



Research Article

Evaluation of vitamin D and calcium mineral metabolism in patients with chronic urticaria

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Abstract

Objectives: Chronic urticaria (CU) is a skin disease characterized by the spontaneous occurrence of itchy, swollen welts lasting 6 weeks or more. The aim of this study was to assess the potential influence of vitamin D and calcium mineral metabolism in patients with CU.

Methods: Patients over the age of 18 who presented at a dermatology outpatient clinic between November 2020 and February 2021 and diagnosed with CU were included in the study. Volunteers with no disease were selected as a control group. The level of 25-hydroxy vitamin D and calcium metabolism parameters (calcium [Ca], phosphorus [P], parathyroid [PTH] hormone) were measured in both groups and compared.

Results: The mean age of the participants was 35.01±11.96 years in the urticaria group and 34.89±11.75 years in the control group (p>0.05). The mean serum Ca level was 9.14±0.75 mg/dL in the urticaria group and 9.46±0.43 mg/dL in the control group (p=0.003). The mean serum P level was 3.3±0.71 mg/dL in the urticaria group and 3.3±0.56 mg/dL in the control group (p=0.76). The mean serum level of PTH was 46.28±16.29 pg/mL in the urticaria group and 41.95±14.09 pg/mL in the control group (p=0.091). The mean serum level of vitamin D in the CU and the control group was as 13.8±5.67 ng/mL and 18.12±8.42 ng/mL, respectively (p<0.001). The 7-day Urticaria Activity Score (UAS7) was 19.99±8.61 in the patients with urticaria. There was a negative correlation between the UAS7 score and the vitamin D level (p=0.001). The mean duration of disease was 20±15.22 months. No correlation was seen between disease duration and the vitamin D level (p=0.49).

Conclusion: The study findings indicated that the Ca and vitamin D levels in patients with CU were statistically significantly lower than those of the control group. However, additional studies are needed to further explore the possible contribution of this analysis to the diagnosis and treatment of urticaria.

Keywords: Calcium, parathyroid hormone, urticaria, vitamin D

Chronic urticaria (CU) is an inflammatory skin disease observed in 0.5% to 1% of the population. CU patients experience attacks of urticaria and/or angioedema that persist for more than 6 weeks, which may adversely affect quality of life [1]. Approximately 40% of patients with urticaria experience angioedema, a reaction that includes swelling of the lower layers of the skin [2]. CU is typically characterized by pink or red welts of different shapes and sizes, and burn-

ing and itching that may occur on various parts of the body. The lesions typically present in a form similar to macular erythema or papules, which may be localized or have a general distribution [3]. CU is more common in adults, and affects women more often than men, with an average ratio of nearly 2:1 [4]. CU can also occur as a clinical progression of immunological and inflammatory mechanisms and may have idiopathic properties [5].

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Vitamins are chemical molecules required in small quantities for various biochemical functions. Many cannot be synthesized by the body, and therefore must be supplied through the diet. Vitamin D is a secosteroid; 1 of the cyclopentanoperhydrophenanthrene rings is broken [6]. Dietary vitamin D can be obtained in the form of ergocalciferol (vitamin D₂), found in plants, and cholecalciferol (vitamin D₃), found in animal tissue. Vitamin D₃ is synthesized in the human body [7]. Vitamin D can be absorbed through the skin and through diet, and is converted to 25(OH)D₃ by the enzyme hydroxylase. It then undergoes 1- α hydroxylation in the kidneys and becomes 1,25 dihydroxyvitamin D (calcitriol), which is the active form of vitamin D. The vitamin D-binding protein is the key transport protein which, along with albumin, is responsible for over 99% of the binding of circulating vitamin D metabolites [8]. PTH, Ca, and P also have a role in the regulation of vitamin D₃ [9].

The measurement of the serum 25(OH)D₃ level can assess vitamin D status and provide useful information. An adequate or normal level of vitamin D has been defined as >30 ng/mL, 20-30 ng/mL has been classified as insufficient, <20 ng/mL vitamin D as deficient, and <10 ng/mL as severely deficient [10]. In recent years, vitamin D deficiency and insufficiency have been associated with many chronic diseases, including common cancers, cardiovascular disease, metabolic syndrome, and infectious and autoimmune diseases [11].

