

Oral lichen planus among patients from Lublin Region in relation to 25-hydroxy-vitamin D3 serum level

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Abstract

Introduction. Lichen planus is a chronic inflammatory skin disease involving the mucous membrane of the oral cavity. It is postulated that different factors play a role in the occurrence of the disease and may activate the immune system, thus influencing the development of lichen planus. Vitamin D is a steroid prohormone with multiple systemic effects.

Objective. The aim of this study was to assess oral lichen planus against 25-hydroxy-vitamin D3 serum level. Vitamin D takes an active part in the pathogenesis of immunisation diseases, may have also a beneficial effect on oral health.

Materials and method. The clinical picture of lichen planus was analyzed according to the concentration of 25-hydroxy-vitamin D3. Patients were given a questionnaire interview which included questions about the co-existence of systemic diseases, subjective complaints, and information relating to the individual course of the disease. In the next stage of the study, patients were underwent a physical examination. Laboratory determinations of the concentration of 25-hydroxy-vitamin D3 were also performed.

Results. The mean vitamin D concentration in patients with lichen planus in the oral cavity was 14.37 ± 4.95 ng/ml. An insufficient level (10–30 ng/ml) was detected in 84.91% of the examined patients, whereas a deficiency (< 10 ng/ml) was observed in 15.09% of those patients. None of the analyzed patients had vitamin D level in the range of established clinical standards. A substantially lowered vitamin D level was found in patients reporting bleeding and pain of the gums.

Conclusions. The study enhances relationship between reduced levels of vitamin D3 and lichen planus in patients with oral lesions. Thus, vitamin D3 control and supplementation may play an important role in the treatment of lichen planus.

Key words

periodontitis, vitamin D deficiency, oral lichen planus (OLP)

INTRODUCTION

Lichen planus (LP) is a chronic inflammatory skin disease involving the skin, nails and mucous membranes. The incidence of the disease is estimated to be not more than 2% of the total population. Most commonly it affects people between the ages of 30 and 50. The disease has a predilection for the female gender with women constituting about 60% of patients [1, 2]. The etiopathogenesis of the disease is poorly understood but its multi-causal character is underlined. It is postulated that genetic, infectious, post-traumatic, toxic and psychological factors, as well as disturbances of the immunological system, play a role in the process of lichen planus formation [2, 3]. The influence of an immunological background on the disease may be indicated by comorbidity between lichen planus and auto-immune diseases, such as Hashimoto's disease, dermatomyositis, scleroderma, diabetes, and ulcerative colitis, as well as the presence of lichen planus in graft-versus-host disease (GvHD). The changes in the area of oral mucosa only, are observed in 25% – 30% of patients, while approximately 50% of the patients with skin lesions have also mucosal changes.

Lichen planus lesions may be located throughout the body. While taking the medical history, it is always necessary to include the question of the prior presence of skin lesions and lesions on the mucous membranes, because during the examination they may be absent. The disease may adopt different forms: reticular, atrophic, erosive or the plaque-like form of oral lichen planus (Fig. 1) [4–6]. Generally, they include the cheek mucosa, tongue, gums, lips, soft palate, and the floor of the mouth. Lesions are usually bilateral but



Figure 1. Erosive form of lichen planus in the oral cavity

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Figure 2. Reticular form of lichen planus in the oral cavity

not always symmetrical, and the most common form of all is the reticular form (Fig. 2). The lesions manifest themselves as small, flat-topped papules, and white or white and grey, shiny lines forming ring-shaped or irregular snowflake shaped system of lesions called Wickham's striae. These lichen planus lesions do not cause any disorders and they may only constitute an aesthetic issue. The atrophic and erosive forms of lichen planus are symptomatic, as they may be characterized by persistent pain. The changes in the mucous membrane of the mouth of OLP rarely resolve spontaneously. They can last for years with periods of exacerbation and patients therefore require long-term symptomatic treatment [7].

