

Original Article

Comparing Vitamin D Serum Levels in Patients with Oral Lichen Planus and Healthy Subjects

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KEY WORDS

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ABSTRACT

Statement of the Problem: Lichen planus disease is a chronic inflammatory lesion without a known etiology. Recent studies have indicated the role of vitamin D on immune system and proposed its anti-inflammatory effects.

Purpose: This study aimed to compare vitamin D serum levels in patients with oral lichen planus and healthy subjects.

Materials and Method: In this case-control study, 18 patients suffering from oral lichen planus referred to the Department of Oral Medicine, Tabriz Faculty of Dentistry were chosen as the case group and 18 healthy people were chosen as the control group. A 5-mL blood sample was taken from all subjects and the subjects' vitamin D serum levels were assessed with a vitamin D total (25-hydroxy vitamin D) kit by employing the electrochemiluminescence technique. The results were analyzed and compared by using SPSS17 statistic software. $p < 0.05$ was considered statistically significant.

Results: The mean vitamin D level in serum of patients with oral lichen planus was 30.7 ± 20.38 ng/ml and in healthy subjects was 36.45 ± 15.33 ng/ml, the difference was not statistically significant ($p = 0.346$).

Conclusion: The difference between the level of vitamin D in the serum of patients suffering from oral lichen planus and healthy individuals was not significant.

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Introduction

Lichen planus (LP) is a chronic and relatively common mucocutaneous disease and is considered a premalignant condition. It affects approximately 0.5–2% of the population worldwide. [1] Most of affected individuals are middle-aged and in their 4th decade of life but it may affect children and young adults either. Female-to-male ratio of affliction is 3:2 and the mean age of the diagnosis of the lesions is 55 years. [1]

The etiology of oral lichen planus (OLP) is unknown.

Over the years, a large mass of evidence has accumulated, indicating the primary role of the immune system in the development of this disease. [1-2] Histopathological features in relation to the infiltration of T lymphocytes into the sub epithelial band and destruction of basal cells, referred to as liquefaction degeneration, confirms this postulation. [1] These characteristics can be interpreted as the immune system cell-mediated pathway emergence, with a role in the pathogenesis of OLP through direct toxicity of T lymphocytes against

the antigens exposed by the basal cell layer. [2] The immune system T lymphocytes might have an important initial role in the progression of OLP. These cells cannot make a distinction between the innate molecules of the body and foreign antigens. Activation of autoimmune T lymphocytes is a process that might move from oral mucosa to other parts of the body. It might even occur simultaneously with the initiation of mucosal lesions. [1-2]

Several treatments have been used for OLP; however, there is no definite treatment for this condition and various treatment modalities only relieve signs and symptoms. Therefore, widespread studies are still underway on the etiology and pathogenesis of the disease. [1-2]

Calcitriol exerts a direct regulatory effect on the function of T lymphocytes through inhibition of the proliferation of Th1 cells, increasing Th2 cell counts by a direct effect on CD4 cells or on DC/APC and subsequent facilitation of IL-4, IL-5 and IL-10, and increasing in the number of cells regulating CD4⁺ and CD25⁺ T cells that secrete IL-10. [3-4]

Recent studies have shown that vitamin D has an endocrine effect on immune system cells, and exhibits anti-inflammatory and regulatory effects on the immune system. [5] In addition, it has potential therapeutic effects on autoimmune diseases, psoriasis, and neoplasms. [6] Although the basic mechanisms of vitamin D in autoimmune diseases is not well elucidated, vitamin D deficiency has been shown in some autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus, type I diabetes mellitus, multiple sclerosis, inflammatory diseases of the intestine, autoimmune diseases of the thyroid (such as Hashimoto and Graves diseases), and autoimmune gastritis. [7]

In a study by El-Komy *et al.*, [8] evaluation of vitamin D levels in patients with pemphigus vulgaris (PV) showed that these patients had lower vitamin D serum levels compared to healthy subjects. Vitamin D deficiency in patients with PV might exacerbate the disease through various immune system-related mechanisms. [8] The results of a study by Joshi *et al.* [9] in Northern India on patients with PV were similar to those of aforementioned study.

