Correlation of Oral Vitamin D Administration with the Severity of Psoriasis and the Presence of Metabolic Syndrome

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To improve the management of psoriasis, we have started from the hypothesis that normalization of vitamin D serum reduces the severity of psoriasis and positively influences the diagnostic criteria of metabolic syndrome. Experimental part. The objective of the prospective study was to evaluate the impact of oral vitamin D on psoriazis and metabolic syndrome in a group of 184 patients diagnosed with psoriazis and metabolic syndrome, between 2010-2017. In all patients included in the study, we evaluated family history, personal medical history, the living and working conditions, the history of psoriatic disease (control group only), clinical data (waist circumference), height (cm), body mass index, blood pressure (mmHg)) and laboratory examinations. Regarding the severity of psoriasis, in all 141 patients treated with vitamin D, a significant improvement was seen after 12 months of treatment. We bring a new approach to the treatment of psoriasis with vitamin D.

Keywords: psoriasis, vitamin D, metabolic syndrome.

Psoriasis is a chronic, inflammatory, proliferative disease [1]. It is most often characterized by well-defined, red, erythematous plaques, covered with thick white patches [2,3]. Psoriasis is associated with multiple comorbidities, such as metabolic syndrome, cardiac disorders, arthritis [4-7].

The reported lifetime prevalence of psoriasis increased from 4.8% in 1979-1980 to 11.4% in 2007-2008. Recent studies showed an increase in psoriasis prevalence, the number of cases nearly doubled between the 1970s and 2000, the reason being still unknown [8,9].

Psoriasis can occur regardless of age, from birth to old age; generally, the age of onset is between 15 and 30 years [10,11]. It is common in both men and women, and there are no morphological differences between the sexes [10,12-14].

Pathogenesis of psoriasis is still unknown, however it is generally accepted to be a chronic inflammatory disease with a complex skin reaction. The dendritic cells of the dermis and epidermis are activated at onset and worsening of the disease, producing TNF-alpha and IL-23 messengers, leading to the preferential development of T, Th1 and Th17 cells that migrate and proliferate epidermal cells [15,16].

Topical treatment of psoriasis includes: corticosteroids, anthralin, vitamin A, synthetic vitamin D3. Phototherapy includes UVB, UVB laser and PUVA. Systemic therapy includes: cyclosporine, methotrexate, retinoid receptor inhibitors; in biological therapy: TNF-alpha inhibitors and cytokine inhibitors such as anti-IL23p40 and IL-17 inhibitors [17].

Over time, the metabolic syndrome was known as: plurimetabolic syndrome, X syndrome, X plus syndrome, metabolic syndrome X, cardiovascular metabolic syndrome, insulin resistance syndrome - dyslipidemia, etc [18,19].

Studies in many countries show a considerable difference in the prevalence of metabolic syndrome, from 10 to 84%, depending on race, age, gender, ethnicity [20,21].

Recent studies have estimated a prevalence of metabolic syndrome of 15%-24% in the general population and 30% -50% in psoriasis patients, this high percentage necessitating an appropriate treatment approach for these patients [22,23].

The relationship between psoriasis and metabolic syndrome is probably bidirectional, meaning that psoriasis favors metabolic syndrome and metabolic syndrome predisposes to psoriasis, both of which have vitamin D deficiency, the essential hormone that has the effect of chronic inflammation, the common element in the pathophysiology of the two diseases [18,24].

In addition to its well established function as the central regulator of bone and mineral homeostasis, 1,25 $(OH)_2$ D3 (1,25-dihydroxyvitamin D_3) (fig. 1), the active form of vitamin D, has been rediscovered as a modulator of cell growth and differentiation, including immune system cells [25-28].

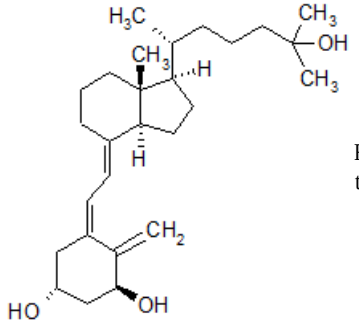

Fig. 1. Chemical structure of the 1,25-dihydroxyvitamin D_3 (Calcitriol)

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Vitamin D deficiency (25-hydroxyvitamin D3 or 25 (OH) D3) (fig 2.) influences health and exacerbates pre-existing diseases such as psoriasis, osteoporosis, rickets, autoimmune diseases, cancer, diabetes and cardiovascular diseases [29,30].

