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Is Laser Therapy Effective at Relieving Pain in Adult Patients with Recurrent Aphthous Stomatitis?

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A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements For

The Degree of Master of Science

In

Health Sciences – Physician Assistant

Department of Physician Assistant Studies
Philadelphia College of Osteopathic Medicine
Philadelphia, Pennsylvania

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ABSTRACT

OBJECTIVE

The objective of this selective EBM review is to determine whether or not laser therapy is effective at relieving pain in adult patients with recurrent aphthous stomatitis.

STUDY DESIGN


DATA SOURCES

Three randomized controlled trials were obtained using PubMed.

OUTCOMES MEASURED

The symptom of pain was measured for improvement by patient survey of visual analog pain scales.

RESULTS

Prasad et al. (2013), Tezel et al. (2009), and Zand et al. (2009) all demonstrated improvement in a majority of the subjects’ pain relief from treatment with laser therapy.

CONCLUSION

Evidence to support the efficacy of laser therapy as a treatment of pain relief for recurrent aphthous stomatitis in adults is strong at this point in time, due to a relevant subject population, fixed standard of measurement, and a wide spectrum of subject age. The data strongly supports the efficacy of laser therapy as a superior method of pain relief for adult patients suffering from recurrent aphthous stomatitis.

KEY WORDS
Laser therapy and aphthous stomatitis
INTRODUCTION

Recurrent oral aphthous stomatitis is a common disorder that affects up to 25% of the population in the United States.\(^1\) The etiology behind recurrent aphthous stomatitis (RAS) is idiopathic, but it is believed there is a genetic predisposition.\(^1,2\) RAS can be classified into three clinical forms; minor recurrent aphthous stomatitis, major recurrent aphthous stomatitis, or herpetiformis.\(^3\) Minor RAS comprise the majority of cases and are involved in 80%-90% of RAS.\(^3\) Minor recurrent aphthous stomatitis are classified as being less then 1 centimeter in diameter and last anywhere from 7-14 days.\(^3\) The current theory on how these ulcers appear involves cell mediated mechanisms, although the exact immunopathogenesis is uncertain.\(^4\) RAS is routinely diagnosed based on a detailed history and physical examination. There is currently no cure for recurrent oral aphthous ulcers and there have been few investigations into treatment options. Aphthous ulcers are not overtly dangerous to one’s health, but can be quite painful, with pain usually subsiding after 4-5 days.\(^3\) This systematic review is aimed at determining whether or not laser therapy is an effective option at relieving pain in adult patients with recurrent oral stomatitis. This paper evaluates three randomized control trials comparing pain relief using laser therapy versus placebo and topical medication options for recurrent ulcers.

In the United States, there is no clear cut answer to how many individuals are affected by oral aphthous stomatitis. Since there is no known cure for RAS and because outbreaks can occur so frequently, many afflicted patients do not seek care for the pain they endure from RAS. Because of this, there is not an exact statistical number of patients that can be identified as having RAS. Estimates range anywhere from 5%-25% of the population in the United States are affected by aphthous stomatitis.\(^2,3\) By extrapolating 5% of the population in the United States, it
is estimated that upwards of ten million people are affected by recurrent aphthous stomatitis. Many afflicted patients do not seek medical care due to the lack of a cure or the fact that ulcers resolve on their own after up to two weeks of pain. Although many have spontaneous healing of ulcers within ten to fourteen days, treatment is sought by many individuals to reduce the time it takes RAS to heal and the pain that is associated with ulcerations. Reducing healing time and pain returns the patient’s ability to speak, eat, and swallow, hence improving their quality of life. Reports estimate anywhere between 5-25% of the population in the United States are affected by RAS and most common age range is between 10 to 30 years old. RAS have been reported in all races and there is a slight female predominance. Most patients with RAS are otherwise healthy and do not face an increased morbidity or mortality rate. The challenges faced with finding a precipitating event for RAS are its nonspecific histological features and a lack of ability to reproduce the causes. Predisposing factors for RAS are believed to include; oral trauma, genetic background, allergic agents, or nutritional deficiencies. RAS has been associated with deficits of vitamin B1, vitamin B2, vitamin B6, vitamin B12, folic acid, zinc, iron; Crohn’s disease, celiac disease, Behcet’s syndrome, and immunodeficiency.

Current management of Recurrent oral aphthous stomatitis is multifaceted. Currently there is no preferred management method. Numerous treatment modalities have been used to manage RAS. The current goal of therapy is to lessen the pain and duration of ulcers and to avoid local trauma that may cause them to return. Management conventionally consists of systemic medications, topical medications, or corticosteroids. Newer methods of treatment have included acupuncture, psychotherapy, and most recently laser therapy.
OBJECTIVE

The objective of this systematic review is to determine whether or not laser therapy is effective at relieving pain in adult patients with recurrent aphthous stomatitis.

