AJDS LAZHAR Al-Azhar Journal of Dental Science Print ISSN 1110-6751 | online ISSN 2682 - 3314
Vol. 27- No. 4- 503:510- October 2024 https://ajdsm.journals.ekb.eg
Oral Biology, Medicine & Surgical Sciences Issue *(Oral Biology, Oral Pathology, Oral Periodontology, Medicine, Oral & Maxillofacial Surgery)*

THE EFFECT OF TOPICAL HYALURONIC ACID COMPARED TO LOW LEVEL LASER THERAPY IN TREATMENT OF ORAL LICHEN PLANUS PATIENTS

Abdel-Latif Galal Borhamy[1], Mahmoud Taha El-Destawy[2]

ABSTRACT

Objectives: To evaluate clinically the effectiveness of topical hyaluronic acid compared to low level laser therapy in treatment of oral lichen planus patients. **Subjects and Methods:** Forty two Patients with clinical and histological diagnosis of EOLP were included in randomized clinical trials. They were divided into two groups:Group A:21 Patientswas treated with HA (0.2%) for local application directly on the affected area. Group B: 21 patients treated by Low level laser therapy performed by using a semiconductor diode laser 635 nm. Application of 635 nm wavelength will transmitted to the lesion via an optical fiber equipped with a diffuser tip. The laser power from the end of the optical fiber did not exceed 300 mW. Each session will be 10 min. **Results:** Both groups showeda statistically significant difference from baseline to follow -up periods. Where both groups showed a remarkable reduction in pain andsize of lesions. **Conclusion:** Topical application of hyaluronic acid was effective and can be considered as an alternative therapy for low level laser therapyin the treatment of erosive-atrophic OLP.

KEY WORDS: Lichen planus, Hyaluronic acid, low level laser.

INTRODUCTION

Oral lichen planus (OLP) is a chronic mucocutaneous inflammatory illness with an unknown cause that affects 0.5% to 2% of the general population(1). It often affects individuals over the age of thirty, with a small feminine predisposition(2). Although any mucosal region may be impacted, the buccal mucosa is the most commonly afflicted, followed by the tongue and gingiva (3, 4) .

Oral lichen planus (OLP) can appear clinically in three different patterns: reticular, atrophic, and bullous, erosive; each has distinct features and can be seen alone or in combination. The most common variety is the reticular type, which is distinguished by the presence of Wickham striae, which are usually symmetric, bilateral, asymptomatic, and located mostly in the buccal mucosa. The erosive variant, albeit being less common, is more clinically significant since the lesions are generally symptomatic, ranging from mild discomfort to severe pain (5).

OLP etiology is assumed to be a T-cell-mediated autoimmune illness involving both specific and non-specific antigen specificity (6). Antigen specificity is defined as antigen presentation by basal keratinocytes and antigen-specific keratinocytes

1. Lecturer of Oral Medicine, Periodontology, Diagnosis and Oral Radiology Faculty of Dental Medicine Al-Azhar University, Egypt
2. Associate Professor of Oral Medicine, Periodontology, Diagnosis and Oral Radiology Faculty of Dental Medicine Al-Azhar University, Egypt

• ***Corresponding author*:** galalabdo357@gmail.com

DOI: *10.21608/AJDSM.2023.227422.1444*

by CD8+cytotoxic T-lymphocytes, whereas non-specific antigen comprises mast cell degranulation and matrix metalloproteinase activation[7]. IL-6, TNF-α, and GM-CSF trigger local inflammation[8,9].

In dentistry, hyaluronic acid has been used to accelerate tooth socket healing, treat temporomandibular joint osteoarthritis, maintain space in non-grafted sinus lifting, manage soreness from recurrent aphthous ulceration (RAU), as monotherapy, or as an adjunct to non-surgical and/or surgical periodontal treatment to reduce inflammation and promote wound healing [10].

Although corticosteroid medication is often effective due to its potent anti-inflammatory characteristics, it can induce candidiasis, burning or stinging sensations, mucosal atrophy, unpleasant taste, nausea, sore throat, and dry or swollen mouths. Superpotent topical and systemic steroids have also been linked to systemic absorption and adrenal suppression, particularly when used to treat chronic disorders like OLP [11]. Thus, an alternate therapy is preferable. For example, HA may be used to handle OLP [12].

