CLINICAL SCIENCE

Vitamin D status in patients with Behcet’s Disease

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OBJECTIVES: This study investigated the serum 25-hydroxyvitamin D levels of patients with Behcet’s Disease.

DESIGN AND METHODS: Thirty-two patients with Behcet’s Disease and 31 matched healthy controls were enrolled in this study. The erythrocyte sedimentation rate (ESR) and the levels of C-reactive protein (CRP), serum 25-hydroxyvitamin D, calcium (Ca), phosphate (P), and total alkaline phosphatase (ALP) were measured in both groups.

RESULTS: There were no significant differences between the two groups regarding demographic data. The serum 25-hydroxyvitamin D levels of patients and controls were 13.76 (range: 4.00-35.79) and 18.97 (range: 12.05-36.94) ng/ml, respectively. In patients with Behcet’s Disease, 25-hydroxyvitamin D values were significantly lower than those of the healthy controls (p<0.001). Serum Ca, P, and ALP levels were similar in both groups. Serum ESR and CRP levels were significantly higher in patients than controls (p<0.05). There was no correlation between 25-hydroxyvitamin D levels and age, body mass index (BMI), disease duration, ESR, or CRP levels. Multivariate regression analysis parameters showed that smoking, alcohol intake, and use of colchicine were the main predictors of 25-hydroxyvitamin D levels. Of the parameters studied, the largest impact was due to colchicine therapy (p<0.001). We did not find a significant relationship between the use of corticosteroids and 25-hydroxyvitamin D levels.

CONCLUSION: Our results suggest that serum 25-hydroxyvitamin D levels are decreased in patients with Behcet’s Disease. Smoking, alcohol intake, and use of colchicine appear to affect vitamin D levels.

KEYWORDS: Behcet’s Disease; vitamin D; inflammation; 25-hydroxyvitamin D; colchicine.

INTRODUCTION

Behcet’s Disease is a chronic inflammatory disease with exacerbations and remissions characterized by recurrent orogenital ulcerations, ocular manifestations, arthritis, and vasculitis. In addition, neurological and large vessel involvement can occur in some cases.1 Occasionally it appears associated with ankylosing spondilitis.2 The infiltration of lymphocytes and monocytes through small veins without microscopic changes in the vessel walls are major features in the inflamed tissues.3 The etiology and pathogenesis of Behcet’s Disease have not been clearly defined. However, several genetic, environmental, and immunological factors have been suggested as causative factors in this disease.4 In addition, the role of the HLA-B51 gene in genetic susceptibility to Behcet’s Disease has been defined in recent years.5-6 Vitamin D has long been known to be important for bone health and turnover.7 In recent studies, vitamin D has been demonstrated to play a significant role in malignancy, immune system functioning, and cardiovascular events.8-10 The measurement of serum 25-hydroxyvitamin D levels, commonly used by clinicians, is accepted as a clinical indicator of vitamin D status because of its correlation with low vitamin D values.11 The metabolite 1,25-dihydroxyvitamin D is formed by 1-hydroxylation of 25-hydroxyvitamin D in the kidneys.12 Although it is the active metabolite of vitamin D, 1,25-dihydroxyvitamin D serum values do not correlate well with vitamin D deficiency. Therefore, these values are not preferred for routine testing of vitamin D levels.

Vitamin D deficiency is particularly common in patients with rheumatological disorders, such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE).12 Vitamin D status has been inversely correlated with disease activity in those disorders due to the immunomodulatory effects of vitamin D.13,14 Vitamin D has been proposed as a new preventive treatment of inflammatory diseases. Environmental and inflammatory factors, renal and hepatic involvement, and certain drugs could be involved in the pathophysiology of vitamin D deficiency in rheumatological disorders.15 To our knowledge, vitamin D levels have not been previously studied in Behcet’s Disease. The aim of this study was to characterize the vitamin D status of patients...
with Behcet’s Disease and the relationship between vitamin D levels and the inflammatory process.

MATERIALS AND METHODS

The diagnostic criteria for Behcet’s Disease proposed by the International Study Group for Behcet’s Disease were used for diagnosis.16 Thirty-two patients with Behcet’s Disease and thirty-one matched healthy controls were included in the study. All participants were informed of the study protocol, and their written informed consent was obtained according to the Declaration of Helsinki. The study was approved by the local ethics committee of Ataturk University.

Subjects in the patient and control groups had a history of liver and kidney diseases, diabetes mellitus, familial hypercholesterolemia, thyroid and parathyroid diseases, and malignancy were excluded from the study. Individuals with osteoporosis or a history of osteoporosis treatment, liver and kidney diseases, endocrine diseases, and postmenopausal women were excluded from the study.

In the study group, three patients were on active phase of the disease. Twenty-seven of the patients were under colchicine therapy at doses of 1 to 1.5 mg/day, and two patients were taking colchicine along with low-dose steroids. Three patients had a history of steroid use.

The heights and weights of all subjects were on record, and body mass index (BMI) was calculated as weight (kg)/height (m²). Laboratory testing of serum calcium (Ca), phosphate (P), total alkaline phosphatase (ALP), and 25-hydroxyvitamin D levels was conducted for all patients and control subjects. The erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) level were determined in whole blood and serum aliquots, respectively. ESR was determined according to the Westergren method and CRP by a nephelometric method (Beckman Array Protein System, USA). 25-hydroxyvitamin D levels were determined in an E-170 ECL system (Roche, Japan) with an electrochemiluminescence method.