The results of the studies conducted by Marzano *et al.* [10-11] indicated the presence and possible role of

vitamin D deficiency in the pathogenesis of bullous mucocutaneous autoimmune diseases and PV. In addition, the prevalence of fractures in such patients was reported to be higher. [10-11]

Limited studies have been conducted on the role of vitamin D as an associated factor in LP. The only study carried out in this respect, based on a literature review, is a case report, which suggested that vitamin D levels should be evaluated, especially when patients with LP exhibit associated risk factor for vitamin D deficiency such as low exposure to sunlight, genetic predisposition and basic symptoms such as low back pain, multiple arthralgia, and so on. [12]

Given the importance of LP as a premalignant condition and the possible role of immunologic factors in its etiology, and considering the effect of vitamin D on the immune system, the present study was designed to compare vitamin D serum levels in patients with OLP and healthy subjects.

Materials and Method

The Ethics Committee of Tabriz University of Medical Sciences (IRIC: IRTBZMED. REC.1395.419) approved the protocol of the present case-control study. All the patients signed informed consent forms before being included in the study. No therapeutic intervention was made and the patients' data were kept confidential. No costs were inflicted on the patients for the laboratory tests.

Determination of the sample size

Since the present study was a new study and there was no similar previous study available, the sample size was determined at $n=15$ in each group. This was based on the results of a pilot study by considering a difference of 18 units in the vitamin D serum levels between patients with OLP and healthy subjects with standard deviations of 15.25 and 18.67, respectively ($\alpha=5\%$, study power=80%). In order to increase the reliability of the study, the sample size in each group was increased 20% to reach $n=18$ in each group.

The Inclusion criteria were affliction with OLP based on clinical views or clinical-pathological criteria and willingness to participate in the study. The exclusion criteria were:

- Presence of any factor that induced lichenoid reactions, including amalgam restorations adjacent to the

lesion or use of medications associated with lichenoid lesions.

- Congenital and acquired deficiencies of the immune system such as AIDS, chemotherapy, injection drug abuse, hemophilia, and patients undergoing hemodialysis. Such subjects were excluded due to problems with biopsies and infection control and doubts about their cooperation in future.
- Presence of any contraindication for taking biopsies from the lesions (in the case of lesions that should undergo biopsy for the process of diagnosis)
- Use of medications affecting the serum levels of vitamin D, including vitamin D supplements, calcium and calcium channel blockers.
- Active infections such as hepatitis, HIV, and tuberculosis
- Use of medications for the treatment of LP during the past two months
- Diseases that alter vitamin D serum levels such as thyroid or parathyroid disease and hyperparathyroidism
- Presence of dysplasia in histopathological evaluations [13-14]

In the present study, 18 patients with OLP, and 18 healthy subjects referring to the Department of Oral Medicine, Tabriz Faculty of Dentistry, were included after taking medical history, clinical examinations, and completion of informed consent forms. A 5-mL blood sample was taken from all the subjects and the subjects' vitamin D serum levels were determined with a vitamin D total (25-hydroxy vitamin D) kit using the electrochemiluminescence technique and then were compared between the OLP patients and healthy subjects.

Data were analyzed with mean differences test in independent groups (independent samples t-test) or its non-parametric equivalent, using SPSS 17. Statistical significance was set at $p < 0.05$.

Results

Eighteen subjects were evaluated in the control group, consisting of female (77.8%) and male (22.2%) subjects. In the OLP group, 18 patients were evaluated, consisting of female (61.1%) and male (38.9%) subjects. The mean age of the subjects in the control group was 49.94 years, with an age range of 21-76 years. The mean age of the subjects in the OLP group was 44.16 years,

with an age range of 30-71 years.

The mean vitamin D serum levels in the OLP and control group subjects were 30.7 ± 20.38 and 36.45 ± 15.33 (ng/mL), respectively, with a mean difference of 5.7 units, which was higher in the healthy subjects. Due to the homogeneity of variances in the two groups as evaluated by the Levene's test ($p = 0.145$), independent t-test was used to compare vitamin D serum levels between the healthy subjects and OLP patients, which showed no significant differences between the two groups ($p = 0.346$).

