The role of serum vitamin D levels in vitiligo

Ebru Karagün1, Can Ergin2, Sevim Baysak3, Günel Erden4, Habibullah Aktaş5, Özlem Ekiz6

1Department of Dermatology, Ağrı State Hospital, Ağrı, Turkey
2Department of Dermatology, Dışkapı Yıldırım Beyazıt Education and Research Hospital, Ankara, Turkey
3Department of Dermatology, Bandırma State Hospital, Balıkesir, Turkey
4Department of Medical Biochemistry, Faculty of Medicine, Hacettepe University, Ankara, Turkey
5Department of Dermatology, Education and Research Hospital, Karabük University, Karabük, Turkey
6Department of Dermatology, Faculty of Medicine, Mustafa Kemal University, Hatay, Turkey

Abstract

Introduction: Vitiligo is a common acquired pigmentary skin disorder. Vitamin D is responsible for skin pigmentation, increases tyrosinase activity and melanogenesis, and exhibits immunoregulatory functions. Low levels of vitamin D are associated with many autoimmune diseases, including systemic lupus, diabetes mellitus, rheumatoid arthritis, multiple sclerosis and alopecia areata. Few reports have evaluated serum vitamin D levels in vitiligo patients, and their results are conflicting.

Aim: To evaluate serum vitamin D levels of vitiligo patients and compare the results with controls.

Material and methods: In total, 50 vitiligo patients and 47 controls were enrolled in the study. Vitamin D levels were measured from blood samples. Group comparisons were performed using appropriate statistical methods.

Results: The patients had lower serum vitamin D levels than the controls, but this difference was not significant (p = 0.570).

Conclusions: It remains unknown whether vitamin D deficiency causes vitiligo. Larger controlled studies are required to prove whether low circulating vitamin D is a causative factor in vitiligo.

Key words: vitiligo, vitamin D, autoimmune diseases, etiopathogenesis.

Introduction

Vitiligo, an autoimmune disorder caused by the destruction of melanocytes in the skin, is characterized by depigmented macules of different shapes [1]. The disease may affect both genders and all skin types [2] and may also be associated with systemic autoimmune diseases such as lupus erythematosus, scleroderma, autoimmune thyroiditis and alopecia areata [3]. Reduced serum vitamin D levels are found in many autoimmune diseases including systemic lupus erythematosus, diabetes mellitus, rheumatoid arthritis, multiple sclerosis and alopecia areata [1, 4, 5].

Vitamin D is an essential hormone that is synthesized in the skin [6]. The active form of vitamin D, 1,25-dihydroxyvitamin D3, is a hormone that regulates calcium and bone metabolism, controls cell proliferation and differentiation and also exhibits certain immunoregulatory functions [1]. Vitamin D may affect both innate and adaptive immune responses through receptors in T and B lymphocytes, macrophages and dendritic cells [7]. In addition, vitamin D increases tyrosinase activity and melanogenesis via a nuclear hormone receptor – the vitamin D receptor (VDR) in melanocytes [1, 8]. Vitamin D and its analogues are used to treat skin disorders, including psoriasis and vitiligo [1]. Patients with vitiligo have been treated with topical calcipotriene [1].

Few reports have investigated the association between vitiligo and reduced vitamin D levels, but these studies provide conflicting results [9, 10].

Aim

This study aimed to determine whether patients with vitiligo have lower serum vitamin D levels compared to controls.
Material and methods

In total, 50 patients diagnosed with vitiligo, in our outpatient department from 1 December 2013 to 31 March 2014, were enrolled in the study; 47 age-, gender- and skin phototype-matched healthy controls also participated.

The patients were examined by the same dermatologist and the diagnosis of vitiligo was made according to clinical findings and a Wood's lamp examination. Punch biopsy was performed on suspicious cases, with the diagnosis then verified. Detailed disease and family histories were obtained from all patients. Various demographic and lifestyle factors were recorded, including age, gender, skin phototype and sunscreen usage.

Participants with liver or kidney disorders, hyperparathyroidism, hypoparathyroidism, any metabolic bone disorders (e.g. osteoporosis or osteopenia) or inflammatory diseases were excluded from the study, as were those taking vitamin D- or calcium-including drugs, or any systemic or topical treatment for vitiligo within the previous month. Controls were recruited from the partners or relatives of patients, if not affected by vitiligo, to minimize differences due to dietary intake of vitamin D.

Informed consent was obtained from all participants and the local Ethics Committee approved the study, which was conducted in accordance with the tenets of the Declaration of Helsinki.

Blood samples were taken in the morning after a minimum fasting period of 8 h. Serum free T3, free T4, thyroid stimulating hormone, fasting glucose, anti-thyroid peroxidase antibodies, anti-thyroglobulin antibodies, vitamin B₁₂, and vitamin D levels were measured.

