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Research Article

TO INVESTIGATE THE VITAMIN D SUPPLEMENTARY AS AN ADJECTIVE METHOD TO CURE LICHEN PLANUS IN PERI-MENOPAUSAL FEMALES; A CROSS SECTIONAL STUDY

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Abstract:

Objective: The aim of our study was to investigate the vitamin D supplementary to cure lichen planus in peri-menopausal females as an adjective method.

Study Design: A cross sectional study.

Place and Duration: This study was conducted at the department of Medicine and Diagnosis, Allied Hospital Faisalabad for the duration of eight months starting from January, 2020 to September, 2020.

Methodology: In our present study 100 patients age range from 35-45 years were included. We distribute patients in two groups with use of flip coin method, these group categorized as receiving conventional therapy and vitamin D supplementary with conventional therapy altogether. Significance level were considered as less than 0.05. SPSS v. 20 was used for the analysis of data.

Result: In our study 100 patients were included. In these patients 50 were having vitamin D deficiency and 50 were having vitamin D insufficiency and 40.04±41.2 years. For standard therapy we recorded pain scores amongst week 1 and week 4 with pain intensity score was 1.80±0.40 and 5.04±2.20 (p-value=0.001). patients of group 2 show improvement in clinical appearance of lesion between week 1 and week 2.

Conclusion: At the end of our study, we concluded that in peri menopausal females the most common thing is vitamin D deficiency which is associated with oral lichen planus.

Key Words: Oral Lichen, Visual Analogue Scale, Vitamin D deficiency, Vitamin D insufficiency

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INTRODUCTION:

Lichen planus (LP) was a common chronic autoimmune disorder of mucosa and skin of unspecified cause which frequently affects the oral mucosa [1]. Oral Lichen Planus (OLP) commonly present as bilateral, symmetrical lesion appearing as white hyperkeratotic papules and striae on the buccal mucosa, tongue and/ or gingiva. Clinically subtypes are recognized as reticular, popular, plaque-like, atrophic, ulcerative/erosive, and bullous. Oral lichen planus is mostly common on the buccal mucosa associated most commonly with the reticular type of OLP with no symptoms. Patients presenting with symptoms like burning sensation and pain are mostly associated with erosive or atrophic lichen planus. OLP is associated with dysfunction of T-cell-mediated immunity, affecting females 2 to 3 times as compared to male in between 3rd and 5th decade of life and the reported average malignant transformation rate of it is approximately 1.09% [2].

The prevalence of OLP independently as an oral disease is 1-3 % in South Asian population whereas it is mostly associated with any metabolic disorder, drug-induced, hypersensitivity reaction, autoimmune disease, chronic graft-versus host disease and hepatitis-C [3-5]. Different studies have recorded the influence of female hormones (progesterone and estrogen) on the oral mucosal changes and also these comprehensively associates with autoimmune diseases but still no direct relationship has been established in developing oral lichen planus. Perimenopausal women usually presents dry, shiny, atrophic pale oral mucosa with gingivostomatitis, burning sensation and taste disturbances. As there is limited data available to specify the exact treatment of OLP and considering it as an autoimmune disease the clinician just targets to lower the sign and symptoms mostly by administering local agents such as corticosteroids in the form gel, ointment or mouthwash without any specific treatment. The rationale of the study was to identify whether treating vitamin D deficiency in OLP lesions improves treatment outcome and to investigate Vitamin D supplementation as an adjunctive method in curing the progression of lichen planus among perimenopausal.

METHODOLOGY:

This cross-sectional study was conducted at the department of Medicine and Diagnosis, Allied Hospital Faisalabad for the duration of eight months starting from January, 2020 to September, 2020. The study was carried after the ethical permission by the head of institution. Purposive sampling technique was used to include Peri-menopausal patients with an age

between 35-45 years diagnosed with any form of Oral lichen planus [6] and presenting with Serum 25 Hydroxy vitamin D levels below 30ng/ml (in investigation) were included in this study. All those who reported of consuming tobacco in any form or with history of betel nut chewing, any dermatological disease, endocrine dysfunction, co-morbid or malignancy; patients on hormone replacement therapy, steroid medications, or reported to have consumed pain killers (NSAID's) during last four weeks were excluded from this study. The sample size of 100 was calculated in each group (50 patients) using Rao soft software with margin of error 5% confidence level of 95%, population size of 102 and response distribution of 50% [7]. The study participants were initially explained the purpose of research study after which a written and verbal consent was obtained. All study subjects were examined and managed by an experienced clinician of Oral medicine. A double-blind randomization with flip coin method was used to assign study participants into any of two groups.