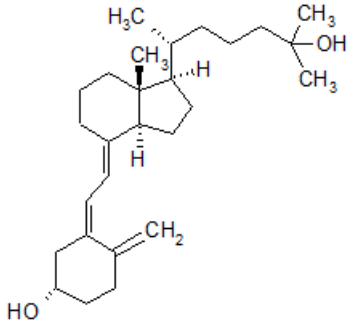

Fig. 2. Chemical structure of the 25-hydroxyvitamin D_3

Hypervitaminosis D can cause cardiac arrhythmias, anorexia, polyuria, weight loss, increased calcium levels, leading to tissue calcification and vascular wall damage to the heart, kidneys and arteries.

The importance of vitamin D in psoriasis has been shown to be both the efficacy of vitamin D derivatives in the skin's treatment of this disease, as well as the effectiveness of ultraviolet exposure, resulting in increased plasma concentrations and regression of psoriatic lesions in the skin [31].

Experimental part

The main objective of the study was to assess the correlation between oral vitamin D and evolution of patients diagnosed with vulgar psoriasis and vitamin D deficiency. The study period was between 2010-2017.

Criteria for inclusion in the study

The study group included 141 patients with psoriasis and 43 with metabolic syndrome, selected with the help of family doctors from Bucharest and Ilfov, and from Elias Emergency University Hospital, Bucharest. The control group included patients who came to control for other diseases, not influencing the research, and the general population, ≥ 18 years of age.

Patients with contraindications for standard systemic therapy and/or biological treatment were included in the study.

Exclusion criteria from the study

Patients who received treatment that may lower vitamin D levels have been excluded from the study. Regarding patients with psoriasis, those who underwent standard or biological systemic therapy were excluded.

Also, those who took oral vitamin D supplements in the last 6 months before enrolling in the study were excluded. In addition to medication, the exclusion criteria was applied to those who suffered from epilepsy, asthma, tuberculosis, Crohn disease, malabsorption (intestinal resection, cystic fibrosis, celiac disease), genetic malformations, liver disease, endocrine disorders, kidney disease, sarcoidosis.

Tracking Parameters

In phase I, the baseline of the study, we followed the control of the severity of psoriasis that was calculated according to the BSA (Body Surface Area) score, taking into account the affected skin surface [32].

We searched the presence of metabolic syndrome in both groups. We used the diagnostic criteria of the metabolic syndrome, the criteria of the International Diabetes Federation (IDF) [33].

The serum level of vitamin D was determined, in order to assess the deficiency. Then, vitamin D oral administration was recommended in all patients, with both psoriasis and metabolic syndrome, which have been found with deficient or insufficient levels of vitamin D.

Statistical analysis

All the data obtained was introduced into Microsoft Excel, in order to be processed and statistically analyzed. For the relationship coefficient, we took into account R = 1 = perfect correlation. We took into account the statistical significance threshold $p < 0.05$ for the validity test. The confidence interval of 95% for the variance ranges of the studied parameters has been respected.

Study limitations

Urban predominance, time limitation (12 months) and territorial limitation (Bucharest and Ilfov).

It was difficult to quantify the sun exposure, influenced by season, latitude, pollution, clouds, fog, skin color, age.

The daily intake of vitamin D from food sources during the study was not monitored. There were patients in the study groups with topical vitamin D treatment, and the degree of dermal absorption was difficult to quantify.

Results and discussions

Comparison of values of Vitamina D before and after administration

Following oral vitamin D administration, increases in serum were observed (fig 3). Following these increases of vitamin D, changes in the severity of psoriasis have been observed.

Influence oral vitamin on the severity of Psoriasis

Following the severity of psoriasis in all 141 patients treated with vitamin D, a significant improvement was seen after 12 months of treatment (fig. 4)

We analyzed the downward trend of each category and outlined it in figures 5, 6 and 7.

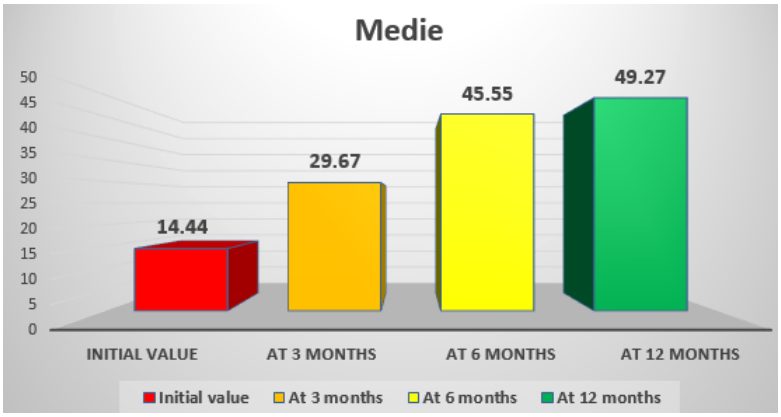

Fig. 3. Graphic representation of increase in mean vitamin D values after administration, depending on control time (the values of vitamin D are expressed in ng/mL)

