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Evaluation of 25-HydroxyVitamin D Levels in Patients with Chronic Telogen Effluvium: A Retrospective Analysis of 291 Cases

Kronik Telogen Effluvium Hastalarında 25 Hidroksi Vitamin D Düzeylerinin Değerlendirilmesi: 291 Olguluk Retrospektif Analiz

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ABSTRACT Objective: Telogen effluvium is a common diluted, non-scarring, and frequently observed hair loss type classified into acute (less than 6 months) and chronic (more than 6 months). Some etiological reasons are hypothesized to contribute to telogen effluvium pathogenesis, one of which is the vitamin D inadequacy. Various researches stated conflicting consequences on "serum 25 hydroxy vitamin D" (25-OH vitamin D) levels, and also relationship regarding telogen effluvium. In this retrospective analysis, it is targeted to evaluate and compare serum "25-OH vitamin D" levels in chronic telogen effluvium patients with control group in a large research group. **Material and Methods:** Results of serum 25-OH vitamin D levels in 291 chronic telogen effluvium patients and 258 healthy individuals were evaluated retrospectively and compared to each other. **Results:** A statistically significantly lower serum amount of 25-OH vitamin D was observed in patients of chronic telogen effluvium compared with the stable control group ($p<0.001$). Prevalence of vitamin D deficiency was seen to be 82.1% in chronic telogen effluvium patient group. **Conclusion:** Based on these findings, it is believed that serum 25-OH levels of vitamin D may be routinely evaluated in patients with chronic telogen effluvium and vitamin D supplementation choice for such patients can be recommended for further research.

Keywords: Vitamin D; telogen effluvium; vitamin D deficiency; hair disorder

ÖZET Amaç: Telogen effluvium skar yapmayan, yaygın tutulumlu ve toplumda yaygın görülen saç dökülmesi tipi olup; 6 aydan kısa sürenler akut, 6 aydan uzun sürenler kronik olarak sınıflandırılır. Birçok faktörün telogen effluvium patogenezi için katkıda bulunduğu üzerinde düşünülmüş olup bunlardan bir tanesi vitamin D eksikliğidir. Serum 25 hydroksi vitamin D (25-OH vitamin D) düzeyi ile telogen effluvium arasındaki ilişkiyi araştıran önceki çalışmaların sonuçları çelişkilidir. Bu retrospektif analizde, katılımcı sayısı yüksek çalışma grubunda biz 25-OH vitamin D düzeyleri açısından kronik telogen effluvium hastaları ile kontrol grubunu karşılaştırıp değerlendirmeyi amaçladık. **Gereç ve Yöntemler:** İki yüz doksan bir kronik telogen effluvium hastası ve 258 sağlıklı bireyin serum 25-OH vitamin D seviyeleri retrospektif olarak değerlendirildi ve birbiriyle karşılaştırıldı. **Bulgular:** Kronik telogen effluvium hasta grubunun serum 25-OH vitamin D düzeyleri sağlıklı kontrol grubu ile karşılaştırıldığında hasta grubunda kontrol grubuna gore istatiksel olarak anlamlı oranda düşük serum 25-OH vitamin D seviyeleri gözlendi ($p<0,001$). Vitamin D eksikliğinin kronik telogen effluvium hasta grubundaki prevalansı %82.1 idi. **Sonuç:** Çalışma bulgularına göre, kronik telogen effluvium hastalarında serum 25-OH vitamin D düzeylerinin rutin olarak değerlendirilebileceğini, bu hastalarda vitamin D takviyesinin tedavi seçeneği olarak düşünülebileceğini ileri sürmekteyiz.

