ORIGINAL STUDY

Oral Vitamin D Therapy for Chronic Plaque-Psoriasis among Iraqi Patients, Efficacy, and Safety

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ABSTRACT

Background: Psoriasis is an immune-mediated disorder that results from a polygenic predisposition combined with environmental triggers. Any problem in the optimal function of the skin due to psoriasis may lead to a decrease in the ability of vitamin D3 cutaneous production. Up-to-date, the effective management of psoriasis built on sufficient nutritional consumption of vitamin D, while oral intake of vitamin D in psoriasis still not fulfilled clinical necessity, and its effect still controversial.

Aim: The aim of the current study was to evaluate the safety and efficacy of oral vitamin D in the treatment of moderate to severe classical plaque psoriasis.

Patients and methods: 76 patients enrolled in the study were allocated randomly into two groups. Group A (38 psoriasis patients) were given only topical potent corticosteroid (clobetasol propionate) therapy for 3 months' duration, while group B (38 psoriasis patients) were taken topical potent corticosteroid (clobetasol propionate) in addition to oral vitamin D (50,000 IU weekly dose for 3 months' duration). The severity of psoriasis was assessed monthly for the 3 months' duration of the study based on photography and evaluation of psoriasis area severity index (PASI) score, and vitamin D serum level was also assessed.

Results: There was no significant difference in mean age, basal metabolic rate (BMR), and gender between the two groups in the study. No significant difference between the mean of serum vitamin D of two groups, and also no statistical difference between PASI score of two groups. Regarding vitamin D serum level evaluation among patients in group A, it was 13.2 + 6.12 ng/mL at baseline, then after 3 months, its level was 13.6 + 3.82 ng/mL with non-significant differences between the two serum levels (improvement 3.03 + 6.21%, $p = 0.62$). Otherwise, serum vitamin D level among patients in group B was 13.5 + 4.16 ng/mL, then this level was significantly and constantly increased to reach 42.12 + 5.63 (improvement 212 + 47.82%, $p = 0.0012$), and this increment of vitamin D serum level was statistically significant inverse relationship with the improvement in PASI score ($r = –0.4$) throughout the 3 months' period of study. There was a significant improvement in PASI score among patients who took in addition to the topical steroid oral vitamin D ($p = 0.033$).

Conclusion: The oral vitamin D supplementation can be safe, effective, and cheap therapeutic modality to psoriasis patients. Other drugs used for treatment of psoriasis systemically are costly and widely side effects.

Keywords: Chronic plaque-psoriasis, Iraqi patients, Oral vitamin D.

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INTRODUCTION

Psoriasis is a common, chronic, and recurrent inflammatory disease of the skin.[1] It is a group of chronic inflammatory and hyperproliferative conditions of the skin, associated with systemic manifestations in many organ systems.[2] Psoriasis is an immune-mediated disorder, both genetic and environmental influences have a critical role in the etiology and pathogenesis.[2,3] T cells and cytokines play pivotal roles in the pathophysiology of psoriasis.[1,4] Any problem in optimal function of skin due to psoriasis may lead to a decrease in the ability of vitamin D3 cutaneous production. It stimulates a nasty loop that weakens skin hemostasis and leads to advanced reduction in vitamin D level in entire body of humans, even skin.[5] Vitamin D prevents epidermal propagation, controls keratinocyte growing, and distinguishing and finally modify the immune system; this occurs when hyperproliferative of epidermis.[3] Chronic plaque psoriasis is the most common type of psoriasis, accounting for about 80 to 90% of all cases. It presents as a papulosquamous rash, and the diagnosis is based on the typical appearance of individual lesions, and