The use of low-level laser therapy (LLLT) as an alternate technique for treating OLP has sparked widespread attention in recent years. LLLT, also known as photobiomodulation, is a non-pharmacological, non-invasive therapeutic application with potential analgesic, anti-inflammatory, immunomodulatory, and biostimulatory benefits that have few side effects [13-17]. Dillenburg et al. [13] found that the laser-treated group improved much more in terms of OLP signs and symptoms, with a lower recurrence rate, than the clobetasol group. Furthermore, Jajram et al. [18] found that laser therapy was equally efficient as dexamethasone in the treatment of OLP, with no known adverse effects. On the other hand, Kazancioglu and Erisen [19] discovered that corticosteroids and ozone were more beneficial in pain relief and clinical improvement in individuals with erosive OLP than laser management.

SUBJECT AND METHODS

Forty-two patients with ulcerative erosive OLP were identified clinically and histologically. In a randomized parallel trial design, patients will be recruited from the Departments of Oral Medicine, Periodotology, Oral Diagnosis, and Oral Radiology at Al Azhar University's Faculty of Dental Medicine (Boys in Cairo). They were selected based on the criteria listed below.

Inclusion criteria:

Patients with histologically proven diagnosis of OLP according to modified WHO criteria [20].

Exclusion criteria:

(a) Patient on immunosuppressive medication, chemotherapy, or history of radiation for the previous 6 months. (b) Pregnant or breastfeeding women; (c) Patients with uncontrolled diabetes or hypertension and a positive Hepatitis C virus antibody or Hepatitis Bs Ag.(d) Patients who have taken any medicines that might provoke a lichenoid response, have undergone topical treatment for oral lichen planus in the recent two weeks or systemic treatment for OLP in the last three months, or are heavy smokers.

Each patient gave informed permission after receiving thorough information and a description of the trial.

Sample size calculation:

The sample size was calculated using GPower software (Version 3.0.10). According to the study design, the appropriate statistical test will be an independent t-test to investigate the statistical differences in pain degree based on the visual analogue score (VAS) between various treatments (Hyaluronic acid and laser beam). The following estimates are based on the effect size (0.79) determined by Hashem et al.[21]. To achieve 81.6% test power at $\alpha = 0.05$ and determine the clinical relevance of therapy, a total sample size of 42 persons (21 cases per group) is proposed. The diagnosis of erosive OLP is based on:

Clinical examination:

It included documented patient data and intraoralexamination (signs and symptoms, onset and duration ofdisease, site, and size of the lesions) and skin examination of anydermatological sign of lichen planus. Patients werehistopathologically confirmed as oral lichen planus.

Grouping and intervention:

Patients were randomly assigned using an electronically created set of random numbers by computer program (Random allocation software version 1.0, Pass 2022.USA) into two groups: Group A patients were treated with hyaluronic acid (0.2%) (Gingegel. Turkey) for topical application to the afflicted region. The patients were encouraged to apply the medications three times a day after eating and to leave them on for 30 minutes. During the medication application, the patient did not ingest any food or beverages. Group B received low-level laser treatment utilizing a semiconductor diode laser (Lasotronic. Poland) at 635 nm.

The laser power at the end of the optical fiber did not surpass 300 mW. Each low-level laser treatment session lasted 10 minutes and delivered a total dosage of 120 J/cm2. The treatment was repeated on the third, seventh, and fifteenth days. The patients were followed up after the fourth week, three months, and six months of therapy. The healing process after each laser treatment was painless, with no edema or bleeding.

Group A: Hyaluronic acid group.

