Comparison of Anxiety and Depression Scores in Patients with Oral Lichen Planus and Normal Individuals

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ABSTRACT

Introduction: Oral lichen planus (OLP) is a common chronic inflammatory, psycho-mucocutaneous disease affecting about 1%–4% of the general population associated with psychoneuroendocrine and psychoimmunological comorbidities. Lichen planus although it is not an infectious disease, its cause is unknown, it is classified as an autoimmune disorder that may be precipitated or exacerbated by psychosocial stress. The Hospital Anxiety and Depression Scale (HADS) was originally developed to indicate the possible presence of anxiety and depressive states in the setting of a medical outpatient clinic and was found to perform well in assessing the anxiety disorders and depression in both somatic, psychiatric and primary care patients and in the general population. **Aims:** The aim of this study is to evaluate the levels of psychological status and the impact of treatment on psychological status in OLP individuals and compare it with normal individuals. **Materials and Methods:** Forty OLP patients along with the same number of age- and gender-matched healthy controls were included in the study. HADS questionnaire was administered to all 40 OLP (start of therapy) and 40 non-OLP individuals. In the OLP Group (40 participants): 20 were given "active" intervention with Cyclosporine Oral Solution (Group A), 20 were given "placebo" intervention (Group P). HADS questionnaire was given to all the twenty participants of Group A and all twenty participants of Group P at the end of therapy. The questionnaire consisted of 14 questions; 7 questions pertaining to anxiety and 7 pertaining to depression. **Results:** High level of anxiety (47.5%) and depression (85%) was observed in participants with OLP as compared to non-OLP (0%). After the active intervention, 14 participants were relieved of anxiety as compared to 8. Comparison of the prevalence of depression in OLP individuals before and after getting "active" intervention revealed that on getting active intervention the depression present in all 20; 1 (10%) mild and 9 (90%) frank came down to 1 (10%), and 4 (40%) mild. Five (50%) participants were completely relieved of depression. **Conclusion:** Lichen planus is to some extent a psychosomatic or somatopsychic disease or both. The present study results matches with the majority of the studies, showing a positive association between anxiety and depression levels in OLP patients, suggesting counseling along with traditional

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treatment can be effective in reducing the size of the lesions. Oral healthcare providers should pay attention to the emotional state of their patients. Emotional factors are important as evidenced by higher frequency of psychiatric symptoms, poor quality of life, higher level of anxiety, and neuroendocrine and immune dysregulations. Counseling may help in ameliorating symptoms, improving quality of life, and enhancing recovery.

Keywords: *Anxiety, cyclosporine oral solution, depression, Hospital Anxiety and Depression Scale, oral lichen planus*

Introduction

Oral lichen planus (OLP) is a common chronic inflammatory, psycho-mucocutaneous disease affecting about 1%–4% of the general population associated with psychoneuroendocrine, psychoimmunological comorbidities.[1] It occurs at any age (mean age of onset middle age), affecting both sexes with females being at higher risk for oral mucosal and genital involvement. It is an obstinate disorder baffling not only the patients but also the practitioner.[2,3]

Psychologically, the skin is an erogenous zone and channel for emotional discharge so that troubled skin could be a manifestation of unexpressed anger or an inner conflict due to external stress.[4] Brig *et al*. suggested that there is a diversionary symbiosis between the skin and psyche.[5] Psychological stress could have a negative impact on healthy skin, exacerbating or precipitating dermatological disorders suggesting the presence of interface between psychiatry and dermatology.[6]

Lichen planus is not an infectious disease. The cause is unknown, but it is classified as an autoimmune disorder which may be precipitated or exacerbated by psychosocial stressors.[7] Patients with lichen planus experience stressful events before the onset of the disease and also a higher level of anxiety along with high salivary cortisol levels.[3,8]

Andreasen was the first to point out in 1968 that OLP patients are found to be in conditions of stress leading to anxiety and depression. Colella *et al*. applying the Hamilton scale, found anxiety as well as depression in patients with OLP. McCartan, Jose L, Rojo-Moreno carried out trials to prove the same.