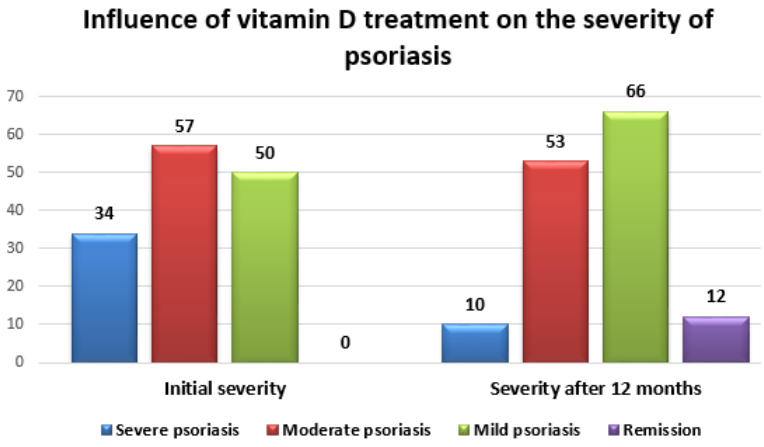

Fig. 4. Numeric distribution of patients by baseline severity of psoriasis and 12 months of treatment

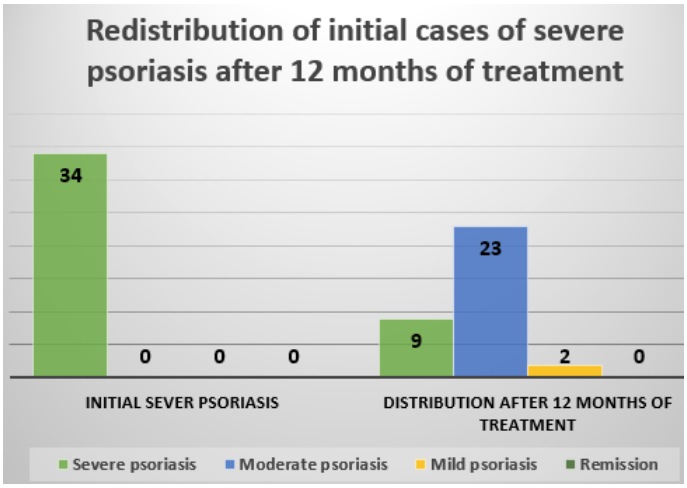

Fig. 5. Decrease trend of psoriasis severity in patients with severe psoriasis at baseline. Out of 34 patients with severe psoriasis, after vitamin D administration only 9 patients experienced severe psoriasis, 23 patients had moderate psoriasis, 2 were mild psoriasis and no patient had remission

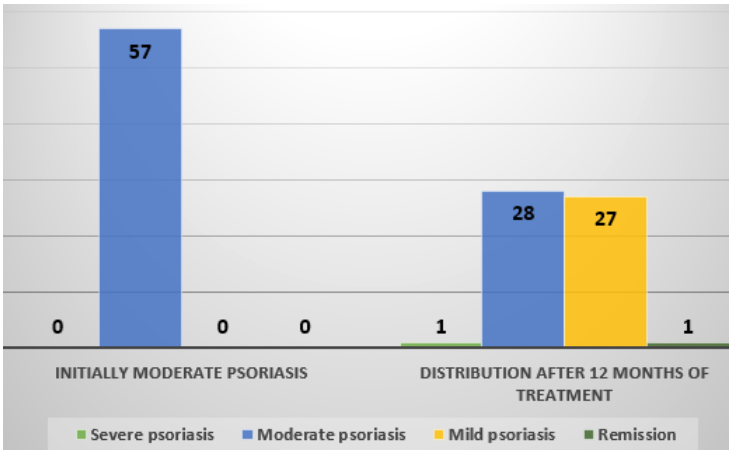

Fig. 6. Decrease trend of psoriasis severity in patients with moderate psoriasis at baseline and after 12 months of treatment. Out of 57 patients with moderate psoriasis, after vitamin D administration only 1 patient experienced severe psoriasis, 28 patients had moderate psoriasis, 27 mild psoriasis and 1 patient had remission

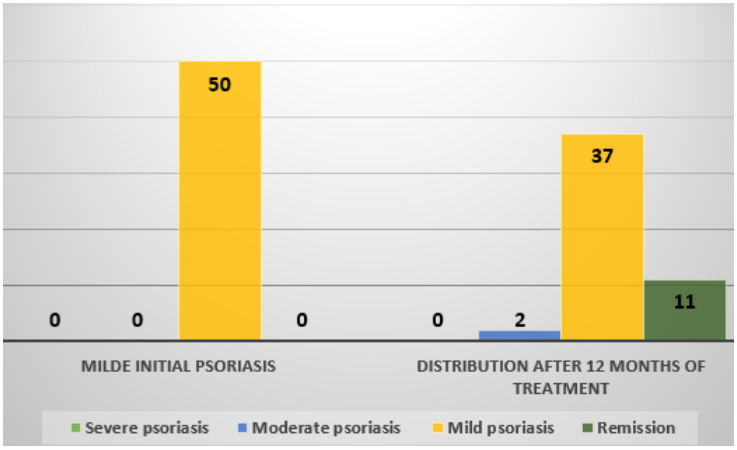

Fig. 7. Decrease trend of psoriasis severity in patients with mild psoriasis at baseline. Out of 50 patients with milde psoriasis, after vitamin D administration no patients experienced severe psoriasis, 2 patients had moderate psoriasis, 37 were mild psoriasis and 11 patients had remission

