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EXPLORING THE CHANGES OF SERUM VITAMIN D LEVELS IN PATIENTS WITH MUSCULOSKELETAL DISEASES

E. Slavov[1*], Kr. Nancheva[2], A. Avramova[3], S. Zheleva[4]

[1]Department of Molecular Biology, Immunology and Genetics, Medical Faculty, Trakia University, Stara Zagora, Bulgaria
[2]Clinical Laboratory, University Hospital "Prof. d-r Stoyan Kirkovich" AD, Stara Zagora, Bulgaria
[3]Medical Center "SELENA-L" EOOD, Stara Zagora, Bulgaria
[4]Medical Center "ORFEI", Stara Zagora, Bulgaria

ABSTRACT

Vitamin D plays an important role in the calcium-phosphorous homeostasis, and its levels are critical for bone growth and development. Existing data for insufficient levels of vitamin D among the people of Europe and USA allow us to survey the serum vitamin D levels of patients with musculoskeletal diseases. 73 patients afflicted with osteoporosis, osteopenia, rheumatoid arthritis or osteoarthritis were included in the study. The serum levels of vitamin D were evaluated using electrochemiluminescence (ECL) technology. Suboptimal levels of vitamin D were found in 76,7% of the patients irrespective of the diseases. The supplementary therapy with Cholecalciferol for six months has significantly improved their vitamin D status. The obtained results aim to focus on the importance to estimate the vitamin D serum levels in patients with musculoskeletal diseases.

Vitamin D is a biomolecule with a variety of biological effects (1). It plays an important role in the calcium-phosphorous homeostasis, and its levels are critical for bone growth and development (2). The term "vitamin D" includes both vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol). A major source of vitamin D is the UV radiation which mediates the conversion of 7-dehydrocholesterol into a pre-vitamin D, followed by its convertion into a native vitamin D3 (3). The accepted normal serum levels of vitamin D (25 (OH) D) are between 30 and 50 ng/ml (4). Recently, a number of studies discuss a serious decrease of vitamin D serum levels in patients with musculoskeletal disease, as well as in pulmonary diseases, malignancies and autoimmune diseases (3, 5, 6). Even pandemic decrease of vitamin D levels in Europe and the USA were discussed (7). Over one billion people in the world have manifested a deficiency of vitamin D.

A cross-sectional study conducted in Bulgaria showed deficiency of vitamin D in Bulgarian population, as well (8).

Deficiency of vitamin D is associated not only with impaired bone mineralization, but with many systemic effects as disturbances in the function of the immune system, fatigue, weakness, susceptibility to viral infections and tumor development (6, 9).

According to current guidelines, daily intake for infants should be 400 IU of the vitamin D daily (10). For the prevention of rachitis during the first year of life 1000-2000 IU are applied. In men and women over the age of 50 the recommended daily intake of vitamin D3 is between 800-1000 IU, which should result in serum levels of 25 (OH) D over 75 nmol/l (30 ng/ml) (11).

PATIENTS AND METHODS

73 patients (average age 51,4 ± 14 years), all with musculoskeletal diseases were included in the study. The patient cohort was divided according to the diagnostic criteria in several groups: osteoporosis (38 patients), osteopenia (4 patients), rheumatoid arthritis (9 patients), osteoarthritis (11 patients) and a group "other diseases" (11 patients) including single cases of

sacroiliitis, hypermobility syndrome, vasculitis and fibromyalgia.

7 women of the patients group were studied again, after a 6-month supplementary therapy with Cholecalciferol.

A written informed consent was obtained from all patients involved in the study.

Blood samples were obtained via venipuncture from all patients. The serum levels of total vitamin D were evaluated within 2 h of blood collection with Roche Elecsys 2010 chemistry analyzer test for detection of total vitamin D (25(OH)D).

According to Schoindre et al. all patients with serum vitamin D levels above 30 ng/ml were considered to have optimal vitamin D status, and these with levels lower than 30 ng/ml – suboptimal vitamin D status (4).

The STATISTICA 7 system for data analyses was used to determine mean vitamin D concentration in different groups and prove statistical significant differences.

RESULTS

The results we obtained show that 17 (23,3 %) women only were with normal serum levels **(Figure 1).** While 56 (76,7 %) of the patients were with suboptimal levels of vitamin D.

