Review Article

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Dentistry Section

Low Level Laser as a Therapeutic Alternative in Treatment of Oral Lichen Planus- Review of Literature

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ABSTRACT

Oral Lichen Planus (OLP) is a chronic mucocutaneous disease having oral and systemic manifestations. Topical Steroids are the first line of treatment in OLP. Adjuncts like retinoids, placental extracts, immunomodulators like tacrolimus are supplemented with topical steroids for the management of unresponsive lesions of OLP before the administration of systemic corticosteroids, which has its own complications. There are reports of some lesions of OLP that become unresponsive after prolonged steroid therapy. Low Level Laser Therapy (LLLT) has been used in dentistry for a wide range of therapeutic procedures like de-pigmentation, incisions, curing of composite, frenectomy etc. LLLT has been tried and tested for management of skin lesions in psoriasis and vitiligo successfully that prompted many authors to use LLLT in the management of the oral lesions in Lichen Planus. This review aimed to evaluate the role of LLLT as a therapeutic adjunct in the management of un-responsive and/or symptomatic cases of OLP before the administration of systemic corticosteroids. It also attempts to evaluate if the use of LLLT supplemented with topical steroids can reduce the incidence of unresponsive or resistant lesions of OLP.

Keywords: Corticosteroids, Skin lesions, Therapeutic adjunct

INTRODUCTION

OLP is a T-cell mediated chronic mucocutaneous disease affecting 0.5-2.2% of population which is associated with burning sensation that undergoes periods of remission and exacerbation. Its prevalence has been reported between 1% and 18.2% with an annual malignant transformation rate of 0.27% [1].

The currently accepted protocol for the management of oral lesions in Lichen planus is to administer topical steroids as the first line of therapy. This can be done in the form of ointment as well as local injections. Topical steroids are first administered at a loading dose of 2-3 times/day for three weeks followed by a maintenance dose of 1-2 times/day for six months. Most of the reticular forms and few of the erosive/ulcerative forms of OLP respond to this treatment. The effect of topical steroids may be enhanced by the use of adjuncts. The commonly used adjuncts include retinoids, immuno-modulators like cyclosporins, tacrolimus and human placental extracts like placentrix. If the symptoms of OLP do not subside with the combination of topical steroids and adjuncts, systemic steroids are recommended, the adverse effects of which includes resistance to steroids, secondary infections like candidiasis and mucosal atrophy. One of the recently accepted management modality for the treatment of unresponsive and/or resistant cases of OLP, before administration of systemic steroids is LLLT [2,3].

Most authors have opined that oral lesions of Lichen Planus that are not responding to the conventional treatment protocols for a period of three or more months are considered unresponsive [4,5].

It is not clear as to why certain cases of OLP develop resistance to steroids. One theory suggests that a subpopulation of CD4+T-lymphocytes develop resistance to the anti-proliferative effects of steroids on prolonged use [6,7].

Some authors have also suggested that a mutation in the *p53* gene may be responsible for certain cases of OLP to become recalcitrant. An oral lesion of lichen planus that suddenly becomes unresponsive to topical steroids, after an initial responsiveness implies the potential of the lesion to harbour dysplastic features and increased malignant transformation [3,7].

Previously, LLLT was used only for treatment of lesions in Psoriasis and Vitiligo [8]. Kollner K et al., in Germany were amongst the first reported ones to use a 308 nm wavelength excimer laser for treatment of erosive OLP that was unresponsive to topical steroids in 8 patients with good results [8,9].

In 1960, Miaman TH, [10] introduced lasers in dentistry. Lasers in dentistry can be classified according to the lasing medium used, such as gas laser and solid laser; according to tissue applicability, such as hard tissue and soft tissue lasers; according to the range of wavelength etc., [11].