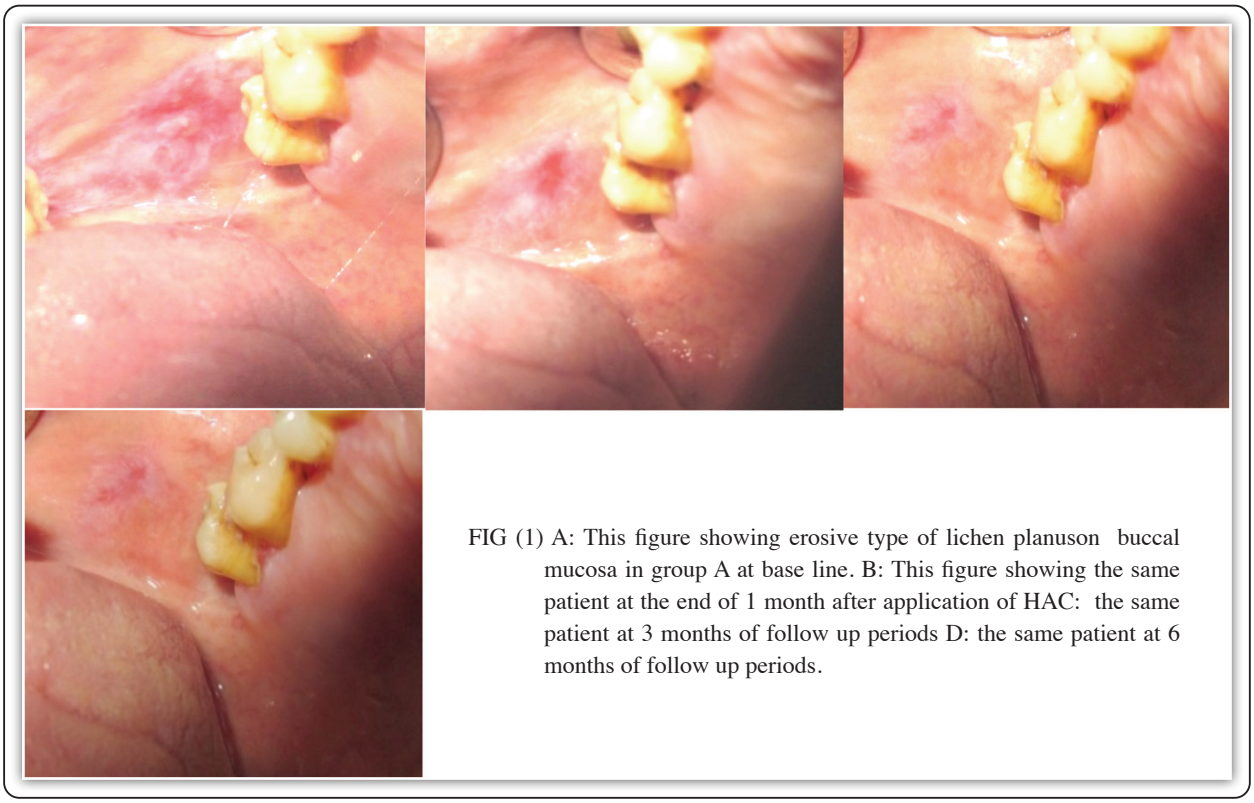

FIG (1) A: This figure showing erosive type of lichen planuson buccal mucosa in group A at base line. B: This figure showing the same patient at the end of 1 month after application of HAC: the same patient at 3 months of follow up periods D: the same patient at 6 months of follow up periods.

Group B: low level laser therapy group.

