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Evaluation of Vitamin D Levels in Patients with Lichen Planus

Liken Planuslu Hastalarda D Vitamini Düzeyinin Değerlendirilmesi

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ABSTRACT Objective: In recent years, vitamin D has been shown to be effective on cell regulation, proliferation, differentiation, apoptosis and immune modulation. The aim of this study was to investigate vitamin D levels in patients with lichen planus and to determine their relationship with the disease. **Material and Methods:** The study included 40 patients with lichen planus who did not receive topical or systemic treatment in the last 3 months and 40 healthy controls. Clinical evaluation of the disease was made according to the condition of the lesions and severity of itching. Vitamin D level was determined by high pressure liquid chromatography method. **Results:** Vitamin D levels were 14.59±5.63 ng/mL in the control group and 10.86±4.45 ng/mL in the patient group and statistically significantly lower in the patients with lichen planus (p=0.002). There was a negative correlation between the plaque height and the level of itching and vitamin D (r and p values respectively -0.300, 0.007; -0.284, 0.011). **Conclusion:** In this study, although vitamin D levels were lower in both groups, it was found to be significantly lower in patients with lichen planus. Vitamin D deficiency has been shown to exacerbate the clinical manifestations of the disease.

Keywords: Lichen planus; 25-hydroxyvitamin D

ÖZET Amaç: Son yıllarda, vitamin D'nin hücre regülasyonu, proliferasyon, farklılaşma, apoptoz ve bağışıklık modülasyonu üzerinde etkili olduğu gösterilmiştir. Bu çalışmanın amacı liken planuslu hastalarda vitamin D düzeylerini araştırmak ve hastalık ile ilişkisini saptamaktır. **Gereç ve Yöntemler:** Çalışmaya son 3 ay içinde topikal veya sistemik tedavi almayan 40 liken planus hastası ve 40 sağlıklı kontrol dahil edildi. Hastalığın klinik değerlendirmesi, lezyonların durumuna ve kaşınmanın şiddetine göre yapıldı. D vitamini seviyesi, yüksek basınçlı sıvı kromatografi yöntemi ile belirlenmiştir. **Bulgular:** D vitamini düzeyi, kontrol grubunda 14.59 ±5.63 ng/mL, hasta grubunda 10.86 ±4.45 ng/mL idi ve liken planuslu hastalarda istatistiksel olarak anlamlı derecede daha düşüktü (p = 0.002). Plak yüksekliği ve kaşıntı şiddeti ile vitamin D düzeyi arasında negatif korelasyon vardı (sırasıyla r ve p değerleri -0.300, 0.007; -0.284, 0.011). **Sonuç:** Bu çalışmada her iki grupta da D vitamini düzeyi düşük olmasına rağmen liken planuslu hastalarda anlamlı olarak daha düşük bulunmuştur. D vitamini eksikliğinin hastalığın klinik belirtilerini şiddetlendirdiği gözlenmiştir.

Anahtar Kelimeler: Liken planus; 25-hidroksivitamin D

Lichen planus is a chronic inflammatory disease characterized by itchy, purplish, polygonal, and flat papules, often located on the extremities. The disease may also affect the scalp and mucous membranes. Although the exact cause is not known, it is emphasized that many factors such as autoimmunity, materials used in the treatment of dental diseases, drugs, infections trigger disease.[1]

In recent years, vitamin D has been shown to be effective on cell regulation, proliferation, differentiation, apoptosis and immune modulation.[2]

There was a significant relationship between vitamin D deficiency and increased incidence of autoimmune disease. In a study by Van Belle et al., it was concluded that vitamin D deficiency was effective in autoimmune diseases such as Type 1 diabetes, multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, and asthma.[3] In recent years, the role of vitamin D in various skin diseases is emphasized. It has been reported that vitamin D level and vitamin D-related treatment protocols are effective in diseases such as psoriasis, atopic dermatitis, vitiligo, and alopecia areata.[4] The aim of this study was to investigate vitamin D levels in patients with lichen planus and to determine their relationship with the disease.

