



The Role of High-Dose Vitamin D Supplementation on Disease Severity and Lipid Profile in Psoriatic Patients - a Pilot Study

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Abstract

Background/Aim: Psoriasis is a chronic inflammatory skin disease that is associated with a higher prevalence of cardiovascular (CV) risk factors. The effect of vitamin D on bone health has been long known, but its extraskeletal role especially in cardiovascular disease and skin disease, is the subject of recent research. This study aimed to assess the influence of high-dose vitamin D supplementation on the Psoriasis Area and Severity Index (PASI) score and lipid profile in patients with psoriasis.

Methods: The study included 20 adult patients with chronic plaque psoriasis. They received vitamin D capsules in a daily dose of 5,000 IU over 12 weeks. Measured serum concentrations of lipid metabolism parameters were triglycerides (TG), total cholesterol (TC), low-density lipoproteins (LDL) and high-density lipoproteins (HDL). PASI was used to determine the severity of the disease.

Results: High-doses vitamin D supplementation had a significant influence on reduction in PASI score in all patients (17.99 ± 12.42 vs 10.27 ± 8.53 ; $p < 0.001$). The supplementation of high dose vitamin D induced statistically significant lowering of the TC, LDL-C and TG in the psoriatic patients ($p < 0.05$). Furthermore, significant increase in serum HDL-C level was observed. The change of PASI score showed week positive correlation with the changes in serum TC and LDL-C ($r = 0.303$, $p = 0.03$ and $r = 0.357$ $p = 0.013$).

Conclusion: High-dose vitamin D supplementation had a positive impact on clinical status of the chronic plaque psoriasis patients, measured by PASI score. It also improved the serum lipid profile of these patients. Double-blinded prospective studies are needed in order to get more comprehensive data related to vitamin D, lipid metabolism and severity of psoriasis.

Key words: Psoriasis; Disease severity; Lipid profile; High-dose; Vitamin D.

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Introduction

Psoriasis is a very common chronic inflammatory skin and systemic disease with various clinical manifestation that affects 2-3 % of the general population.^{1,2} Aetiopathogenesis of the disease has not been fully understood yet and includes complex interaction of immune system, genetic background, autoantigens and environmental factors.³

A connection between psoriasis and higher cardiovascular (CV) morbidity and mortality is well recognised.⁴ The CV risk factors such as lipid disturbance, hypertension, oxidative stress, diabetes mellitus and metabolic syndrome are more prevalent in patients with psoriasis.^{4, 5} Dyslipidaemia is one of the most common CV risk factors and many authors have shown a direct link be-

tween the serum levels of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and the risk of cardiovascular disease (CVD).⁶

The features of dyslipidaemia in psoriatic patients are very often associated with elevated triglyceride (TG) level, predominance of LDL-C and low level of HDL-C, all of which contribute to the increased CV risk. Therefore, more attention should be paid to routine screening for lipid disturbances in the psoriatic patients, which can contribute to an early determination of the risk for CVD.⁷

Vitamin D deficiency reached an epidemic proportions in the general population and has recently been associated with many CV risk factors like obesity, hypertension, insulin resistance, dyslipidaemia and chronic low-grade inflammation.⁸ Besides that, there is a lot of data from available literature that have shown low vitamin D status in many non-skeletal diseases, including psoriasis. Some authors found that hypovitaminosis D in psoriatic patients correlated with clinical severity of disease calculated by the Psoriasis Area Severity Index (PASI) score.⁹ It is unclear whether this association is causal or due to the underlying disease and the importance of hypovitaminosis D in psoriasis is still not entirely clear.¹⁰

There are limited data from available literature about the influence of high-dose vitamin D supplementation on disease severity and lipid profile in the psoriatic patients. The study aimed to assess influence of high-dose vitamin D supplementation on PASI score and lipid metabolism in patients with psoriasis.

Methods

Study design

This was a clinical study in chronic plaque psoriasis patients performed between June and December 2018. The patients were recruited at the Skin and Venereal Disease Clinic of the University Clinical Centre of the Republic of Srpska, Banja Luka, Bosnia & Herzegovina. A total of 20 adult psoriatic patients completed the study. All participants (> 40 years), received an oral dose of vitamin D (5,000 IU per day) for three months.

