Short Communication

Treatment of Herpes Labialis Virus by Low-Level Laser Therapy in Comparison with Acyclovir Cream

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Abstract

Background: Acyclovir is one of many medications that might help with reducing symptoms and promoting healing of labial herpes. However, only low-level laser therapy (LLLT) has been shown to have an impact on the duration of the recurrence phase. It is beneficial for the field of oral medicine to be able to perform chair-side treatment for oral soft tissue using lasers due to their small area coverage. **Objectives:** In this work, we aim to evaluate the effects of LLLT on the healing and recurrence of labial herpes simplex infections in patients. **Materials and Methods:** The study included 60 patients, who were divided into two groups: one group was treated with acyclovir cream, and the second group received LLLT at an intensity of 60 mW/cm^2, a wavelength of 830 nm, and a dose of 4.8 J/cm^2. **Results:** There was no statistically significant difference between the two groups for the first day ($P = 0.886$), but a statistically significant difference was observed during the course of the treatment. The virus counts in both groups significantly decreased on the fourth day ($P < 0.0001$), with a significantly greater reduction in the LLLT-treated group. **Conclusions:** LLLT is a safe, noninvasive, and successful treatment for labial herpes infection, with no negative effects reported. By using a low-intensity laser device, we were able to show that a total of four daily irradiations considerably reduced the effectiveness of herpes virus infection. The underlying mechanisms and the potential function of the therapy will be the main topics of future research. Larger studies are additionally required to assess the impact of the HSV type (HSV-1 against HSV-2) and various irradiation methods on the effects of laser therapy in herpes virus infection, as well as follow-up for each patient after laser treatment to determine if recurrent infection occurs.

Keywords: Acyclovir cream, herpes labialis, HSV-1, low-level laser therapy (LLLT)

Introduction

Herpes is derived from the Greek term "herpein," which is considered to be spread by creep. In the past, it was utilized for describing wounds that appear on the skin and spread slowly over time for a variety of reasons.[1] Currently, it is referred to as self-healing vesicular lesions with HSV as the primary cause. HSV is a very contagious virus that is spread by coming into touch with a bodily fluid that is infected. In the case when antibodies pass from mother to child, they lose their defense, and primary HSV infection happens.[2] When immunity is compromised, the virus reactivates in the body's nerve cells, which remains latent and continues to result in infections. Although the capability of HSV to result in infections was first demonstrated in 1919, it was discovered that adults with recurrent herpetic lesions had neutralizing antibodies against HSV in the year 1930. Herpes simplex virus-1 (HSV-1), which affects roughly 67% of the population, infects the mucosa and skin, whereas herpes simplex virus-2 (HSV-2), one of the HSV infections with two sub kinds, causes infections in the anal and genital areas.[3]

The most prevalent HSV-1 infection is recurrent herpes labialis (RHL), which typically affects the oral region.

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The cold, stress, high fever, UV light, menstruation, and trauma are immune system-weakening conditions that have a significant role in the recurrence of lesions.[4] Viral titers reach their highest within the first 24 h of lesion formation when the majority of lesions are still in the vesicle stage, and after that, gradually decline into crusts and ulcers. Before papules and erythema form, patients commonly go through a prodromal stage marked by burning, itchiness, and paresthesia. The lesions in some people are prevented or blocked before they reach the vesicle stage.[5] RHL is persistent, painful, and debilitating despite being self-limiting and benign, and it could drastically lower the quality of life, particularly during the vesicle and ulcer stages. Symptoms including burning, pain, paresthesia, and itching are seen at the lesion site prior to the lesions developing. Papules, erythema, pustules, vesicles, and ulcers are examples of lesions. Crust development, vesicle bursting, and recovery take place in 7–10 days in people with healthy immune systems who do not experience a subsequent bacterial infection. Recently, the possibility of treating herpes labialis using (LLLT) was raised.[6] The anti-inflammatory and analgesic effects of laser phototherapy also promote tissue regeneration and fibroblast growth. A coherent, collimated, monochromatic beam of light or laser is produced when an excited atom drives photon emission. This following photon is released as a result of the first photon's release from the excited atom. It's regarded as a lightweight scalpel.[7] With increasingly targeted treatments for both soft tissue and hard tissue, like photo bio-modulation and photodynamic therapy, laser technology has advanced significantly. It is advantageous for the fields of oral medicine and radiology to be able to do chair-side procedures for the treatment of oral soft tissue utilizing lasers due to the little pain, bloodless environment, and simplicity of post-operative healing.[8] In recent years, the possibility of treating herpes labialis has increased using LLLT.[9] Application of light, often using a low-power laser or LED with a power range of 10–500 mW, is known as LLLT.[10]