The study participants were allocated in two groups: Group A was given Treatment 1 as conventional therapy and group B was supplemented with Vitamin D (50000 I.U) after every week for a period of one month (the serum Vitamin D levels were not sufficient (below 30ng/ml) [8]. Conventional therapy consisted of alternate use of 2 Tablet Betnesol 0.5mg dissolve in 10ml of bezydymaine chlorhexidine mouth wash and 4 to 5 drops of Nilstat taken 3 times a day. The symptoms and signs of the patients in both arms were clinically assessed at baseline, after week one and four weeks of initial visit by single investigator. Pain was assessed using Visual Analogue scale ranging from 0-10 where 1-4 was considered as mild pain, 5-7 as moderate pain and a score above 8 was recognized as pain of severe intensity. Furthermore, we had used an objective and subjective parameter to assess OLP combination scoring as defined by Silverman et al. and Escudier et al [9,10]. Clinical presentation of the lesion was calculated by multiplying (Sub-site score A) into (Severity score B).

Finally, the lesion was considered as persisting at follow-up if the clinical presentation score was greater than 0 where as a score of 0 indicated a healed lesion. The data was analyzed using SPSS version 20 for those subjects in which follow-up information regarding outcome variable was complete. The level of significance was considered to be less than 0.05 ($p > 0.05$). The difference in pain intensity scores and clinical presentation was reported as mean and standard deviation. Paired-sample t-test was applied to measure difference in pain intensity and sub site scores

at week 1 and week 4 of the therapy. The difference in the level of significance was considered to be less than 0.05.

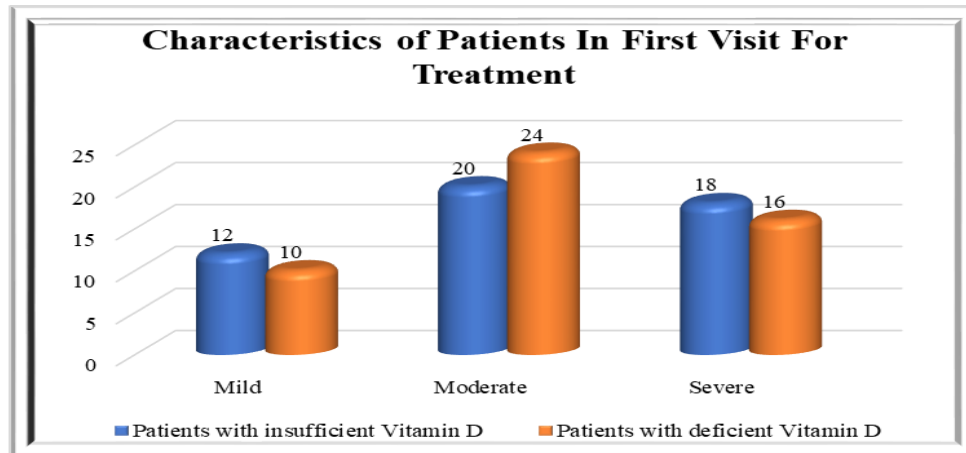
RESULTS:

Our study consisted of hundred (N=100) subjects, with Vitamin D insufficiency (n=50) and Vitamin D deficiency (n=50) and a mean age of 40.04 and 41.2

years respectively. In first treatment 12(24%) patients were having mild insufficiency of vitamin D, 20(40%) were having moderate insufficiency of vitamin D, 18(36%) were having severe insufficiency of vitamin D, 10(20%) patients were having mild deficiency of vitamin D, 24(48%) were having moderate deficiency of vitamin D and 16(32%) were having severe deficiency of vitamin D,