Vitamin D, a steroid prohormone with multiple systemic effects, plays an important role in the regulation of calcium-phosphorus balance and bone metabolism. Current studies show that vitamin D deficiency is common. It has been proven that vitamin D receptors (VDR) take an active part in the pathogenesis of cancer, infections, diabetes, cardiovascular, neurological, pulmonary, periodontal, and immunization diseases [8–10]. The main source of vitamin D in the organism is skin synthesis (90%). Lichen planus is a disease based on immunological mechanisms, while the influence of vitamin D on the immune system is commonly known. However, the literature about the capability of using vitamin D derivative remains poor. In dermatological treatment, vitamin D may be used in the cases of hypersensitivity to solar radiation, as light rays are a factor that triggers or exacerbates lesions, for example, in lupus erythematosus, dermatomyositis, pemphigoid or pemphigus. Due to different levels of vitamin D in the body, recommendations for daily vitamin D supplementation are presented depending on age: adults (19–75 years): 800–2,000 IU/day; seniors (>75 years): 2,000–4,000 IU/day [8]. Vitamin D may have also a beneficial effect on oral health by improving the innate immune system, bone mineral density and production of anti-microbial agents [11].

OBJECTIVE

The aim of the study was to assess oral lichen planus against 25-hydroxy-vitamin D3 serum level. The clinical picture of oral lichen planus was analyzed according to the subjective complaints and the examination of the oral cavity. The patients' demographic characteristics that may affect both the disease and the condition of the oral cavity were included in the study.

MATERIALS AND METHOD

The study was conducted among the population of the Lublin Province in Eastern Poland. The study group consisted of 53 patients diagnosed with oral lichen planus, who received behavioural, dental or periodontal treatment in the University Clinic of the Medical University in Lublin. The study protocol was approved by the Ethics Committee of the Medical University (Approval No.: KE-0254/214/2007). All patients received a detailed description of the proposed study protocol and provided written informed consent to participate. Physical examination of the oral cavity was performed to determine the form of the lichen planus, its exact location and additional extraoral locations. The clinical examination was supplemented by information relating to the demography, co-existence of systemic diseases, subjective complaints, including those located in the oral cavity. Additionally, information about nicotine addiction was obtained and assessment made of exposure to excessive emotional tension in everyday life.

The mucous membrane of lips, cheeks, tongue, floor of the mouth and the palate was intraorally evaluated. Attention was drawn to other anomalies within these areas. The level of vitamin D in the group of oral lichen planus changes were assessed in the peripheral blood collected for diagnostic examinations. Laboratory determinations of the concentration of 25-hydroxy-vitamin D3 in the serum of patients with lichen planus were performed using the CHILIA method (Liaison analyser, Diasorin). The research results were introduced into a Microsoft Excel spreadsheet. In all tests, a P-value <0.05 was considered statistically significant. All statistical analyses were conducted using Statistica 5.1 software.

RESULTS

The study group consisted of 44 women and 9 men aged from 25 – 83 years; average age – 55.72 ± 12.02 years. The mean vitamin D concentration in patients with lichen planus in the oral cavity was 14.37 ± 4.95 ng/ml (Tab. 1). The reticular form was the most commonly observed (88.68%), whereas forms such as atrophic (16.99%), bullous (9.43%) and plaque-like, were less frequently observed. The co-occurrence of a few forms of oral lichen planus was observed in 18.86% of the examined patients. In most of the patients, lesions were located on the cheeks (81.13%), gums (22.64%), and in a lower proportion, on the tongue (18.86%) and lips (7.55%). The so-called symptomatic changes which are usually followed by various ailments (96.22%) were distinguished from asymptomatic changes which occurred only in 2 patients suffering from oral lichen planus (3.77%). Lesions in the

Table 1. Interpretation of the levels of vitamin D in analyzed group

Reference range		n	%
Deficiency	< 10 ng/ml	8	15.09
Insufficient level	10 – 30 ng/ml	45	84.91
Sufficient level	30 – 100 ng/ml	0	0
Toxicity	> 100 ng/ml	0	0.00
		53	100.00

n – sample size

oral cavity were found in 41 patients, whereas simultaneous presence of cutaneous eruptions was found in 12 patients (22.64%).