MATERIAL AND METHODS

The study was approved by the local ethics committee. The research was performed in agreement with the Helsinki Declaration and informed consent obtained from participants. The study was conducted between November 2017 and February 2018. The study included 40 lichen planus patients older than 18 years and 40 healthy controls without any known systemic or dermatological disease. Patients with lichen planus who received topical, systemic therapy or phototherapy in the last 3 months were not included in the study. Cases who received vitamin mineral supplements in the last 6 months, lichen planus cases with only oral lesions or only scalp involvement were excluded from the study. The diagnosis of lichen planus was made by dermatological examination but histopathological examination was performed in suspicious cases. Type 1 diabetes mellitus, pernicious anemia, autoimmune thyroiditis and other autoimmune diseases associated with lichen planus were recorded. In patients' anamnesis, the presence of drug used in the last 6 weeks, emotional stress, dental treatment and viral infection were investigated. Clinical and demographic data of the patients were recorded. Because there was no disease index used for lichen planus, clinical evaluation was made according to the condition of the lesions and the severity of itching. The lesions were evaluated at 3 levels according to their height at the same level as the skin, mild swollen lesions and significant swollen lesions. Involvement of scalp as well as oral, genital and nail involvement associated with typical rashes was recorded.

Venous blood samples taken from the patients were transferred to anticoagulant tubes containing EDTA. The samples were centrifuged at 4000 rpm for 10 minutes. 25 (OH) vitamin D levels in plasma samples were determined by high pressure liquid chromatography method with Thermo Scientific Dionex Ultimate 3000 device in biochemistry laboratory. 25 (OH) vitamin D is the biomarker that provides the best information about the level of vitamin D present in the circulation. Serum calcium (Ca), alkaline phosphatase (ALP) and phosphor (P) levels were measured sperctrophotometrically in ADVIA 1800 Chemistry (Siemens Healthcare GmbH) autoanalyser. Serum parathyroid hormone (PTH) levels were determined by the electrochemiluminescence principle in the Centaur XP (Siemens Healthcare GmbH) immunoassay.

STATISTICAL ANALYSIS

SPSS v.17.0 package program was used for statistical evaluation of obtained data in study (SPSS Inc, Chicago, Illinois, USA). While continuous data were summarized as mean, standard deviation, categorical data were summarized in terms of number and percentage. Chi-square test was used to evaluate the relationship between two categorical variables. Pearson correlation test was used to evaluate the relationship between two continuous variables. Independent T test was used to compare continuous variables between groups. P values below 0.05 were considered statistically significant.

RESULTS

Demographic features of the participants are given in Table 1. Clinical features of the patients with lichen panus are given in Table 2. When the current plaques were evaluated, lesions of 10% (n=4) of the cases were at the same level with the skin, 45% (n=18) of the cases had mild swelling and 45% (n=18) had a significant swelling. 27.5% (n=11) of the cases had mild, 35% (n=14) moderate, 37.5% (n=15) had severe itching. Vitamin D levels were significantly lower in patients with lichen planus

TABLE 1: Demographic features of the participants.

	Lichen Planus Group	Control Group	p
Gender			
Female	23(57.5%)	21(52.5%)	0.653*
Male	17(42.5%)	19(47.5%)	
Age (year)	35.98±9.86	33.40±7.76	0.198**

* The chi-square test was used.

** Student t test was used. The statistical significance level was p <0.05.

TABLE 2: Clinical features of the patients with lichen planus.

Accompanying diseases	
Vitiligo	2.5% (n=1)
Autoimmune thyroiditis	7.5% (n=3)
Type 1 diabetes mellitus	2.5% (n=1)
Etiology	
Stress	20% (n=8)
Drug use	5% (n=2)
Infection	2.5%(n=1)
Dental treatment	2.5%(n=1)
The mean disease duration	10.18 ± 6.79 (min-max:1-24) months
Affected body areas	
Oral	17.5% (n=7)
Genital	12.5% (n=5)
Nail	5% (n=2)
Scalp	0%(n=0)

TABLE 3: Laboratory parameters of the groups.

