Effects of Low Level Laser Therapy on Erosive-atrophic Oral Lichen Planus

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Background: The erosive-atrophic form of oral lichen planus (OLP) is associated with severe pain and burning sensation and is often unresponsive to treatment. Topical corticosteroids are considered as a medication of first choice but they can produce adverse effects. Therefore, new therapeutic approaches are required.

Aim: The aim of this study was to investigate the effectiveness of biomodulation with diode laser in patients presenting with long-standing erosive-atrophic OLP.

Materials and methods: Twelve patients, clinically and histologically diagnosed with OLP, participated in this study. The level of pain and the clinical scores of total 59 lesions were recorded before treatment using visual analog scale and Thongprasom sign scoring system respectively. All patients received low level laser therapy (LLLT) with diode laser (810 nm) with parameters (0.5 W, 30 s, 1.2 J/cm²) three times weekly for a month. The response rate was assessed according to the decrease in pain and sign scores. Treatment efficacy index was calculated.

Results: There was a significant reduction in pain after LLLT (p<0.0001). Improvement in clinical signs was achieved in 59.3% of the lesions. At the end of the treatment 5.1% of the lesions exhibited score 5; 6.8% - score 4, 11.9% of the lesions were scored 3 and 8.5% and 30.5% showed score 2 and score 1, respectively. Complete resolution was revealed in 37.3% of the lesions. All patients experienced some degree of improvement. Most of the cases showed moderate recovery.

Conclusion: The present results indicate that LLLT is an effective and harmless modality for management of erosive-atrophic OLP.

BACKGROUND

Lichen planus (LP) is a chronic inflammatory mucocutaneous disease of unknown etiology, in which CD8+ T cells induce apoptosis of basal keratinocytes. People in the age range of 30 to 60 years are affected and the ratio of males to females is 1:2.1,2 Typically the disease presents with multiple lesions with bilateral symmetric distribution. Andreasen’s classification distinguishes six clinical forms of OLP: reticular, papular, plaque-like, atrophic (erythematous), erosive-ulcerous and bullous-erosive.3-7 Reticular, papular and plaque-like forms are usually painless and present clinically as white keratotic lesions. The other non-keratotic forms are associated with severe pain and intolerance of patients to consume hot or spicy food. Furthermore, the risk of malignant transformation in erosive and atrophic lesions may be higher than other types of OLP.3,4,8 Therefore, treatment of this forms and monitoring in the long term are vital.

Despite the great attempts to develop efficient modalities for managing OLP lesions the results of administering agents are often unsatisfactory. Treatment is aimed primarily at abolishing the symptoms and at extending the periods of remission. At this stage, complete eradication of the disease cannot be achieved by any method.9 Topical corticosteroids are considered a gold standard in the treatment of OLP but they can produce adverse effects including thinning of the oral mucosa, secondary candidiasis and tachyphylaxis.5,9,10 Retinoids and several potent immunosuppressive agents like cyclosporine and tacrolimus have been proposed as alternatives to corticosteroids for influencing the symptoms but they all may cause adverse effects.8
is the phototherapy using various types of lasers. In patients with OLP, laser-assisted surgery (laser ablation and laser excision) and laser biomodulation (low level laser therapy - LLLT and photodynamic laser therapy - PDLT) may be applied.10

Low level laser therapy has the ability to non-thermally and non-destructively change the cell function, inducing an increase of cell metabolism and acceleration of tissue healing, without side effects. Furthermore, LLLT has anti-inflammatory potential and has been proven to reduce pain.8,10 Because of the immediate pain relief it produces LLLT has been suggested as a possible treatment for oral erosive lichen planus.

AIM

The aim of this study was to investigate the effectiveness of biomodulation with diode laser (810 nm) in patients presenting with long-standing erosive-atrophic OLP.

MATERIALS AND METHODS

Twelve patients with erosive-atrophic OLP were selected from those attending the Department of Periodontology and Oral Diseases of the Faculty of Dental Medicine, Medical University Plovdiv. The diagnosis of lichen planus was made by an oral medicine specialist based on 'a modified definition of the World Health Organization'11 and then was confirmed by histological examination where presence of a well-defined band-like zone of lymphocytes, confined to the superficial part of the connective tissue, and signs of 'liquefaction degeneration' in the basal cell layer were evident. Patients demonstrating histological signs of dysplasia, lichenoid reactions as well as those taking corticosteroids or other immunosuppressive treatment in the past month were excluded from the study. All of the lesions were symptomatic. The research protocol was approved by the ethics committee of Medical University Plovdiv. Informed consent was obtained from all participants.