The co-existence of systemic diseases was noted in 38 patients among the examined group. The cardiovascular diseases were the most frequent (54.72%). While taking the medical history, 8 patients (15.09%) revealed bone, joint or muscle diseases. Diseases of the gastro-intestinal, respiratory and nervous systems constituted a small part of the diseases noted. Diabetes and allergic diseases occurred, respectively, in 11.32% and 18.87% of patients. Depression was noted in 15.09% of those in the examined group. The patients' subjective sensations there were a feeling of dryness (62.26%), burning in the oral cavity (52.83%) and numbness of the region affected by lesions (49.06%). Slightly fewer people reported teeth hypersensitivity (35.85%), bleeding gums (30.19%) and their painfulness (26.42%). Nicotine addiction was found in 9 patients (16.98%) who smoked cigarettes. Exposure to constantly and frequently occurring emotionally involving events was found in 33.96% of patients in the examined group. Gingival recession (86.79%) as well as dental calculus (84.91%) were most frequently found during the intra-oral examination. Gingival inflammation occurred in almost half of the patients (49.06%). Pathological mobility of teeth was found in 28.30%, while desquamative gingivitis was observed in 11.32%. Dryness, tension and reddening of the cheek mucous membrane occurred in 73.58%, 45.28% and 28.30% of patients, respectively.

DISCUSSION

The study included 53 patients suffering from lichen planus in the oral cavity. There were 44 women (83.02%) and 9 men (16.98%) in the group. The mean age of the examined group was 55.72 ± 12.02 years. Most of the available studies present a dominantly greater number of women compared to men in the overall number of cases of lichen planus [5, 6, 12]. Fernandez-Gonzales et al. [13] present results which are the most similar to the current study, as there were 78% of women and 22% of men in the group of 50 examined patients, and mean age of the examined group was 56.06 years. Other research conducted by Goncalves de Lima et al. in 41 patients with diagnose of oral lichen planus present that women were also more affected (70.7%) than men (29.3%); mean age 45 ± 13.6 years for women and 42 ± 13.6 years for men [12]. In the study, no predominance of a particular form of oral lichen planus neither to the age of patients ($p=0.52$), nor to the gender of patients ($p=0.73$) was found.

In the current study, the patients lesions within the oral cavity, while only 22.64% had skin lesions which are characteristic for this disease. The obtained results are

slightly higher than those presented by other authors: Cassol-Spanemberg et al. – 19%, Chiang et al. – 15% and Radochova et al. – 17.3% [5, 6, 14]. The most frequently observed skin lesion locations were body's flexor surfaces: 60.1% [5]. The current study shows a less frequent occurrence of skin lesions in the areas of limbs (18.87%), back (3.77%) and head (1.89%), which may be caused by the oral lichen planus selection criterion. Skin lesions occurred significantly more frequently in older people (63.38 ± 9.56 years versus 54.36 ± 11.98 years; $p=0.04$), although these lesions were not significantly associated with particular forms of lichen planus. Similar results concerning an association of skin lesions with some forms of lichen planus have been presented by Radochova et al. [14]. The reticular form with characteristic Wickham striae on the lesion surface was the most frequently observed (88.68%). All the available publications declare the reticular form as the most frequently observed in patients with lichen planus in the oral cavity (frequency of the reticular form occurrence according to different sources: Lauritano et al. – 58.5%; Fernandez-Gonzales et al. – 78%; Gupta et al. – 84.3%; Radochova et al. – 95.6% [13, 14, 15, 16]. In our material, the reticular form affected the cheeks more frequently (93.02%) than the tongue and gums. Radochova et al. obtained similar results, as the reticular form was mainly found on the mucous membrane of cheeks affecting 91.5% of the patients, on the tongue in 42.5% of the patients and on the alveolar ridges in 21.7% of the examined patients [14]. The second most frequently observed form in the current study was the atrophic lesion (16.99%).