Discussion

LP is a relatively common chronic mucocutaneous lesion and is considered a premalignant condition. A large mass of evidence collected over many years reveals the primary role of the immune system in the development of this condition. [1-2]

Vitamin D can play a great role in the initiation or severity of OLP through regulation of the function of the human body immune system. On the other hand, the active form of vitamin D has a role in the regulation of the expression of many important genes of the body in different pathways, and its relationship with many cancers and autoimmune diseases has been shown. Vitamin D deficiency results in a decrease in Th2 cell counts compared to other T cells, especially those involved in inflammatory pathways, such as Th1 and Th17 cells. This results in more injuries in inflammatory conditions such as LP. Therefore, it is necessary to pay attention to vitamin D levels in community members, especially in those with LP. It is of interest that although Iran lies in geographical latitude suitable for receiving adequate UV, there is a high rate of vitamin D deficiency in Iran, predominantly in Iranian women. [15]

In the present study, the serum levels of vitamin D were evaluated in a control group and in a group of patients with OLP. The results showed no significant difference in vitamin D serum levels between the two groups. No recent similar study has compared vitamin D serum levels between OLP patients and healthy subjects. In this respect, the present study is considered a pioneer study. Various studies have determined vitamin D serum levels in different autoimmune diseases; however, there is controversy in this respect, which necessitates more future investigations.

Based on a study by El-Komy *et al.* [8] on the vitamin D serum levels of 34 patients with pemphigus vulgaris (PV), patients with PV had vitamin D serum levels lower than those in healthy subjects which is different from the results of the present study. Vitamin D serum levels are different depending on sampling season, the duration of exposure to sunlight, BMI, age, the number of pregnancies, the serum levels of parathyroid hormone, and serum levels of calcium. In addition, ethnicity affects vitamin D serum levels and various studies have shown that European and Egyptian PV patients have the lowest vitamin D serum levels. [8]

The results of a study by Joshi *et al.* [9] in Northern India on 30 PV patients and 10 healthy subjects were consistent with those of the study by El-Komy *et al.* [8] They indicated that vitamin D insufficiency might be a predisposing factor in PV and possibly exacerbates the disease through various immune related mechanisms that regulate T cell functions *in vivo*.

A study by Silverberg *et al.* [16] showed that vitamin D serum levels in patients with vitiligo were less than normal levels. Vitiligo is a skin disorder in which the loss of the function of melanocytes creates non-pigmented areas on the skin. Although the etiology of the disorder is unknown, an autoimmune origin has been suggested for it in recent years. [16]

The difference between the results of our study and studies above might be attributed to ethnical, geographical differences, different techniques which used to measure serum vitamin D levels of the patients and nutrition status as a confounding factor.

In a study by Baldini *et al.*, [17] the vitamin D serum levels in the patient with Sjögren's disease and healthy subjects were compared and the results showed no significant differences between the two groups, consistent with the results of the present study.

In a study by Moravvej *et al.* [18] on 52 pemphigus patients, data on demographics, body mass index, disease severity, and surface body area were obtained. There was no significant association between vitamin D levels and presence of pemphigus, season of sampling, age, BMI, or smoking habit, consistent with the results of the present study. [18]

In a study by Tukaj *et al.*, [19] on 12 bullous pemphigoid patients, there was no significant difference in vitamin D serum levels between the healthy and af-

ected subjects. They correlated their results to the different techniques employed to measure serum vitamin D levels of the patients (such as ELISA and radioimmunoassay) and the heterogeneity in disease activity i.e. active disease and clinical remission. [19]

Evaluation of vitamin D serum levels in different forms of OLP and its relation to the severity of autoimmune diseases with larger samples is recommended for future studies.

Conclusion

The mean serum levels of vitamin D in patients with OLP were less than that in healthy subjects but the difference was not significant. This might be attributed to various factors affecting vitamin D serum levels, including sampling season, the duration of exposure to sunlight, BMI, age, the number of pregnancies, the serum levels of parathyroid hormone and the calcium serum level.

Conflict of Interest

The authors disclose no potential conflicts of interest.

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