Before treatment (T0) type (atrophic, erosive or bullous), site and size of the lesions were recorded. The degree of pain/discomfort was also evaluated and digital photos were taken. All twelve patients received LLLT with diode laser (810 nm) with parameters 0.5 W, 30 s, 1.2 J/cm², 3 times per week at intervals of a day for a month. To assess the effectiveness of treatment the size and clinical scores of the lesions and pain level were reevaluated after therapy (T1).

The lesion size was defined as the longest distance in mm from end to end of the atrophic and erosive areas of the OLP lesion using a periodontal probe. The severity of pain was determined using a visual analog scale (VAS) from 0 to 10 where 0 indicated no pain and 10 indicated the worst possible pain. The symptoms data were then scored according to the following classification: score 3: severe pain/discomfort (7<VAS<10); score 2: moderate pain/discomfort (3.5<VAS<7); score 1: mild pain/discomfort (0<VAS<3.5); score 0: without pain/discomfort (VAS=0)

The change in clinical signs was assessed by Thongprasom sign scoring system as follows: score 5: white striae with erosive area >1 cm²; score 4: white striae with erosive area <1 cm²; score 3: white striae with atrophic area >1 cm²; score 2: white striae with atrophic area <1 cm²; score 1: white striae only; score 0: no lesions, normal mucosa.

Treatment efficacy index (EI) was calculated, using the following formula:

\[(Total\ \text{score\ of\ the\ lesion\ before\ treatment} – \text{Total\ score\ of\ the\ lesion\ after\ treatment}) / \text{Total\ score\ of\ the\ lesion\ before\ treatment}] \times 100\%

The EI was categorized into 5 rank scale as follows: healed: EI=100%; marked improvement: 75%≤EI<100%; moderate improvement: 25%≤EI<75%; mild improvement: 0<EI<25%; no improvement: EI=0.

STATISTICAL ANALYSIS

The data were analyzed with SPSS software (11.5 Inc, Chicago, IL, USA), Excel 7.0 VB for applications and PrapPad Prism 3.0 (PrapPad, Soft, USA). A Wilcoxon matched paired test was used to determine any difference in pain and clinical scores before and after treatment. P values less than 0.05 were considered statistically significant. The data were presented as mean ± SDM, where mean is the average value and SDM is its standard deviation of the mean.

RESULTS

Eleven females and one male participated in this study. The mean age of the patients was 54.4 years (age range 24 to 73). Six patients were diagnosed with erosive form, five patients with atrophic form, and blisters were found in only one female. Most of the patients had multiple lesions where the buccal mucosa was the most common site for OLP (83.3%), followed by the gingiva (33.3%), tongue (25%), labial mucosa (16.7%) and palate (8.3%).
Lesions of the skin were diagnosed in one patient. Regarding pain scores, most patients (75%) reported severe degree of oral discomfort before treatment - VAS score 3 – three patients (25%) and VAS score 2 – six patients (50%). After therapy all patients experienced relief of their symptoms – 66% of the patients felt mild discomfort (score 1) and two patients reported no pain (score 0). The Wilcoxon matched paired test revealed that the degree of pain/discomfort decreased significantly from pretreatment to after laser therapy (p=0.0005) (Fig. 1).

The total number of the recorded lesions during the initial clinical examination was 59. 45.7% of the lesions presented as erosive destruction less or more than 1 cm², score 4 and score 5, respectively. After LLLT, improvement in clinical signs was achieved in 59.3% of the lesions (Fig. 2). According to the Thongprasom sign scoring system, at the end of the treatment 5.1% of the lesions exhibited score 5; 6.8% - score 4, 11.9% of the lesions were scored 3 and 8.5% and 30.5% showed score 2 and score 1. Complete resolution was revealed in 37.3% of the lesions (Fig. 3). According to the statistical analysis, the sign scores decreased significantly from pretreatment to after therapy (p<0.0001).

The efficacy index (EI) of LLLT was defined as the reduction in total (sign score and pain score) score of the lesions compared to the pretreatment level. All patients experienced some degree of improvement (Fig. 4). In most of the cases we found moderate recovery whereas in one patient complete remission was achieved with clinically normal mucosa and no pain.

**DISCUSSION**

OLP is a common chronic immunological disease the treatment of which remains a challenge for clinicians. In contrast to cutaneous lichen planus, which is characterized by acute onset and rapid resolution, OLP tends to persist for years. Corticosteroids are the most widely accepted treatment for OLP. However, prolonged use of this group of medication should be avoided because the suppression of the immune system increases the risk of malignancies, which in the case of erosive-atrophic OLP, which is considered a premalignant condition, would be irrelevant. This requires the introduction of alternative harmless methods for treatment.