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their characteristic distribution on the skin.[2] Psoriasis guttata is steady lesions, occur in trunk and limbs, like water drop in size. Psoriasis follicularis lesion is a little, scaly occur at hair follicles opening. Psoriasis annulata, gyrate, or figurata lesion, which is curved line occurs as a result of chief involution. Psoriasis discoidea with no central involution and fix firm patches. Psoriasis rupioides lesion look like syphilitic rupia.[1] Psoriasis prevalence in different populations varies from 0.1 to 11.8%.[6] Psoriasis occurs with equal frequency in both genders. Between 1 and 2% of the US population has psoriasis.[1] There are wide variations in the reported prevalence of psoriasis in different populations. This may reflect variations in study methodology or ethnic and environmental differences between populations. Psoriasis appears to be more common in white people.[2] Because psoriasis is a chronic disease, it requires a long-term treatment strategy, which takes into account potential medication side effects and individual needs.[3] In the 1930s, they used vitamin D for osteoporotic patients also; they have psoriasis; they look that patients become well.[4] Vitamin D3 is well tolerated and continues to be clinically effective with minimum of adverse effects in long-term use. It exerts its actions by binding to the vitamin D receptor.[7] It regulates cell growth, differentiation, and immune function, as well as, calcium and phosphorous metabolism, and inhibits creation of numerous pro-inflammatory cytokines counting IL-2 besides IFN-γ.[6,8] The cutaneous production of vitamin D is considered the core source of it, that stimulated by UV radioactivity, so the contact to UV light radiation in safe dose does not lead to developing skin cancer. Daily life exposure to the sunlight is considered safe, but exposure to high amounts of radiation during sunbathing and holiday lead to increase in the risk of cutaneous cancer development (melanoma).[9] So, alternative to sun exposure, we give vitamin D3 supplementation and some food but most meals and food contain small amounts of vitamin D, another food contain high amounts eaten sporadically.[10] Vitamin D plays an important role in numerous inflammatory cutaneous disorders, including atopic dermatitis, and chronic urticarial and rosacea.[11] A decrease in 25-hydroxycholecalciferol might be a dangerous factor for psoriasis progression and lead to abnormality in cellular defense system.[12] Research on the relationship between blood level of vitamin D and several diseases in dermatology, such as, vitiligo, psoriasis, atopic dermatitis, urticarial, and melanoma is currently very advanced. Oral vitamin D current use as primary or supplemental therapy has been widely studied. Vitamin D offers many therapeutic benefits in dermatology, both as monotherapy and combination with other medications.[13] The therapy with vitamin D, is first-line recently recommended topical drugs for this disease, alone or with topical steroids.[14] Therefore, the objectives of the current study were to evaluate the safety and efficacy of oral vitamin D in the treatment of moderate to severe classical plaque psoriasis.

PATIENTS AND METHODS

This study was a comparative therapeutic study, involved 76 patients with chronic plaque psoriasis. Patients were eligible from those attending the out-patient clinic of dermatology in Merjan Teaching Hospital from January 2018 to July 2019. The 76 patients enrolled in the study were allocated randomly into two groups to assess the efficacy and safety of vitamin D on psoriasis. Group A (38 psoriasis patients) were given only topical potent corticosteroid (clobetasol propionate) therapy for 3 months' duration, while group B (38 psoriasis patients) were taken topical potent corticosteroid (clobetasol propionate) in addition to oral vitamin D (50,000 IU weekly dose for 3 months' duration). Both groups were statistically matched regarding age, gender (male:female ratio), psoriasis severity, and PASI score.

Full information from each patient was taken in a questionnaire regarding age, gender, weight, medical history, and drug history.

Inclusion criteria: Patients older than 18 years with chronic plaque psoriasis.

Exclusion criteria: It included the following conditions:

- Patients on systemic or topical therapy or phototherapy for psoriasis in the last one month.
- Pregnant, as well as, lactating females.
- Patients with an age less than 18 years old.
- Patients with kidney, hematological or liver damage, diabetes mellitus, marginal neuropathy, insufficient peripheral flow, renal stone, and parathyroid complaint.
- Patients with elevated blood calcium or exposure to ultra violate B (UVB) phototherapy.
- Patients tack chemotherapy, vitamin D, Ca tablets, drug for epilepsy, anticoagulant, and bisphosphonate, currently or within the last one month for any other cause.
- Patients with pustular, guttate, or any other variant of psoriasis rather than classical plaque psoriasis.

The diagnosis of psoriasis: This established on clinical basis by the dermatologist.

Baseline evaluations: At the initial visit, baseline assessment included psoriatic lesions photography, the PASI scores, and serum level of vitamin D for both groups, while patients on vitamin D treatment group were further investigated about level of parathyroid hormones, Ca, creatinine, and phosphate.

Follow-up: The severity of psoriasis was assessed monthly for the 3 months' duration of the study basing on photography and evaluation of PASI score, and vitamin D serum level was also assessed. Follow up for the treatment group patients also involved monitoring of any alternation in lab data: parathyroid hormone, serum phosphate, Ca, serum creatinine, and C reactive protien (CPR).

Adverse effects: Adverse effects of vitamin D were also monitored and follow up monthly for any new signs and symptoms exacerbation of old lesions present at baseline or any change in the baseline laboratory investigations.

Ethical approval: Verbal agreement was taken for each patient before starting oral vitamin D routine after detailed information about the aim and purpose of this research. This approval supply by the health ethics agency of Babylon Medical College.

Statistical analysis: Done by SPSS 22, where mean SD and percentage of variables measure, and chi square used for categorical data with significant p value less than 0.05.