Hard Lasers are used for cutting both hard and soft tissues whereas soft tissue lasers are used exclusively for soft tissue. Hard tissue lasers include ER:YAG and Excimer. Soft tissue lasers include Carbon dioxide (CO_2) and Neodymium Yttrium Aluminum Garnet (Nd: YAG). Low Level Laser (LLL) is a type of soft tissue laser are based on semi-conductor diode devices [11].

LLL is a modification of surgical laser with some minor adjustments. They are as follows [Table/Fig-1] [12].

	Surgical lasers	LLLT
Power	1-5 W	10-500 mW
Diameter of tip	300-400 m	1 cm
Heat generated	Adequately high	<1C

[Table/Fig-1]: Showing the differences between surgical lasers and LLLT.

LLLT as a therapeutic modality was introduced by the work of Dr. Endre Mester (1966) and colleagues, who noted improvement in wound healing with application of a low-energy (1 J/cm^2) ruby laser. LLLT is defined by several parameters. The primary defining factor is power with a range of 10^{-3} to 10^{-1} W. Other significant parameters include a wavelength between 300 and 10,600 nm, a pulse rate of 0 (continuous) to 5,000 Hz, a pulse duration of 1 to 500 milliseconds, an inter-pulse interval of 1 to 500 milliseconds, a total irradiation time of 10 to 3,000 seconds, an intensity (power/area) of 10^{-2} to 100 W/cm^2, and a dose (power irradiation time/area irradiated) of 10^{-2} to 102 J/cm^2 [13].

The principle site of action of LLLT is at the mitochondria of the cells in the irradiated area. When LLLT is focussed over any tissue, multiple small packets of energy called Photons are absorbed by the mitochondria of the cells in the irradiated region. The activated mitochondrial enzymes cause increased proliferation of cells and also protein synthesis, which in turn controls the oxidative stress by release of several cytokines that has a twofold result- on one hand; it promotes the release of endorphin which inhibits the nociceptive receptors and produces an analgesic effect. On the other hand, these cytokines regulate the genes resulting in increased Adenosine Tri-Phosphate (ATP) synthesis that results in accelerated wound healing [14].

The cellular level changes of LLLT, clinically manifest as a tissue change that helps to bring about the desired effects in the site of irradiation. These changes are discussed in [Table/Fig-2] [5,15,16].

The tissue level effects of LLLT at various wavelengths are presented in [Table/Fig-3] [13].

Tissue/cellular level changes	Clinical outcome
Increased lymphatic flow	Reduced swelling and oedema
Stimulation of endorphins	Analgesic effect (due to inhibition of nociceptive receptors)
Reduction in conduction of C-fibres	Analgesic effect (reduced conduction of pulpal pain)
Reduction in the release of histamines, bradykinin and acetylcholine	Reduction of pain associated with inflammation
Stimulation of osteoblasts, odontoblasts and fibroblasts	Accelerated tissue healing
Increased activity of neutrophils and macrophages	Reduced post-procedural complications
Stimulation of vessels and nerve regeneration	Rapid tissue healing due to angiogenesis

[Table/Fig-2]: Showing the various cellular level changes with the respective tissue outcomes for LLLT.

Wavelengths (Nm)	Effects produced	Tissue level changes
980	Water retention	Detumescence
810	Penetrate the sub cutaneous tissues upto a depth of 5-7 cm	Pain inhibition due to decreased metabolism of painful mediators
660	Stimulate blood circulation, anti-inflammation and anti-bacterial effect	Boosting tissue repair

[Table/Fig-3]: Showing the tissue level changes at various wavelengths of LLLT.

The advantages of LLLT in the management of OLP are good patient compliance [16] as it is a non-invasive technique that leads to rapid post-operative tissue healing due to easy clot formation resulting from denaturation of proteins, increase in cellular metabolism, modulation of the immune system, reduced pain and oedema and anti-inflammatory and analgesic effects [14].

The limitations of LLLT include a delicate armamentarium, technique sensitive procedure, skilled procedure and time consuming as LLLT takes more time to achieve a greater depth [4].

In this review, the present authors have highlighted the role of LLLT in the management of symptomatic cases of OLP not responding to conventional therapy.