There are various reports concerning the frequency of lesion occurrence in other locations within the oral cavity. According to Radochova et al., desquamative gingivitis was present in 12.9% of patients, and the forms most frequently found on the gingiva and alveolar mucosa were the red forms (32.6%), white forms were found less frequently (17.7%). These results were statistically significant ($p=0.0264$) [17]. Similar results were obtained in the analysis of patients in the current study with symptom of desquamative gingivitis, which showed a less frequent occurrence of this symptom in the reticular form.

The mean vitamin D concentration in patients with lichen planus in the oral cavity was 14.37 ± 4.95 ng/ml. An insufficient level (10 – 30 ng/ml) was detected in 84.91% of the examined patients, whereas a deficiency (< 10 ng/ml) was observed in 15.09% of patients. None of the analyzed patients had a vitamin D level within the range of established clinical standards (Tab. 1). All analyzed studies showed a lower mean vitamin D concentration in patients with oral lichen planus changes, in comparison with healthy subjects [16, 18, 19, 20, 21, 22]. Only 2 studies proved to be statistically significant [16, 20]. Studies conducted by Gupta et al. presented a lower mean vitamin D concentration 20.40 ng/ml, compared to the control group – 32.67 ng/ml. These differences were statistically significant [16]. The current study revealed no significant difference in the mean vitamin D concentration in men and women ($p=0.65$) and in patients in different age groups ($p=0.61$). Despite the lack of significant difference in this study, only women had a deficiency of vitamin D, while all the examined men had an insufficient vitamin D level. According to Gupta et al. more female patients (77.3%) had vitamin D deficiency, compared to male patients 58.3%. The insufficiency of vitamin D was more often found in males 27.8% than in females 10.6% [16]. Their results

are very similar with those in the current study with the differences in vitamin D levels: an insufficient level (20 – 30 ng/ml); deficiency (< 20 ng/ml). It seems that the population living in regions with good insolation should not have any problem in providing the organism with a normal supply of vitamin D. However, studies confirm that in regions in Spain, where there is a lot of sunlight, there is a deficit of vitamin D [23]. The main cause of the deficiency may be its postulated relation to auto-immune diseases, for example, systemic lupus erythematosus. Arshad et al. carried out research on vitamin D concentration in 98 patients with lupus, because of the solar hypersensitivity and increased risk of vitamin D deficiency in this group of patients. The results obtained indicated a substantial vitamin deficiency (mean vitamin D concentration – 19.9 ± 17.8 ng/ml), which is similar to the current study, including patients with lichen planus (14.37 ± 4.95 ng/ml). The deficiency in vitamin D (less than 20 ng/ml) was found in 65 patients with lupus, and of those 46 were severely deficient (less than 12 ng/ml) [24]. The mean vitamin D concentration was also evaluated according to lesion location on the cheek mucous membrane and desquamative gingivitis. Patients with lesions located on the cheeks did not present a significant vitamin D concentration difference, compared with patients with lesions in other locations within the oral cavity (14.23 ± 5.04 ng/ml versus 14.95 ± 4.77 ng/ml; $p=0.76$) (Tab. 2).