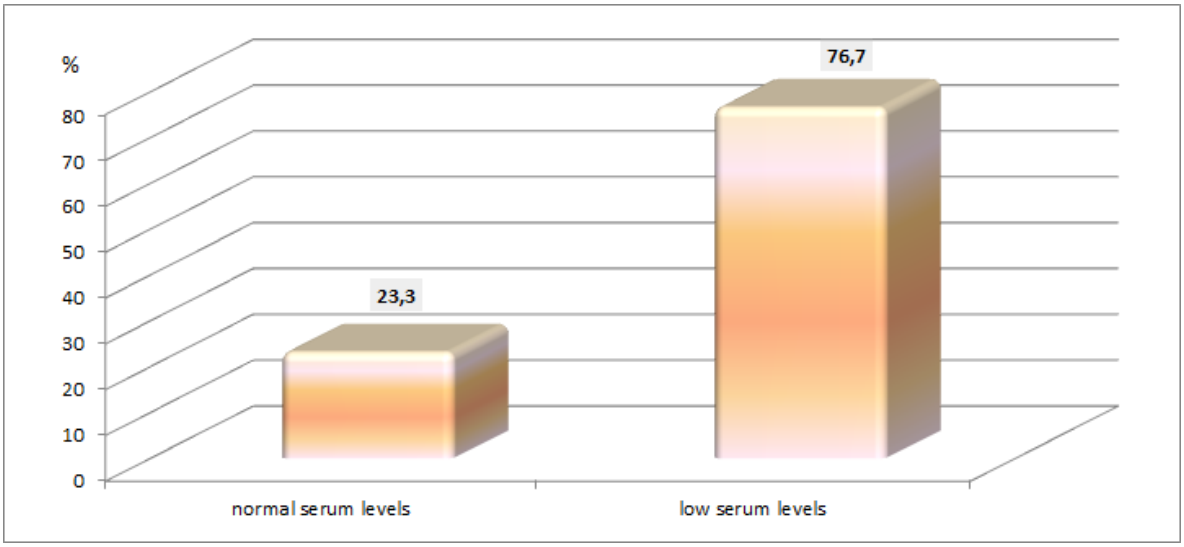

Figure 1. Distribution of patients according to serum levels of vitamin D

The distribution of patients with suboptimal levels of vitamin D was performed according to the staging of vitamin D deficiency, proposed in 2001 by Lips et all (12). We found that most of the patients with suboptimal levels of vitamin D had a mild form of vitamin D deficiency (35,6%), followed by a moderate form of deficiency of vitamin D (4,1%) **(Table 1)**. One patient only (1,3%) had severe vitamin D deficiency.

Table 1. *Distribution of patients according to the severity of vitamin D deficiency.*

Stages	**Serum vitamin D (ng/ml)***	**Patients n (%)**
Mild vitamin D deficiency (or insufficiency)	< 10-20	26 (35.6)
Moderate vitamin D deficiency	< 10	3 (4.1)
Severe vitamin D deficiency	< 5	1 (1.3)

We also found suboptimal vitamin D levels in all patients group studied **(Figure 2).** There were no significant statistical differences between vitamin D serum levels in all groups studied. Meanwhile the patient group with osteoarthrosis had lowest serum levels (20,8 ng/ml) among all patients.

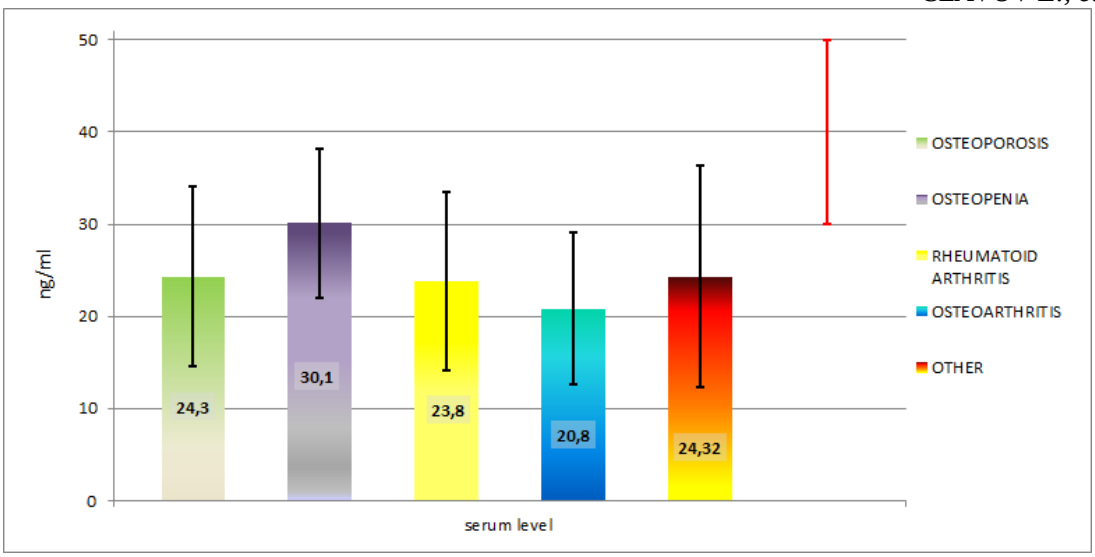

Figure 2. Mean serum vitamin D levels of patient groups with different musculoskeletal diseases.

The dynamics of vitamin D levels after supplementation with Cholecalciferol is presented on **Figure 3**. All the patients in therapy increased vitamin D serum level. However, the patients were found not to respond equally to the therapy. It appears that the supplementary therapy had a stronger effect on patients suffering from a more severe vitamin D deficiency and led to faster compensatory effect.