There have been very few cases where psoriasis has worsened after vitamin D treatment, namely a case with moderate psoriasis evoluated to severe psoriasis and two cases of mild psoriasis worsend to moderate psoriasis. The worsening may be due to the patient's failure to take the treatment as recommended.

We analyzed the severity distribution based on the presence or absence of metabolic syndrome.

The presence of metabolic syndrome negatively influences the severity of psoriasis, the number of cases of severe psoriasis with metabolic syndrome and vitamin D

Table 1

DISTRIBUTION OF SEVERITY AFTER TREATMENT, DEPENDING ON PRESENCE OR ABSENCE OF METABOLIC SYNDROME (MS)

Initial severity of psoriasis in patients with MS (N)	Severity after 12 months of treatment with vitamin D (N)	Initial severity of psoriasis in patients without MS at 12 months (N)	Severity after 12 months of treatment with vitamin D (N)
Severe (28)	Severe - 8 Moderate - 20 Mild - 0 Remission - 0	Severe (6)	Severe - 1 Moderate - 3 Mild - 2 Remission - 0
Moderate (32)	Severe - 1 Moderate - 15 Mild - 16 Remission - 0	Moderat (25)	Severe - 0 Moderate - 13 Mild - 11 Remission - 1
Mild (19)	Severe - 0 Moderate - 0 Mild -12 Remission - 7	Mild (31)	Severe - 0 Moderate - 2 Mild - 25 Remission - 4

deficiency being initially 28, compared to cases of severe psoriasis without vitamin D deficiency and no metabolic syndrome [10].

The proportion of patients with metabolic syndrome, psoriasis and vitamin D deficiency is 56%. In the studied group, 44% were patients with psoriasis, without metabolic syndrome, with vitamin D deficiency, out of a total of 141 who have psoriasis and vitamin D deficiency.

The downward trend in the severity of psoriasis following vitamin D treatment can be observed. There is a clear and significant reduction in the number of severe psoriasis patients. In general, severity reduction occurred gradually, there were no patients with severe psoriasis who, after 12 months of treatment, entered the remission.

Taking into account the maximum allowed dose of vitamin D of 4000 IU/day for adults, we considered the maximum allowed dose as a threshold for administration to deficient patients.

Sun exposure and sun protection were analyzed in all study participants. The degree of sun exposure decreases with the increase in the severity of psoriasis in the studied group.

Sayre and Dowdy demonstrated that SFP-15 solar protection reduces pre-vitamin D3 production below the body's requirement and greater protection completely blocks the production of pre-vitamin D3. For an optimal intake of vitamin D, exposure to the sun in the middle of the day without sunscreen is preferable, however negative effects such as burns and skin cancers may occur [34, 35].

Botella-Corretero et al have found the vitamin D level below 5 percentile (20 ng/mL) in 50.7% of the 73 morbidly obese patients. In their study, vitamin D deficiency was associated with the metabolic syndrome pathways in patients with morbid obesity [36].

In our study, we have found an increase in the mean baseline values of vitamin D in patients with metabolic syndrome from 18.27 ± 6.744 to 47.81 ± 6.107, after 12 months of treatment.

A 12-month study on 59 patients with metabolic syndrome showed elevations of vitamin D serum by diet and exposure to the sun with an initial mean of 19.1 ± 1.5 and a mean after 12 months of 28, 4 ± 1.5 [37].

The results of our study sustain the necessity of an awareness campaign among family doctors on the correlation of psoriasis - metabolic syndrome - vitamin D.

In addition to the awareness campaign, a screening program for the presence of metabolic syndrome, risk factors and evaluation of vitamin D serum levels among psoriasis patients is required [38,39].

Conclusions

In conclusion, the results of the current study open a new perspective in addressing and treating psoriasis. Patients with psoriasis are prone to develop metabolic syndrome. The predisposition increases in parallel with the severity of psoriasis and the number of years of illness.

The main novelty of our study is represented by the beneficial effects of systemic treatment with vitamin D on the severity of psoriasis, as well as on the components of the metabolic syndrome. There is no other research on this topic in the national and international literature.

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