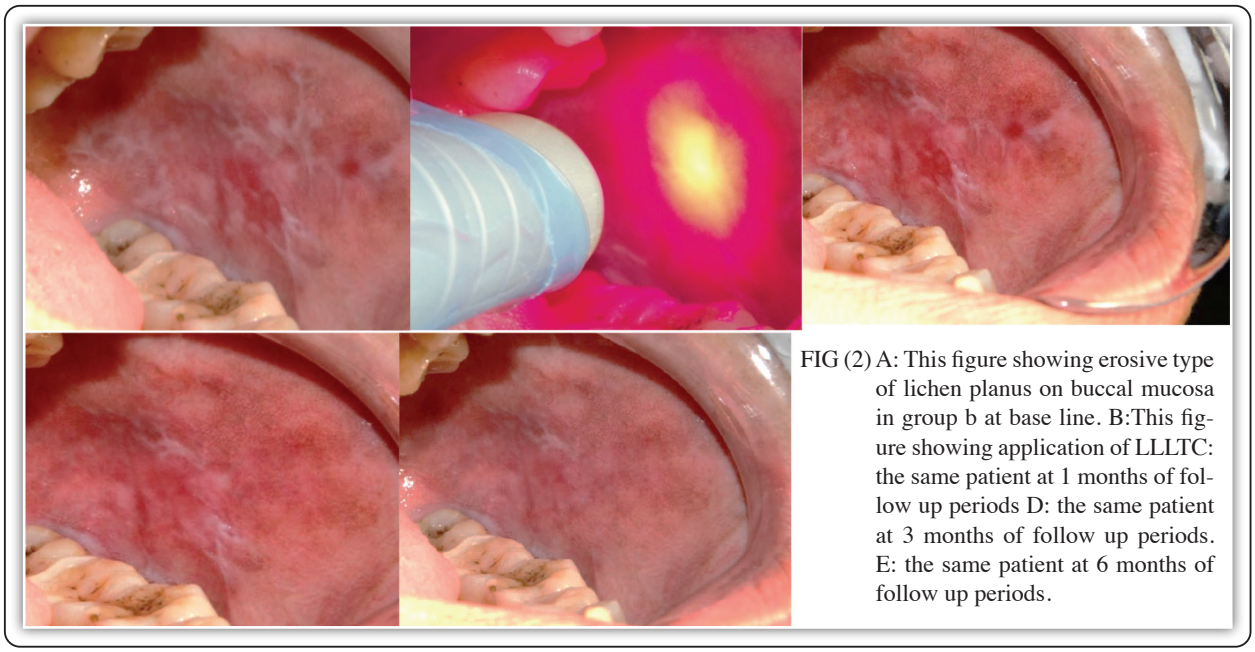

FIG (2) A: This figure showing erosive type of lichen planus on buccal mucosa in group b at base line. B:This figure showing application of LLLTC: the same patient at 1 months of follow up periods D: the same patient at 3 months of follow up periods. E: the same patient at 6 months of follow up periods.

Clinical Assessment:

The clinical data were rated using the criterion scale developed by Thongprasom et al. (1992) [22]. Oral lichen planus lesions were scored using a scaled tongue blade: 0 = no lesion, 1 = mild white striae without erythematous area, 2 = white striae with atrophic area <1cm2, 3 = white striae with atrophic area >1cm2, 4 = white striae with erosive area <1cm2, and 5 = white striae with erosive area >1cm2.

The intensity of the lesions' symptoms was measured using a visual analog scale (VAS), which ranged from zero to ten, with zero representing no pain and ten representing acute discomfort [23]. Discomfort scores and a questionnaire detailing any potential side effects were completed. Patients were asked to rate the degree of their discomfort on a visual analog scale ranging from 0 to 10; answers were collected at the beginning of the trial, after treatment, and at follow-up.Digital images were taken at the initial presentation, after therapy, and during follow-up periods to visually record improvements.

Total improvement (complete resolution of clinical signs) was defined as the disappearance of all erosive lesions, regardless of any remaining hyperkeratotic lesions; partial response meant a decrease in pain and lesion size compared to baseline; and no improvement meant no changes in the lesion.

Statistical analysis of the data:

Statistical analyses were carried out using IBM-SPSS version 23. The Kruskal-Wallis test was used to investigate the influence of treatment time on the examined parameters. The Mann-Whitney test was employed to demonstrate statistical differences between experimental groups. Data is presented as median and range. $P<0.05$ indicated a statistically significant difference.

RESULTS

Table 1 shows the data visual analogue score (VAS) of pain scale for all cases before and after 1, 3, and 6 months of LLLT and HA therapies. The degree of discomfort on the VAS system was substantially impacted (P<0.000) by the change in follow-up time, according to Kruskal-Wallis test.

Before therapy, all patients caused a significant level of pain on the VAS scale. After one month of therapy with LLLT or HA, the pain was greatly decreased to moderate. After three months, the discomfort was significantly decreased to minimal or no pain in all treatments. After one month of treatment, those treated with HA had much less pain than those treated with LLLT.

Table (1) The change in visual analogue score (VAS) of pain scale before and after 1, 3, and 6 months of treatment with low-level laser therapy (LLLT) and hyaluronic acid (HA) in oral lichen planus patients. Data is presented as a median (and range).

Follow up time	Treatment		Effect of treatment[(b)]
	LLLT (n=21)	HA (n=21)	
Before	9 (8-10)	10 (7-10)	P=0.45
After 1m	5 (4-5)*	5 (3-5)*	P=0.55
After 3m	0 (0-3)*	0 (0-2)*	P=0.131
After 6m	0 (0-1)8*	0 (0)*	P=0.155
Effect of time[(a)]	P=0.000	P=0.000	

**: significant difference (P<0.000), as compared to the values before treatment.*

P<0.000: represent significant effect according to Kruskal-Willis (a) or Mann-Whitney (b) tests.

