007) and a significant positive correlation between age and Vitamin D levels (r=0.488; p=0.001). Due to significant differences between our groups regarding age and gender, we used covariance analysis to compare Vitamin D levels (Table 1).

Table 1. Summary of our variables and analysis results between our groups

	Allergic with asthma (n=31)	Allergic without asthma (n=28)	Healthy individuals (n=31)	p
Age	32.19±14.06[a]	25.86±15.15[a]	41.74±14.86[b]	<0.001
Gender				
Male	17 (54.8%)[a]	14 (50.0%)[a]	8 (25.8%)[b]	0.048
Female	14 (45.2%)[a]	14 (50.0%)[a]	23 (74.2%)[b]	
Allergic factor				
Absent	0 (0.0%)[a]	0 (0.0%)[a]	31 (100.0%)[b]	
Single	23 (74.2%)[a]	20 (71.4%)[a]	0 (0.0%)[b]	<0.001
Multiple	8 (25.8%)[a]	8 (28.6%)[a]	0 (0.0%)[b]	
PFT				
Normal	9 (30.0%)[a]	27 (100.0%)[b]	31 (100.0%)[b]	<0.001
Abnormal	21 (70.0%)[a]	0 (0.0%)[b]	0 (0.0%)[b]	
Ig E	130.5 (18.0-2477.0)[a]	87.5 (23.0-323.0)[a]	21.0 (5.0-40.0)[b]	<0.001
Vitamin D	14.60±8.52[a]	12.40±6.1[a]	30.98±10.47[b]	<0.001[(1)]

Ig E: Immunoglobulin E, PFT: Pulmonary function test

Same letters denote lack of significant difference between groups

[(1)]p value calculated by using Analysis of Covariances with age correction

The analysis showed that age was a significant covariate (p=0.002) while gender was non-significant (p=0.438). After Vitamin D levels were corrected according to age, we found that levels were higher in the healthy group compared to the other groups (p<0.001).

Finally, groups were also compared in subgroups according to the number of allergic factors (single vs multiple). No significant differences were observed between these subgroups (p=0.927).

Discussion

In this study we compared vitamin D levels with IgE and PFT results in allergic patients with and without asthma and healthy controls. We did not find a significant difference in terms of vitamin D levels between the asthma and non-asthma groups after adjusting for age. A study comparing asthmatic patients with healthy volunteers reported that asthmatic patients had lower levels of vitamin D levels than healthy volunteers, but no difference between patients with allergic and nonallergic asthma were determined (5). A large collaborative study by the Childhood Asthma Management Program Research Group found that, asthmatic patients with vitamin D level lower than 30 ng/mL (adjusted for various factors) were at higher risk for hospitalization or emergency department visit (Odds ratio, 1.5; 95% CI, 1.1-1.9; p=0.01) (15). In another study, those with vitamin D levels lower than 20 ng/mL were found to be 50% more likely to have asthma compared to those with a vitamin D level between 20-30 ng/mL (16). Shahin et al. (9) defined vitamin D sufficiency as >25 ng/mL and reported lower vitamin D in asthmatic patients compared to healthy controls (19.88±9.6 ng/mL vs 33.5±6.1 ng/mL). In comparison, the whole of our study group showed significantly lower levels than their patients. While our controls had higher vitamin D levels than allergic patients, compared to other studies, overall vitamin D levels were significantly lower in our study group. There may be various explanations for this, including differences in measurement method, race, and location; each of which may be the cause for remarkably low vitamin D levels in the whole of our study group.

The role of IgE in the pathogenesis of allergic diseases is well established. Despite the fact that the patient groups displayed similar allergic characteristics, mean IgE level in the asthma group was significantly higher than that of the control group. However, no correlations were found between IgE and vitamin D levels. In a study comparing allergic and nonallergic asthmatics, IgE levels were reported to be higher in allergic asthmatics and there was also no correlation between IgE level and vitamin D concentration. In the same study, patients with asthma were divided into three groups (hypersensitivity to one inhaled allergen, to more than one inhaled allergen, and to mixed allergens). After evaluation of the comparisons between these groups, the authors of the study suggested that vitamin D insufficiency could be an important part of asthma pathogenesis in patients with hypersensitivity to more than one inhaled allergen (5). We also divided our patients into subgroups according to the presence of single or multiple allergic factors. However, we found no significant difference between single factor and multiple factor groups in the current study. Recent studies have presented controversial data on the correlation between vitamin D and total IgE, some authors suggest that there is no link, while others put forth various associations (5,17,18,19,20). Further studies are needed to clarify this hypothesis.

In the current study, patients were divided into two groups based on PFT result (normal and abnormal PFT). All patients with abnormal PFT were from the asthma group (allergic asthmatic patients). In other words, there was a strong relationship between allergic asthma and abnormal PFT. However, no statistically significant association was found between vitamin D levels and PFT. Tolppanen et al. (21) found a significant association between FEV1 and 25(OH) D2 but no significant correlation between lung function and 25(OH)D3. In another study, it was reported that there was no correlation between vitamin D levels and lung function (5). There are also studies which report contrasting findings; Shahin et al. (9) reported that they found a positive correlation between 25(OH)D level and FEV1% in asthmatic patients. Similarly, Damera et al. (22) reported that higher serum 25(OH)D concentrations in asthmatic patients were associated with higher FEV1%. They suggested that the inhibition of matrix metalloproteinase formation and fibroblast proliferation by vitamin D (which effects collagen synthesis) may be the underlying cause of this association. They also explained that the tissue remodeling effects of 1.25(OH) vitamin D may have significant influence on lung function.

Study Limitations

There are some limitations in our study. Firstly, our study was single-centered, which can be considered as a limitation. Secondly, the observed low levels of vitamin D in all of our participants may be associated with poor health and nutritional or lifestyle factors in general. Apart from some lifestyle factors, other factors which may have

had an effect on vitamin D levels were not considered in the current study.

Conclusion

The results of our study indicate that vitamin D levels are lowered in patients with allergies; however, there was no difference regarding vitamin D levels between allergic patients with and without asthma. Also, there were no correlations between IgE levels and the results of PFT and vitamin D. We also evaluated whether there were any differences between patients in regard to the number of allergic factors (single vs multiple); however, we found no significant differences. Further studies are required to determine whether vitamin D and IgE levels are effective on the pathophysiologic characteristics of asthma.

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Ethics

Ethics Committee Approval: Ethical approval was obtained from the local Clinical Research Ethical Committee (approval no: 25.12.2017/052).

Informed Consent: Patients who accepted to participate the study were included in the study after they completed the questionnaire in full.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: A.S.Ş., Design: A.S.Ş., Data Collection or Processing: A.S.Ş., F.B., Analysis or Interpretation: F.B., Literature Search: A.S.Ş., F.B., Writing: A.S.Ş., F.B.

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