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EFFICACY OF LOW LEVEL LASER THERAPY USING DIODE LASER IN THE TREATMENT OF RECURRENT APHTHOUS STOMATITIS

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ABSTRACT

Objective- To evaluate reduction in pain intensity and duration of pain relief,reduction in size of ulcer,duration for healing of ulcer (healing time) in patients with recurrent aphthous stomatitis(RAS) after application of Low Level Light Amplification by Stimulated Emission of Radiation therapy (LLLT) comparing with topical anaesthetic agent and placebo group. **Materials & Methods-** A total number of 150 individuals diagnosed as RAS were divided into three equal groups as follows: **Group 1:** Minor aphthous ulcer was treated by giving LLLT using Diode LASER; **Group 2**: Minor aphthous ulcer was treated by placebo/sham non activated LASER application.; **Group 3:** Minor aphthous ulcer was treated by local application of anaesthetic Benzocaine gel 20%. **Results-** In this randomized controlled experimental study LLLT using Diode LASER causes significant reduction in pain intensity caused by RAS hence reducing the morbidity, there is also significant improvement in reduction in the size and healing time of the ulcer as compared to Benzocaine gel 20% and placebo group. **Conclusion-** Although various treatment modalities have been used and LLLT is not commonly used to treat aphthous ulcers but this study is suggestive that using LLLT would be a safe and effective treatment modality for RAS patients.

KEYWORDS: Recurrent apthous stomatitis; LLLT; healing time.

INTRODUCTION

Recurrent aphthous stomatitis (RAS), also known as canker sores or aphthae, are frequent lesions that affect the oral cavity.[1] These ulcerations affect 5–66% of the population.[2] The lesions are characterized by recurrent bouts of single or multiple rounded, flat, painful oral ulcers.[2] Ulceration is a breach in the oral epithelium, which typically exposes nerve endings in the underlying lamina propria, resulting in pain or soreness.[3] The pain inhibits patients' abilities to eat, drink, and maintain oral hygiene.[4] RAUs typically appear with grey-white pseudomembranes surrounded by thin erythematous halos.[2] These lesions typically take occur in the non-keratinized mobile oral mucosa. The normal progression of the lesions requires 10–14 days for healing.

Oral ulcers are usually classified based on the number of lesions (single or multiple), the duration of the ulcers (acute or chronic), the presence of disease in the past (primary or recurrent). Based on the causes, a proper treatment is selected. In most cases, a symptomatic treatment (viscous lidocaine, liquid diphenhydramine, diclonine hydrochloride, benzydamine, systemic analgesia) is necessary against pain to permit nutrition, hydration and for speech. Recently LASER therapy have been used for treatment of oral ulcers.[5]

Low-level laser therapy (LLLT) is also known as 'soft laser therapy,' 'laser phototherapy' (LPT) and 'cold laser therapy'. A Light source treatment that produces a single light wavelength is Low Level Laser therapy (LLLT). It is the output power and density of the lasers which determine if the laser is a low or high-power one. If the density is less than 670mW/cm^2, the laser is called a low power one. The output power of these lasers is usually less than 250 mW. Low level lasers are usually settled in wave length of 650-1200 nm.[5]

LLLT does not effect through emitting heat, sound or vibration, but it can act via photobiologic or biostimulation which are nonthermal and photochemical reactions in the cells.[5] LASERS using red light induce powerful analgesic and anti-inflammatory effects. Healing of the ulcerations is mainly achieved by stimulating epithelial growth and angiogenesis.[3]

Based on this rationale, the present study was conducted with the aim of assessing the efficacy of LLLT in treating aphthous ulcers using a protocol developed by us especially for the purpose. We also evaluated reduction in pain intensity and duration of pain relief and healing of ulcer (healing time), reduction in size of ulcer.

Also patients with RAS after application of Low Level LASER therapy were compared with topical anaesthetic agent and placebo group.

MATERIALS AND METHODS

Subjects included in present study were selected from the outpatient Department of Oral Medicine and Radiology. The proposal for study was approved by the Institutional Ethical Committee.

A total number of 150 individuals, both males and females in the age range of 14 – 45 years, diagnosed as recurrent aphthous stomatitis on the basis of natural history and clinical features were enrolled in the study after explaining the procedure and taking informed consent of the patients. They were divided into three equal groups as follows:

Group 1: Comprised of randomly selected 50 patients of either gender in whom minor aphthous ulcer was treated by giving LLLT using Diode LASER

Group 2: Comprised of randomly selected 50 patients of either gender in whom minor aphthous ulcer was treated by placebo non activated LASER application.

