Research Article (Araştırma Makalesi)

Serum 25-Hydroxy Vitamin D Level Does Not Reflect The Severity of Wart: A Cross-Sectional Study

Serum 25-Hidroksi Vitamin D Düzeyi Siğil Şiddetini Yansıtmaz: Kesitsel Bir Çalışma

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Özet

Amaç: Verruka vulgaris, human papilloma virüslerinin neden olduğu benign epiteliyal proliferatif bir hastalıktır. Siğil tedavisinde topikal ve intralezyonel D vitamini uygulamaları etkili yöntemlerdir. Bununla birlikte, hastalık ile serum D vitamini düzeyleri arasındaki ilişki belirsizdir. Hastalığın şiddeti ile serum 25-hidroksi D vitamini (25-OH vit D) düzeyleri arasındaki ilişki daha önce araştırılmamıştır. Bu çalışmada verruka vulgarisli hastalarda serum 25-OH vit D düzeyleri ile hastalık şiddeti arasındaki ilişkinin belirlenmesi amaçlanmıştır.

Gereç ve Yöntemler: Verruka vulgarisli 40 hasta ile cinsiyet ve yaş açısından eşleştirilmiş 43 sağlıklı gönüllünün serum 25-OH vit D düzeyleri ölçüldü. Hastalar verruka vulgaris hastalık şiddeti ve süresine göre gruplandırılarak serum 25-OH vit D düzeyleri kaşılaştırıldı.

Bulgular: Verruka vulgaris hastaları ile kontrol grubu arasında serum 25-OH vit D düzeylerinde anlamlı fark yoktu (p=0.760). Hastalar verruka vulgaris hastalık şiddeti ve süresine göre gruplandırıldığında hafif hastalığı olanlar ile şiddetli hastalığı olanlar arasında serum 25-OH vit D düzeyleri farklı değildi.

Sonuç: Serum 25-OH vit D düzeyi verruka vulgaris ile ilişkili değildir. Serum 25-OH vit D düzeyleri hastalık şiddeti ve süresi ile de ilişkili değildir. Verilerimiz verruka vulgarisin önlenmesi veya tedavisi için D vitamini takviyesini desteklememektedir.

Anahtar kelimeler: Hastalık şiddeti, Serum 25-hidroksi D vitamini, Verruka vulgaris

Abstract

Objective: Verruca vulgaris is a benign epithelial proliferative disease caused by human papilloma viruses. Topical and intralesional vitamin D applications are effective methods in the treatment of warts. However, the relationship between the disease and serum vitamin D levels is unclear. The correlation between the severity of the disease and serum 25-hydroxy vitamin D (25-OH vit D) levels have not been previously investigated. This study aimed to determine the relationship between serum 25-OH vit D levels and disease severity in patients with verruca vulgaris.

Material and Methods: Serum 25-OH vit D levels were evaluated in 40 patients with verruca vulgaris and 43 sex and age-matched healthy volunteers. Serum 25-OH vit D levels were compared by grouping the patients according to the severity and duration of verruca vulgaris disease

Results: There was no significant difference in serum 25-OH vit D levels between verruca vulgaris patients and the control group (p=0.760). There was no significant difference between serum 25-OH vit D level, disease severity and disease duration in the verruca vulgaris group (p =0.102, p=0.257, respectively).

Conclusion: Serum 25-OH vit D level was not associated with verruca vulgaris. Serum 25-OH vit D levels are not related to disease severity and duration. Our data do not support vitamin D supplementation for the prevention or treatment of verruca vulgaris.

Keywords: Disease severity, Serum 25-hydroxy vitamin D, Verruca vulgaris

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INTRODUCTION

Verruca vulgaris is a self-limiting benign epidermal proliferation secondary to human papilloma virus infection in the skin and mucous membranes. It can be a single wart or sometimes appear as dozens of warts or mosaic warts. Although there are numerous therapeutic options in the treatment of warts, none of them are considered as the gold standard treatment method. Topical vitamin D administration is one of the effective treatment methods for warts (1-4). Vitamin D (25-OH vit D) is thought to be effective by regulating epidermal cell proliferation and differentiation and modulating cytokine production (5). For the first time in 2016, Aktaş et al. (6) reported that intralesional vitamin D injection may be an effective treatment option in patients with warts. However, the authors reported that their study was limited by the fact that patients' serum vitamin D levels were not measured. Many studies in recent years have supported the effectiveness of intralesional vitamin D injection for the treatment of warts (7-9). However, serum vitamin D levels were not investigated in any of these studies.

The effectiveness of the topical application or intralesional injection of vitamin D in the treatment of warts suggests that there may be a relationship between serum vitamin D levels and verruca vulgaris. To the best of our knowledge, serum 25-hydroxy vitamin D (25-OH vit D) levels was investigated in only two studies in patients with warts (10,11). Although the results of these studies are contradictory, the relationship between disease severity and serum 25-OH vit D level was not evaluated in these studies. In this study, for the first time in the literature, we investigate the relationship between disease severity and serum 25-OH vit D level in patients with verruca vulgaris.