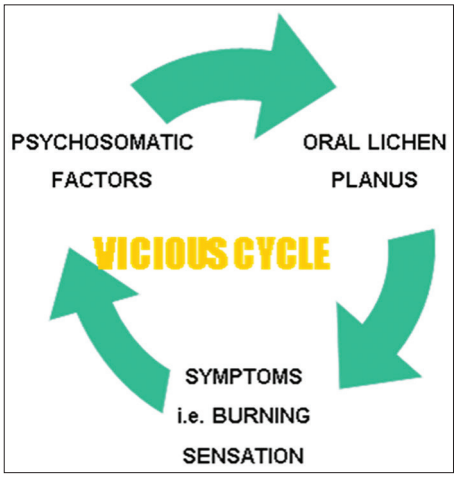


Figure 1: vicious cycle of oral lichen planus

Hegarthy AM, Hodgson A suggested that OLP does affect the quality of life, and effective treatment improves patient well-being [Figure 1].

The Hospital Anxiety and Depression Scale (HADS) is a 14-item self-report screening scale that was originally developed to indicate the possible presence of anxiety and depressive states in the setting of a medical outpatient clinic (Zigmond and Snaith, 1983). It contains two seven-item scales: one for anxiety and one for depression, both with a score range of 0 ± 21.[9] Validity of HADS was assessed by Ingvar Bjelland, Alv A Dahl *et al*. in 2001, and HADS was found to perform well in assessing the anxiety disorders and depression in both somatic, psychiatric, and primary care patients and in the general population.

Soto Araya *et al*. (2004) recently established a positive relationship between psychological alterations and OLP, considering the stress and anxiety levels in OLP patients as high [Figure 2]. According to these findings, it is possible to assume that psychological factors should be taken into account when maintaining oral health as such patients showed increased values on the Hamilton anxiety scale and Hamilton depression scale (Colella *et al*. 1993). There are reported differences in psychoimmune interactions between patients afflicted with nonerosive OLP lesions compared with those with erosive OLP lesions (Chiappelli *et al*. 1997). Andreasen (1968) reported that 49% of OLP patients had been subjected to strong stress in their lives, while others have reported stress-related history in OLP patients with the erosive form, as compared with reticular form (Lowental and Pisanti 1984).[10]

Eisen *et al*. in 1990[11] recommended "Swish and Spit" method of use cyclosporine in patients with OLP. They conducted a randomized double-blind trial in 16 symptomatic OLP patients. All of the eight recipients of cyclosporine receiving 5 ml of medication (containing 100 mg/ml of cyclosporine per mL) three times daily showed significant improvement in signs and symptoms. When all the 16 were treated openly, 50% of the lesions were almost or completely clear after 8 weeks.

Pacor *et al*. in 1994[12] evaluated the efficacy of topical cyclosporine (5 ml of solution [500 mg]) used as a mouth rinse in swish and spit manner three times a day for 3 months in 14 OLP patients and found beneficial effects on signs and symptoms after only 1 month of therapy. They thus concluded that cyclosporine is useful in the treatment of OLP.

To begin to address this uncertainty and to explore the possibility of psychosomatization as a possible pathogenic mechanism of initiation and clinical expression of this oral disorder, we evaluated the levels of psychological status in OLP individuals and the impact of treatment in psychosocial status in OLP individuals.