Group 3: Comprised of randomly selected 50 patients of either gender in whom minor aphthous ulcer was treated by local application of anaesthetic Benzocaine gel 20%.

Inclusion criteria

1. Patients with single Minor recurrent aphthous ulcer.
2. Patients with duration of onset of ulcer of one day only when reported to department.

Exclusion criteria

1. Patients with more than one minor aphthous ulcer
2. Patients with duration of onset of ulcer of more than one day
3. Patients who have not started taking any treatment for aphthous ulcer
4. Patients with Major and Herpetiform Ulcers
5. Patient with any systemic disease causing oral ulcerations
6. Patient having other mucosal lesions, with recurrent minor aphthous ulcers
7. Pregnant and lactating mothers
8. Patients who are receiving or have received chemotherapeutic drugs, Immune-modulators or systemic corticosteroids

Case history was recorded and all the patients were informed regarding the purpose of study and were asked to sign the consent form. The pre-procedural evaluation was done for the following parameters –

1. Size of ulcer – using Williams Graduated Periodontal Probe.
2. Pain scale – using VAS.
3. Total healing time

Following this, the LASER unit was set up and the patient was comfortably seated. The treatment consisted of only one sitting. Each sitting consisted of 4 sessions of Low Level LASER application lasting about 45 seconds each with a gap of about 20 - 25 seconds between each session, for a total LASER application time of 3 minutes. The laser unit which was utilized in the current study was 'AMD Diode LASER unit - Picasso lite 3.0' The LASER unit was set at an output power of 0.5W, wavelength of 810 nm, applied in Non-Contact, Continuous (NCC) mode with a distance of 2-3mm between the LASER tip and ulcer surface. The LASER beam was applied in a continuous sweeping motion so as to cover the entire ulcer surface.

For the Placebo/Sham group, the exact same technique was followed, without actually activating the LASER beam.

For the Benzocaine group, benzocaine gel 20% was applied over the ulcer for 1 minute and patients were advised to apply it over the ulcer three times daily over next one week.

The pain and size of the ulcer were evaluated at the following times –

1. Immediately Pre Diode LASER and Benzocaine gel 20% application procedure.
2. After 20 minutes Post Diode LASER and Benzocaine gel 20% application procedure.
3. At third and sixth day follow up

After that patients were recalled on complete resolution of ulcer to calculate the duration of healing for aphthous ulcer.

The patients were asked to refrain from using any medication for ulcer treatment over the next 6 to 7 days. Also, the patients were asked to keep a record of any post procedural adverse effects such as burning sensation, pain, bleeding over the next few days.

The data was compiled and the resultant data for the size of ulcer, pain VAS score and duration of healing of aphthous ulcer for all the individuals was subjected to statistical analysis to determine the significance of LLLT using Diode LASER and Benzocaine gel 20% in treating minor aphthous ulcer. The statistical analysis was carried out with the help of SPSS Software version 16.

RESULTS

The overall age range was 14 – 45 years, of which 63 were males and 87 were females. The mean age of individuals constituting Group 1 was 28.24 years, Group 2 was 27.9 years and Group 3 was 24.9 years. Table 1.

Table 1: Mean Age and Sex distribution of the Study Groups

	No. of Individuals	Mean Age	Sex distribution	
			Males	Females
Group 1	50	28.24	21 (42%)	29 (58%)
Group 2	50	27.9	20 (40%)	30 (60%)
Group 3	50	24.9	22 (44%)	28 (56%)
Total	150	27.01	63 (42%)	87 (58%)

Size of ulcer

The mean size of ulcer with standard deviation in Group 1 on day 0, 3 and 6 was 2.00 ± 0.53, 0.88 ± 0.31 and 0.00 ± 0.00 mm respectively. In Group 2 mean size of ulcer with standard deviation on day 0, 3 and 6 was 2.15 ± 0.31, 1.13 ± 0.30 and 0.50 ± 0.00 respectively. Followed by Group 3 where the mean size of ulcer with standard deviation on day 0, 3 and 6 was 2.06 ± 0.42, 0.95 ± 0.18 and 0.29 ± 0.24 respectively. P value was significant in group 1 and was non significant in both group 2 & 3.Table 2.