	Lichen Planus Group	Control Group	p*
Ca (mg/dl)	8.76±0.1	8.73±0.1	0.164
P (mg/dl)	3.37±0.52	3.27±0.71	0.472
PTH (pg/mL)	58.59±15.79	57.82±14.38	0.820
ALP (U/L)	64.50±11.74	66.17±9.9	0.493
Vitamin D (ng/mL)	10.86±4.45	14.59±5.63	0.002

*Student t test was used. The statistical significance level was p <0.05.

Ca: Calcium, P:Phosphor, PTH:Parathyroid hormone, ALP: Alkaline phosphatase.

compared to the control group (p=0.002). There was a significant negative correlation between the height of the plaque and the severity of itching and the vitamin D level (r and p values, respectively -0.300,0.007; -0.284,0.011). Laboratory parameters of the groups are given in the Table 3. There was no correlation between vitamin D and Ca, P and ALP levels (respectively p values 0.802, 0.847, 0.916), and vitamin D and PTH levels were negatively correlated (r = -0.261, p = 0.020).

DISCUSSION

Most of vitamin D is synthesized in the skin in the presence of UVB. Lesser part is provided from vegetable and animal foods.[5] Serum vitamin D level is regulated by Ca, P, PTH, fibroblast growth factor and vitamin D feedback system.[6] Vitamin D has many different roles on skin physiology. It is involved in epidermal differentiation, proliferation, barrier function of the skin, apoptosis in keratinocytes and effective steps in maintaining the structure and function of the skin, which are immunregulatory processes.[7]

Lichen planus is a papulo-squamous disease characterized by chronic inflammation that may affect mucous membranes, skin and mucosa. This disease is triggered by autoimmunity, infection, drugs, exposure to some chemicals, psychogenic and genetic factors. Basal keratinocytes damaged by T lymphocytes indicate that immunological mechanisms are effective in the development of this disease.[8] Even though vitamin D is a known immunomodulator, the number of data associated with connecting vitamin D deficiency to lichen planus is limited. In this study, vitamin D levels were significantly lower in patients with lichen planus. There was a significant negative correlation between plaque height and itching intensity and vitamin D.

The active form of vitamin D is involved in the regulation of the expression of many important genes of the body in different ways and has been shown to be associated with many cancers and autoimmune diseases.[9] Calcitriol has a direct regulatory effect on T lymphocytes. It inhibits the proliferation of Th1 and increases the number of Th 2 cells.[10] Vitamin D deficiency results in a reduction in Th2 cell counts compared to other T cells involved in inflammatory pathways such as Th1 and Th17 cells. This causes exacerbation of the disease in inflammatory diseases such as Lichen Planus.[9]

In a study by Varma et al., three patients with oral lichen planus and accompanying vitamin D deficiency were evaluated. It was emphasized that the clinical findings in patients decreased with vitamin D supplementation and that vitamin D deficiency might be the predisposing factor for lichen planus. Erosive oral lichen planus is known to have malignancy potential. Antiproliferative, antiangiogenic and apoptotic effects of vitamin D in erosive oral lichen planus have been emphasized to prevent malignant transformation.[7]

The effects of topical calcipotriol treatment on patients with lichen planus were investigated by Bayramgürler et al. While 56.3% of the patients responded to the treatment, 43.8% of the cases did not. The authors concluded that calsipotriol is not the first choice for lichen planus but may be a treatment option[8]. In another study by Theng et al. in patients with lichen planus, the effect of calsipotriol and betamethasone valerate on the treatment was compared. When the lesion thickness, pigmentation and pruritus were evaluated after 12 weeks of use, there was no significant difference between the groups.[11]