METHODS

This review is comprised of three randomized controlled clinical trials that meet specific criteria for the comparison of laser therapy for pain relief in patients with recurrent aphthous ulcers. The first trial was a randomized control trial study comparing pain relief between laser therapy and a topical corticosteroid. The corticosteroid used was triamcinolone acetonide 0.1%. The second trial was a randomized control trial, single blind study, that examined the efficacy of laser therapy versus an active placebo. The third RCT single blind study also compared pain relief between laser therapy and placebo in patients with recurrent aphthous ulcers. The populations within all of these trials consisted of adults over the age of 18 who had recurrent aphthous ulcerations that had appeared within 72 hours of the study. The populations excluded from these studies were patients under the age of 18 years old, those with history of systemic disease related to RAS, or RAS that appeared more then 72 hours before the study began.

Keywords used in the research for these studies were laser therapy and aphthous stomatitis. All articles used in this research were peer-reviewed journals and were found via PubMed. Selection of the articles researched had to meet several inclusion criteria including: relevance to the proposed clinical question, publication date in the year 2000 or later, and the articles had to be presented as a patient oriented outcome studies. Exclusion criteria included articles published prior to the year 2000, articles that focused on disease oriented outcomes
versus patient oriented outcomes, or articles that included patients suffering from any other type of pain. Statistics used within these studies used p-value, confidence intervals, and standard deviation. Below, Table 1 displays the demographics and characteristics of the studies reviewed and used.

Table 1: Demographics and Characteristics of included studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Type</th>
<th># of patients</th>
<th>Age (yrs)</th>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
<th>W/D</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prasad (2013)</td>
<td>Single blind RCT</td>
<td>25</td>
<td>18-40</td>
<td>-History of RAS -2 or more RAS that presented within 3 days of study</td>
<td>-Pregnancy -History of systemic disease -traumatic ulcerations -ulcers currently being treated or CAUSED by medication</td>
<td>None</td>
<td>Single session CO₂ laser at 0.7W power for 5-8 seconds</td>
</tr>
<tr>
<td>Tezel (2009)</td>
<td>Single blind RCT</td>
<td>20</td>
<td>25-39</td>
<td>-1 to 5 ulcers that appeared within 3 days of trial -normal sense of pain</td>
<td>-pregnancy -lactation -history of hypersensitivity reaction -Ulcers caused by a systemic disease -treatment of ulcers within 1 month -Liver, kidney, or heart disease</td>
<td>None</td>
<td>ND:YAG laser operated at 2W power for 2-3 minutes</td>
</tr>
<tr>
<td>Zand (2009)</td>
<td>Single blind RCT</td>
<td>15</td>
<td>24-56</td>
<td>-History of RAS -2 or more RAS that presented within 3 days of study</td>
<td>- patient under age 12 -pregnancy -systemic disease -treatment of current ulcers -systemic treatment in the past 3 months</td>
<td>None</td>
<td>Single session CO₂ laser at 1W power for 5-10 seconds</td>
</tr>
</tbody>
</table>
OUTCOME MEASURED

All three studies measured the desired outcome of pain reduction using a 10 centimeter visual analog pain scale that ranged from 0 to 10. Participants in all studies were informed that the left most side of the scale assigned with a 0 signaled no pain or discomfort and the scale elevated sequentially to 10 on the right most side of the scale indicating the worst pain or most severe discomfort. In the Tezel study, pain was initially assessed pretreatment and then post treatment on days 1, 4, and 7. All assessments were carried out in the same clinic, in an area free of music, noise, or conversation. In the Prasad study, pain was assessed prior to treatment, immediately after treatment, and twenty-four hours post treatment. Pain was assessed in the Zand study before treatment, immediately after treatment, and post treatment at intervals of 4 hours, 8 hours, 12 hours, 24 hours, 48 hours, 72 hours, and 96 hours.

RESULTS

In all three randomly controlled trials, the efficacy of laser therapy is compared to a placebo or an alternate medication. In the Tezel study, a total of 20 patients entered the study and all patients completed the study. The exclusion parameters for this study included patients who were pregnant or breastfeeding, those with concurrent clinical conditions that could pose a health risk, those with ulcers that manifested as a result of a systemic disease process, those currently undergoing treatment for their ulcers or have used nonsteroidal anti-inflammatory drugs or antihistamines within one month of the study, and those under the age of 18 years old. The patients in this study were well matched in demographics including age, sex, medical history, baseline ulcer location, ulcer history, and number of ulcers. A randomizing table was used to split patients into two groups. The two types of therapy were allocated randomly to
patients using the randomizing table. Group 1 was treated with triamcinolone acetonide 0.1%, applied to the ulcers three times a day for one week. Group 2 was treated once using an Nd:YAG laser for 2-3 minutes. Prior to treatment, mean ulcer pain was collected and was found to be even between the two groups. Day one post treatment, the patients treated with laser therapy (group 2) saw their pain decrease drastically. By day 4, the patients in group 2 had their pain almost completely vanish. By the end of the study on day 7, patients in group 2 had no pain. Patients treated with a topical corticosteroid in group 1 also showed a decrease in pain with each recorded score, but it was not nearly as drastic a reduction as the patients in group 2. By the end of the week, both groups exhibited a statistically significant (p <0.05) decrease in pain compared to their initial presentation. This trial was safe and there were no reported adverse reactions to treatment in either group. There were no limitations to this study.