Table 2: Shows Intra-Group comparison of Size of Ulcer

	Day 0	Day 3	Day 6	p value
Group 1 (Mean ± SD)	2.00 ± 0.53	0.88 ± 0.31	0.00 ± 0.00	0.001
Group 2 (Mean ± SD)	2.15 ± 0.31	1.13 ± 0.30	0.50 ± 0.00	0.12
Group 3 (Mean ± SD)	2.06 ± 0.42	0.95 ± 0.18	0.29 ± 0.24	0.08

Statically significant difference at p=0.05.
Test of significance- One way ANOVA test, SD: Standard Deviation.

On Inter-group comparison in mean size of ulcer on day 0, all the three Groups showed p value as non significant. On comparing on day 3, p value was significant between Group 1 & 2 and Group 2 & 3 but was non significant between Group 1 & 3. On day 6, all the three Groups showed p value as statistically significant. Table 3, Figure 1.

Table 3: Shows Inter-Group comparison of Size of Ulcer

	Day 0	Day 3	Day 6
Group 1 (Mean ± SD)	2.00 ± 0.53	0.88 ± 0.31	0.00 ± 0.00
Group 2 (Mean ± SD)	2.15 ± 0.31	1.13 ± 0.30	0.50 ± 0.00
Group 3 (Mean ± SD)	2.06 ± 0.42	0.95 ± 0.18	0.29 ± 0.24
p value between Group 1 & 2	0.889	0.001	0.001
p value between Group 2 & 3	0.753	0.002	0.001
p value between Group 1 & 3	0.088	0.273	0.001

Statistically significant difference at p=0.05.
Test of significance- Student t test, SD: Standard Deviation.

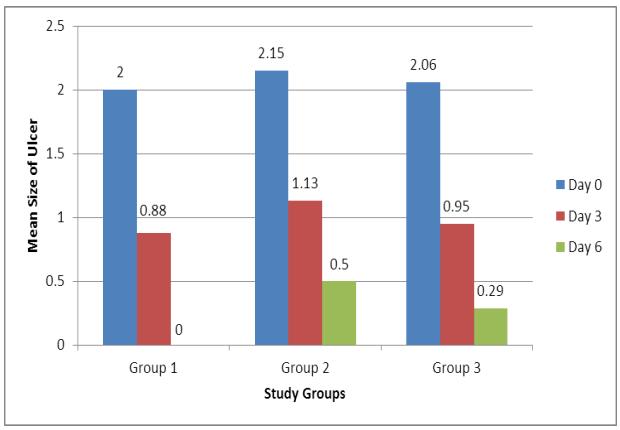

Figure 1: Compares of Mean of Size of Ulcer in all Study Groups

Pain VAS score

The mean value of Pain VAS score with standard deviation on day 0 before and after treatment in Group 1 was 6.02 ± 1.32 and 5.49 ± 0.62. In Group 2 the mean value on day 0 before and after treatment was 6.63 ± 0.49 and 6.51 ± 0.50. For Group 3 the mean was 6.67 ± 1.27 and 6.35 ± 0.90. p value was significant for both Groups 1 and 3 but was non-significant for Group 2.

Also duration of action was noted, both after Diode LASER at 0.5W in NCC mode application and Benzocaine 20% gel application. It was observed that Diode LASER at 0.5W in NCC mode application had rapid onset of 1-2 minutes and duration of pain free period after Diode LASER at 0.5W in NCC mode application was 40-50 minutes. After recurrence, pain intensity was much lesser as compared to the intensity before treatment was given. Topical application of

Benzocaine 20% gel too had a rapid onset of 1-2 minutes but duration of pain free period was only 15-20 minutes. And after recurrence, pain intensity was similar to the intensity before treatment was given but after recurrence, pain intensity was less as compared to the intensity before treatment after Diode LASER at 0.5W in NCC mode application. Patients in whom non-activated Diode LASER at 0.5W in NCC mode application was given as placebo there was only slight reduction in pain intensity after few minutes and also duration of pain free period was shortest. Table 4.