The results of rating erosive lesions according to Thongprasom in all instances are shown (Table 2). There was no significant change in Thongprasom scores between the groups before treatment. However, after one month of therapy, the median Thongprasom scale scores with HA were lower than those with LLLT. After 3 and 6 months, Thongprasom ratings were considerably lower than before therapy.

Table (2) The change in Thongprasomscore before and after 1, 3 and 6 months of treatment with Low level laser therapy (LLLT) and hyaluronic acid (HA) in oral lichen planus patients. Data are displayed as median (and range).

Follow up time	Treatment		Effect of treatment[(b)]
	LLLT (n=21)	HA (n=21)	
Before	4 (2-5)	3 (2-5)	0.448
After 1m	2 (1-3)*	1 (1-3)*	0.343
After 3m	1 (0-3)*	1 (0-1)*	0.129
After 6m	0 (0-1)*	0 (0)*	0.155
Effect of time[(a)]	0.000	0.000	

**: significant difference (P<0.000), as compared to the values before treatment.*

P<0.000: represent significant effect according to Kruskal-Willis (a) or Mann-Whitney (b) test

DISCUSSION

Lichen planus is a chronic mucocutaneous illness, and it has been believed that cell-mediated immunity and cytokines generated by keratinocytes and lymphocytes play an important role in its progression. TNF-α, IL-8, and INF-γ cytokines activate lymphocytes and induce keratinocyte death. Therefore, systemic and local corticosteroid therapy are the cornerstone of its treatment. However, these therapies have a number of adverse effects, including candidiasis, xerostomia, sore throat, osteoporosis, adrenal insufficiency, hypertension, and diabetes mellitus [(24)]. The primary goal of OLP treatment is to reduce the duration and severity of symptomatic

outbreaks. Tacrolimus, systemic and topical retinoids, calcineurin inhibitors, cryotherapy, CO2 laser, PUVA therapy, and toluidine blue-mediated photodynamic treatment have all been proposed as ways to alleviate symptoms [25].

The topical use of 0.2% HA is a new and promising therapy for OLP. Extensive study has been done on the chemical and physicochemical characteristics of HA, as well as its physiological function in humans. Its diverse features, including biocompatibility, non-immunogenicity, biodegradability, and viscoelasticity, make it an excellent biomaterial for cosmetic, medicinal, and pharmaceutical applications. Measuring the size of the erosive/ulcerated region indicates that 0.2% HA can aid in healing [26].

In the current study, both groups had significantly lower VAS ratings, erythema levels, and lesion sizes.The current study's findings are consistent with those of Nolan et al. [27]. Who investigated the effectiveness of a topical HA gel formulation (0.2%) in the treatment of OLP and discovered a substantial reduction in discomfort and lesions.

Shetty et al.[26] discovered a substantial decrease in VAS ratings, degree of erythema, and size of lesions in the HA group compared to the placebo group. Both results are consistent with those of the current investigation, showing that 0.2% HA might be a viable treatment option for OLP. Both human and animal research have proven that HA promotes tissue repair. The activity may be mediated by moderating inflammatory responses, boosting cell proliferation, or stimulating re-epithelization through basal keratinocyte proliferation [27].

Low-level laser treatment is being utilized to treat a wide range of lesions, including skin and breast malignancies, immunologic disorders (such as acne, psoriasis, lichen planus, and scleroderma), and infectious illnesses (such as HPV, osteomyelitis, and candidiasis) [19].

According to the findings, both groups showed statistically significant changes between the baseline and follow-up periods. The current study's findings were consistent with those of Dillenburg et al.[13] who found that the laser-treated group had considerably greater recovery in signs and symptoms of OLP and a lower recurrence rate than the clobetasol group. Furthermore, Jajram et al. [18] discovered that laser therapy was equally efficient as dexamethasone in the treatment of OLP, with no known adverse effects. In contrast, Kazancioglu and Erisen [19] found that corticosteroids and ozone were more effective than laser treatment in reducing pain and improving clinical outcomes in patients with erosive OLP.