The participants were given a precise number of capsules for three months of treatment and their compliance was checked on a monthly basis.

The participants who received some form of antipsoriatic systemic or local therapy, phototherapy and topical or oral vitamin D preparations not less than three months prior to being enrolled in the study were not included in the study. Participants who were treated with lipid metabolism affecting medications were not included in the study, either. Besides, the participants who had hypercalcaemia were not included. During the study, calcium values were measured on a monthly basis for all patients.

Ethical consideration

The study was approved by the Ethics Committee of the University Clinical Centre of the Republic of Srpska. All of the participants were informed of the study purpose and protocol, risks/benefits in the treatment course and the study schedule and signed informed permission prior to enrolment to the study.

Clinical and anthropometric measurements

Disease severity of skin lesions in chronic plaque psoriasis patients was scored by PASI values. Chronic skin lesions were monitored during this study. Based on PASI scores, the patients were divided into three groups: mild, moderate, and severe (PASI values < 10, PASI values from 10-20, PASI values > 20), respectively.¹¹

Based on anamnestic data, psoriatic patients were split into two groups: early and late form of psoriasis (early form had onset of the disease before 30 years of age, and late form of psoriasis had onset of the disease after 30 years of age).

At the beginning of the intervention period, anthropometric measurements were taken in the morning, by qualified staff. Height was determined with an accuracy of 1 mm. Weight measurement was conducted using a standard scale to the nearest 0.1 kg. Body mass index (BMI) was derived using the standard formula.

Biochemical analysis

Lipid status profile and serum calcium levels were analysed. Blood samples were taken at the beginning and at the end of the treatment period, after 12-14 hours overnight fasting. Standard biochemical methods at Cobas 6000 analyser

(Roche Diagnostics, Mannheim, Germany) were used to analysed lipid profile parameters and serum calcium levels.

Statistical analyses

The Shapiro-Wilk's test was used for assessing data distribution normality. After the distribution check, an appropriate parametric or non-parametric test was used. The paired sample t-test or Wilcoxon Signed Rang test was performed for analysis of differences in the outcome variables. Correlation coefficients were assessed using the Pearson's correlation. Correlation coefficients are considered negligible if $r = 0.0 < 0.30$, week if $r = 0.30 < 0.50$, moderate if $r = 0.50 < 0.70$, and strong if $r > 0.70$.

The SPSS Statistic for Windows, version 20, was used to analyse data. Statistical significance was considered by p -value < 0.05 . Numerical/categorical data were represented as mean \pm standard deviation or number (%) where is appropriate.

Results

There were 20 patients of both genders that completed the study (10 males, 50.00 %). Demographic date concerning gender, age, BMI, disease duration, current smoking status, family history of psoriasis, and beginning of disease were presented in Table 1. The mean value of BMI was 27.67 kg/m², and higher BMI was noticed in the

Table 1: Demographic characteristic of psoriatic patients

Variable	Total n = 20
Gender	
Male	18 (46.2)
Female	21 (53.8)
Age (year)	46.82 \pm 15.05
Body Mass Index (kg/ m ²)	26.43 \pm 2.60
Disease Duration (year)	13.69 \pm 11.90
Smoking status	
Smoker	27 (69.2)
Non-smoker	12 (30.8)
Family history of psoriasis	
positive	21 (53.8)
negative	18 (46.2)
Beginning of disease	
early	19 (48.70)
late	20 (51.30)

Values are presented as number (%) or Mean \pm Standard deviation

more severe form of disease group (28.38 kg/m²) compared to the patients with mild or moderate forms of diseases. Nevertheless, this difference was found not to be statistically significant.

Twelve-week supplementation of vitamin D had a significant effect on the reduction in PASI score in all patients. The PASI score decreased from 15.54 \pm 10.77 to 8.87 \pm 7.38 (< 0.001) in all psoriatic patients. A significant reduction of PASI score after twelve-week supplementation of vitamin D in female and male patients (13.81 \pm 10.58 vs 8.22 \pm 7.41 and 17.58 \pm 11.09 vs 9.67 \pm 7.48) was noticed, respectively.

