Original paper

The role of serum vitamin D levels in vitiligo

Ebru Karagün[1], Can Ergin[2], Sevim Baysak[3], Gönül Erden[4], Habibullah Aktaş[5], Özlem Ekiz[6]

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

Adv Dermatol Allergol 2016; XXXIII (4): 300–302
DOI: 10.5114/pdia.2016.59507

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 D_3, 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_3 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.

Address for correspondence: Can Ergin MD, Department of Dermatology, Dışkapı Yıldırım Beyazıt Education and Research Hospital, Cinnah Cad. Yeşilyurt Sok. No: 15/7, Kavaklıdere, Ankara, 06690 Turkey, phone: +90 505 6831264, e-mail: drcanergin@hotmail.com
Received: 10.08.2015, **accepted:** 18.09.2015.

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 B_{12} and vitamin D levels were measured.

Statistical analysis

Group comparisons were performed using Student's *t*-test for continuous variables and a χ^2 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 B_{12} 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, autocytotoxic 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 adrenocortical 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 D_3, 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 D_3 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.

References

1. AlGhamdi K, Kumar A, Moussa N. The role of vitamin D in melanogenesis with an emphasis on vitiligo. Indian J Dermatol Venereol Leprol 2013; 79: 750-8.
2. Nordlund JJ. The epidemiology and genetics of vitiligo. Clin Dermatol 1997; 15: 875-78.
3. Lee H, Lee MH, Lee DY, et al. Prevalence of vitiligo and associated comorbidities in Korea. Yonsei Med J 2015; 56: 719-25.
4. Kamen DL, Aranow C. The link between vitamin D deficiency and systemic lupus erythematosus. Curr Rheumatol Rep 2008; 10: 273-80.
5. Aksu Cerman A, Sarikaya Solak S, Kivanc Altunay I. Vitamin D deficiency in alopecia areata. Br J Dermatol 2014; 170: 1299-304.
6. Lips P. Vitamin D physiology. Prog Biophys Mol Biol 2006; 92: 4-8.
7. Adorini L, Penna G. Control of autoimmune diseases by the vitamin D endocrine system. Nat Clin Pract Rheumatol 2008; 4: 404-12.
8. Oikawa A, Nakayasu M. Stimulation of melanogenesis in cultured melanoma cells by calciferols. FEBS Lett 1974; 42: 32-5.
9. Ustun I, Seraslan G, Gokce C, et al. Investigation of vitamin D levels in patients with vitiligo vulgaris. Acta Dermatovenerol Croat 2014; 22: 110-3.
10. Saleh HM, Abdel Fattah NS, Hamza HT. Evaluation of serum 25-hydroxyvitamin D levels in vitiligo patients with and without autoimmune diseases. Photodermatol Photoimmunol Photomed 2013; 29: 34-40.
11. Czajkowski R, Męcińska-Jundziłł K. Current aspects of vitiligo genetics. Postep Dermatol Alergol 2014; 31: 247-55.
12. Laddha NC, Dwivedi M, Mansuri MS, et al. Role of oxidative stress and autoimmunity in onset and progression of vitiligo. Exp Dermatol 2014; 23: 352-3.
13. Silverberg JI, Silverberg AI, Malka E, Silverberg NB. A pilot study assessing the role of 25 hydroxy vitamin D levels in patients with vitiligo vulgaris. J Am Acad Dermatol 2010; 62: 937-41.
14. Ersoy-Evans S. Commentary: vitamin D and autoimmunity: is there an association? J Am Acad Dermatol 2010; 62: 942-4.
15. Birlea SA, Costin GE, Norri DA. New insights on therapy with vitamin D analogs targeting the intracellular pathways that control repigmentation in human vitiligo. Med Res Rev 2009; 29: 514-46.
16. Parsad D, Saini R, Verma N. Combination of PUVAsol and topical calcipotriol in vitiligo. Dermatology 1998; 197: 167-70.
17. Oh SH, Kim T, Jee H, et al. Combination treatment of non-segmental vitiligo with a 308-nm xenon chloride excimer laser and topical high-concentration tacalcitol: a prospective, single-blinded, paired, comparative study. J Am Acad Dermatol 2011; 65: 428-30.
18. Koizumi H, Kaplan A, Shimizu T, Ohkawara A. 1,25-dihydroxyvitamin D3 and a new analogue, 22-oxacalcitriol, modulate proliferation and interleukin-8 secretion of normal human keratinocytes. J Dermatol Sci 1997; 15: 207-13.