Table 4: Shows Intra-Group comparison of Pain VAS score at Day 0 - Before and After treatment is given

	Day 0 Before Treatment	Day 0 After Treatment	p value
Group 1 (Mean ± SD)	6.02 ± 1.32	5.49 ± 0.62	0.001
Group 2 (Mean ± SD)	6.63 ± 0.49	6.51 ± 0.50	0.07
Group 3 (Mean ± SD)	6.67 ± 1.27	6.35 ± 0.90	0.03

Statically significant difference at p=0.05.
Test of significance- Paired t test, SD: Standard Deviation.

The mean of Pain VAS score with standard deviation for Group 1 on day 0 before treatment, after treatment, on day 3 and day 6 was 6.02 ± 1.32, 5.49 ± 0.62, 1.5 ± 0.50 and 0.00 ± 0.00 respectively. In Group 2 the mean with standard deviation at day 0 before treatment, after treatment, on day 3 and day 6 was 6.63 ± 0.49, 6.51 ± 0.50, 2.44 ± 0.50 and 1.00 ± 0.00 respectively. For Group 3, mean of pain VAS score with standard deviation on day 0 before treatment, after treatment, on day 3 and day 6 was 6.67 ±1.27, 6.35 ± 0.90, 1.75 ± 0.50 and 0.54 ± 0.50 respectively. p value was significant in all the study groups. Table 5.

Table 5: Shows Intra-Group comparison of Pain VAS score

	Day 0 Before Treatment	Day 0 After Treatment	Day 3	Day 6	p value
Group 1 (Mean ± SD)	6.02 ± 1.32	5.49 ± 0.62	1.50 ± 0.50	0.00 ± 0.00	0.001
Group 2 (Mean ± SD)	6.63 ± 0.49	6.51 ± 0.50	2.44 ± 0.50	1.00 ± 0.00	0.002
Group 3 (Mean ± SD)	6.67 ± 1.27	6.35 ± 0.90	1.75 ± 0.50	0.54 ± 0.50	0.001

Statically significant difference at p=0.05.
Test of significance- One way ANOVA test, SD: Standard Deviation.

On Inter Group comparison of pain VAS score on day 0 before treatment, all the three Groups showed p value as non significant. On day 0 after treatment p value is significant between Group 1 & 2 but is non significant between Group 2 & 3 and Group 1 & 3. On day 3, p value is significant between Group 1 & 2 and Group 1 & 3 but is non significant between Group 2 & 3. On day 6, all the three Groups showed p value as statistically significant. Table 6, Figure 2.

Table 6: Shows Inter-Group comparison of Pain VAS score

	Day 0 Before Treatment	Day 0 After Treatment	Day 3	Day 6
Group 1 (Mean ± SD)	6.02 ± 1.32	5.49 ± 0.62	1.50 ± 0.50	0.00 ± 0.00
Group 2 (Mean ± SD)	6.63 ± 0.49	6.51 ± 0.50	2.44 ± 0.50	1.00 ± 0.00
Group 3 (Mean ± SD)	6.67 ± 1.27	6.35 ± 0.90	1.75 ± 0.50	0.54 ± 0.50
p value between Group 1 & 2	0.78	0.04	0.03	0.001
p value between Group 2 & 3	0.11	0.65	0.69	0.001
p value between Group 1 & 3	0.31	0.83	0.02	0.001

Statically significant difference at p=0.05.
Test of significance- Student t test, SD: Standard Deviation.

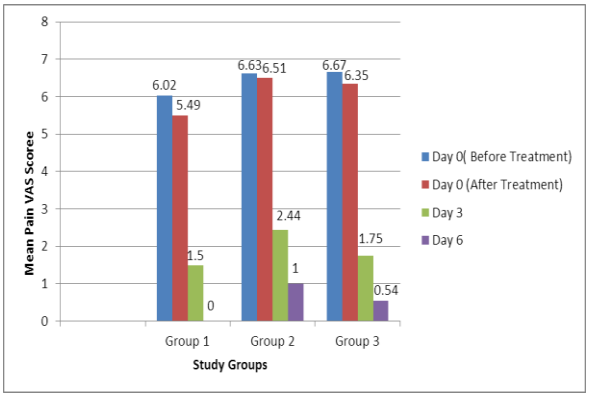

Figure 2: Compares Mean of Pain VAS Score in all Study Groups

Healing time

On comparison of duration of healing in the all three groups, the mean with standard deviation is 4.42 ± 0.49, 8.2 ± 0.70 and 6.54 ± 0.50 for Group 1, 2 and 3 respectively. The p value obtained is statistically significant. Table 7, Figure 3.