Othman et al. [28] evaluated the effect of laser on clinical symptoms and serum pro-inflammatory tumour necrosis factor (TNF-) levels in individuals with OLP. The participants were separated into two groups: laser and topical steroids. The authors found substantial decreases in lesion size and serum TNF- in both groups.LLLTs' capacity to reduce indicators (clinical appearance) and symptoms (pain) in OLP can be linked to a number of factors. LLLT promotes the creation of ß-endorphins and encephalins, as well as the lowering of bradykinin and histamine levels, all of which contribute to analgesia and pain alleviation. The analgesic effect of LLLT is also supported by its influence on C fibers, which decreases their activity and consequently the conductance of pain stimuli [29].

The biological activity of LLLT in boosting enhanced fibroblast proliferation, differentiation, and migration, as well as stimulation of epithelial cells, which are regarded major players in the healing process of the oral mucosa, may explain the reduction in clinical manifestations of OLP following LLLT. Furthermore, LLLT plays a crucial role in immunomodulation. LLLT modulates mast cell activity, which enhances leukocyte release into oral tissues and so plays a significant role in the regulation of oral mucosa inflammation [30].

CONCLUSION AND RECOMMENDATION

The current study discovered that 0.2% HA efficiently alleviates OLP symptoms with no worsening or recurrence of lesions even after treatment was discontinued, and that it may be utilized as an alternate therapy to LLLT for the treatment of erosive-atrophic OLP. The research samples only included findings from these specific patient categories. More study with bigger samples and longer follow-up periods is required to validate these findings.

REFERENCES

1. Alaizari N, Al-Maweri S, Al-Shamiri M, Tarakji B, Shugaa-Addin B. Hepatitis C virus infections in oral lichen planus: A systematic review and meta-analysis. Aust Dent J. 2016; 61: 282-87.
2. McCartan B, Healy M. The reported prevalence of oral lichen planus: A review and critique. J Oral Pathol Med. 2008;37: 447-53.
3. Radochova V, Drizhal I, Slezak R. A retrospective study of 171patients with oral lichen planus in the East Bohemia - Czech Republic- Single center experience.J ClinExp Dent.2014; 6: 556-61.
4. Al-Maweri S, Kalakonda B, Al-Soneidar W, Al-Shamiri M, Alakhali M, Alaizari N. Efficacy of low-level laser therapy in management of symptomatic oral lichen planus: A systematic review. Lasers Med Sci. 2017;32:1429- 37.
5. Payeras M, Cherubini K, Figueiredo M, Salum G. Oral lichen planus: focus on etiopathogenesis. Arch Oral Biol. 2013; 58:1057-69.
6. Sugerman B, Savage N, Walsh J, Zhao Z, Bigby M. The pathogenesis of oral lichen planus.Crit Rev Oral Biol Med. 2002; 13: 350-65.
7. Roopashree M, Gondhalekar R, Shashikanth M, George J, Thippeswamy S, Shukla A. Pathogenesis of oral lichen planus -a review. J Oral Pathol Med. 2010; 39: 729-34.
8. Ismail B, Kumar K, Zain R. Oral lichen planus and lichenoid reactions: Etiopathogenesis, diagnosis, management and malignant transformation. J Oral Sci. 2007; 49: 89-106.
9. Thongprasom K, Dhanuthai K, Sarideechaigul W, Chaiyarit P, Chaimusig M. Expression of TNF-alpha in oral lichen planus treated with fluocinoloneacetonide 0.1%. J Oral Pathol Med. 2006; 35: 161-6
10. Yildirim S, OzenerO, Dogan B, Kuru B. Effect of topically applied hyaluronic acid on pain and palatal epithelial wound healing: an examiner-masked, randomized, controlled clinical trial. J Periodontol 2018;89:36-45.
11. Keshari D, Patil K, Mahima VG. Efficacy of topical curcumin in the management of oral lichen planus: a randomized controlled-trial.JAdvClin Res Insights. 2015;2:197-203.
12. Kia J, Shirazian S, Mansourian A, KhodadadiFard L, Ashnagar S. Comparative efficacy of topical curcumin and triamcinolone for oral lichen planus: a randomized controlled clinical trial. J Dent (Tehran). 2015;12(11):789-96.
13. DillenburgC,MartinsM, MuneratoMC, MarquesMM, Carrard VC, Sant'AnaFilho M, etal.Efficacy of laser phototherapy in comparison to topical clobetasol for the treatment of oral lichen planus: a randomized controlled trial. J Biomed Opt .2014;19(6):068002.
14. Al-Maweri S, Javed F, Kalakonda B, AlAizariA, Al-Soneidar W, Al-Akwa A .Efficacy of low level laser therapy in the treatment of burning mouth syndrome: a systematic review. PhotodiagnosisPhotodyn Therapy.2016(17):188–93.
15. Pandeshwar P, Roa M, Das R, ShastryP, Kaul R, Srinivasreddy. MB Photobiomodulation in oral medicine: a review. J InvestigClin Dent (2016) 7(2):114–26.
16. Cafaro A, ArduinoG, Massolini G, Romagnoli E, Broccoletti R. Clinical evaluation of the efficiency of low-level laser therapy for oral lichen planus: a prospective case series. LasersMedSci (2014) 29(1):185–90.
17. Abduljabbar T, Javed F, Shah A, Samer MS, Vohra F, Akram Z. Role of lasers as an adjunct to scaling and root planning in patients with type 2 diabetes mellitus: a systematic review. Lasers Med Sci(2017):32(2):449–59.
18. JajarmH, Falaki F, Mahdavi O. A comparative pilot study of low intensity laser versus topical corticosteroids in the treatment of erosive-atrophic oral lichen planus. Photomed Laser Surg.2011:29(6): 421–25.
19. Kazancioglu H, Erisen M Comparison of low-level laser therapy versus ozone therapy in the treatment of oral lichen planus. Ann Dermatol.2015: 27(5):485–91.
20. Rad M, Hashemipoor M, Mojtahedi A. Correlation between clinical and histopathologic diagnosis of oral lichen planus based on modified WHO diagnostic criteria. Oral Surg Oral Med Oral Pathol Oral RadiolEndod 2009; 107: 796–800.
21. Hashem, A, Issrani, R., Elsayed, E., &Prabhu, N. Topical hyaluronic acid in the management of oral lichen planus:

A comparative study. Journal of Investigative and Clinical Dentistry, (2019).10(2) .170-85.

22. Thongprasom K, Luangjarmekorn L, Sererat T, Taweesap W. Relative efficacy of fluocinoloneacetonide compared with triamcinolone acetonide in treatment of oral lichen planus. J Oral Pathol Med. 1992; 21: 456-8
23. Cafaro A, Albanese G, Arduino P, Mario C, Massolini G, Mozzati M, et al. Effect of low-level laser irradiation on unresponsive oral lichen planus. Photomed Laser Surg. 2010; 28: 99-103.
24. Abduljabbar T, Javed F, Shah A, Samer MS, Vohra F, Akram Z. Role of lasers as an adjunct to scaling and root planning in patients with type 2 diabetes mellitus: a systematic review. Lasers Med Sci(2017) :32(2):449–59.
25. Jajarm H, Falaki F, Mahdavi O.A comparative pilot study of low intensity laser versus topical corticosteroids in the treatment of erosive-atrophic oral lichen planus.Photomed Laser Surg(2011): 29(6): 421–25.
26. Shetty R, Burde K, GuttalS. The efficacy of topical hyaluronicacid 0.2% in the management of symptomatic oral lichen planus.JClinDiagn Res. 2016;10(1):46-50.
27. Nolan A, Badminton J, Maguire J, Seymour A. The efficacy of topicalhyaluronic acid in the management of oral lichen planus. J OralPathol Med. 2009;38:299-303.
28. Othman A, Shaker G, ElshenawyM, Abd-Elmoniem W,EldinM, Fakhr M.The effect of diode laser and topical-steroid on serum level of TNF-alpha in oral lichen planus patients. JClinExp Dent (2016) .8(5):566–70
29. Kalakonda B, Farista S, Koppolu P, Baroudi K, Uppada U, MishraA, et al . Evaluation of patient perceptionsafter vestibuloplasty procedure: a comparison of diode laserand scalpel techniques. J ClinDiagn Res.(2016) : 10(5):96–100.
30. Najeeb S, Khurshid Z, Zohaib S, Najeeb B, Qasim SB, ZafarM.Management of recurrent aphthous ulcers using low-levellasers: a systematic review. Medicina (Kaunas, Lithuania) (2016) :52(5):263–68.