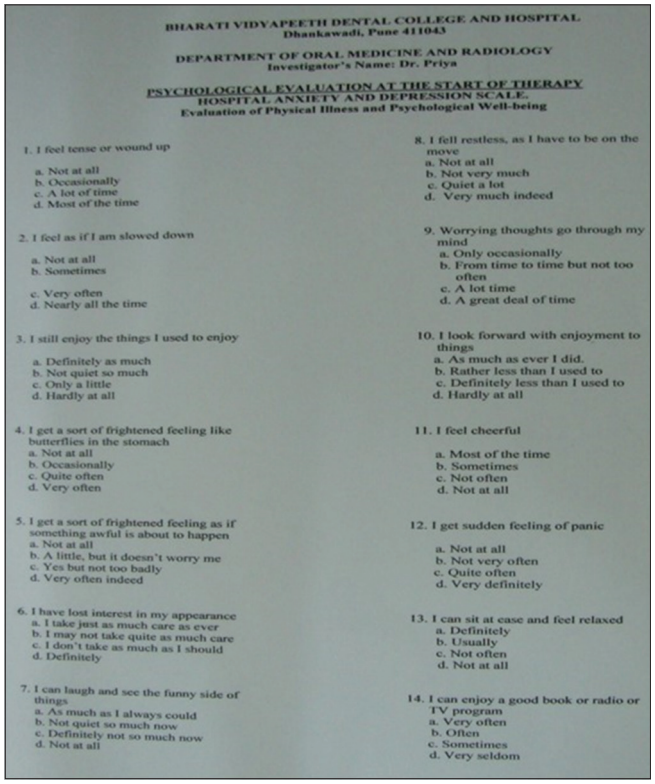
Aims

1. To evaluate the levels of psychological status in OLP individuals and compare the same in normal individuals
2. To evaluate the impact of treatment in psychosocial status in OLP individuals and compare the same in normal individuals.

Materials and Methods

Study setting

The study was conducted in the Department of oral medicine and radiology.



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PSYCHOLOGICAL EVALUATION AT THE START OF THERAPY
HOSPITAL ANXIETY AND DEPRESSION SCALE.
Evaluation of Physical Illness and Psychological Well-being

1. I feel tense or wound up
a. Not at all
b. Occasionally
c. A lot of time
d. Most of the time

2. I feel as if I am slowed down
a. Not at all
b. Sometimes
c. Very often
d. Nearly all the time

3. I still enjoy the things I used to enjoy
a. Definitely as much
b. Not quiet so much
c. Only a little
d. Hardly at all

4. I get a sort of frightened feeling like butterflies in the stomach
a. Not at all
b. Occasionally
c. Quite often
d. Very often

5. I get a sort of frightened feeling as if something awful is about to happen
a. Not at all
b. A little, but it doesn't worry me
c. Yes but not too badly
d. Very often indeed

6. I have lost interest in my appearance
a. I take just as much care as ever
b. I may not take quite as much care
c. I don't take as much as I should
d. Definitely

7. I can laugh and see the funny side of things
a. As much as I always could
b. Not quiet so much now
c. Definitely not so much now
d. Not at all

8. I fell restless, as I have to be on the move
a. Not at all
b. Not very much
c. Quiet a lot
d. Very much indeed

9. Worrying thoughts go through my mind
a. Only occasionally
b. From time to time but not too often
c. A lot time
d. A great deal of time

10. I look forward with enjoyment to things
a. As much as ever I did.
b. Rather less than I used to
c. Definitely less than I used to
d. Hardly at all

11. I feel cheerful
a. Most of the time
b. Sometimes
c. Not often
d. Not at all

12. I get sudden feeling of panic
a. Not at all
b. Not very often
c. Quite often
d. Very definitely

13. I can sit at ease and feel relaxed
a. Definitely
b. Usually
c. Not often
d. Not at all

14. I can enjoy a good book or radio or TV program
a. Very often
b. Often
c. Sometimes
d. Very seldom

Figure 2: HADS Questionnaire

Study population

Patients coming in the OPD of the Department Of Oral Medicine & Radiology.

Inclusion criteria for oral lichen planus participants

- Self reporting individuals, 18 years and above, clinically and histologically proven OLP
- Burning sensation as one of the presenting symptoms.

Inclusion criteria for nonoral lichen planus participants

- Otherwise healthy individuals reporting with the dental complaint of short duration, age- and gender-matched to OLP participants.

The patients fulfilling the inclusion and exclusion criteria were explained the need and procedure of the trial. Informed consent was obtained.