RESULTS

Eighty-five patients with chronic plaque psoriasis (mild, moderate, and severe) were assessed to be enrolled in the study. Nine patients were excluded because seven of them dropped to participate, one patient was taking systemic immunosuppressive agents, and another patient had hypercalcemia. Ultimately, only 76 patients were appropriate and randomized into two groups, each containing 38 patients, as shown in Figure 1.

The baseline demographic data distribution for patients in both groups are summarized in Table 1. The two groups were statistically matched regarding the demographic data (age, BMI**,** gender ratio, PASI score, and serum vitamin D level). No significant difference in mean of age (group A: 34.63 + 2.1 *vs.* group B: 36.54 + 4.7, p = 0.34), BMI (group A: 26.82 + 5.4 *vs.* group B: 28.19 + 1.4, p = 0.82), and gender (male:female ratio) (group A: 1.9:1 *vs.* group B: 2.1:1, p = 0.53) between the two groups in the study. No difference between the mean of two groups, group A: 13.2 ng/mL to group B: 13.5 ng/mL, p-value = 0.24). The score of PASI also showed no difference significantly between the mean of two groups (group A: 15.1 + 3.72 *vs.* group B: 15.3 + 1.14, p = 0.76).

At baseline, mean PASI score among patients in group A who received only topical potent steroid therapy was 15.1, then it was gradually decreased to 10.4 + 2.32 after 3 months' period representing a 31.12 + 56.44% improvement (p = 0.033). Likewise, the baseline mean PASI score among patients in group B who received topical potent steroid therapy in addition to oral vitamin D (50,000 IU weekly) was 15.3, then it was significantly decreased to reach 5.2 + 4.43 after 3 months of continuous therapy, and represented 66.01 + 30.13% of improvement (p = 0.014), as illustrated in Figure 2 and Table 2.

Regarding vitamin D serum level evaluation among patients in group A, it was 13.2 + 6.12 ng/mL at baseline, then after 3 months, its level was 13.6 + 3.82 ng/mL with non-significant differences between the two serum levels (improvement 3.03 + 6.21%, p = 0.62). Otherwise, serum vitamin D level among patients in group B was 13.5 + 4.16 ng/mL, then this level was significantly and constantly increased to reach 42.12 + 5.63 (improvement 212 + 47.82%, p = 0.0012), and this increment of vitamin D serum level was statistically significant inverse relationship with the improvement in PASI score (r = –0.4) throughout the 3 months' period of study, as illustrated in Figure 2 and Table 2.

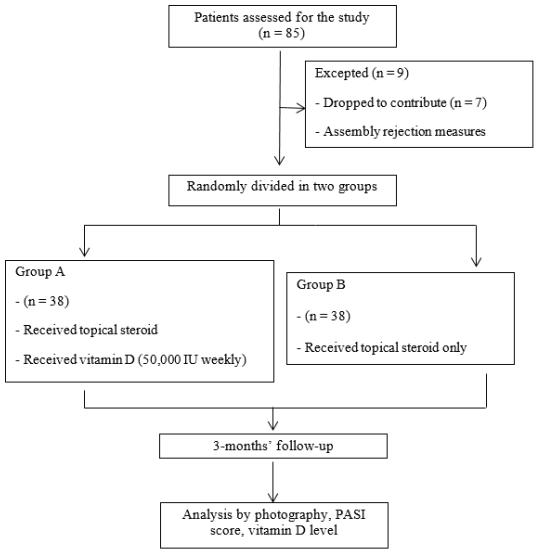

Figure 1: Scheme of the study

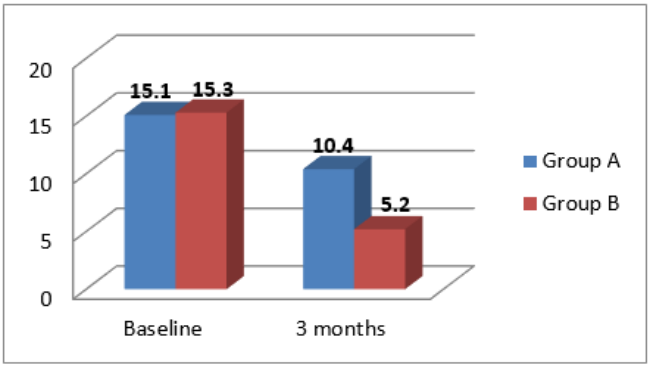

Figure 2: PASI improvement at the 3 months' follow-up

Table 1: Baseline demographic data distribution between the two groups in the study