Table 2: The effect of vitamin D supplementation 5,000 IU/day over 12 weeks on PASI score in psoriatic patients (n = 20)

PASI score	Before vitamin D supplementation	After vitamin D supplementation	p
Female	16.17 \pm 13.14	9.62 \pm 9.09	0.002
Male	19.81 \pm 12.01	10.92 \pm 8.38	< 0.001
All patients	17.99 \pm 12.42	10.27 \pm 8.53	< 0.001

Data are expressed as Mean \pm Standard deviation; PASI, Psoriasis Area and Severity Index

Serum lipid profile was analysed after 12 weeks of the intervention period. The supplementation of high dose vitamin D (5,000 IU) had a significant influence on the lipid parameters in psoriatic patients. As shown in Figure 1, the levels of TC, LDL-C, and TG were significantly decreased at the end of the study when compared with baseline values (5.61 \pm 1.30 vs 5.37 \pm 1.08; 3.25 \pm 0.91 vs 2.98 \pm 0.82 and 2.31 \pm 1.53 vs 2.13 \pm 1.37), respectively. Furthermore, a significant increase in serum HDL-C level was observed 1.22 \pm 0.28 vs 1.47 \pm 0.31, ($p < 0.001$).

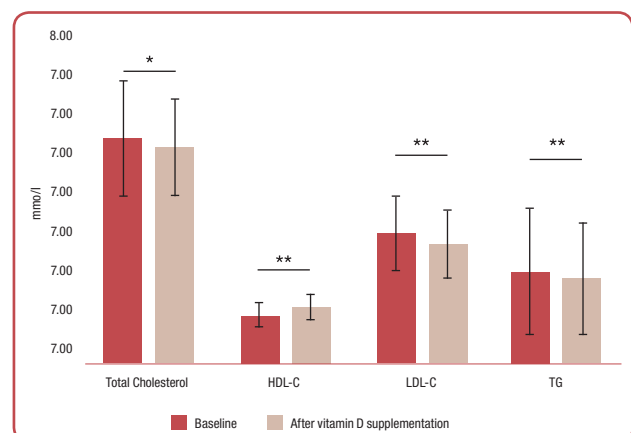


Figure 1: Effects of twelve weeks' supplementation with high dose of Vitamin D on serum lipid profile in psoriatic patients

Data are expressed as the mean \pm SD. HDL-C, High-density lipoprotein cholesterol; LDL-C, Low-density lipoprotein cholesterol; TG, triglycerides; * $p < 0.01$ ** $p < 0.001$

Table 3: Correlation between changes of PASI score with change of serum lipid profile after twelve-week of supplementation with high dose of Vitamin D (5,000 IU/day)

Lipid profile changes	r	p
Δ Total Cholesterol mmol/l	0.303	0.030
Δ HDL - C mmol/l	0.099	0.274
Δ LDL - C mmol/l	0.357	0.013
Δ TG mmol/l	0.043	0.398

Pearson's correlation was applied for verification of the relationship between the lipid profiles level changes in patients with psoriasis in relevance to PASI score after 12 weeks of vitamin D supplementation. Table 3 shows a weak, but statistically significant positive correlations between the change of PASI score with serum total cholesterol and LDL-C changes (Pearson's $r = 0.303$, $p = 0.03$ and Pearson's $r = 0.357$, $p = 0.013$, respectively), but there were no significant correlations between PASI score change with serum HDL-C and triglycerides changes.

Discussion

Psoriasis is a chronic skin and systemic disease interrelated with an increased risk of metabolic syndrome and CVD.⁴ The chronic inflammation, usually common in psoriasis patients, can be a trigger for the structural protein changes, including the creation of neo-epitopes, which stimulate the HDL-C alterations and production of autoantibodies (anti-aHDL, anti-aApo-AI). Batuca et al found that elevated levels of autoantibodies were related with an increased cardiovascular risk and they could be involved in the development of atherosclerotic plaques.¹² These antibodies were also detected in patients with other autoimmune disease and their presence correlated with the severity of disease.¹³ The previous studies reported that the vitamin D deficiency may be associated with dyslipidaemia in apparently healthy people and in diabetic patients.¹⁴⁻¹⁶ Besides, vitamin D deficiency was related to an increased risk of CVD. A meta-analysis of 24 observational studies indicated an inverse relationship between the vitamin D serum level and risk of CVD.¹⁷ The outcomes obtained by Bashir et al indicated that the vitamin D insufficiency or deficiency had significant effects on the lipid profiles, decreasing HDL-C level by almost 30 % and increasing the levels of TC, LDL-C and TG more than double.¹⁸