Since such wavelengths can penetrate soft-hard tissues and skin, light with a wavelength in red to near infra-red spectrum range of 660–905 nm is typically used.[11] Clinical research has demonstrated that the power density (irradiance), which is typically between 4.5 and 5 W/cm^2, has a positive impact on inflammation, pain, and tissue repair.

The interactions between the laser light and the biological elements (chromophores) of hard and soft tissues determine how these lasers affect oral tissues.[12] The present literature lists certain elements, such as varied wavelengths, exposure times, energy densities, and tissue composition, that could affect how well a laser interacts with the target tissue.[13]

The aim of this study was to evaluate the effect of low-level laser therapy (LLLT) on the treatment of patients with herpes labialis compared with acyclovir. LLLT significantly decreased the healing time and pain intensity compared to acyclovir and turned-off laser groups.

Materials and Methods

This work, which was conducted at a private clinic in Hilla city, lasted from July 2022 to March 2023 and involved 60 patients who had herpes simplex infections. Two groups of patients were created. The first group, which consisted of 30 patients, received acyclovir cream (15 mg) topically three times per day for at least one week. The second group, which consisted of 30 patients, used LLLT with the following settings: intensity of 60 mW/cm^2, wavelength of 830 nm, and dose of 4.8 J/cm^2. The patients were irradiated three times at a distance of 1–3 mm for 30 s.

Twenty-two of patients were so satisfied with the result after the first treatment that they did not require a second treatment. Five patients were treated twice, and the other 3 patients were treated three times. After treatment, the patients were followed daily for 4 days. The pain severity was rated by the patient on a numerical rating scale from 0 to 10. The surface area of the lesion was measured in mm^2 using a ruler. After treatment, some patients confirmed that certain symptoms no longer occurred. This indicates that the duration of the herpes infection is reduced by means of laser treatment.

Statistical analysis

The statistical analysis for all results in this study was performed using SPSS version 21. Continuous variables were expressed as mean ± standard deviation (SD) by using descriptive and frequency analysis. Cross-tabulation and *t* test was used to analyze some categorical and continuous data. The level of P value < 0.001 was regarded as statistically significant.

Ethical approval

The study was conducted in accordance with the ethical principles that originate from the Declaration of Helsinki. It was carried out with patients' verbal and analytical approval before the sample was taken. The study protocol, the subject information, and the consent form were reviewed and approved by a local ethics committee according to document number 2004 on June 19, 2022.

Results

This study enrolled 60 patients (20 males and 40 females), and two groups were created. Both groups included 30 infected patients [Table 1].

Prior to treatment, the levels of the area were 4.57 ± 2.53 mm in the laser group on the first day and 4.77 ± 2.38 mm in the acyclovir-treated group; none-the-less, there have not been any statistically significant differences between the two groups (P = 0.976). The results of the ANOVA test

revealed a statistically significant difference between the two groups during the course of treatment. On the second day, the level area 0.94 ± 0.73 mm in the laser group, while 3.62 ± 1.8 mm in acyclovir group ($P = 0.003$). Also, on the third day, the level area was 0.08 ± 0.22 mm in the laser group and 0.9 ± 1.08 mm in acyclovir ($P < 0.002$). On the fourth day, the level area was 0.00 ± 0.00 mm in the laser group and 0.00 ± 0.00 mm in the acyclovir group ($P < 0.0001$) [Table 2].