A lower mean concentration, although not statistically significant, was found in patients with desquamative gingivitis symptoms (12.32 ± 4.63 ng/ml versus 14.63 ± 4.98 ng/ml; $p=0.29$) (Tab. 2). Studies conducted by Tak et al. presented a statistically significant association of serum vitamin D levels between patients with oral lichen planus and healthy subjects. There were 20 patients with oral lichen planus and 20 healthy subjects included in study. The authors observed a statistically significant decreased level of vitamin D in 4 patients (50%) with erosive lichen planus, in 1 patient (12.5%) with the reticular form, and in 3 patients (37.5%) with reticular and and erosive component [20]. Similar results are presented in the current study on patients with the red forms and symptoms characteristic of desquamative gingivitis: a lower mean concentration, but not statistically significant, compared to patients without symptoms of desquamative gingivitis (Tab. 2). All patients in the current study had changes in the oral cavity, while only a part of the group, i.e. 22.64%, additionally had skin changes. A significant relation between the co-occurrence of lichen planus cutaneous eruptions and the lower vitamin D level (11.30 ± 3.12 ng/ml versus 14.91 ± 5.04 ng/ml; $p=0.03$) was stated based on the obtained results (Tab. 2).

The literature emphasizes the activity of vitamin D in preventing, for example, cardiovascular diseases and type 2 diabetes [25], and the current study there were various systemic diseases in patients with lichen planus. However, no statistically important relation was confirmed between vitamin D concentration and the co-existence of a systemic disease ($p=0.63$) (Tab. 2). In studies carried out by different authors an insignificantly lower vitamin D concentration was observed in patients with schizophrenia, depression or alcoholism, compared with the control group [26, 27, 28]. Scientific descriptions indicate the advantages of vitamin D supplementation which, when applied during infancy, is related to lowering the risk of schizophrenia [29].

What is more, completing vitamin D deficiency influences

Table 2. Vitamin D serum level and chosen parameters

	Women			Men			p
	n	M	SD	n	M	SD	
	44	14.52	5.33	9	13.63	2.45	0.65
	≤ 57 years old			> 57 years old			p
	n	M	SD	n	M	SD	
	30	14.82	5.43	23	13.78	4.30	0.61
	Patients with lesions on the cheeks			Patients without lesions on the cheeks			p
	n	M	SD	n	M	SD	
	43	14.23	5.04	10	14.95	4.77	0.76
	Patients with desquamative gingivitis			Patients without desquamative gingivitis			p
	n	M	SD	n	M	SD	
	6	12.32	4.63	47	14.63	4.98	0.29
	Patients with skin lesions			Patients without skin lesions			p
Vitamin 25OH-D3 (ng/ml)	n	M	SD	n	M	SD	
	8	11.30	3.12	45	14.91	5.04	0.03
	Patients with systemic diseases			Patients without systemic diseases			p
	n	M	SD	n	M	SD	
	38	14.53	4.93	15	13.95	5.16	0.63
	Patients with bleeding gums			Patients without bleeding gums			p
	n	M	SD	n	M	SD	
	16	12.08	4.44	37	15.35	4.89	0.02
	Patients with painful gums			Patients without painful gums			p
	n	M	SD	n	M	SD	
	14	12.02	4.08	39	15.21	5.01	0.03
	Patients with numbness of the region affected by lesions			Patients without numbness of the region affected by lesions			p
	n	M	SD	n	M	SD	
	26	14.10	4.98	27	14.63	5.01	0.72

M – mean; n – sample size; p – value; SD – standard deviation

the reduction of symptoms of depression [30]. Depression was noted in 15.09% of people in the examined group. In the current study, the patients were also analyzed in terms of exposure to strong emotional stress. Exposure to frequent or constantly occurring emotional events was found in 33.96% of patients in the examined group. However, this did not prove to be a parameter significantly influencing lichen planus lesions in the oral cavity, according to laboratory test results or health state of the oral cavity. A study including 102 patients diagnosed with oral lichen planus who were evaluated by depression, anxiety and stress scales, showed their prevalence in proportion (14.7%, 6.9% and 5.9%, respectively). All the other patients suffered from varying degree of depression, anxiety and stress. In these studies vitamin D concentration lower than 20 ng/ml was revealed in 78.6% patients with mild depression, 77.3% patients with mild anxiety and in 87.9% with severe stress [16]. The results show the association between psychological factors, vitamin D deficiency and oral lichen planus. Most of the addicted people were males under the age of 57 who were exposed to frequent stress situations.

