



Transdermal Application of Vitamin D Cream in Individuals with Osteoporosis and Osteopenia

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Abstract

It is estimated that over a billion people worldwide have low vitamin D concentrations, justifying the term "pandemic" of vitamin D deficiency, with severe consequences for public health. Vitamin D is a key factor in the prevention and treatment of osteoporosis as it promotes the intestinal absorption of calcium, which is a fundamental prerequisite for normal bone homeostasis. Numerous therapeutic options are available for the prevention and treatment of bone loss, particularly crucial for postmenopausal women and older individuals. The primary measures for preventing bone loss include proper nutrition, physical activity, and adequate intake of vitamin D and calcium. Endocrine societies worldwide provide guidelines recommending calcium and vitamin D intake, typically ranging from 800 to 1200 mg of calcium (from food and supplements) and 800–2000 IU of vitamin D for postmenopausal women with osteoporosis. Osteoporosis leads to a reduction in bone density and quality, exposing women to a higher risk of fractures even with minor injuries or spontaneous falls. The risk of osteoporosis in individuals over 50 is estimated to be about 50% higher in women and 20% higher in men, meaning that women are 2.5 times more likely to be at risk. Vitamin D deficiency also increases the risk of other diseases (comorbidities) such as diabetes, high blood pressure, asthma, and heart disease. Our research focused on the transdermal application of vitamin D, especially in diseases like osteoporosis and osteopenia. The results show that after 2 months of transdermal vitamin D application (twice daily: morning and evening), osteopenia in participants subsided, and the findings returned to normal. Transdermal application of vitamin D is scarcely represented in literature and research, making our study one of the first to address this issue and providing a foundation for further research.

Keywords: *osteoporosis, osteopenia, vitamin D, studies, disease.*

1. Introduction

Vitamin D, along with its active analogs and metabolites, constitutes a group of compounds with numerous functions in the body. Vitamin D is the name for a group of fat-soluble secosteroids and prohormones [1]. There are two forms of vitamin D: vitamin D₂ (ergocalciferol) and D₃ (cholecalciferol). Vitamin D can be synthesized in the body, specifically in the skin, from endogenous cholesterol (7-dehydrocholesterol) under the influence of UV B (290–315 nm) radiation. It transforms from its prohormone form into the active form of vitamin D. In the liver, it is metabolized into 25-hydroxyvitamin D (25-OH D) and further converted in the kidneys into the active form, calcitriol (1,25 (OH)₂ vitamin D) [3]. Its primary role lies in the metabolism of calcium and phosphorus. Vitamin D, as one of the essential vitamins, reduces the physiological activity of parathormone both directly: by acting on the parathyroid gland cells and indirectly: through hypercalcemia. Its function is also reflected in bone breakdown and formation. By acting on osteoblasts through vitamin D receptors, it increases the synthesis of osteocalcin, alkaline phosphatase and collagen type 1. Its influence on osteoclasts is direct: suppressing the differentiation of promyelocytes into monocytes, which are precursors of osteoclasts and indirect: through osteoblasts [5]. Vitamin D deficiency is widespread worldwide today and poses a significant threat to public health. Osteoporosis, according to the World Health Organization (WHO) definition is

characterized by bone density more than 2.5 standard deviations (SD) below the average for the same age and gender in a healthy population. The incidence of osteoporosis increases with age and is most common in the female population, even up to 80% more than in males, particularly in postmenopausal women. Due to the reduction in ovarian estrogen levels, there is an accelerated loss of bone mass and a decrease in the ability to remodel bones. The risk of fractures in postmenopausal women is 30–40% [4]. Vitamin D deficiency can cause and worsen many diseases such as: heart disease, cancer, rheumatoid arthritis, high blood pressure, depression, muscle weakness, muscle loss, autoimmune diseases and periodontal diseases (: !!). The prevalence of vitamin D₃ deficiency is much higher in patients with type 2 diabetes mellitus than in the healthy population, posing a significantly increased risk of developing diabetic nephropathy. The average prevalence of vitamin D deficiency is associated with a twofold increase in the risk of coronary heart disease, cerebral disease and 1.5-fold increased risk of mortality (Lin et al., 2019).