Table 1: Demographic characteristics of patients in both groups

Demographic feature	Acyclovir treated group	LLLT treated group
Age, years 23.66 ± 15.24 21.23 ± 15.46		
Mean ± SD	31.48 ± 8.12	30.5 ± 9.21
Sex, N(%)		
Male	10 (50.0%)	10 (50.0%)
Female	20 (50.0%)	20 (50.0%)
Total	30(100.0%)	30 (100.0%)

Table 2: The level of pain after treatment

Day pain level	1st day Mean ±SD	2nd day Mean ±SD	3rd day Mean ±SD	4th day Mean ±SD
Laser	4.57 ± 2.53	0.94 ± 0.73	0.08 ± 0.22	0.00 ± 0.00
Acyclovir	4.77 ± 2.38	3.62 ± 1.8	0.9 ± 1.08	0.00 ± 0.00
P value	0.995	0.003	0.0001 >	0.0001 >

Table 3: Assessment of surface area of lesion area after different treatment days

Day group	1st day Mean ± SD (mm^2)	2nd day Mean ± SD (mm^2)	3rd day Mean ± SD (mm^2)	4th day Mean ± SD (mm^2)
Laser	23.66 ± 15.24	21.23 ± 15.46	6.70 ± 13.57	0.00 ± 0.00
Acyclovir	23.71 ± 13.81	22.71 ± 13.62	20.64 ± 13.00	8.52 ± 9.00
P value	0.886	0.724	0.001	0.001

Assessment of the surface area of the lesion following various treatment days is also included in the work. On the first day, the surface area was 23.66 ± 15.24 mm^2 for the laser-treated group and 23.71 ± 13.81 mm^2 for the acyclovir-treated group. There was no statistically significant difference between the two groups ($P = 0.886$).

The results of the ANOVA test revealed a statistically significant difference between the two groups during the course of the treatment. On the second day, the surface area of the lesion was 21.23 ± 15.46 mm^2 in the laser-treated group and 22.71 ± 13.62 mm^2 in the acyclovir-treated group ($P = 0.724$). Also, on the third day, the surface area was 6.70 ± 13.57 mm^2 in the laser group and 20.64 ± 13.00 mm^2 in the acyclovir group ($P = 0.001$). On the fourth day, the surface area was 0.00 ± 0.00 mm^2 in the laser group and 8.52 ± 9.00 mm^2 in the acyclovir group ($P = 0.0010$) [Table 3 and Figure 1].

Discussion

The vast majority of reports confirm the therapeutic effects of LLLT on HSV-1 and HSV-2 infections. LLLT shortens the duration of symptoms and reduces the pain and rate of recurrence. However, The clinical effect, most likely mediated, is caused by both the activation of the sonogenetic processes in the patient's body and immune system modulation.[14] The therapeutic effects of LLLT were attributed to a number of processes. The use of laser lowers cellular oxygen consumption and increases mitochondrial ATP generation. Inflammation is reduced, and the healing process is accelerated when serotonin and endorphin levels rise, prostaglandin synthesis falls, and cytokine and growth factor expression increases.[15,16] Additionally, improved lymphatic drainage, skin blood circulation, and hyperpolarization all help to decrease edema. Based on the findings of this work and previous research, it could be said that LLLT, as opposed to acyclovir, shortens recovery times, eases pain, and speeds up the healing process.[17] In the present study, the effect of LLLT compared to acyclovir cream was evaluated in 60 patients. The mean age of patients in the acyclovir-treated

