

CLINICAL STUDY

Is there an association between serum 25-hydroxyvitamin d concentrations and disease activity in rheumatoid arthritis?

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Abstract: *Background:* Recently, it has been recognized that vitamin D not only is important for calcium metabolism and maintenance of bone healthy, but also plays an important role in reducing risk of many chronic diseases including rheumatoid arthritis (RA), systemic lupus erythematosus, insulin-dependent diabetes mellitus, multiple sclerosis, several cancers, heart and infectious diseases. In RA, the role of vitamin D is undefined. *Methods:* The objective of this present study was to determine serum 25-hydroxyvitamin D (25(OH)D) concentrations in patients with RA and to establish its correlation with disease activity. This study was performed on fifty-five consecutive patients RA fulfilling the American Collage of Rheumatology (ACR) criteria for the classification of RA and forty-five healthy subjects. Serum 25(OH)D levels were measured using Elecsys 25(OH)D reactive kit. Disease activity was assessed according to DAS28, the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). The association between serum levels of 25(OH)D and age, gender, disease duration and disease activity parameters were established.

Results: The mean serum 25(OH)D levels were significantly decreased in RA patients compared to healthy controls ($p < 0.01$) and were associated with higher levels of parathyroid hormone. Vitamin D deficiency (i.e. < 30 ng/ml) was found in 50 patients (90.9 %). Serum levels of vitamin D lower than 20 ng/ml were found in 72 % of patients. We did not find the correlation between serum 25(OH)D levels and disease activity parameters.

Conclusions: Our findings have demonstrated that serum 25(OH)D levels is highly prevalent in patient with RA. We believe that it will be helpful to investigate the vitamin D levels in order to determine the osteomalacia risk of RA patients (Tab. 2, Ref. 11). Full Text in PDF www.elis.sk.

Key words: rheumatoid arthritis, 25-hydroxyvitamin D, disease activity.

Epidemiologic and clinical studies support that vitamin D is a important enviromental factor that can increase the prevalence of certain autoimmune diseases such as rheumatoid arthritis (RA), systemic lupus erythematosus, insulin-dependent diabetes mellitus and inflammatory bowel disease.

Several studies have reported that insufficiency and/or deficiency vitamin D levels have been found in patients with RA. The link between vitamin D status and RA is unclear. It has been suggested that lower vitamin D levels may be associated with increased disease severity or activity (1, 2).

The aim of this present study was to determine serum 25-hydroxyvitamin D (25(OH)D) concentrations in patients with RA and to establish its correlation with disease activity.

Methods

This study was performed on fifty-five (40 women and 15 men) consecutive patients RA fulfilling the American Collage of

Rheumatology (ACR) criteria for the classification of RA and forty five (33 women and 12 men) age and sex matched healthy controls. The patients' ages ranged from 28 to 68 years, the mean was 45 years. The patients were receiving with immunosuppressives, sulphasalazine, antimalarials, corticosteroids and anti-TNF drugs.

A standardized examination was used to assess the clinical and laboratory findings. Serum 25(OH) D levels were measured using Elecsys 25 (OH)D reactive kit. Disease activity was assessed according to DAS28, the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). The associations between serum levels of 25(OH)D and age, gender, disease duration and disease activity parameters were established.

According to current recommendations, serum 25(OH)D levels < 30 ng/ml and 20 ng/ml were defined as vitamin D insufficiency and deficiency, respectively.

The Statistical Package for Social Science (SPSS) software, version 11.0 for Windows was used for all statistical analysis. The Pearson correlation coefficient was performed for correlation between results. The level of significance was set at p value lower than 0.05.

Results

In comparison with the healthy control group, serum 25(OH) D levels were significantly decreased in RA patients ($p < 0.01$)

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Tab. 1. Results of the laboratory parameters in RA patients and controls.

	RA	Controls	p
ESR (mm/h)	65±24	8±6	<0.05
CRP (mg/dl)	35±12	negative	<0.05
DAS28	5.4±3.2	negative	<0.05
25(OH)D (ng/ml)	12.2±7.8	19.3±8.8	<0.05
PTH (pg/ml)	80±22	28±15	<0.05

We did not find the correlation between serum 25 (OH) D levels and disease activity parameters (p>0.05, see Table 2)

Tab. 2. Correlation between the disease activity parameters and 25(OH)D levels in RA patients.

	DAS28	ESR	CRP
25(OH)D	-0.15*	-0.12*	-0.14*

*p > 0.05

and were associated with higher levels of parathyroid hormone (p < 0.01) (Tab. 1). Approximately 90.9 % of RA patients had less than 30 ng/ml of serum 25(OH)D. Serum levels of vitamin D lower than 20 ng/ml were found in 72 % of patients, and included 14 patients (25.4 %) with the level lower than 10 ng/ml. A reduction in 25(OH)D levels was seen with age in both groups (Tab. 2).

Discussion

Vitamin D is a steroid hormone with important skeletal and non-skeletal biologic functions. Also, it has been suggested that vitamin D had an immunomodulator role. The existence of vitamin D receptors in T and B lymphocytes, macrophages and dendritic cells is well known. Vitamin D deficiency is common and is manifested with musculoskeletal symptoms (3).

In RA, the role of vitamin D is controversial (4–8). Several studies have reported that low vitamin D levels is a common condition in patients with RA. More than 60 % of RA patients have vitamin D levels below the normal range (9, 10). Als et al found decreased serum vitamin D concentrations in RA patients compared to healthy controls (10). Our findings were consistent with these studies (9, 10). However, Nielen et al found no difference between 25(OH)D levels in patients with RA and healthy subjects (11).

Some studies found a negative correlation between vitamin D levels and disease activity (8–10). However, we did not find the correlation between serum 25(OH)D levels and disease activity. We found that the serum concentrations of 25(OH)D were significantly below those of healthy subjects in most patients with RA. Low concentrations of vitamin D may result from severely impaired liver function but our patients had no signs of liver disease. It is known that many analgesic drugs have a negative effect on liver enzymes. Our patients had been receiving long-term analgesics and anti-inflammatory drug therapy. Our findings may be the result of drug-induced disturbance of vitamin D metabolism. In addition,

the physical activity of majority of our patients was limited, and the intake of vitamin D significantly reduced.

The serum 25(OH)D level is a more reliable indicator of vitamin D status. Concentrations of vitamin D are influenced by several factors such as diet, season, skin pigmentation, clothing, supplementation, obesity. Also, anti-malarials seemed to be a predictor of lower 25(OH)D levels; hydroxychloroquine is known to inhibit the 1-hydroxylation of 25(OH)D. Our results may be due to the climate of our region and season features (1–3).

In conclusion, our findings have demonstrated that serum 25(OH)D levels was highly prevalent in patients with RA. Our results suggest that vitamin D deficiency in RA may play a possible role in the pathogenesis of RA. We believe that it will be helpful to investigate the vitamin D levels in order to determine the osteomalacia risk of RA patients.

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