Table 7: Shows Inter-Group comparison of Duration of Healing of ulcers

	Total Days	p value
Group 1 (Mean ± SD)	4.42 ± 0.49	0.008
Group 2 (Mean ± SD)	8.2 ± 0.70	
Group 3 (Mean ± SD)	6.54 ± 0.50	

Statically significant difference at p=0.05.

Test of significance- One way ANOVA test, SD: Standard Deviation.

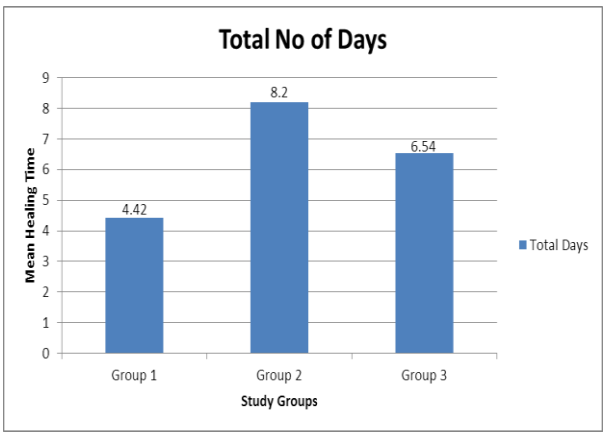

Figure 3: Compares Mean of Duration of Healing of Ulcers in all Study Groups

No adverse reactions were observed immediately post Diode LASER at 0.5W in NCC mode application.

DISCUSSION

Since the main etiology of RAS is still unknown, a definitive cure does not exist and the present treatments are aimed toward alleviating the symptoms. Some treatments have been suggested, however, such treatments are palliative, not curative. A challenge to patient management is to significantly stimulate the healing process and minimize patient discomfort, without side effects These factors necessitate the research of new methods of treatment without the use of medicines. One of the most effective methods is physical therapy using a low intensity laser radiation.

REDUCTION IN PAIN INTENSITY

In The present study, reduction in the pain intensity, VAS score was evaluated in all the Groups before and after treatment at day 0. Group 1 revealed significant (p value 0.001) reduction in pain VAS score after LASER application with mean value being 6.02 ± 1.32 and 5.49 ± 0.62 respectively. The results are in accordance with study conducted by Muhannad A. Kashmoola(2005), Hadeel Samanet al (2008), Khademi H et al (2009), De Souza TO et al(2010) who have concluded that 75% of the patients reported a reduction in pain in the same session after LASER treatment(8-11). Group 2 revealed non significant reduction in pain with mean value being 6.63 ± 0.49 and 6.51 ± 0.50, before and after treatment respectively. Whereas in Group 3, although there was reduction in pain before and after application of Benzocaine gel with mean values being 6.67 ± 1.27 and 6.35 ± 0.90 respectively but the results were not statistically significant. Also duration of action was noted, both after Diode LASER at 0.5W in NCC mode application and Benzocaine 20% gel application. It was observed that Diode LASER at 0.5W in NCC mode application had rapid onset of 1-2 minutes and duration of pain free period after Diode LASER at 0.5W in NCC mode application was 40-50 minutes. After recurrence, pain intensity was much lesser as compared to the intensity before treatment was given. Topical application of Benzocaine 20% gel too had a rapid onset of 1-2 minutes but duration of pain free period was only 15-20 minutes. And after recurrence, pain intensity was less as compared to the intensity before treatment was given but results were better after Diode LASER at 0.5W in NCC mode application. Patients in whom non-activated Diode LASER at 0.5W in NCC mode application was given as placebo there was only slight reduction in pain intensity after few minutes and also duration of pain free period was shortest.

Thus, it can be said that the reduction in pain intensity after the application of LLLT was more in comparison to Benzocaine 20% gel. Till date no such study has been performed to compare the efficacy of Local Anesthetic and Diode LASER at 0.5W in NCC mode in treatment of aphthous ulcers.