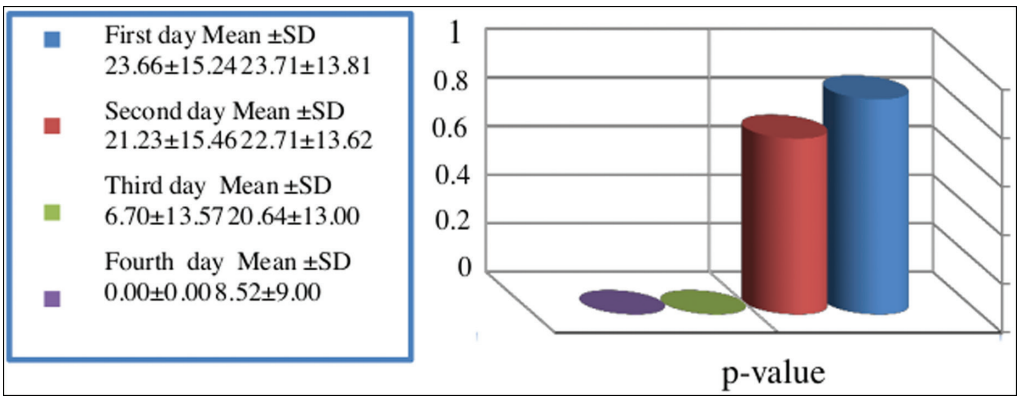

Figure 1: The lesion area in infection groups after different days of treatment LLLT

group and LLLT group was 31.48 ± 8.12 and 30.5 ± 9.21, respectively. This result was comparable to the study of Senti *et al.*, with a mean age of patients 32.6 years.[18] The sex ratio favored females (66.6%). This could be explained by the higher prevalence of labial herpes simplex infection in females.[19] The assessment of pain intensity in both groups was evaluated and showed a significant difference in pain intensity, mainly on the 4th day between the two groups. The mean pain was 0.00 ± 0.00 in the laser group and 0.00 ± 0.00 in the acyclovir group ($P < 0.0001$). The assessment of lesion area in the infection groups following various treatment days was also included in the study, and the results revealed a statistically significant difference between the two groups during the course of the treatment.

The lesion area was 21.23 ± 15.46 mm in the laser group while it was 22.71 ± 13.62 mm in the acyclovir group ($P = 0.724$) on the second day of therapy. On the fourth day, the lesion area was 0.00 ± 0.00 mm in the laser group and 8.52 ± 9.00 mm in the acyclovir group ($P = 0.0010$). The result of this study was comparable to the result demonstrated by Stona *et al.* in 2014, which evaluated the effect of low-level laser therapy for both children and adults. The laser parameters were wavelength (780 nm), power (70 mW, PD 62.5 mW/cm^2), and exposure 80 s on each of four lesions.[11,12] Moreover, Lacour *et al.* evaluated the effect of low-level light therapy with the same previous parameters and detected a mean increase in HSV latency of 4 to 37.5 weeks in a group treated with laser light, while a placebo group demonstrated a mean increase of 3 weeks.[13] In line with other works, the (LLLT) considerably reduced both pain severity and healing time in comparison with acyclovir and turned-off laser groups. In 2013, Lee and Dougal[20] evaluated the impact of a diode laser (1072 nm) on oral herpes simplex infection. According to the findings, the healing and crusting times of herpes labialis in the laser group were shorter than those of the control group.

A study by Hargate *et al.*[21] evaluated the impact of a diode laser (1072 nm) on the herpes labialis. According to the findings, the experimental group's mean crust time was 2 days, whereas the control group's was 2.88 days. For the control and experimental groups, the average healing times were 9.40 and 6.33 days, respectively. Diode lasers with a wavelength of 660 nm were used in several studies to treat herpes labialis patients who were in the vesicle stage.[22-24]

Conclusion

Through using a low-intensity laser device, the present study shows that a total of four daily irradiations considerably reduces the duration and pain severity of oral herpes virus infection compared to the use of acyclovir therapy. The clarification of the underlying mechanisms and the potential function of the therapy will be the main topics of future research. Larger studies are additionally required to assess the impact of the HSV type (HSV-1 against HSV-2) and various irradiation methods on the effects of laser therapy in herpes virus infection as well as follow-up for each patient after laser treatment to determine if recurrent infection occurs.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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