The study design underwent the Institute Research Board and Ethical Board clearance and approval.

Forty OLP (Group OLP) and forty normal individuals (Group non-OLP) age- and gender-matched to OLP participants were enrolled in the study.

Hospital Anxiety and Depression Questionnaire was given to all forty OLP (start of therapy) and forty non-OLP individuals.

In the OLP Group (forty participants): Twenty were given "active" intervention (Group A) with Cyclosporine Oral Solution (Commercially available as PanimunBioral™ 100 mg/ml), twenty were given "placebo" intervention (Group P) [Figures 3 and 4].

The placebo was prepared at institute pharmacy similar in appearance and taste and contained only the vehicle, i.e., hydrogenated castor oil and labrafilm, minus the active ingredient, i.e., Cyclosporine.

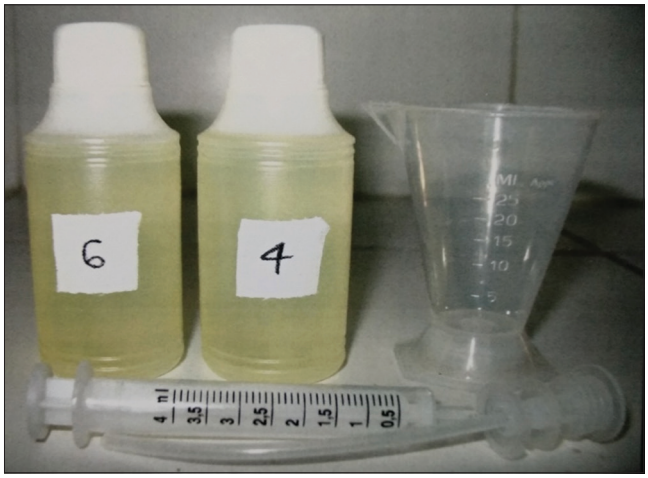


Figure 3: active and placebo formulation along with dispenser

Patients were given 150 ml (dispensed in three bottles of 50 ml each) of either the active drug or placebo. Patients in both the groups were instructed to use 5 ml of the solution in a "Swish and Spit" manner once a day in the morning after breakfast for 5 min for 30 days. Instructions for use were given to participants and a copy given in the English and/or vernacular language.

Randomization was done for both the active drug and placebo samples by generating a series of ten random numbers for both the groups. Participants were numbered serially as they entered the trial. Based on the two series, the participants got assigned either to the active group (Group A) or placebo group (Group P).

Concealment of Allocation and Binding: The principal investigator carried out the initial as well as the posttreatment evaluation of all the participants.

To minimize the bias, the investigator was unaware of intervention received during all stages of the trial. The intervention material (cyclosporine or placebo) were delivered to participants by another person unrelated to the trial.

The participants, too, were blinded by preparing the placebo similar in taste and color to cyclosporine preparation.

Hospital Anxiety and Depression Questionnaire was given to 20 (Group A) and 20 (Group P) at the end of the therapy.

Questionnaire consisted of 14 questions; 7 questions pertaining to anxiety and 7 pertaining to depression.

Each item had to be answered on a four point (0–3) response category.

- 0–7 = No anxiety/depression
- 8–10 = Mild anxiety/depression
- ≥11 = Frank anxiety/depression.

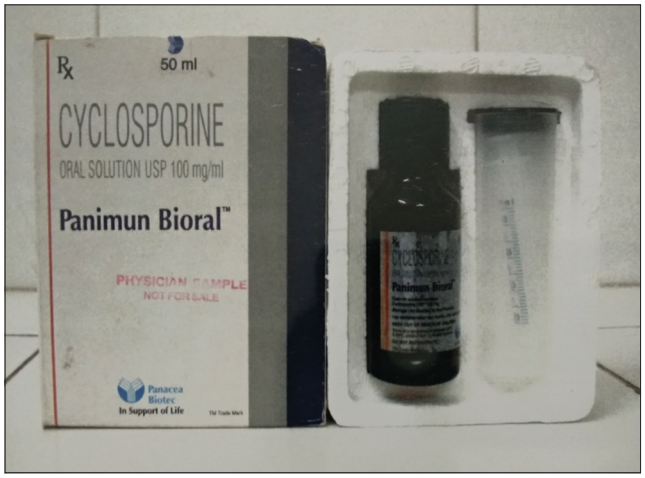


Figure 4: commercially available cyclosporine product

The patients were assessed at baseline (day 1) and at the end of the therapy period (30th day) and the patient were kept on follow-up for the next 6 months.