The effects of vitamin D on both the innate and the acquired immune system play an important role in immune homeostasis, and several studies have investigated the relationship between autoimmune and inflammatory diseases. The vitamin D level has been found to be low and high in CU patients; however, to the best of our knowledge, no study has evaluated the additional role of Ca metabolism and PTH. This study was designed to investigate to vitamin D level and related Ca metabolism changes in patients with CU and to explore the relationship to disease activity.

Materials and Methods

Approval for this study was granted by the Selcuk University Faculty of Medicine Local Ethics Committee on November 18, 2020 (No: 2020/507), and all of the participants provided written, informed consent prior to the study.

Patients over the age of 18 years who presented at a dermatology outpatient clinic between November 2020 and February 2021 and were diagnosed with CU (male: n=33, female: n=38) were enrolled in the study. Patients with liver disease, kidney disease, thyroid disease, diabetes mellitus, other systemic connective tissue disease, tumor, neurological disease, pregnancy, or alcohol dependence were excluded. The 7-day Urticaria Activity Score (UAS7) was used to record the severity of itching and swelling. Routine 25-hydroxy vitamin D level and Ca metabolism parameters (Ca, P, PTH) were evaluated. Participants who presented at the same dermatology outpatient clinic with a diagnosis of no disease were enrolled as the control group (male: n=33, female: n=38).

The measurement of 25(OH)D₃ and PTH was performed using an ADVIA Centaur XPT immunoassay system (Siemens Healthineers GmbH, Erlangen, Germany) and an ADVIA Centaur Vitamin D Total Assay chemiluminescent immunoassay system (Siemens Healthineers GmbH, Erlangen, Germany) using the electrochemiluminescence immunoassay method. Ca and P were measured using a Mindray BS-800M analyzer (Mindray Bio-medical Electronics Co., Ltd., Shenzhen, China) using the calorimetric method.

Statistical analysis

The statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 software (IBM Corp., Armonk, NY, USA). The differences between the CU patients and the healthy control group were evaluated with the Mann-Whitney U test. The data were expressed as mean \pm SD. One-way analysis of variance and the Kruskal-Wallis test were used to assess the sample distribution. Pearson's correlation analysis was used to examine the relationship between parameters. The results were considered to be statistically significant at a p level of <0.05.

Results

The mean age of the study participants was 35.01 \pm 11.96 years in the CU group and 34.89 \pm 11.75 years in the control group. There was no significant difference between the groups in terms of age and gender. The mean serum Ca value was 9.14 \pm 0.75 mg/dL in the urticaria group and 9.46 \pm 0.43 mg/dL in the control group; the difference between the groups was statistically significant (p=0.003). The mean serum P level was 3.3 \pm 0.71 mg/dL in the urticaria group and 3.3 \pm 0.56 mg/dL in the control group. The difference in the P level was not statistically significant (p=0.76). The mean serum PTH level was 46.28 \pm 16.29 pg/mL in the CU group and 41.95 \pm 14.09 pg/mL in the control group, which also was not statistically significant (p=0.091). The mean serum vitamin D value was 13.8 \pm 5.67 ng/mL in the CU group and 18.12 \pm 8.42 ng/mL in the control group. The difference in the vitamin D level between the groups was statistically significant (p<0.001). The measurement data of both groups are presented in Table 1.

The mean UAS7 score was 19.99 \pm 8.61 in the CU patients, and a negative correlation was seen between the UAS7 score and the vitamin D level (p=0.001), as illustrated in Figure 1. The mean disease duration was 20 \pm 15.22 months; no correlation was seen between disease duration and the level of vitamin D (p=0.49).