Statistical analysis

Group comparisons were performed using Student’s t-test for continuous variables and a χ² test for categorical variables. Statistical analysis was performed using the SPSS for Windows software package (ver. 17; SPSS Inc., Chicago, IL, USA).

Results

In total, 28 (56%) males and 22 (44%) females were included in the study group. The control group consisted of 30 (63%) males and 17 (37%) females. The mean ages of the patient and control groups were 30.96 ±10.57 and 31.45 ±8.33 years, respectively. There was no significant difference between the patient and controls in terms of age (p = 0.53) or gender (p = 0.43). No participants declared sunscreen usage.

All patients had generalized vitiligo as determined by the presence of bilateral symmetrically distributed depigmented macules in characteristic locations. The mean age at vitiligo macules onset was 18.84 ±8.84 years. The duration of the lesions ranged from 2 to 25 years. A family history of vitiligo was reported in one patient. No patients had diabetes mellitus or vitamin B₁₂ deficiency. Autoimmune thyroid diseases were reported in 12 (24%) patients. Vitamin D levels were tested during the winter months, from December 2013 to March 2014. The patients’ serum vitamin D levels ranged from 6 to 42 ng/ml (mean: 12.04 ±8.84 ng/ml); in the control group they ranged from 8 to 39 ng/ml (mean: 12.91 ±6.08 ng/ml). The patients had lower circulating vitamin D levels than controls, but this difference was not significant (p = 0.570).

Discussion

In the present study, we found lower serum vitamin D levels in patients with vitiligo relative to controls; however, this difference was not significant. Both the patients and controls had very low circulating vitamin D levels. This may be because the blood samples were collected during winter months.

There are very few studies evaluating serum vitamin D levels in vitiligo patients [9, 10]. Ustun et al. investigated 25 vitiligo patients and 41 controls; insufficient (< 30 ng/ml) or very low (< 15 ng/ml) levels of vitamin D were observed in the majority of patients, but the difference was not significant compared to controls [9]. These investigators stated that a large number of studies had reported low levels of circulating vitamin D in autoimmune diseases, but it remains unclear whether this is a cause or result of autoimmune diseases [9]. Another study investigated 40 vitiligo patients and 40 age- and gender-matched controls. Significantly lower serum vitamin D levels were seen in the patients relative to controls. The authors speculated on the possibility of vitamin D supplementation for the treatment of vitiligo patients in the future [10].

The pathogenesis of vitiligo remains largely unknown. There are different theories explaining the pathogenesis of vitiligo, with all genetic, autoimmune, autotoxicotic and neurogenic causes postulated. The autoimmune theory is the best-supported one, because vitiligo may be associated with other autoimmune diseases including pernicious anemia, hyperthyroidism, Hashimoto’s thyroiditis, alopecia areata and adenocortical failure. Furthermore, histological studies have demonstrated a high frequency of cytotoxic T lymphocytes specific to melanocytic antigens in vitiligo lesions, suggesting a direct, melanocyte-specific T cell attack [9, 11, 12].

Vitamin D, which is a fat-soluble vitamin obtained by humans through diet, is of particular interest to dermatologists because it is synthesized in the skin by ultraviolet light. It has been used to treat psoriasis, vitiligo and other skin diseases for many years [9]. The active form of vitamin D, 1,25-dihydroxyvitamin D₃, not only regulates calcium and bone metabolism, but also controls cell proliferation and differentiation and exerts immunoregulatory activities [1]. In a previous study, it was reported that...
patients with comorbid autoimmune illnesses are more likely to have very low serum vitamin D levels [13].

Vitamin D has a nuclear receptor called vitamin D receptor (VDR). Vitamin D receptors are present in the cells involved in calcium and bone metabolism, and also in keratinocytes, melanocytes, fibroblasts and immune system cells of the skin [1]. Polymorphisms in VDR are correlated with increased susceptibility to multiple sclerosis, inflammatory bowel disease, rheumatoid arthritis and type 1 diabetes mellitus [14].

Vitamin D exerts a significant effect on melanocytes and keratinocytes via various mechanisms. In vitro studies have shown that vitamin D₃ is associated with an increase in tyrosinase activity and melanogenesis [7], which may contribute to repigmentation in vitiligo macules. Vitamin D analogues, including calcipotriol and tacalcitol, are known to enhance repigmentation in vitiligo patients [15–17]. Another study reported that vitamin D exerts immunomodulatory effects by inhibiting the expression of interleukin (IL)-6, IL-8, tumor necrosis factor (TNF)-α, and TNF-γ [18]. Furthermore, it has also been shown that the active form of vitamin D reduces the apoptotic activity induced by UVB in melanocytes [1].

Conclusions

Further study is required to delineate the relationship between vitamin D and vitiligo, to evaluate whether a low level of serum vitamin D is a causative factor in vitiligo, and to ascertain whether vitamin D supplements are useful for both the prevention and treatment of vitiligo.

Conflict of interest

The authors declare no conflict of interest.

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