Results

Nineteen (47.5%) of the participants with OLP had "frank anxiety," thirty-four (85%) of the participants had "frank depression" [Table 1].

None of the participants in the non-OLP group had anxiety, whereas only two participants had mild depression [Table 2].

Anxiety is more prevalent in OLP individuals (47.5%) as compared to non-OLP individuals (0%) [Table 3a and Graph 1].

Depression (85%) like anxiety too is more common in OLP as compared to non-OLP individuals (5%) [Table 3b and Graph 2].

Comparison of the prevalence of anxiety in OLP individuals before and after getting "active" intervention

Table 1: Levels of psychological status in oral lichen planus individuals

Groups	Group OLP			Total
	Absent (%)	Mild (%)	Frank (%)	
Anxiety	14 (35)	7 (17.5)	19 (47.5)	40
Depression	4 (10)	2 (5)	34 (85)	40

OLP=Oral lichen planus

Table 2: Levels of psychological status in normal individuals

Groups	Group non-OLP			Total
	Absent (%)	Mild (%)	Frank (%)	
Anxiety	40 (100)	00 (0)	00 (0)	40
Depression	38 (95)	2 (5)	00 (0)	40

OLP=Oral lichen planus

Table 3a: Comparison of levels of psychological status (anxiety) in oral lichen planus and nonoral lichen planus individuals

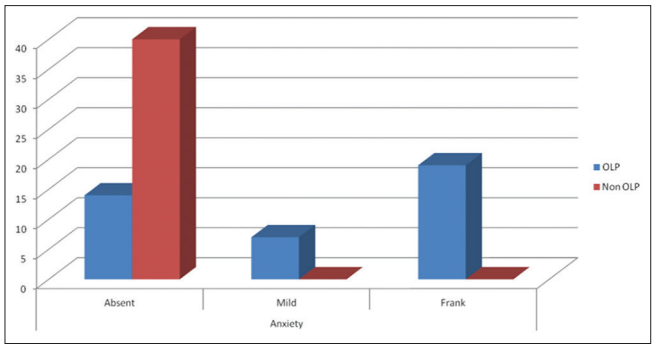
Groups	Anxiety			Total
	Absent (%)	Mild (%)	Frank (%)	
Group OLP	14 (35)	7 (17.5)	19 (47.5)	40
Group non-OLP	38 (95)	2 (5)	00 (0)	40

OLP=Oral lichen planus

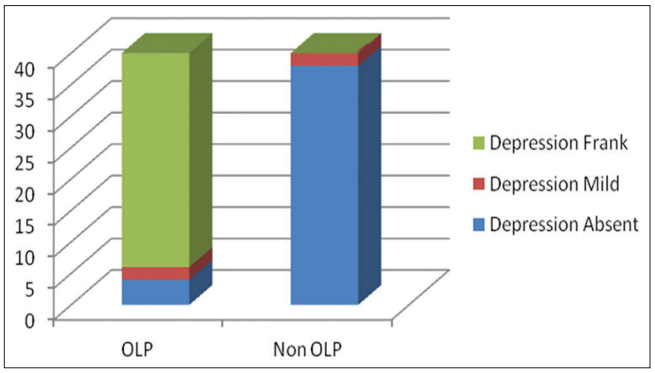
Table 3b: Comparison of levels of psychological status (depression) in oral lichen planus and nonoral lichen planus individuals