Anahtar Kelimeler: Vitamin D; telogen effluvium vitamin D eksikliği; saç hastalığı

As a frequently seen type of diffuse noncicatricial alopecia, Telogen Effluvium (TE), is defined as loss of hair in the stage of telogen.[1] Many etiologic factors such as acute hemorrhage, surgical operations, pregnancy, crash diet and chronic diseases including thyroid dysfunction, liver and renal diseases, malignancies, severe vitamin and mineral deficiency, systemic lupus erythematosus can cause telogen

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effluvium.[2,3] This is classified as acute TE if hair loss continues for less than six months. Chronic TE lasts longer than 6 months. Hair loss in patients with acute TE is diffuse and starts suddenly. Self-limiting occurs two or three months after trigger factors. Chronic TE is hair loss that lasts more than six months without identifiable trigger factors.[4,5]

Skin is not only target tissue for vitamin D. Two types of vitamin D can be seen. Cholecalciferol is synthesized with food in the skin and ergocalciferol is obtained orally. Due to natural circumstances, the influence of sunlight releases 90-95 percent of vitamin D on the skin. Skin is the tissue where the synthesis of vitamin D from 7-dehydrocholesterol to cholecalciferol in epidermal keratinocytes, dermal fibroblasts starts by the effect of sunlight.[6] Then, cholecalciferol is hydroxylated to the active form of 1,25-dihydroxy vitamin D in the liver and kidney.[7] Vitamin D is believed to have an impact on hair follicle differentiation and deficiency of vitamin D is a reason suspected of TE ethiopathogenesis.[2,4,8]

Reported details about the serum vitamin D level and its interaction with TE seems to be contradictory. In this study, it is targeted to assess levels of serum 25-OH vitamin D and its effect on hair loss in chronic TE patients.

MATERIAL AND METHODS

The institutional review board protocal approval was obtained from the local committee of Clinical and Laboratory Research Ethics of Aksaray University (Approval date: 19.04.2019 and decision number: 19/03-58). The study was conducted at Aksaray University Training and Research Hospital, Dermatology Department between January 2017 and March 2017. These months are known to be winter, with minimum ultraviolet exposure in central Anatolia, where both patients and controls were living in. This research was carried out compatible with the Declaration of Helsinki principles. This retrospective and single-centered research contained patients admitting to outpatient dermatology clinics with diffuse hair loss and diagnosing as chronic telogen effluvium. Patients' files were reviewed, and according to the anamnesis and dermatological examination written in the files, the patients who were examined by the same dermatologists, whose hair pull tests were positive and who didn't have bitemporal hair loss were involved in the research. Patients with cicatricial, female type androgenetic alopecia and local alopecia, systemic diseases, infections, malignancy, pregnancy, lactation and drug users for at least one year were excluded from the study. Female participants who were in menapause periods were also excluded from the study.

Files of 291 patients were reviewed and analyzed. Healthy control group (n=258) which applied to the outpatient clinics for check-up without no history of systemic diseases and drug use was included in the study and their files were reviewed. Participants' serum 25-OH vitamin D which were measured by using Roche Cobas E601 Modular Diagnostic System levels and demographic features were recorded. Status of vitamin D was classified by using the acceptable cut off points like deficiency of vitamin D (<20 ng/ml), inadequacy of vitamin D (21-29 ng/ml) and adequacy of vitamin D (>30).[9]

STATISTICAL ANALYSIS

SPSS 23.0 version package program was used to analyze the data. The data distribution normality was assessed through Shapiro-Wilk test. Continued variables were represented by numbers and percentages as mean±standard deviation and categorical variables. Examination of the difference between categorical variables was assessed with the test of chi-square and the analysis of the difference between repeated variables using the Mann-Whitney-U test. A p value of <0.05 was evaluated as statistically significant.

RESULTS

Of the patients diagnosed with chronic TE (n=291), 84 (28.9%) were male and 207 (71.1%) female, and mean age was 24.13±7.7 years. The mean serum 25-OH vitamin D level was 14.39±7.81 ng/ml in patients with chronic TE. Chronic TE patient group consisted of 239 (82.1%) patients with vitamin D deficiency (Table 1). A statistically significantly lower level of serum 25-OH vitamin D was observed in patients with chronic TE in comparison with the healthy con-

TABLE 1: Comparison of chronic TE and control group with regard to demographic features and levels of serum 25-OH vitamin D.