Statistical Analysis

Statistical analysis was performed with PASW Statistics 18 (SPSS Inc., Chicago, U.S.A.) for Windows. Statistical analyses were performed using the Mann-Whitney U test. A p value of less than 0.05 was accepted as statistically significant. Correlations among parameters were analyzed using Pearson’s correlation coefficient. A multivariable regression model was established to evaluate the effects of different variables on vitamin D levels.

RESULTS

Table I lists the clinical and demographic characteristics of the patient and control groups. The findings are expressed as median (min-max). The demographic and BMI values were similar between groups. The acute-phase reactant levels of ESR and CRP were significantly higher in patients with Behcet’s Disease than in the control subjects (p<0.05).

After the data were weighted by age, vitamin D levels were significantly lower in the patient group than in the control group (p<0.001). There was no significant difference between the patients and the controls in terms of Ca, P, or ALP levels (p>0.05). There was no correlation between vitamin D levels and age, BMI, disease duration, ESR, or CRP levels (Table II). Multivariable regression analysis was performed to determine the main predictors of vitamin D levels (Table III). The variables included in the model were age, smoking, alcohol intake, and use of colchicine and corticosteroid drugs. Age, smoking, alcohol intake, and use of colchicine were found to be the main predictors. Colchicine therapy was found to have the greatest effect on levels of vitamin D (p<0.001). We did not find a significant relationship between the use of steroids and 25-hydroxyvitamin D (p=0.62).

DISCUSSION

Behcet’s Disease is a systemic and immunoinflammatory form of vasculitis with endothelial dysfunction.17 The inflammation is generally mediated by cytokines derived from Th1 lymphocytes, such as tumour necrosis factor-α (TNF-α), interleukin-6 (IL-6), and IL-1β.18 Vitamin D is a hormone that has important roles in calcium homeostasis and bone turnover.19 There is an increasing interest in the relationship between vitamin D deficiency and a number of autoimmune diseases.12

Decreased vitamin D levels have been reported to correlate with increased SLE disease activity.14 Animal model studies of SLE have shown that some aspects of the disease decreased in severity when vitamin D intake was increased.20 Vitamin D has also been related to disease activity in RA. Values of 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D showed significant negative correlations with RA disease activity.13,21

Vitamin D has immunosuppressant properties and has been considered as a therapeutic intervention for several autoimmune diseases.22 In an in vitro study, Do et al.23 showed

Table I - Clinical and laboratory features of patients with Behcet’s Disease and healthy controls.

|                        | Patient group | Control group | p-value |
|------------------------|---------------|---------------|---------|
| Sex (male/female)      | 14/18         | 11/20         | ns      |
| Age (years)            | 29 (18-50)    | 33 (21-57)    | ns      |
| Disease duration (months) | 33 (3-216) | -             |         |
| Height (cm)            | 164.5 (143-183) | 162 (150-182) | ns      |
| Weight (kg)            | 65.5 (43-92)  | 66 (50-95)    | ns      |
| BMI (kg/m²)            | 24.7 (16.8-30.5) | 25.4 (19.5-33.5) | ns |
| Pathergy test positivity (%) | 14 (43.8 %) | -             |         |
| ESR (mm/h)             | 13.5 (1-89)   | 10 (2-25)     | p<0.05  |
| CRP (mg/L)             | 0.5 (0.3-12.6) | 0.3 (0.3-1.1) | p<0.05  |
| Ca (mg/dl)             | 9.4 (8.1-10.5) | 9.4 (8.5-10.6) | ns      |
| P (mg/dl)              | 3.5 (2.6-5.3) | 3.5 (2.7-5.3) | ns      |
| ALP (U/L)              | 84 (38-167)   | 76 (42-141)   | ns      |
| 25-hydroxyvitamin D (ng/ml) | 13.76 (4-35.79) | 18.97 (12.05-36.94) | p<0.001 |

ns: not significant.

Table II - Correlation between 25-hydroxyvitamin D levels and clinical parameters in patients with Behcet’s Disease.

|                        | Median (min-max) | r      | p-value |
|------------------------|------------------|-------|---------|
| Age (years)            | 29 (18-50)       | 0.126 | ns      |
| BMI (kg/m²)            | 24.7 (16.8-30.5) | 0.323 | ns      |
| Disease duration (months) | 33 (3-216) | 0.303 | ns      |
| ESR (mm/h)             | 13.5 (1-89)      | 0.258 | ns      |
| CRP (mg/L)             | 0.5 (0.3-12.6)   | 0.244 | ns      |

ns: not significant.
Table III - Multivariate regression analysis of vitamin D levels with demographic and clinical parameters in patients with Behcet's Disease.

| Model          | B    | Std. error | t    | p-value |
|----------------|------|------------|------|---------|
| Constant       | 22.787 | 1.065      | 21.404 | p<0.001 |
| Age            | -0.064 | 0.023      | -2.855 | p<0.01  |
| Smoking        | 1.179  | 0.121      | 9.743  | p<0.001 |
| Alcohol intake | 1.196  | 0.298      | 4.010  | p<0.001 |
| Colchicine     | -5.101 | 0.357      | -14.304| p<0.001 |
| therapy        |       |            |       |         |
| Corticosterone | -0.174 | 0.346      | -0.504 | ns      |

ns: not significant.

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