Demographic data	*Group A (n: 38)*	*Group B (n: 38)*	*p value*
Age/ years	34.63 + 2.1	36.54 + 4.7	0.34
BMI	26.82 + 5.4	28.19 + 1.4	0.82
Gender; male:female n (ratio)	25:13 (1.9:1)	26:12 (2.1:1)	0.53
Serum vitamin D levels/ ng/mL	13.2 + 6.12	13.5 + 4.16	0.24
PASI score	15.1 + 3.72	15.3 + 1.14	0.76

Significant difference when p-value < 0.5

Table 2: PASI score and serum vitamin D level evaluation after 3 months

Evaluation data	*Groups*	*Baseline*	*After 3 months*	*% of improvement*	*p value*
PASI score	Group A	15.1 + 3.72	10.4 + 2.32	31.12 + 56.44	0.033
	Group B	15.3 + 1.14	5.2 + 4.43	66.01 + 30.13	0.014
Vitamin D serum level	Group A	13.2 + 6.12	13.6 + 3.82	3.03 + 6.21	0.62
	Group B	13.5 + 4.16	42.12 + 5.63	212 + 47.82	0.0012

Significant difference when p-value < 0.05

DISCUSSION

Results reached through this study showed that the mean age for psoriasis patients in group A was 34.63 + 2.1 years, and in group B was 36.54 + 4.7 years. These results came in line with another study displaying that people at their thirties are more prone to manifest psoriasis signs and symptoms than others.[15] Conferment also came from other study pointing that the onset of psoriasis is at late twenties and early thirties, but the range is wide, from the neonatal period to the seventies.[1] Psoriasis may begin at any age, but it is uncommon under the age of 10 years, most likely, it appears between the ages of 15 and 30 years.[6] Similarly, the results reached by this work about gender distribution of psoriasis showed that males were about two folds more likely to get psoriasis than females (male:female ratio in group A = 1.9:1 and in group B = 2.1:1). These results were strengthened by a previous study, men were most patients record their data in Sweden for management of psoriasis with two to three folds' male:female ratio.[16] Likewise, a similar male:female ratio to our study found by a study from Ireland, twice as many men had psoriasis compared with women.[17]

The present study results established that vitamin D serum levels were found to be lower than the normal value in both groups, as presented in Table 1. The extent of psoriasis improvement among patients of this study, as a response to oral vitamin D intake was evaluated after 3 months of the establishment of the study regimen by assessing the percentage of improvement in their PASI score along with the monthly visits following the participation in the study as a comparison to their baseline records, and results displayed that there was a significant improvement of PASI score among patients, who took in addition to the topical steroid oral vitamin D ($p = 0.033$), as presented in Figure 2 and Table 2.

This study results about the correlation between PASI score improvement and duration of vitamin D therapy was sustained by a previous study among psoriasis patients receiving daily oral vitamin D for months. Study found 88% of patients improved, 26.5% had total remission, 26.3% had partial remission, and 25.3% only had little remission. Likewise, Danilo *et al*. evaluated patients by PASI score calculation before and after the therapy, all patients had significant improvement. The higher the vitamin D level, the smaller the patient's PASI score.[18] Recently, researchers look that long duration of vitamin D supply is very useful to the patients with psoriasis, patients with psoriasis need Vitamin D more than normal patients so significant association between improvement of PASI score and vitamin D supply for all patients.[15,18]

Patients keep the area of skin with psoriasis cover, so no more UV light exposure and lead to decrease vitamin D levels and decrease in S. Vitamin D all these lead to increase in PASI score.[5,19] More recently, enforcement for the present study came from Ingram *et al*. (2018). There was a significant association between high PASI score and decrease vitamin D level concentration, and psoriasis severity, so high vitamin level in blood due to oral intake is useful for patients with psoriasis,[20] 10,000 IU daily intake of vitamin D is useful for psoriasis patients with no adverse effects.[21]

This monotherapy has been shown to result in an ~60% reduction of PASI after 8 weeks of treatment.[3] Throughout the period of this study, vitamin D therapy among psoriasis patients was consistently found to be safe treatment choice. No abnormalities in the baseline investigations was recorded for any patient in-group B that may be attributed to vitamin D intake, and no appearance of side effects due to vitamin D or exacerbation of the disease. Similar finding observed that in (Zittermann *et al*.) that stated there are no changes or abnormalities appear in level of vitamin D after vitamin intake with no any adverse effects due to vitamin D taken.[21]

CONCLUSIONS

Oral vitamin D supplementation can be safe, effective, and cheap therapeutic modality to psoriasis patients. Unlike most systemic drugs currently used in psoriasis, the adverse effects of which are significant, and many of them are costly.

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