	Chronic TE Patient Group (n=291)	Control Group (n=258)	p value
Age n (%)	24.13±7.7	24.70±10.5	p>0.05
Sex n (%)	Female Male	Female Male	
	207 (71.4) 84 (28.9)	174 (67.4) 84 (32.6)	p>0.05
BMI (Mean ± SD)	21.46±1.37	21.23±1.23	p>0.05
Serum vitamin D level (Mean ± SD)	14.39±7.81	30.63±9.12	p<0.001
Vitamin D deficiency (<20 ng/ml) n (%)	239 (82.1)	32 (12.4)	p<0.001
Vitamin D inadequacy (20-30 ng/ml) n (%)	43 (14.8)	100 (38.8)	p<0.001
Vitamin D adequacy (>30 ng/ml) n (%)	9 (3.1)	126 (48.8)	p<0.001

TABLE 2: Comparison of levels of serum 25-OH vitamin D in chronic TE patient group according to gender (n=291).

	Serum vitamin 25-OH vitamin D levels			
	Deficiency (<20 ng/ml)	Inadequacy (20-30 ng/ml)	Adequacy (>30 ng/ml)	Total
Sex	n (%)	n (%)	n (%)	n (%)
Female	174 (84.1)	26 (12.6)	7 (3.4)	207 (100)
Male	65 (77.4)	17 (20.2)	2 (2.4)	84 (100)

trol group (p<0.001). No impartant statistically difference was ascertained in serum 25-OH vitamin D levels of chronic TE patients when they were compared according to gender (p=0.234) (Table 2).

DISCUSSION

Although vitamin D is particularly considered as the major hormone to control bone and calcium metabolism for years, it is shown with the studies that vitamin D plays important roles in cutaneous homeostasis and immunoregulation, it protects from ultraviolet radiation, infectious agents, oxidative stress and malignancy.[3,10,11] Cell proliferation and differentiation, immunological functional are the vital functions of vitamin D and on account of these, vitamin D is related with various systemic and dermatologic diseases and has been a significant treatment option for those diseases.[12]

Vitamin D has a hand in the regulation of keratinocyte growth and differentiation through a binding receptor for nuclear vitamin D (VDR). Macrophages, keratinocytes, lymphocytes, dendritic cells, especially "mesodermal dermal papilla cells and epidermal keratinocytes", which are dense in hair follicle, expressed VDR. This receptor plays an important role for the integrity of hair follicules. This expression is essential for normal hair follicle cycle.[3] It was discovered in a study with murine hair follicle that for VDR hair follicle keratinocytes are immunoreactive and showed the best performance in the anagen level.[13] In literature hair loss has been reported in patients regarding type II vitamin D-dependent rickets, thereby disclosing vitamin D function in the hair follicle. Patients with VDR gene mutations resulted in resistance to vitamin D, sparse body hair often concerning total scalp and body alopecia.[7] According to their study, Seleit et al. suggested about VDR gene polimorphism and its association with chronic TE, that new anagen proliferation was prohibited due to hair stem cell proliferation in patients' inhibition with VDR gene polimorphism (Taq1 and Cdx1 polimorphism) after exposure of physical or mental stress and for this reason, TE was persistent and chronic.[14]

It was found that, in comparison with our study's control group, serum 25-OH vitamin D levels were slightly lower in the chronic TE patient population, and 82.1 percent of 291 chronic TE patients had vitamin D inadequacy. Parallel to our findings, Gürel et al. compared 80 healthy individuals with 80 TE patients. It was revealed that the serum levels of 25-OH vitamin D were significantly lower in patients with TE compared to healthy individuals.[2] Rasheed et al., in the study with 80 TE and female type hair loss patient group, 40 control group, found both ferritin and levels of vitamin D

lower in patient group than in healthy individuals.[15] Nayak et al., in the study with 44 female patients, found low levels of vitamin D in patients with diffuse hair loss compared with control group and it was found that 81.8% cases had vitamin D deficiency. They suggest that vitamin D assessment is significant in diffuse hair loss, it is required to search the hair growth pattern following vitamin D supplementation in the affected group.[16]