Groups	Depression			Total
	Absent (%)	Mild (%)	Frank (%)	
Group OLP	4 (10)	2 (5)	34 (85)	40
Group non-OLP	38 (95)	2 (5)	0 (0)	40

OLP=Oral lichen planus



Graph 1: comparison of levels of psychological status (Anxiety) in OLP and Non-OLP Individuals



Graph 2: comparison of levels of psychological status (Depression) in OLP and Non-OLP individuals

Table 4a: Intervention Group (A) - Anxiety scores (before and after active intervention)

Groups	Anxiety			Total
	Absent (%)	Mild (%)	Frank (%)	
Group A				
Before	8 (40)	4 (20)	8 (40)	20
After	14 (70)	4 (20)	2 (10)	

Table 4b: Intervention Group (A) - Depression scores (before and after active intervention)

Groups	Depression			Total
	Absent (%)	Mild (%)	Frank (%)	
Group A				
Before	0 (0)	2 (10)	18 (90)	20
After	10 (50)	8 (40)	2 (10)	

Table 5a: Placebo Group (P) - Anxiety scores (before and after active intervention)

Groups	Anxiety			Total
	Absent (%)	Mild (%)	Frank (%)	
Group P				
Before	3 (15)	3 (15)	14 (70)	20
After	6 (30)	4 (20)	10 (50)	

Table 5b: Placebo Group (P) - Depression scores (before and after active intervention)

Groups	Depression			Total
	Absent (%)	Mild (%)	Frank (%)	
Group P				
Before	3 (15)	0 (0)	17 (85)	20
After	4 (20)	2 (10)	14 (70)	

revealed that on receiving active intervention the anxiety scores in OLP individuals dropped from 12 participants having the combination of mild and frank anxiety to 6 participants. After active intervention, 14 participants were relieved of anxiety as compared to 8 [Table 4a].

Comparison of the prevalence of depression in OLP individuals before and after getting "active" intervention revealed that on getting active intervention the depression present in all 20; 1 (10%) mild and 9 (90%) frank came down to 1 (10%) and 4 (40%) mild. Five (50%) participants were completely relieved of depression [Table 4b].

Comparison of the prevalence of anxiety in OLP individuals before and after getting "placebo" intervention revealed that not much change in anxiety registered in group receiving passive intervention before and after the intervention [Table 5a].

Comparison of the prevalence of depression in OLP individuals before and after getting "placebo" intervention revealed that there was no change in depression in OLP individuals before and after getting passive intervention [Table 5b].

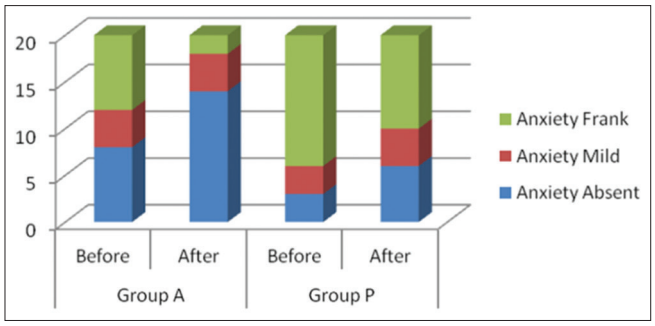
Comparison of anxiety in Group A and Group P after getting respective intervention [Table 6a and Graph 3].

Comparison of depression in Group A and Group P after getting respective intervention [Table 6b and Graph 4].

In our study, according to HADS scale, depression level in OLP patients was 85% compared to the control group (0%) and anxiety level in OLP patients was 47.5% compared to the control group 0%. The present study showed that there is significant increase in depression and anxiety in OLP patients than control groups.