The aim of this study was to evaluate the serum 25-OH vit D levels of patients with verruca vulgaris and to determine the relationship between serum 25-OH vit D levels and disease severity.

MATERIALS AND METHODS

In this prospective case-control study, patients diagnosed with verruca vulgaris who were admitted to the dermatology outpatient clinic between September 2018 and March 2020 were evaluated. Patients under 18 and over 65 were excluded from the study. Patients with conditions affecting serum 25-OH vit D levels; pregnant patients, breastfeeding mothers, systemic disease (liver, kidney and bone metabolism diseases, etc.), history of smoking and alcohol use, and history of drug use (vitamin D and calcium supplements, bisphosphonates, corticosteroid, etc.) were excluded from the study. In order to keep the skin type distribution similar, individuals with Fitzpatrick's skin types 2 and 3, which are common in our country, were included in the study, while individuals with more rare Fitzpatrick skin types 1, 4, 5 and 6, were excluded from the study. Patients with a history of a disease that may cause immune deficiency and patients on immunosuppressive drugs were also excluded from the study, as they may affect the severity of the warts. Forty patients with verruca vulgaris and 43 sex-age and Fitzpatrick's skin type matched healthy volunteers were included in the study. Age, gender, number of warts, disease duration and serum 25-OH vit D levels were recorded. If the number of warts was less than 3, it was considered a mild disease. If the number of warts was 3 and above and/or mosaic wart, it was considered as a severe disease. Serum 25-OH vit D levels of the groups were compared. Serum 25-OH vit D levels were compared with disease severity and disease duration. The study was performed in accordance with the principles of the Declaration of Helsinki and approved by our Institutional Ethical Committee (2018/8-4). Written informed consent was obtained from all patients.

Statistical analysis

SPSS version 21 (SPSS software, Chicago, IL, USA) was used for data analysis. Descriptive statistics were expressed as percentage, mean, standard deviation, median, and minimum and maximum values. The Mann Whitney-U test was used to compare the serum 25-OH vit D values of the case group and the control group and to evaluate the relationship between disease severity and serum 25-OH vit D level. The Spearman correlation test was used to determine the relationship between disease duration and serum 25-OH vit D level. P-values <0.05 were considered to indicate statistical significance.

RESULTS

There were no significant differences between the groups in age, gender and Fitzpatrick's skin type ratio (**Table 1**). Mean serum 25-OH vit D level was 13.98±7.83 (5-50, range) ng/ml in the case group and 13.83±8.21 (4-41, range) ng/ml in the control group. There was no difference between 25-OH vit D levels between the groups (p=0.760). Serum 25-OH vit D levels are given in **Table 2** in patients with verruca vulgaris and control group.

Table 1. Age, gender, and Fitzpatrick's skin type distribution of verruca vulgaris and control group			
	Verruca vulgaris (n= 40)	**Control (n=43)**	**P-value**
Age (years)			
Mean ± SD	26.33±10.80	29.67±12.90	0.179[a]
min-max	18-64	18-65	
Sex - n (%)			0.400[b]
Female	32 (80.0)	31 (72.1)	
Male	8 (20.0)	12 (27.9)	
Fitzpatrick's skin type - n (%)			0.562[b]
Type 2	16 (40)	17 (39.5)	
Type 3	24 (60)	26 (60.5)	

[a] Mann Whitney-U test, b Chi-square test

Table 2. Serum 25-Hydroxy Vitamin D levels in patients with verruca vulgaris and the control group.				
Serum 25-Hydroxy Vitamin D levels (ng/ml)	**Verruca vulgaris (n=40)**		**Control (n=43)**	
	n	**%**	**n**	**%**
≤10	11	27.5	16	37.2
>10 - ≤20	24	60.0	21	48.8
>20 - ≤30	4	10.0	4	9.3
>30	1	2.5	2	4.7

Table 3. Disease severity and serum 25-Hydroxy Vitamin D levels in patients with verruca vulgaris			
Serum 25-Hydroxy Vitamin D levels	**Mild n = 13**	**Severe n = 27**	**P-value**
Mean ± SD	11.20±5.01	15.31±8.65	0.102[a]
min-max	5-21	5-50	

[a] Mann Whitney-U test

Of the 40 patients with verruca vulgaris, 13 (32.5%) had mild and 27 (67.5%) had severe disease. There was no significant relationship between disease severity and serum 25-OH vit D level (**Table 3**). The mean duration of disease in patients with verruca vulgaris was 12.05±15.52 (1-72, range) months. There was no significant relationship between disease duration and serum 25-OH vit D level (p=0.257).

DISCUSSION

This study is the first study to investigate the relationship between disease severity and serum 25-OH vit D level in patients with verruca vulgaris. In the current study, the serum 25-OH vit D levels of patients with warts were similar to the control group, and serum 25-OH vit D levels in patients with verruca vulgaris did not correlate with the severity of disease and disease duration. The results of our study suggest that serum 25-OH vit D level is not a factor in the disease aetiology. Furthermore, this study shows that although topical and intralesional vitamin D applications are effective in wart treatment, vitamin D supplements may not show the same effect.