In a retrospective study with 115 patients diagnosed as acute and chronic TE, deficiency vitamin D deficiency was observed in 33.9% of the patients with acute and chronic TE. Besides, ferritin, vitamin B12, folate, and zinc were examined and no control population was included in the study. Deficiency in ferritin (45.2%) and zinc (9.6%), vitamin B12 (2.6%) were detected, and no one had folate deficiency in the study.[1]

Karadağ et al., in the study with 63 female patients and 50 control group, classified as acute TE (n=29) and chronic TE (n=34). In acute and chronic TE patient group, serum 25-OH vitamin D levels were found quite higher than in control group. Due to the same study, serum ferritin and hemoglobin levels were found to be low in TE patients in comparison with the control group. They suggested that iron deficiency was the main trigger factor in TE patients, and vitamin D level increase might be seen as a compensator way to TE.[4] The other hypothesis for this is that melanin synthesis loss in telogen hair follicles can cause a huge vitamin D synthesis in the skin.[17]

According to Conic et. al.'s research, vitamin D levels were compared between different kinds of alopecia in 358 patients [TE (n=121), alopecia areata (n=77), androgenic alopecia (n=73), lichen planopilaris (n=58), and central centrifugal scarring alopecia (n=29)]. They found that patients with TE had 3.7 times higher odds of serious vitamin D inadequacy compared with alopecia areata. And men suffered from a larger rate of vitamin D inadequacy. According to the study, they suggested that inadequacy of vitamin D testing should be evaluated in alopecia patients and they recommended giving vitamin D supplementation.[18] However, in this research it was pointed that supplementation efficacy of vitamin D was questionable, and some researches showed detrimental supplementation impacts.[19]

In a study of Poonia et. al., it is found that 81 of 100 cases with non-scarring diffuse hair loss [chronic TE (62%), female pattern hair loss (22%), acute TE (16%)] had low levels of serum vitamin D3 (< 30 ng/mL). Besides, low levels of serum ferritin were seen in 20 patients, low levels of vitamin B12 were seen in 76 patients in the study. They suggest that serum vitamin D, ferritin, and vitamin B12 levels have an important impact on the loss of hair pathogenesis, and their supplementation may be required for the patients with non-scarring diffuse hair loss.[20]

According to the results of our study, compatible with previous researches, we reveal that chronic TE may be associated with vitamin D inadequacy. Our study has the comparison data with the largest patient and control group ever as compared to the other studies. Another difference of our study from others the is that patient group consisted of only patients with chronic TE. We did not evaluate the files of patients with acute TE and other diffuse hair loss. Retrospective design could be assessed as a limitation of the research. Due to many reports, levels of serum vitamin D were lessened in comparison with the controls that is thought one of the main factors leading to loss of hair. And also it is not obvious whether low serum vitamin D levels are secondary to hair loss or hair loss secondary to low vitamin D levels. Thus, there are many question marks that should be investigated about vitamin D and its connection with chronic TE.

CONCLUSION

Our research highlights the significance of performing serum vitamin D in chronic TE patients as a routine laboratory work. Supplementation of vitamin D may be considered as an option of treatment and this topic may be investigated in further studies whether supplementation of vitamin D is successful or not for chronic TE treatment.

Source of Finance

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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: *Funda Kemeriz, Sibel Çiğdem Tuncer, Burcu Tuğrul;* ***Design:*** *Funda Kemeriz, Sibel Çiğdem Tuncer, Burcu Tuğrul;* ***Control/Supervision:*** *Funda Kemeriz, Sibel Çiğdem Tuncer, Burcu Tuğrul;* ***Data Collection and/or Processing:*** *Funda Kemeriz, Sibel Çiğdem Tuncer;* ***Analysis and/or Interpretation:*** *Funda Kemeriz, Sibel Çiğdem Tuncer, Burcu Tuğrul;* ***Literature Review:*** *Funda Kemeriz,Burcu Tuğrul;* ***Writing the Article:*** *Funda Kemeriz;* ***Critical Review:*** *Funda Kemeriz, Burcu Tuğrul.*

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