1.2. Vitamin D Cream

Vitamin D Cream is a product by brand, Dr. Pasha“ from Sarajevo. The cream has the following details of patent claim:

- Cholecalciferol, Vitamin D₃: Ph Eur, BP, USP;
- CAS-br. 67-97-0;
- Molecular formula: C₂₇H₄₄O (Hill);

- EZ-number 200-673-2;

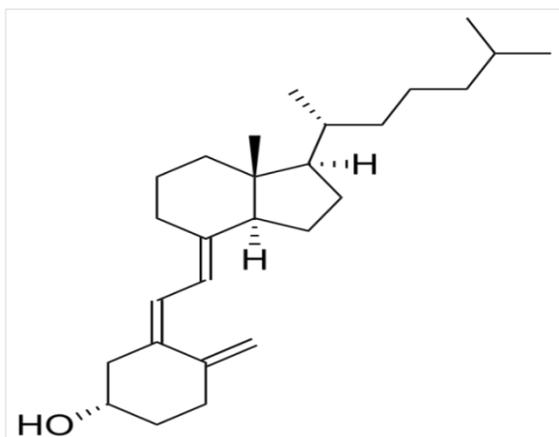


Figure 1: Composition of the general formula of Vitamin D3

The well-known structure of vitamin D3 is integrated into the cream base, which, due to its composition delivers active substances to the application site. These included: Shea butter, Almond oil and Hydrolyzed oat protein in the form of potassium salts and Xanthan gum, whose composition includes: Agua, Prunus Amygdalus Ducis Oil, Butyrospermum Parkii Butter, Potassium Olivoyl Hydrolyzed Oat Protein, Glycerin, Cetearyl Alcohol, Glyceryl Oleate, Glyceryl Stearate, Dehydroacetic Acid, Benzyl Alcohol, Xanthan Gum, Cholecalciferol, Tocopherol. This cream is intended as dermal support in conditions where there is a need to replenish a deficiency of vitamin D, and it is applied with approximately 1200 IU of vitamin D. It is to be applied to the treated skin twice a day, in the morning and evening, with the aim of delivering an adequate dose

of vitamin D to the treated area much faster and more efficiently than would be achieved through oral supplementation.

2. Materials and Methods

The research on transdermal application of vitamin D was conducted over a period of 3 months, involving 3 checkpoints: after 1 months, after 2 months and after 3 months. The total number of participants was 28. The study was conducted using an online survey (Google Forms). The survey was of an anonymous nature and strictly confidential, collecting data on the patients health status and their medical history. Transdermal vitamin D application therapy did not interfere with the routine patient treatment documentation and was carried out with their informed consent. The study adhered to the Convention on human Rights and local law regarding patient rights, including the Law on Rights, Obligations and Responsibilities of Patients in the Federation of Bosnia and Herzegovina; the Law on Personal Data Protection in Bosnia and Herzegovina; and the Regulation on Records in the Field of Health in the Federation of Bosnia and Herzegovina.

3. Results

Table 1. presents the gender and age structure of the 28 participants with detected vitamin D deficiency. The age structure of the participants ranged from 40 years to 90 years. The results show the following: within the male gender group (N=10), the highest percentage of 40% (4 participants) was in the age range of 71-80 years, while the lowest was observed for age groups 40-70 years and 81-90 years. The female gender group (N=18) recorded the highest percentage of 44.4% for participants in the age range of 61-70 years, while the lowest percentage was for the range of 81-90 years.

Table 1. Gender and age structure of participants with vitamin D deficiency

The age group of participants	The gender group of the participants	
	Male (%)	Female (%)
from 40-50 age	1 (10%)	2 (11.1%)
from 51-60 age	1 (10%)	3 (16.6%)
from 61-70 age	3 (30%)	8 (44.4%)
from 71-80 age	4 (40%)	4 (22.2%)
from 80-90 age	1 (10%)	1 (5.55%)
Total:	10	18

Table 2. displays the results for the administration of vitamin D in participants with osteoporosis and osteopenia (male and female populations). The number of participants with osteoporosis was 5 (M=2; F=3), while the number of participants with osteopenia was 23 (M=8; F=15). The table included 3 follow-up periods: control after 1 months; control after 2 months and control after 3 months. Also, in the table, dashes were provided next to each month, indicating the following outcomes: normal findings, improvement, no improvement. The "improvement" indication referred to a better quality of life for individuals with this type of illness. While there were no changes in the findings, participants experienced mitigating circumstances. They were able to move more easily, had improved appetite, and could perform daily activities with significantly reduced pain intensity. Osteoporosis in the male population showed no effects after one month of using vitamin D cream. However, in the female population, there was improvement in one participant. After applying the cream for two months, improvements were

observed in one male participant, while the condition remained unchanged in another. In the female population, one participant showed improvement, while two did not. Following three months of using the vitamin D cream, both male participants and all three female participants experienced improvement. Osteopenia in the male population (8 participants) showed improvement in 7 participants 7 days after the application of vitamin D. The control after 1.5 months showed improvement in 2 participants, while findings were normal in 6 participants. The last control after 2 months showed normal findings in all participants [8]. Osteopenia in the female population (15 participants) showed improvement in 11 participants during the first control (7 days), with normal findings in 4 participants. The second control (1.5 months) revealed normal findings in 10 participants, with improvement in 5 participants. The final control (2 months) showed normal findings in all 15 participants.