16.98% of patients in the analyzed material admitted to smoking, but there was no significant influence of smoking

on the occurrence of lichen planus lesions on the mucous membrane in the oral cavity. Different studies conducted by Radochova et al. present smokers with lichen planus in the similar proportions to the results obtained in the current study (19.2% and 16.9%, respectively), but do not describe any significant effect of smoking on the occurrence of certain forms of lichen planus in the oral cavity [13, 14].

There were three main subjective sensations selected by the patients: bleeding, gum painfulness and numbness of the regions affected by lesions. Results concerning bleeding and painfulness of the gums were very similar, as they are the manifestation of gum inflammation. Vitamin D concentration was significantly lowered in patients with bleeding (12.08 ± 4.44 ng/ml versus 15.35 ± 4.89 ng/ml; $p=0.02$) and painful gums (12.02 ± 4.08 ng/ml versus 15.21 ± 5.01 ng/ml; $p=0.03$) (Tab. 2). There was no significant relation between the numbness of the regions affected by lesions and the concentration of vitamin D in serum of patients with lichen planus ($p=0.72$) (Tab. 2). Bleeding and painfulness were less frequently observed in the reticular and atrophic forms (bleeding: $p=0.59$; painfulness $p=0.50$). Similar results concerning such symptoms as pain were described Radochova et al. Severe, mild and recurring pain observed in most of the patients with red forms of oral lichen planus (red forms – 37.0%, 64.1%, 55.4%, respectively, versus white forms – 3.8%, 63.3%, 12.7%, respectively). The association between severe and recurring pain with white and red form of oral lichen planus were statistically significant [17].

In the current study, numbness of the region affected by lesions was insignificantly more frequent in the reticular form ($p=0.10$). A significantly lowered vitamin D level in the patients reporting bleeding and painfulness of the gums may indicate an increased risk of the periodontal diseases and, as a result, a greater loss of teeth in the case of this vitamin deficiency. This fact is reflected in studies carried out by Machado et al., which describe that 25(OH)D serum levels were significantly lower in patients with chronic periodontitis [31]. Jagelavicine et al. also evaluated the relation between vitamin D concentration and periodontal diseases [32]. Dietrich et al. demonstrated the relation of significantly low vitamin D concentration in serum to greater loss of connective tissue attachment in men (2.3 ± 1.7 mm) and women (1.8 ± 1.3 mm) over 50 years old ($p < 0.001$), which is BMD independent [33]. On the other hand Bonnet et al. observed a statistically significant association between loss of attachment and 25(OH)D levels < 75 nmol/L on multiple regression analysis, although mean 25(OH)D concentrations and those < 50 nmol/L were not associated with loss of attachment [34]. Vitamin D and calcium supplementation positively influences the state of the periodontium. Vitamin D and calcium deficiency is even determined as a periodontal disease risk factor. Low vitamin D concentration in all the examined patients and its significant relation to skin lesions leads to reflection on the necessity of its supplementation in patients with lichen planus, and also the need for further clinical trials on possible therapy with vitamin D.

CONCLUSION

The data suggest that a low concentration of 25-hydroxy-vitamin D3 is a clinical feature of the patients diagnosed with oral lichen planus, which provides evidence of a significant

association of vitamin D with the pathogenesis of this disease in a study group. Furthermore, the presentation of lesions in patients with oral lichen planus enhances the relationship between reduced levels of vitamin D and the disease. It worth pointing out that reduced levels of vitamin D may contribute to the development of periodontal diseases which may need periodontal treatment. Thus, vitamin D supplementation may play an important role in the treatment of lichen planus, and may have a favourable effect on periodontal status.

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