The analgesic effect of laser irradiation have been explained by many studies as the restoration of the sodium pump necessary to maintain the negative resting potential of neuronal membranes. During inflammation, the normal resting potential of nerve fiber is decreased leading to hypersensitivity. LLLT inhibits a range of nociceptive signals arising from peripheral nerves including neuronal discharges elicited by chemical irritation of inflammation because the laser light can

increase the activity of the ATP-dependant Na-K pump and in this case laser increases the potential difference across the cell membrane moving the resting potential further from the firing threshold, thus, decreasing nerve endings sensitivity.[8]

The reduction in pain VAS score showed significant results in all the 3 Groups on subsequent visits at 3rd and 6th day, but the intensity of pain in Group 1 individuals after treatment till the lesion healed was less as compared to Group 3 and was much lesser in comparison to Group 2. As RAS is self limiting disease, the principle objective behind the treatment is to reduce the morbidity associated with this disease. In the present study the goal behind treating this disease was best achieved with Diode LASER at 0.5W in NCC mode application.

REDUCTION IN SIZE OF ULCER

Minor aphthous ulcers are seldom larger than 5 mm but may be as large as 1 cm. In the present study, when the size of ulcer was measured using calibrated probe mean size of ulcer with standard deviation in Group 1 on day 0, 3 and 6 was 2.00 ± 0.53, 0.88 ± 0.31 and 0.00 ± 0.00 respectively with p value 0.001 which means that there was significant reduction in the size of the ulcer on the subsequent visits. This is in accordance with Muhannad A. Kashmoola (2005) and Hadeel Salman et al (2008) who had observed significant decrease in size of lesion.[7,8] The low energy LASER stimulates DNA-RNA-protein system and raise mitotic activity of cell. This occur through modification of cellular homeostasis of the mitochondria promoting a cascade of events in the respiratory chain of cytochromes, cytochrome oxidase and flavin dehydrogenase that permit absorption of light, that lead to increase in mitochondrial content of ATP, transmembrane potential and pH and changes in ultrastructure of organelles. These changes in mitochondria promote cell division. This results in a more rapid epithelialization and regeneration of mucous membrane in the area of the lesion.[7,8]

In Group 2 mean size of ulcer with standard deviation on day 0, 3 and 6 was 2.15 ± 0.31, 1.13 ± 0.30 and 0.50 ± 0.00 respectively with p value 0.12 which was non significant. Followed by Group 3 where the mean size of ulcer with standard deviation on day 0, 3 and 6 was 2.06 ± 0.42, 0.95 ± 0.18 and 0.29 ± 0.24 respectively. This Group showed p value as 0.08 which was non significant as locally acting symptomatic preparations can relieve symptoms. Thus, the results of present study suggest that there was decrease in size of ulcer on subsequent visits more in Group 1 followed by Group 3 and last by Group 2.

HEALING TIME

Although aphthous heals itself in 10-14 days, but still the ulcer is treated to reduce morbidity and healing time. In the present study, the mean duration of healing of lesion in Group 1 was 4.42 ± 0.49, in Group 2 was 8.2 ± 0.70 and 6.54 ± 0.50 for Group 3. The difference was statistically significant with p value 0.008 showing the ulcers treated with LASER healed in much less duration as compared to the other two Groups. The same results were obtained by Muhannad A. Kashmoola(2005), Khademi H et al (2009), De Souza TO et al(2010)[8,10,11] Although Hadeel Salmanet al (2008) were not able to find any significant change in the duration of ulcer on application of LASER.[9] The maximum time taken for healing was in Group 2.

Reduction in healing time can be due to Increased blood flow to local tissues and capillary vasodilation, after LLLT. When it is delivered in appropriate dosage, energy of the photons from the LLLT is converted into photochemical, photophysical and photobiological effects.[12] These effects include lymphocyte stimulation, activation of mast cells and increased ATP production. Also, proliferation of various types of cells such as fibroblasts and macrophages is seen. All these combined factors promote anti-inflammatory effects and biostimulatory effects, thus enhancing wound healing. In addition, reduced production of prostaglandin E2 (PGE2) and an increase in the production of basic fibroblast growth factor have been noted.[1] These effects on fibroblasts may promote wound healing. Of importance is the observation that high doses of laser power suppress both fibroblast proliferation and production of basic fibroblast growth factor.[1] Hence, the need to maintain an appropriate dose of LLLT is clear.

No adverse reactions were observed immediately post Diode LASER at 0.5W in NCC mode application.

CONCLUSION

LLLT is more effective in producing prompt and greater reduction in pain, ulcer size and duration of the apthous ulcer when compared with symptomatic treatment such as 20% benzocaine gel in this patient cohort.

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