LITERATURE SEARCH

A literature search was done in internet explorer, Google and Google scholar using the key search words, "Laser therapy in Oral Lichen Planus" and the recent articles were chosen between 2010 and 2019. Inclusion criteria were clinical studies, systemic analyses and Randomised Control Trials (RCT) done using LLLT for symptomatic cases of OLP. The exclusion criteria were systematic reviews, review of literature, pharmacological and/or microbiological studies, studies conducted on animal models, clinical studies conducted for conditions other than OLP. A total of 7 clinical case reports and series and 7 RCTs fulfilled the inclusion criteria [8,17-29]. Most of the literature was extracted from these 14 articles [8,17-29].

DISCUSSION

Cafaro A et al., conducted a study to assess the LLLT for the management of OLP unresponsive to standard therapy. They reported a significant reduction in lesion size and in reported pain with LLLT. They concluded that LLLT could be a possible treatment option for patients with unresponsive OLP [17]. Another study was conducted by the same group of authors to assess the effectiveness of LLLT for the management of OLP unresponsive to standard topical therapy. The parameters assessed were reduction in the lesion size and pain intensity measured by Visual Analogue Scale (VAS). They concluded that LLLT can be used as a possible treatment option for unresponsive cases of OLP [18].

Jajarm H et al., conducted a study to compare the effect of LLLT with topical corticosteroids in the treatment of oral erosive and atrophic OLP. The response rate was defined based on changes in the appearance score and pain score measured by the VAS of the lesions before and after each treatment. They found that the appearance score, pain score and lesion severity was reduced in both groups. They concluded that LLLT was as effective as topical corticosteroid therapy without any adverse-effects [19]. Mahdavi O et al., reported two cases of erosive OLP who received LLLT of 630 nm wavelength and there was a significant reduction in pain and lesion size. [20]. Jajarm H et al., also used LLLT against dexamethasone mouthwash as a control. They reported a considerable decrease in the lesion size and the pain intensity in the group treated by LLLT [21].

Dillenburg CS et al., used LLLT at 660 nm wavelength on 21 patients with erosive OLP and the outcomes were evaluated at 30 and 60 days interval. Not only, there was a complete resolution of the oral lesions, the frequency of recurrence had also decreased considerably [22].

Mozafari H et al., and Hanaa and Eldin A, used LLLT at 660 nm and 970 nm wavelengths respectively and there was a significant reduction in lesion size and burning sensation of OLP compared to topical steroids. Hanaa commented that usage of LLLT at 970 nm yielded greater reduction with long term follow-up [23,24].

Elshenawy H et al., conducted a similar study with LLLT at 970 nm and concluded that it can be an effective adjunctive treatment modality for relieving pain and clinical symptoms of OLP [25]. Mutafchieva M et al., utilised the VAS to assess the reduction in pain and burning sensation of Erosive OLP. There was a greater reduction in the pain and burning sensation as compared to the lesion size. LLLT can be considered for the long term maintenance therapy of symptomatic cases of OLP [26].

The use of LLLT on paediatric patients has been a matter of considerable debate. Pedro LA et al., used LLLT in an eight-year-old female patient with OLP. Intra-operative and post-operative procedure with LLLT was much better tolerated by the paediatric patient and two years follow-up for the patient showed no recurrence of the lesion [27].

Mirza S et al., tried to assess the efficiency of LLLT and Photodynamic Therapy (PDT) against a control group that received topical steroids in the management of erosive OLP. Although the efficiency index was highest for PDT, maximum reduction in pain and burning sensation was obtained with topical dexamethasone [28]. Rezaei F et al., reported an 84% reduction in the pain, burning sensation as well as the lesion size of the experimental group treated by LLLT as compared to the control group that received only topical steroids [29].