Over the past two decades different kinds of dental lasers have been broadly investigated as a non-pharmacological treatment option for OLP patients. There are two main groups of laser therapy: laser ablation (vaporization) and laser biomodulation - that are assumed to influence different pathological processes in the pathogenesis of LP. Although the cause of the disease is unclear what is known is that CD8+ T cells induce apoptosis of basal keratinocytes of the affected epithelium. These mechanisms are triggered by expression of the putative antigen on the surface of keratinocytes at the early stages or by recognizing the body’s own peptides as foreign antigens. Use of laser ablation in the treatment of OLP is based on the fact that the activator of the immune aggression is located intra-epithelially and the removal of tunica epithelialis in order to eliminate the causal factor results in discontinuation of the self-sustaining autoimmune process. Pakfetrat et al. used CO2 laser ablation in refractory erosive-atrophic forms of OLP and reported significant reduction in subjective complaints and size - up to complete regression of lesions. On the other hand, some authors suggested that LLLT may be more effective than laser evaporation because it can modulate the immune system. A comparative evaluation of low-level laser and CO2 laser therapies was performed by Agha-Hosseini F et al. Improvements in size of lesions, in pain and clinical response scores were achieved in both groups but LLLT displayed better results than CO2.

Some advantages of LLLT are acceleration of wound healing, anti-inflammatory effects, increase in cellular metabolism, modulation of the immune system, vasodilatation and analgesic effects. Also, one of the principal goals in dentistry is to provide painless treatment for the patient. LLLT can provide a non-invasive, sterile and painless treatment. And what is more important, the concern about stimulation of the cancer cells by laser irradiation seems to be absent. However, the efficacy of this kind of therapy depends on a number of parameters such as wavelength, power, intensity, exposure time, number and sequence of sessions, and therefore is still controversial. A series of studies reported positive results in cases of OLP refractory to medication treatment after administration of ultraviolet, KTP laser (532 nm), red - 630 nm, and infrared lasers - 830 nm, 904 nm, 980 nm. In the study of Agha-Hosseini F et al. the authors applied two wavelengths, visible red (633 nm) which is transmitted through the superficial cellular layers and infra-red (890 nm) to stimulate deep cellular functions. In regards to the laser energy, a basic rule in the LLLT-knowledge notes that a low-grade dose of energy (e.g., 2 J/cm²) stimulates biologic...
processes and a high-grade dose of energy (e.g., 16 J/cm²) inhibits them.¹⁴ In our study we used diode laser (810 nm) with dose 1.2 J/cm², 3 times weekly at intervals of a day for a month.

The administration of low intensity laser radiation after prior local or systemic application of photoattractant (methylene blue, photolon, porphyrin etc) is referred to as photodynamic laser therapy. There is evidence of immunomodulating effect of this type of therapy and the ability to induce apoptosis in hyperproliferating inflammatory cells.¹⁰ Most of the photoattractants become active under the influence of red light between 630–700 nm.²² According to our previous study 810 nm wavelength had no gut absorption in methylene blue dye. Therefore we did not use a photoattractant in the selected cases.

Amongst the different clinical presentation of OLP the non-keratotic forms are associated with pain and discomfort and require treatment unlike the keratotic ones. In addition most literature sources

Figure 1. VAS score. Significant decrease in pain level from before to after laser therapy.

Figure 2. A: Erosive lesion of the buccal mucosa initial state (score 5); B: complete resolution of the lesion after LLLT (score 0).
point erosive and atrophic forms as carrying the highest malignant risk.\textsuperscript{3,4,23} In the present study six patients with erosive form, five patients with atrophic form and one patient with bullous-erosive form were included.

According to the results obtained in this study, a downward shift of the VAS score after LLLT occurred in all of the patients. At the end of the laser treatment 66% of the patients felt mild discomfort (score 1) and two patients reported no pain (score 0). This finding is consistent with outcomes of previous authors\textsuperscript{13} and is in support of the proposed theory regarding the analgesic effect of LLLT based on biostimulation. In vivo studies of the effect of low level laser irradiation on nerves supplying the oral cavity have demonstrated that LLLT decreases the firing frequency of nociceptors, with a threshold effect seen in terms of the irradiance required to exert maximal suppression.\textsuperscript{14}