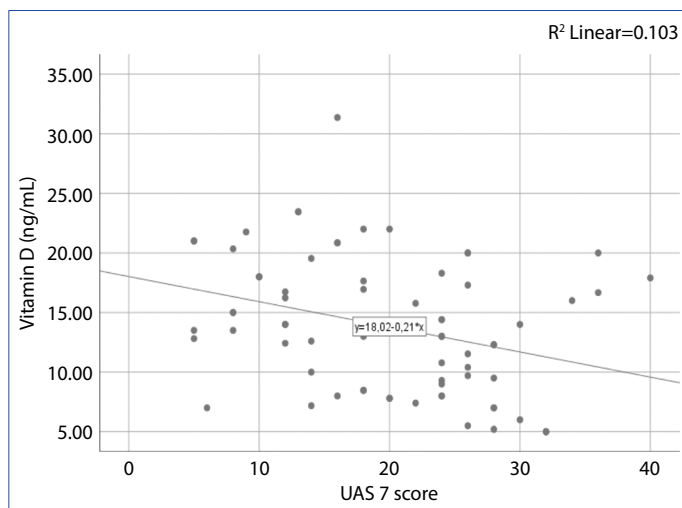
Discussion

CU is characterized by red, and itchy wheals that appear daily or almost daily and lasting for 6 weeks or longer [12]. Although it occurs in 0,5% to 1% of the population, the exact incidence and prevalence of CU remains unknown [13]. It has been sug-

Table 1. Group comparison of vitamin D and some parameters

	CU group	Control group	p
Age (years)	35.01±11.96	34.89±11.75	>0.05
Gender, Female, n (%)	38 (53.5%)	38 (52.8%)	>0.05
Vitamin D, (ng/mL)	13.8±5.67	18.12±8.42	<0.001
Calcium, (mg/dL)	9.14±0.75	9.46±0.43	0.003
Phosphorus, (mg/dL)	3.3±0.71	3.3±0.56	0.76
Parathormone, (pg/mL)	46.28±16.29	41.95±14.09	0.09

CU: Chronic urticaria.

**Figure 1.** Graphic representation of the correlation coefficient between vitamin D and the urticaria score seen in this study.

UAS7: 7-day Urticaria activity score.

gested that vitamin D may be an environmental factor that may trigger or exacerbate some autoimmune disorders [14]. The actions of vitamin D include regulation of cellular proliferation and differentiation, hormone secretion, and the immune system in both innate and adaptive immunity [15].

Vitamin D deficiency and insufficiency have been associated with several chronic diseases, metabolic syndrome, and infectious and autoimmune diseases. The measurement and evaluation of vitamin D can provide a valuable a clinical contribution.

Tsai et al.[16] and Wang et al. [17] reported that the level of vitamin D was significantly higher in CU patients than that of controls. Rather et al. [18] found a significant negative correlation between the level of serum vitamin D and the severity of CSU. The mean serum 25-(OH)D3 level of the CU patients in that study was 19.6±6.9 ng/mL, and 38.5±6.7 ng/mL in the control group, which represented a statistically significant difference ($p < 0.001$). It has also been reported in other studies that the serum 25-(OH)D3 level was significantly lower in patients with CU in comparison with other groups [19, 20].

In our study, the vitamin D value in CU cases was significantly lower than that of the control group, but there was no signifi-

cant difference in PTH or P values. Vitamin D deficiency was associated with the UAS7 score in the CU cases but not correlated with the duration of the disease. Several studies have proposed that hypercalcemia in primary hyperparathyroidism may lead to urticaria. In one study, a mean level of PTH was reported as 67.88±36.46ng/mL in CU patients, which is consistent with our results [21].

Conclusion

In conclusion, it may be a costly or time-consuming problem to measure vitamin D level in all CU cases; however, it may be valuable in CU cases with a high of UAS7 scores. According to the literature, it seems that vitamin D may play a role in the pathomechanism of CU. However, the available data are limited. Further comprehensive studied are needed.

Conflict of Interest: The authors declare that there is no conflict of interest.

Ethics Committee Approval: Approval for this study was granted by the Selcuk University Faculty of Medicine Local Ethics Committee on November 18, 2020 (No: 2020/507).

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