There is no reported parameter to assess which wavelength of LLLT to be considered for symptomatic OLP. Authors have used a wide range of wavelengths (630-980 nm) for the management

of OLP. LLLT has been able to achieve the desired results of pain and lesion size reduction at almost all wavelengths except at 660 nm where decrease in the frequency of the lesions has also been reported [22].

According to Pakfetrat A et al., the mechanism behind lesion improvement in laser treatment is related to the laser power [30]. Agha-Hosseini F et al., stated that when LLLT of two wavelengths are applied, the lower wavelength LLLT stimulates the superficial layers whereas the higher wavelength LLLT stimulates the deep cellular functions [4]. Walsh LJ, pointed out that LLLT with low energy (2 J/cm^2) stimulates biologic processes and LLLT with high energy (16 J/cm^2) inhibits them [31].

OLP is characterised by sub-epithelial inflammation mediated by auto-immunity. Reticular OLP is characterised by wickham striae which is formed by an increase in the granular cell layer in the epithelium, hence high energy and wavelength LLLT should be considered as more structures have to be penetrated in reticular OLP. Erosive/ulcerative OLP is characterised by a defect in the epithelium that makes the penetration of LLLT possible at low energy and wavelength. This can be considered as a guideline to choose which parameters of LLLT to be used in OLP [32].

As mentioned previously, LLLT operates at a wide range of wavelengths and the proper dosage with the proper parameters is imperative for successful treatment outcomes. The parameters of LLLT used by various authors are depicted in [Table/Fig-4].

The case reports and the RCTs discussed in this review, highlight the recent uses of LLLT in the management of OLP. There has been a paradigm shift in the management protocols of OLP over the last few decades. There is an increasing trend among practitioners to switch to more conservative and minimally invasive modality of treatment with better result, that are better tolerated by the patients, for the symptomatic cases of OLP [26,33,34]. LLLT has the advantage of providing a non-invasive, sterile and painless treatment [26]. The success of LLLT in treating OLP can be assessed by a decrease in the pain or burning sensation and/or the lesion size or both. Many authors consider the transformation of an erosive OLP to atrophic or reticular type, a considerable improvement as the risk of malignant transformation is greatly reduced at both molecular level along with the burning sensation [26,33]

Mester E et al., conducted a study to find the correlation between laser irradiation and cancer cell stimulation. They confirmed that