Table No 01: Characteristics of Study Patients for First Visit of Treatment

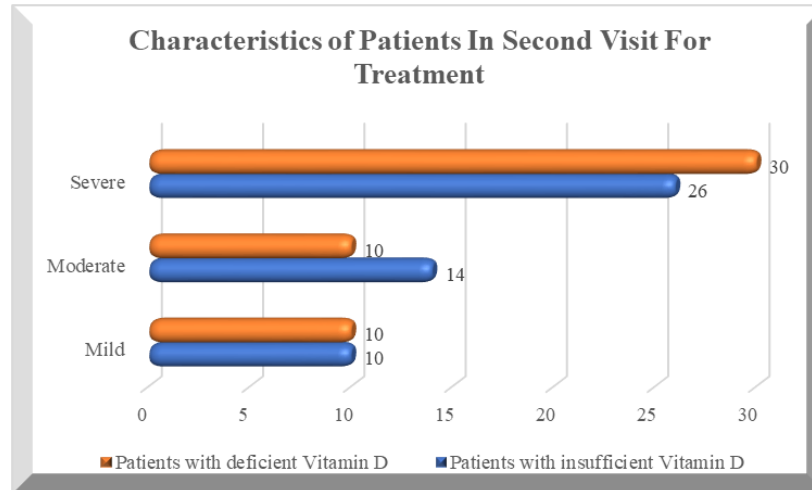
Pain on 1st visit	Patients with insufficient Vitamin D		Patients with deficient Vitamin D	
	Qty	%age	Qty	%age
Mild	12	24%	10	20%
Moderate	20	40%	24	48%
Severe	18	36%	16	32%
Total	50	100%	50	100%



In second treatment 10(20%) patients were having mild insufficiency of vitamin D, 14(28%) were having moderate insufficiency of vitamin D, 26(52%) were having severe insufficiency of vitamin D, 10(20%) patients were having mild deficiency of vitamin D, 10(20%) were having moderate deficiency of vitamin D and 30(60%) were having severe deficiency of vitamin D,

Table No 02: Characteristics of Study Patients for Second Visit of Treatment

Pain on 1st visit1	Patients with insufficient Vitamin D		Patients with deficient Vitamin D	
	Qty	%age	Qty	%age
Mild	10	20%	10	20%
Moderate	14	28%	10	20%
Severe	26	52%	30	60%
Total	50	100%	50	100%



For standard therapy we recorded pain scores amongst week 1 and week 4 with pain intensity score was 1.80 ± 0.40 and 5.04 ± 2.20 (p -value=0.001). patients of group 2 show improvement in clinical appearance of lesion between week 1 and week 2.

DISCUSSION:

In current study the pain was significantly decreased among both groups who were on vitamin D therapy as well as following conventional mode of therapy. However, we found that there was a mark difference in the healing tendency of the lesion in the group with Vitamin D supplementation. The study by Joshi et al [11] which was conducted in Northern India on 30 patients of pemphigus vulgaris and 10 healthy individuals have almost similar results with El-Komy et al [12]. They both consistently reported that vitamin D deficiency might act as a predisposing factor in occurrence of pemphigus vulgaris and possibly aggravates the severity of disease through various immune mediated mechanisms. Majority of the research's have reported about immune regulation of vitamin D and its insufficiency among patients with autoimmune disorders.

One of the oral lesions that is OLP is an outcome of such deficiencies reported among female population of pre and perimenopausal age bracket. OLP induces basal cell degeneration by modified keratinocytes surface antigen in response by cytotoxic T cell. Furthermore, in OLP lesions, Langerhans cells and MHC class II expression is up regulated, followed by keratinocyte apoptosis triggered by CD8+ cytotoxic T-cells [13,14]. Since LP is an autoimmune disease associated with cutaneous manifestation therefore the optimum levels from cutaneous synthesis and total intake as foods and supplements contributes in circulating serum 25(OH)D received by Group B) or

calcidiol (a summation of D3 and D2 forms), which are considered currently as the best available indicator [15,16]. For different precancerous conditions and oral cancers serum calcidiol is considered better predictor of its development than 1,25-dihydroxyvitamin D3 or calcitriol (1,25(OH)2D3). According to Martin et al study it suggests that by natural Vitamin D causes induction of VDR+ cells optically and can be used as chemo preventive agents systemically or locally for the treatment. The pleiotropic hormone vitamin D 1,25(OH)2D3 significantly shows expression by the VDR receptor which is present in the epithelial cells acting as a mucosal barrier. VDR receptor protects the invasion of microbes in the underlying connective tissue and in the case of oral lichen planus the epithelium breakdown implies apoptosis, a programmed cell death mechanism. This helper T-cell type 1 (Th1)-driven chronic inflammatory disorder induces chemokines resulting in the reduction of local VDR levels and so boost the onset of OLP. Thus, Vitamin D levels influences the apoptosis which in turn causes the cessation of invasiveness, and angiogenesis of highly mitotic cells [17].