Discussion

Dermatology shows a distinct relation with psychosomatics as the skin has strong psychological implications. The skin is made up of glands, blood vessels, nerves, and muscle elements, many of which are controlled by the autonomic nervous system and are influenced by psychological stimuli. These have the capacity to cause autonomic arousal and the capability of affecting the skin leading to the development of various skin disorders. Clinical studies have shown that



Graph 3: both groups: Anxiety scores (Before & after intervention)

Table 6a: Both groups - Anxiety scores (before and after intervention)

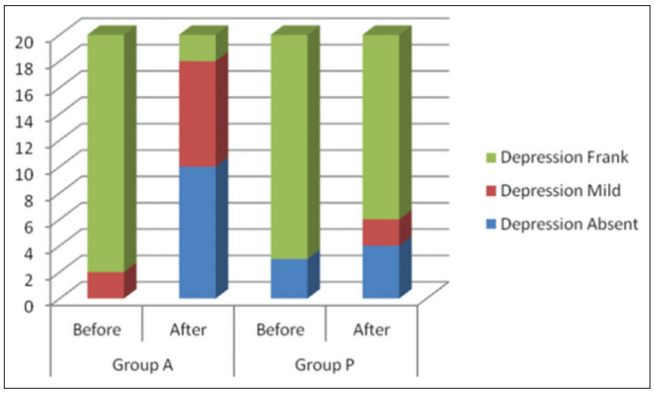
Groups	Anxiety			Total
	Absent (%)	Mild (%)	Frank (%)	
Group A				
Before	8 (40)	4 (20)	8 (40)	20
After	14 (70)	4 (20)	2 (10)	
Group P				
Before	3 (15)	3 (15)	14 (70)	20
After	6 (30)	4 (20)	10 (50)	

Table 6b: Both groups - Depression scores (before and after intervention)

Groups	Depression			Total
	Absent (%)	Mild (%)	Frank (%)	
Group A				
Before	0 (0)	02 (10)	18 (90)	20
After	10 (50)	08 (40)	02 (10)	
Group P				
Before	03 (15)	0 (0)	17 (85)	20
After	04 (20)	02 (10)	14 (70)	

psychological stress can cause suppression of killer T-cells and macrophages, both of which play important roles in skin-related immune reactions. Field described the skin as the "shock organ" for emotional stress, manifesting in the form of several skin diseases. Clinical observations have identified psychological stress as either precipitating, aggravating, or prolonging many skin diseases and the psychosomatic aspects of many disorders.[13]

Brazzini *et al*. proposed the "an active neuro-immune-endocrine interface" or neuroendocrine organ, exhibiting multidirectional and local communication, which is made possible by the production in the skin of cytokines, hormones and neurotransmitters, and anatomical links between the central nervous system (CNS) and skin. In addition, circulating immune cells, recruited in the skin, express receptors for a variety of neuropeptides, cytokines, neurotransmitters, and hormones, identical



Graph 4: both groups: Depression scores (Before & After intervention)

to those expressed centrally, allowing the CNS to communicate with the skin. This means that systemic signals affecting the skin initiate a flow of information between this and other organs, leading to modulation of local immune activity, vascular functions, sensory reception, thermoregulation, exocrine secretion, and the maintenance of skin barrier integrity.[14]

OLP is described as an adult disease. The typical age of presentation is between 30 and 60 years. Exact etiology of the LP is unknown, but a change in cell-mediated immune response has a significant role in the pathogenicity of the lesion.[15] Factors such as stress and psychological problems, especially depression and anxiety, have been mentioned as etiologic factors in OLP. Exacerbations of OLP have been linked to periods of psychological stress and anxiety. Ivonavaski *et al*. proposed that prolonged emotive stress in OLP. Patients has been proposed to lead to psychosomatization which in turn may contribute to the initiation and clinical expression of OLP and also suggested that psychosocial and emotional stress is one possible factor that may precipitate reticular OLP to transform to the erosive form.[16]