Table 2: Application of vitamin D cream in male and female participants in the presence of osteoporosis and osteopenia

Vitamin D deficiency in osteoporosis and osteopenia:		Gender of participants			
		Osteoporosis		Osteopenia	
		Male (N=2)	Female (N=3)	Male (N=8)	Female (N=15)
Application of vitamin D cream after 1 month	Normal findings	0	0	0	4
	Improvement	0	1	7	11
	No improvement	2	2	1	0

Application of vitamin D cream after 2 months	Normal finding	0	0	6	10
	Improvement	1	1	2	5
	No improvement	1	2	0	0
Application of vitamin D cream after 3 months	Normal findings	0	0	8	15
	Improvement	2	3	0	0
	No improvement	0	0	0	0

In Table 3. the results for the presence of comorbidities in participants (male and female) with vitamin D deficiency (osteoporosis and osteopenia) are recorded. The results show the presence of multiple comorbidities in the participants. The majority of male participants (6) have high blood pressure, while 3 participants have type 2 diabetes mellitus, rheumatoid arthritis, heart problems

and asthma each reported by 1 participant. The female population (6) records high blood pressure as the most dominant comorbidity, followed by type 2 diabetes mellitus (5 participants). Heart problems are present in 4 participant, rheumatoid arthritis in 2 participants and hiatal hernia in 1 participant.

Table 3: Presence of comorbidities in participants with osteoporosis and osteopenia

Presence of comorbidities	Gender of participants			
	Male (N=10)	%	Female (N=18)	%
Rheumatoid arthritis	1	10	2	11.11
Heart problems	1	10	4	22.22
Asthma	1	10	0	0
Hiatal hernia	0	0	1	5.55
High blood pressure	6	60	6	33.33
Diabetes mellitus type 2	3	30	5	27.77

4. Discussion

The global interest in vitamin D appears insatiable, given the significant increase in its hypovitaminosis. Literary excerpts on vitamin D span a wide range of clinical specialties, including immunology, endocrinology, nephrology, among many others. The question of how much vitamin D is sufficient on a daily basis, and how much leads to toxicity, is the subject of many significant debates, yet without a clear consensus among scientists. However, much literature is supported by facts about the importance and proliferation of this essential vitamin, and the negative impact on the health of individuals suffering from its deficiency. Among other things, our results indicate that osteoporosis, as well as osteopenia (vitamin D deficiency), is more prevalent in the female population (almost 50%) than in males, and it most commonly occurs in individuals over 40 years of age. Literary excerpts show both agreements and disagreements with our results, where El-Khateeb et al. (2019) state that the prevalence of low vitamin D status was higher in males (88.6%) compared to females (92.4%). Vitamin D was sufficient in 7.6% of males, insufficient in 38.4% of males, and deficient in 54% of males. Among females, vitamin D was insufficient in 10.1%, and deficient in 78.5%. The prevalence of vitamin D deficiency was significantly higher in females than in males (p=0.001). The only variables significantly associated with low vitamin D levels were gender and the age of the participants. Also, in the study by Camara and Brandao (2019), which included 250 participants, of which 115 (46%) were female and 135 (54%) were male. The average age of the participants was 60-70 years. In female participants, the total number with vitamin D deficiency was 40.9%, while in male participants, this number was 59.1%, with a diagnosis of vitamin D deficiency associated with osteopenia. The occurrence of comorbidities is concomitant with defined osteoporosis/osteopenia. The most dominant comorbidities among the participants in our study were high blood pressure, followed by type 2 diabetes mellitus, and heart diseases. Kouvari and Panagiotakos (2019) note that the most common comorbidity among the participants was arterial hypertension in 132 (62.9%) individuals, with diabetes present in 65 (24.6%) participants, and thyroid diseases in 53 (12.5%) participants. Filip et al. (2020) also state that hypertension is the most common comorbidity in patients with osteoporosis and osteopenia, along with heart problems. There are no available literature data on the transdermal application of vitamin D (in the form of cream) in individuals with osteoporosis

and osteopenia. We can say that we are among the first to explore this topic. Our results indicate a very significant achievement with these exceptional ingredients that make up the cream. Osteopenia showed normal reference ranges after only 2 months of treatment with vitamin D cream, which could have a significant impact in the future in improving conditions like these.

5. Conclusion

In the world, there are no forms of transdermal application of vitamin D, nor are there unique guidelines for the prevention, recognition, and treatment of vitamin D deficiency. Therefore, the given results suggest that the transdermal application of vitamin D in 28 participants (male and female populations) showed a significant advancement in its application, and participants had normal findings after 3 months of application. Osteopenia showed normal findings, while osteoporosis demonstrated improvement. Certainly, the participants were of an older age range, from 60 to 90 years old, and the indication of osteoporosis and osteopenia was increased, with the results indicating that women are more susceptible to osteoporosis compared to men.

Conflicts of Interest

Not Applicable

Funding Statement

Not Applicable

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