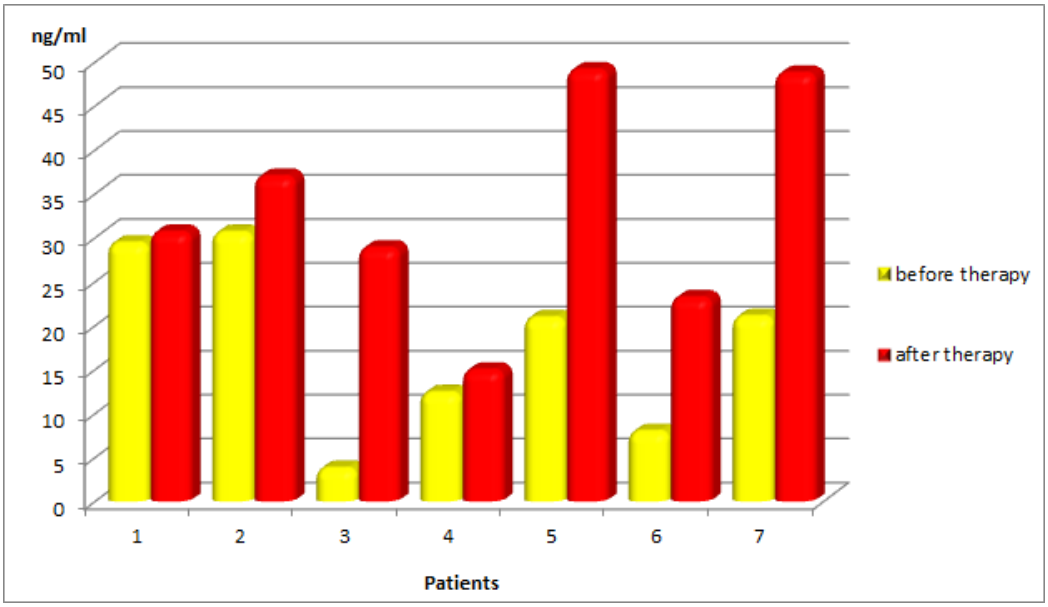

Figure 3. Changes in vitamin D levels in patients after 6 months supplemental therapy with Cholecalciferol.

DISSCUSSION

Vitamin D is defined as a hormone with pleiotropic function (13). The variety of biological effects is based on the interaction between vitamin D and its receptor, expressed on many different cells and tissues (14). A critical role in this activity plays the serum level of vitamin D. A growing number of studies show that vitamin D deficiency is associated with impaired function of endocrine, immune, cardio-vascular system (15). Recent investigation indicate that vitamin D insufficiency could be found not only in patients with health problems (musculoskeletal diseases, diabetes, autoimmunity, viral infections, etc.), but in healthy individuals, as well (16). Furthermore a pandemic decrease of vitamin D levels among the populations from USA, Europe was discussed (7). The results we obtained showed a well expressed suboptimal vitamin D status

among the patients with musculoskeletal diseases. The percentage of vitamin D insufficient patients in our study (41 %) is lower than the winter data on vitamin D levels, found by Borissova et al. in a cross-sectional study conducted in 2012 (8). The authors reported deficiency of vitamin D levels was 21.3 %, and insufficiency 54.5 % of the group studied. In contrast we established that 35,7 % of the subjects had borderline vitamin D levels (20 - 30 ng/ml). On the whole, our data suppose further studies to clarify the status of regulation pathways in vitamin D metabolism, as well as the need of supplementary therapy of individuals with borderline vitamin D levels. In addition, that information could be helpful in clarifying the reasons for a more significant response to supplementary therapy in patients with lower initial vitamin D levels.

To sum up the suboptimal vitamin D levels in all patients groups studied are not surprising. Our results are in agreement with the data of some other studies which find that there is a correlation between vitamin D deficiency and a disease progression. Vitamin D levels are linear to the diseases activity and disease activity score in rheumatoid arthritis patients (17). Moreover, the addition of alfacalcidol (or 1-hydroxycholecalciferol) to the immunosuppressant therapy had positive effect on the activity of the rheumatoid arthritis (18). The reduced levels of vitamin D in patients with osteoporosis could be related to an increased risk of fractures (19). The vitamin D supplementation is recommended for prevention of fractures to risk groups with osteoporosis (12). Moreover the vitamin D insufficiency detected in the group with osteoarthritis has significant association with the structural damage of subchondral bone and cartilage damage (20). Also, the authors pointed out the need of measurement of serum vitamin D levels followed by adequate supplementation. We established that the lowest levels of vitamin D were exactly in this group. Considering the fact that the first loss of knee joint cartilage begins at about the age of 40 (20) we suggest that a screening of vitamin D levels to all patients with elevated risk of osteoarthritis should be performed.

In conclude that a large proportion of individuals with vitamin D deficiency could be found among the patients with musculoskeletal disease. Evaluation of serum vitamin D levels could be helpful in diagnostics of patients with inflammatory joint disease. More studies are needed to clarify the specific dynamics of serum vitamin D levels after supplementary therapy with Cholecalciferol.

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