Sl No.	Author's Name and Reference	Sampling/Grouping	Therapy used	Outcome measures	Results
1.	Kollner K et al., [8]	8 patients unresponsive to topical steroids	Excimer Laser at 308 nm wavelength	Lesion size, burning sensation	Improvement in both the parameters with LLLT
2.	Cafaro A et al., [17]	13 patients unresponsive to topical steroids	Diode Laser at 904 nm wavelength	Lesion size, burning sensation	Improvement in both the parameters with LLLT
3.	Jajarm H et al., [19]	Random sampling Total=30 OLP patients 15-dexamethasone mouthwash, 15-LLLT	Diode Laser at 630 nm wavelength	Lesion size, burning sensation	Same degree of reduction for both with no adverse effects
4.	Cafaro A et al., [18]	82 lesions of OLP unresponsive to topical steroids	Diode Laser at 980 nm wavelength	Lesion size, burning sensation and intensity of pain	Significant reduction in all parameters with LLLT.
5.	Mahdavi O et al., [20]	2 patients with erosive OLP	Diode Laser at 630 nm wavelength	Lesion size, burning sensation and intensity of pain.	Improvement of both the parameters with LLLT.
6.	Dillenburg CS et al., [22]	Random sampling Total=42 OLP patients 21-clobetasol propionate 0.05% 21-LLLT	Diode Laser at 660 nm wavelength	Measured at 30 and 60 days. Lesion size, recurrence, intensity of pain.	Same degree of reduction for both. At 60 days, recurrence rate more reduced for LLLT.
7.	Jajarm H et al., [21]	Random sampling Total= 25 OLP patients 15-dexamethasone mouthwash, 15-LLLT	Diode Laser at 630 nm wavelength	Lesion size, recurrence and intensity of pain.	Significant reduction in all parameters with LLLT.
8.	Mozafari H et al., [23]	Random sampling Total=50 OLP patients 25-dexamethasone mouthwash, 25-LLLT	Carbon dioxide lasers at 660 nm wavelength	Lesion size, burning and pain sensation and recurrence.	Significant reduction in all parameters with LLLT.
9.	Hanaa M et al., [24]	Random sampling Total=24 OLP patients 12-0.1% triamcinolone acetonide, 12-LLLT	Diode Laser at 970 nm wavelength	Burning sensation and intensity of pain	Initially more reduction in pain sensation with triamcinolone but on long term follow-up, more reduction of both pain and burning sensation was with LLLT.
10.	Elshenawy H et al., [25]	10 patients with erosive OLP	Diode Laser at 970 nm wavelength	Lesion size, burning sensation, remission of lesion.	Complete resolution of burning sensation, lesion size in all the patients.
11.	Mutafchieva M et al., [26]	12 patients with 59 lesions histologically diagnosed as OLP.	Diode Laser at 810 nm wavelength	Reduction in pain, burning sensation using the VAS, resolution of the lesion.	59.3% of the lesions showed improvement in the VAS whereas 37.3% lesions showed complete resolution of the lesion.
12.	Pedro LA et al., [27]	8 year old female patient with reticular OLP having multiple erosive areas.	Diode Laser at 660 nm wavelength. Total 20 sessions.	Reduction in burning sensation, lesion size and recurrence.	Complete resolution of both the parameters. 2 years follow-up revealed no evidence of recurrence.
13.	Mirza S et al., [28]	Random sampling- Total=45 patients 15=PDT 15=LLLT 15=topical dexamethasone at 0.5 mg in 5 mL water	Diode Laser at 630 nm wavelength.	Reduction in burning sensation and recurrence.	Best with topical steroids. Efficiency index highest with PDT, followed by LLLT.
14.	Rezaei F et al., [29]	Random sampling Total=50 patients 25=0.1% triamcinolone acetonide, 25=LLLT	Carbon dioxide laser at 630 nm wavelength	Burning sensation, lesion size and recurrence.	84% reduction in pain, burning sensation, recurrence and lesion size with LLLT.

[Table/Fig-4]: Showing the dosage, sampling, outcome measures and results for using LLLT in the management of OLP [8,17-29].

laser irradiation had no role in cancer cell stimulation [33]. Recently, it has been shown that the low doses of irradiation do not induce genomic instability as judged by two distinct markers for genomic integrity. There is a lack in the accumulation of DNA double strand breaks and an absence of the BRCA1 DNA damage repair molecule. These suggest that the low energy densities of LLLT can serve as a safe therapeutic strategy for unresponsive cases and long term follow-up of OLP without any risk [16].

FUTURE DIRECTIONS

Presently there is an increasing trend with the use of LLLT in clinical practise [34]. The safety in using LLLT in the oral mucosa is well established. However, the lack of homogeneous reporting of physical and biologic variables makes summarizing the results particularly complicated and inconclusive [16]. LLLT has been successfully used in a number of clinical trials and found to be quite efficient. Many authors suggest that the use of LLLT should be restricted to those clinical conditions where the potential benefits outweigh the limitations. The previous studies pointed out that, when used at optimum wavelength, LLLT in combination with topical steroids can reduce the frequency of the lesions [21-23,27-29].

CONCLUSION

Topical Corticosteroids still remain the mainstay treatment of OLP. It is recommended that if the symptomatic variants of OLP yield inadequate response to topical steroids, then LLLT should be synergistically used with topical steroids before starting systemic corticosteroids. LLLT in adjunct with topical steroids have shown satisfactory results in treating symptomatic cases of OLP, not responding to conventional therapy. There is enormous scope of LLLT in the management of OLP as the potential benefits outweigh the risks. However, proper clinical assessment and case selection is imperative for the success of LLLT in OLP.

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