In a study by Iraji et al. the effect of narrow band UVB and systemic corticosteroids was compared in the treatment of lichen planus. As a result of 6 weeks of treatment in patients with generalized lichen planus, receiving narrow-band UVB 3 times a week was shown to be statistically more effective than prednisolone 0.3 mg / kg (p=0.008).[12] In another study, the effect of narrowband UVB treatment on vitamin D levels was investigated. It has been found that in patients receiving whole body narrow-band UVB treatment with the minimal erythema dose 3 times a week, they develop a significantly higher vitamin D level than those receiving oral D3 supplementation at 400 IU per day. In addition, narrowband UVB therapy has been shown to increase vitamin D levels in patients with psoriasis, atopic dermatitis, vitiligo and polymorphic light eruption.[4]

25 (OH) vitamin D is considered the standardized biomarker existing in the circulation that provides the best information about the levels of vitamin D. These levels were categorized into severe deficient, if the level is below 10 ng/ml, deficient between 10-20 ng/ml, moderate deficient or insufficient between 20-30 ng/ml and sufficient when more than 30 ng/ml.[13] Despite the fact that our country receives sufficient sunlight, low levels of exposure to daylight, use of sunscreen, increased indoor activities, and inadequate intake because of a diet may cause vitamin D deficiency.[3] In this study, vitamin D was also found to be low in healthy controls. This may be related to the fact that the study was carried out during the winter months and to the clothing style and habits of the population in which the study was conducted.

In the literature, vitamin D levels have been investigated in diseases such as psoriasis, atopic dermatitis and vitiligo associated with chronic inflammation and/or autoimmunity.[14] In studies performed in patients with psoriasis, serum vitamin D was shown to be significantly lower than the control group. A negative correlation between vitamin D level and disease severity was reported.[15,16] It has been shown that oral supplementation of vitamin D decreases the severity of the disease and that topical vitamin D analogs are effective in the treatment. As the serum vitamin D level increases with phototherapy, which is commonly used in the treatment of psoriasis, it is thought to contribute to the beneficial effect of phototherapy.[2]

In a meta-analysis study, it was shown that the prevalence of atopic dermatitis increased in populations living in higher geographic latitudes due to lower exposure to sun exposure and thus decreased vitamin D production. It has been reported that levels of serum vitamin D in children and adults with atopic dermatitis are low.[17] In one study, vitamin D supplementation has been shown to normalize inflammatory mediators in the pathogenesis of atopic dermatitis. The beneficial effect of phototherapy on atopic dermatitis has been associated with positive contributions to vitamin D deficiency or insufficiency.[18,19]

In a meta-analysis study, vitiligo was associated with vitamin D deficiency and topical vitamin D analogues and phototherapy have been shown to be effective in the treatment.[20,21] Alopecia areata is a T-cell mediated disease targeting the hair follicle.

Topical calcipotriol application to the affected areas has been found to improve hair growth in alopecia areata patients.[22,23]

CONCLUSION

Vitamin D interacts with almost every cell of the body and contributes to the maintenance of general well-being. In this study, vitamin D levels were significantly lower in patients with lichen planus and were associated with clinical findings. Vitamin D should be considered in the management of lichen planus disease, where the etiology cannot always be determined and treatment difficulties may be experienced.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Mehmet Kamil Mülayim;* ***Design:*** *Hülya Nazik;* ***Control/Supervision:*** *Perihan Öztürk;* ***Data Collection and/or Processing:*** *Hülya Nazik;* ***Analysis and/or Interpretation:*** *Hülya Nazik;* ***Literature Review:*** *Mehmet Kamil Mülayim;* ***Writing the Article:*** *Mehmet Kamil Mülayim;* ***Critical Review:*** *Hülya Nazik, Perihan Öztürk;* ***References and Fundings:*** *Hülya Nazik;* ***Materials:*** *Mehmet Kamil Mülayim.*

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