Thongprasom sign scoring system showed a decrease in the percentage of lesions during the therapy. Figure 3 shows the OLP lesions showing different Thongprasom sign scores during the initial examination and at the end of the therapy. Figure 4 illustrates the efficacy index of LLLT in OLP patients.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure3.png}
\caption{OLP lesions showing different Thongprasom sign scores during the initial examination and at the end of the therapy.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure4.png}
\caption{Efficacy index of LLLT in OLP patients.}
\end{figure}
crease in lesion size and transformation of erosive to atrophic or reticular forms after LLLT. This is consistent with the effect of this irradiation in improving healing. At the end of the treatment the OLP lesions were scored as follows: score 5 – 5.1%; score 4 – 6.8%; score 3 – 11.9; score 2 – 8.5% and score 1 – 30.5% of the lesions. Complete resolution was found in 37.3% of the lesions. These results are similar to those obtained by Agha-Hosseini F et al., according to which at the 3-month follow-up, 35% of the patients showed 2 degrees of improvement, 31% - 3 degrees, 19% - 4 degrees and 15% - 5 degrees of improvement with LLLT. Furthermore, we agree with the statement of the authors that the transformation of erosive lesions to atrophic or reticular types is of valuable benefit in OLP affected patients as it can reduce painful symptoms and the risk of malignant transformation.

In order to give a numeric value to the effectiveness of the laser therapy we used efficacy index (EI). All participants in the present study experienced some degree of improvement. In most of the cases we found just moderate recovery (25%≤EI<75%) whereas in one patient complete remission was achieved with clinically normal mucosa and no pain. EI was used also by Pakfetrat A et al. to assess the effect of CO2 laser evaporation on OLP lesions. However, in the mentioned study the authors calculated the efficacy of laser treatment as the percentage of the difference between baseline and end-point sign scores of OLP lesions. Since the clinical improvement depends on the objective clinical presentation as well as on the subjective feeling of pain we proposed a modified efficacy index which in our opinion is more reliable. To the best of the authors’ knowledge, in this paper the efficacy index (EI) of LLLT was defined as the reduction in both sign score and pain score for the first time.

A limitation of the present study was the small sample size. In addition, to determine the long-term effectiveness of LLLT a longer period of surveillance after therapy would be advisable for the future studies. Another limitation is the lack of a control group. A recent systematic review failed to determine whether LLLT is more effective as compared to corticosteroids in the treatment of OLP. Hence, comparison of the effectiveness of diode laser with other non-pharmacologic approaches should also be made in future investigation.

CONCLUSION
The LLLT improved the painful symptoms and the clinical score of erosive-atrophic OLP lesions and therefore can be suggested as a useful and harmless treatment modality for that patients.

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Влияние низкоинтенсивной лазерной терапии на эрозивную атрофию oral водного лишайникового плана

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Ключевые слова: ОЛП (оральный лишайниковый план), НИЛТ (низкоинтенсивная лазерная терапия)

Введение: Эрозивная атрофическая форма орального лишайникового плана (ОЛП) проявляется сильной болью и жжением, и часто не поддаётся лечению. Местные кортикостероиды считаются предпочтительными лекарствами, но они могут вызывать нежелательные побочные эффекты. Назревает необходимость в новых формах лечения.

Цель: Целью данного исследования является изучение эффективности биомодуляции с использованием диодного лазера среди больных с длительным эрозивным атрофическим ОЛП.

Материалы и методы: В исследовании приняло участие 12 пациентов, у которых были клинически и диагностики диагностирован ОЛП. Острота боли и клинические результаты 59 поражений были установлены до начала лечения с использованием визуальной аналоговой шкалы и шкалы оценки клинического состояния Thongprasom. Все пациенты прошли низкоинтенсивную лазерную терапию (НИЛТ) с помощью диодного лазера (810 nm) с параметрами (0.5 W, 30 s, 1.2 J/cm²) три раза в неделю в течение месяца. Степень ответа оценивали в соответствии с уменьшением боли и оценкой клинического состояния по шкале Thongprasom. Был рассчитан индекс эффективности лечения.
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Результаты: После НИЛТ установлено значительное уменьшение боли (p<0.0001). Улучшение клинических признаков было достигнуто у 59.3% поражений. По окончании лечения 5.1% поражений достигли оценки 5; 6.8% - оценки 4, 11.9% поражений имели оценку 3 и 8.5% и 30.5% имели показатель, равный соответственно 2 и 1. Полное восстановление было достигнуто в 37.3% поражений. У всех пациентов было налицо улучшение в той или иной степени. В большинстве случаев достигнуто умеренное восстановление.

Заключение: Настоящие результаты показывают, что НИЛТ эффективен и безопасен в борьбе с эрозивным атрофическим ОЛП.