Different studies have been done for the evaluation of the relationship between OLP and psychiatric disorders. In 1961, Altman and Perry conducted a study on of 197 patients with LP, which revealed that "10% were aware of a precipitating stressful incident at the onset of their LP." Andreasen pointed out in 1968 that patients with LP were found to be in conditions of stress, anxiety, and emotional changes. Colella *et al*. conducted a study in 1993 using different psychiatric tests such as "General Health Questionnaire," "Hamilton Anxiety Scale," "Melancholia scale, depression," and "Hamilton Depression Scale" demonstrated that OLP patients had higher depression and anxiety score. McCartan noticed that out of fifty patients with OLP, tendency toward anxiety was in 50% of the cases, but depression scores

were minimal and it could not be related to any specific clinical pattern of OLP.[17]

Other study showed that 63.6% of LP patients had psychiatric symptoms with mixed anxiety and depression being the most frequent (15.7%), followed by social phobia (12.9%), panic symptoms (11.4%), obsessive-compulsive predominantly obsession thoughts and ruminations (10%), and dysthymia (5.7%) arranged in order.[1] In one study, involved 100 patients with OLP and controls were subjected to the following psychometric tests to both groups: Spielberger State-Trait Anxiety Inventory, Cartel Personality Questionnaire 16PF, Hassanyeh Rating of Anxiety-Depression-Vulnerability, Beck Depression Inventory, Raskin Depression Screen, and Covi Anxiety Screen. Despite the higher anxiety scores observed in patients with OLP, it was not established that the observed psychological alterations constitute a direct etiologic factor of OLP, nor was it established that such alterations are a consequence of OLP and its lesions.[17]

Chaudhary conducted an analytical age- and sex-matched double controlled study where the General Health Questionnaire-version 28 and the HADS were used to evaluate psychosocial stressors in terms of stress, anxiety, and depression, respectively. He found that significantly higher stress, anxiety, and depression levels were found in the OLP and positive control than the general population. These suggest that psychological stressors play an important role in the causation of OLP. It may be further hypothesized that these stressors form a starting point for the initiation of various autoimmune reactions, which have been shown to be contributory to the pathogenesis of OLP. Further longitudinal studies need to be done globally before definitive conclusions can be drawn.[18]

Agha-Hosseini *et al*. conducted a study to detect the importance of psychological factors in OLP patients by means of psychological tests and make a meaningful comparison between the levels of anxiety and depression in OLP patients and the healthy population. He saw a significant difference in anxiety scores in two groups, but no statistically significant difference when the depression levels between the two groups were assessed. His results analysis did not appear to support the concept that lichen planus is a disease that is seen in persons who are more depressed than the normal population, but prolonged anxiety in many OLP patients may lead to psychsomatization and may contribute to exacerbation or recurrence of this disease. He concluded that a substantial number of patients might benefit from a mutual collaboration between psychiatrists and oral medicine specialists in OLP management.[19]

Harpenau *et al*. in 1995[20] and Sieg *et al*. in 1995[21] independently in a controlled, randomized prospective trial, consisting of 14 and 13 patients confirm that topical cyclosporine as a rinse (500 mg 1–3 times daily for 5 min) is more effective than placebos but equivalent to topical steroid. No significant side effects were reported in either of the clinical trials. Hence in our trial, we found prescribing 500 mg of cyclosporine as a rinse one time a day gave almost good results.

Conclusion

Though there have been many studies conducted to evaluate the role of anxiety, stress, and depression in the etiopathogenesis of OLP, the results have been conflicting. The present study results matches with the majority of the studies, showing a positive association between anxiety and depression levels in OLP patients, suggesting counseling along with traditional treatment can be effective in reducing the size of the lesions. With regard to the discussion above, it seems logical to claim that psychiatric evaluation and appropriate treatment of the patients along with routine treatment of OLP lesions should be recommended. Lichen planus is to some extent apsychosomatic or somatopsychic disease or both. Oral healthcare providers should pay attention to the emotional state of their patients. Emotional factors are important as evidenced by higher frequency of psychiatric symptoms, poor quality of life, higher level of anxiety, and neuroendocrine and immune dysregulations. Counseling may help in ameliorating symptoms, improving quality of life, and enhancing recovery.

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Conflicts of interest

There are no conflicts of interest.

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