Vitamin D is a hormone required for the proper functioning of the central nervous system, immune system, cardiovascular system, and especially the skeletal system. An increase in the frequency of organ function disorders, cancer and autoimmune diseases has been reported in vitamin D deficiency (12). Vitamin D exerts anti-microbial effects on both natural immunity and adaptive immunity in different ways. In macrophages, vitamin D receptor expression and vitamin D-1-hydroxylase gene expression increase with toll like receptor stimulation, which causes cathedilin stimulation, an

antimicrobial peptide (4). These antimicrobial peptides increase the destruction of Mycobacterium tuberculosis by damaging the cell wall, and increase monocyte chemotaxis to that area (13). Vitamin D shows an immunoregulatory effect by decreasing the formation of T helper 1-9-17 and increasing the differentiation of T helper 2 and regulatory T cells (14). Adequate levels of vitamin D control the T cell antigen receptor signal pathway, enabling killer T cells to eliminate serious infections (13). Indeed, in viral infections such as hepatitis C, human immunodeficiency virus, eczema herpeticum, the body's response to the virus has been associated with vitamin D levels (14). The increase observed in respiratory infections due to influenza virus in the winter season is associated with seasonally decreasing vitamin D values (13). However, in this study, we did not find a relationship between verruca vulgaris and serum 25-OH vit D level. This may be due to the fact that warts do not cause a generalized infection like the aforementioned conditions, and is a result of local infection of the skin. It has been shown that a low vitamin D level is associated with increased cutaneous bacterial infection (15). Since verruca vulgaris is a cutaneous viral infection, serum 25-OH vit D may not be associated with warts.

The relationship between skin diseases and serum 25-OH vit D levels has become a topic of interest and research in recent years. Psoriasis, atopic dermatitis, vitiligo, alopecia areata, mycosis fungoides, systemic lupus erythematosus, systemic sclerosis and acne are skin diseases associated with low serum vitamin D levels (16-24). To the best of our knowledge, the relationship between verruca vulgaris and serum 25-OH vit D has only been investigated in two studies, and the results of these two studies are opposite (10,11). Öztekin et al. reported that serum 25-OH vit D levels of verruca vulgaris patients were significantly lower than the control group (10). Tamer et al. did not find a relationship between verruca vulgaris and serum 25-OH vit D levels similar to our results (11). In the study of Öztekin et al. the fact that verruca patients and the control group did not have similar age distribution, the uncertainty of the distribution of Fitzpatrick's skin types between the two groups, and smokers and alcohol users were not excluded from the study may be factors affecting the results of their studies (10). The common point of these two studies and our study is that the mean serum 25-OH vit D levels of both patient group and control group were lower than normal. Vitamin D deficiency is a problem that is widespread in Turkey and in the world (25,26). Solak et al. reported the mean serum 25-OH vit D value as 15.2±8.8 ng/mL in 35,667 Turkish individuals (26). The control group's serum 25-OH vit D value, such as patients with warts, may be a factor that makes it difficult to determine the relationship between disease and vitamin D level. However, the relationship between verruca vulgaris severity and serum 25-OH vit D level has not been investigated before. In this study, we divided the severity of the disease into mild (patients with less than three warts) and severe (patients with three or more warts and/or patients with mosaic warts). However, we did not find a relationship between severity of disease and serum 25-OH vit D level. In our study, there was no relationship between disease duration and serum 25-OH vit D value. Both the serum 25-OH vit D levels of verruca vulgaris patients were not significantly lower than the healthy individuals and the severity and duration of the disease was not associated with the serum 25-OH vit D level, suggesting that serum 25-OH vit D level is not a factor in the aetiology of verruca vulgaris.

In recent years, it has been reported in many studies that successful treatment has been achieved with both topical and intralesional vitamin D injections (1-4,6-9). Moscarelli et al. applied topical calcitriol to the resistant verruca lesion in the hand of a renal transplant patient and observed complete remission in the lesion (4). Aktaş et al. applied intralesional vitamin D injections to 20 patients with warts and observed complete remission in 80% of patients (6). In verruca vulgaris, it is thought that the possible mechanism of action in local applications, either topical or intralesional injection, is due to the effects of vitamin D on cell proliferation inhibition and differentiation via vitamin D receptors, as well as the immunomodulatory effect on the skin (4,6). However, since the serum 25-OH vit D values of the patients are not known in these studies, it is not possible to establish a relationship between a local application and a possible vitamin D deficiency and response to treatment. We believe that topical and intralesional vitamin D administration in warts patients has been successful in treatment with a local immunomodulatory mechanism rather than raising serum 25-OH vit D level. This will become clearer with studies in which vitamin D levels are measured before and after application in warts patients treated with intralesional vitamin D injection.

In conclusion, serum 25-OH vit D level was not associated with verruca vulgaris. Serum 25-OH vit D levels are not related to disease severity and duration. Our

data do not support vitamin D supplementation for the prevention or treatment verruca vulgaris.

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Ethical Approval: The study was performed in accordance with the principles of the Declaration of Helsinki and approved by our Institutional Ethical Committee (2018/8-4). Written informed consent was obtained from all patients.

Author contributions: All authors contributed equally to the article.

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