The greatest obstacle in estimating approximate age for women at menopause is ascertained in Pakistan. The age of 40 years is frequently used as an arbitrary cutoff point, below it is considered as perimenopausal phase. Hormonal imbalance effects the body metabolism in perimenopausal women resulting in autoimmune disorders such as multiple sclerosis (MS), systemic lupus erythematosus, and rheumatoid arthritis (RA). Immune system is modulated by the sex hormones affecting the cell-mediated immunity by regulating all the subdivisions of CD4+ and CD8+ cells which in turn is involved in the pathogenesis of OLP. Other than this estrogen levels in the serum uplift the humoral immunity. In autoimmune disease

as, multiple sclerosis and rheumatoid arthritis estrogen effects the T-cell regulation and activation resulting in the downregulation of the immune effects and osteoclasts which resorb the bone. There is no direct established relationship with Lichen planus (LP) but the association with deficiency in vitamin D in these individuals can result in such type of oral lesions, as different studies indicate the increase in autoimmune disorder with association with vitamin D deficiency. Varma et al reported in his study a case with presence of lichen planus and vitamin D deficiency and the condition improved after vitamin D treatment [18].

One of the main reasons behind low immunity is deficiency of vitamin D due to which patients report with various autoimmune disorders. LP is one of the skins and oral mucosal condition's which is associated with low immunity. Patients of OLP presents clinically with phases of temporary diminution and worsening of the symptoms and worsening depending upon the pattern of disease.

In current study the mean age of subjects was 40 & 41 years ($SD \pm 0.7$) respectively, which included perimenopausal women who might have tendency of insufficient vitamin D levels in their blood. On the other hand, it is evident that the cases of OLP belong to same age bracket. In these study pain symptoms among both groups at base line was of moderate intensity, which then improved within 4-week span to the level of mild degree with statistically significant difference between the two groups. These finding are in coherence with other studies Carbone et al [19]. Perimenopausal women can influence and have a greater impact on the multifactorial aspects lifestyle and sociocultural status which can affect the symptom severity. Immune mediated disease as oral lichen planus, pemphigus vulgaris, benign mucosal pemphigoid, or Sjögren Syndrome are commonly present in females close to their menopause. The skin and the mucosa are significantly affected during this phase due to the increased levels of estrogen receptors in both dermis and epidermis leading to thin and atrophic epithelium. The oral mucosa and gingival tissues appear dry and pallor in color and bleed easily resulting in gingivostomatitis [20,21].

Furthermore, in current study an improvement in the clinical appearance was comparatively higher in the group supplemented with vitamin D therapy in addition to conventional therapy. These findings were consistent with the studies reported Varma and Gupta. This can be due to possible role of vitamin D in the cutaneous healing of OLP [22,23]. There was a study by Tukaj et al., which he conducted among bullous

pemphigoid patients and healthy subjects but the results showed no significant difference in vitamin D serum levels. They concluded in it as the different methods (Elisa or radioimmunoassay) to measure serum vitamin D levels of the patients can influence the severity of disease and its clinical remission [24].

The epidemiologic distribution of incidence varies in different regions as almost 66% were reported with reticular type in Iran according to the study conducted in 2016 by Nosratzahi et al [18]. The study by El-Komy et al [12] attributes to the ethnicity which affects vitamin D serum levels in European and Egyptian Pemphigus vulgaris. Despite of geographic location and sun exposure still Pakistan is deficient in Vitamin D affecting 53.5% of the general population a drastic state for the Pakistani females and the main reason would be the lack of fortification in the dietary products followed by an indoor living, excessive application of sun block, or wearing a wrong fabric material which is not good for the skin. There are potential limitations in this study. Firstly, confounding factors such as ethnical, demographical differences, different techniques of analyzing Serum Vitamin D levels duration of exposure to sunlight, BMI and serum levels of calcium which were not assessed in our study; should be explored in future studies. Also, follow-up period was kept relatively short to deal with attrition biases as patients deter reporting when their symptoms are resolved. Further studies at molecular level should be conducted to explore plausible mechanisms behind vitamin D receptor (VDR) to give a better supportive treatment plan for patients with precancerous conditions such as OLP. In addition, policy makers must take an action against macro and micro-nutrient deficiencies of peri-menopausal women who equally deserve their attention in addition to women of child bearing age.

CONCLUSION:

At the end of our study, we concluded that in peri menopausal females the most common thing is vitamin D deficiency which is associated with oral lichen planus.

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