Lipid disorders in chronic psoriatic patients and their correlation with clinical progression have been described in the literature. The most common lipid abnormalities in psoriatic patients were reduced concentrations of HDL-C, apolipoprotein A (ApoA) and apolipoprotein B (ApoB) and increased concentrations of TC, LDL-C, and TG.^{6,19-21} In another study, the inverse correlations between vitamin D serum level and atherosclerotic lipid profile in psoriatic patients was described.²²

The current study results revealed a remarkable relationship between the twelve-week vitamin D supplementation and an improvement of lipid profile. A significant blood lipid reduction (TC, LDL-C, and TG), and an increase in HDL-C level after the intervention period were observed. These results are partially in agreement with the previous study conducted in diabetic patients.^{23,24}

However, the other trials have shown that vitamin D supplementation does not appear to improve the lipid profile.^{25,26} Additionally, discrepancies in the results of these studies could be possibly explained by variation in study protocols, different pathophysiologic conditions and the vitamin D interaction with certain drugs.

The decreased lipid absorption and endogenous synthesis are suggested mechanisms by which vitamin D treatment influences the lipid profile (total cholesterol and LDL-C).²⁷ Besides, the previous data have suggested that an increase in intestinal calcium absorption reduces the synthesis and secretion of TG. Another possible lipid-lowering pathway might be via the parathyroid hormone (PTH) regulation and consequent lowering of TG level.¹⁶

Several recent studies have indicated the role of vitamin D in the synthesis of glycosylceramides in the stratum corneum, in differentiation and proliferation of keratinocytes and migration of dendritic cells.^{13,28} Additionally, vitamin D plays an important role in the formation of antimicrobial peptides in epithelial cells of the skin that maintain normal skin integrity.²⁹ Previously, observational studies demonstrated a negative correlation between the reduced level of vitamin D in psoriatic patients and the disease severity according to PASI score.^{9,30} There are limited data in the literature about the influence of high-dose vitamin D supplementation on the disease severity in patients with psoriasis.

The results of the present study demonstrated that a high dose of vitamin D supplementation significantly decreased the disease severity, determined by the PASI score. A significant reduction of PASI scores after twelve-week supplementation with a high dose of vitamin D in female and male patients was noticed.

In the three-quarters of patients, a significant improvement of the lesions was observed after oral treatment with 1 alpha-hydroxyvitamin D₃.³¹ A Brazilian study in 25 psoriasis and vitiligo patients who received a very high daily dose of vitamin D over six months, showed clinical improvement in all psoriatic patients and in 25–75 % of patients with vitiligo had repigmentation.³² Similar results were obtained in the randomised, double-blind, placebo-controlled study conducted by Disphanura et al, however, the treatment period was the same, but the vitamin D supplementation was intermittent every two weeks.³³ In contrast to the results presented in this paper, Jarrett et al found that oral vitamin D administration had no significant difference in the PASI score in patients with mild form of the disease.³⁴

The current study indicated the existence of a significant, but weak correlation between clinical improvements determined by change in PASI score and changes in TC and LDL-C serum level. In another placebo-controlled clinical study, the correlation between the severity of disease and anti-oxLDL and oxLDL concentrations was shown and a higher anti-ox-LDL concentration, along with HDLs antibodies or apolipoprotein was found, which indicated higher cardiovascular risk. It showed that the anti-ox-LDL/ox-LDL ratio correlated significantly with disease severity, its levels increasing linearly with increasing severity.³⁵

Nakhwa et al did not find a statistically significant correlation between PASI score determined severity of disease and lipid profile abnormalities. At the same time, they found a reduced HDL-C level in patients with severe form of psoriasis.⁷

Conclusion

Although there are conflicting data in the literature about the vitamin D role in the pathogenesis of psoriasis, the results of this study found that high-dose vitamin D supplementation had a positive impact on the clinical status of the chronic plaque psoriasis patients, determined by PASI score. Besides, significant improvement in the lipid profile of those patients by lowering TC, LDL-C, and TG and increasing HDL-C, was observed. Nevertheless, prospective, double-blind clinical studies are needed to get more data related to the role of vitamin D supplementation in psoriatic patients.

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Conflict of interest

None.

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