Table 2. Tezel Study: Comparison of VAS Pain Scores

<table>
<thead>
<tr>
<th>Pain</th>
<th>Group 1(topical)</th>
<th>Group 2 (laser)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before treatment</td>
<td>7.72 +/- 0.67</td>
<td>7.78 +/- 0.78</td>
<td>Not statistically significant</td>
</tr>
<tr>
<td>1 day after treatment</td>
<td>6.19 +/- 0.76</td>
<td>1.34 +/- 0.76</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>4 days after treatment</td>
<td>3.71 +/- 0.69</td>
<td>0.18 +/- 0.23</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>1 week after treatment</td>
<td>0.54 +/- 0.60</td>
<td>0</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

*Values are expressed as a group of means +/- standard deviation

In the Prasad study, 25 patients between the ages of 18 to 40 were selected for the study. All 25 patients completed the study. The exclusion parameters in this study included pregnancy, history of systemic disease, traumatic ulcers, or ulcers currently under treatment. The mean age of patients in this cohort was 27.48 years old. The patients in this study all had two aphthous
ulcers in various locations of the oral cavity. Since every person has a different pain threshold, this study had each patient serve as his or her own control. One ulcer was randomly allocated to be treated with a CO$_2$ laser for 5-8 seconds while the other ulcer was treated with a placebo laser. Patients rated their pain score for each ulcer prior to treatment, immediately after treatment, and one-day post treatment. This study was a single blind study and the patients were unaware which lesion was treated with the laser and which was treated with a placebo laser. The study showed that prior to treatment, the mean pain scores experienced in each group were 8.48+/-.71 in the ulcer that was going to be treated with laser and 8.08+/-.70 in the ulcer that was to be treated with placebo. Immediately after treatment, the ulcers treated with the laser showed vast reduction in pain 8.48+/-.71 to 0.68+/-.63, whereas the ulcers treated with the placebo laser showed almost no variability in pain reduction. This trial was safe and there were no reported adverse reactions. There were no limitations to this study.

Table 3. Prasad Study: Comparison of Pain Scores Between Laser Group and Placebo

<table>
<thead>
<tr>
<th>Group</th>
<th>Pain Before Treatment</th>
<th>Pain Immediately After treatment</th>
<th>Pain 24 hours After Treatment</th>
<th>P-Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laser</td>
<td>8.48+/-.071</td>
<td>0.68+/-.063</td>
<td>0.28+/-.054</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Placebo</td>
<td>8.08+/-.070</td>
<td>7.96+/-.084</td>
<td>No change</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Values are expressed as a group of means

The Zand study evaluated the efficacy of pain relief using a single session CO$_2$ laser compared to placebo laser on aphthous ulcers. 15 patients were used in this study, with all 15 completing the study. Each patient in the study had two aphthous ulcers and acted as his or her own control during the study. One of the two ulcers on each patient was randomly allocated to be treated with the carbon dioxide laser for 5-10 seconds, while the other ulcer was treated with a placebo laser. This study was a single blind randomized control clinical trial. Exclusion criteria
included pregnancy, any known systemic disease, or a history of receiving treatment for any ulcers in the past three months. The results of the study were expressed as a mean score +/- standard deviation. The mean age of patients participating in this cohort was 37.9 years old +/- 10.9 years, with ages ranging from 24 to 56 years old. The means of the baseline scores for pain were 6.2 +/- 1.3 and 5.4 +/- 1.3 for the laser group and placebo group respectively. There was no statistical significant difference in baseline pain between the two groups. Immediately following treatment, the laser treatment group showed a drop in pain from 5.4 +/- 1.3 to 0.07 +/- 0.3, whereas there was no change in pain reduction for the placebo group. The differences between the mean scores of pain relief were also significant at all assessments after treatment in the laser group. Pain levels in the placebo group remained static until 48 hours after treatment when the mean pain level slowly decreased to a score around 4 at the 96-hour mark. The P-score in this study was P=<0.001. This study was designed to be a single blind study, but due to the dramatic pain reduction of the ulcers treated with laser therapy, it was not possible to keep patients blind to which ulcer was treated with laser therapy versus placebo. There were no limitations to this study.
DISCUSSION

This systematic review assessed the use of laser therapy for pain relief in patients with recurrent aphthous stomatitis. Currently, laser therapy for eradication of aphthous ulceration outbreaks is not widespread, but the data reported above demonstrates laser therapy may be the leading choice for reducing pain in RAS. The results from these studies show that laser therapy is an effective and safe alternative treatment for RAS. There are no problems or adverse affects reported from using lasers for pain reduction in patients with aphthous ulcerations. There are no drug to drug interactions to worry about, or past problems with this therapy. Laser therapy is a non invasive, highly precise way to treat RAS while causing minimal disturbance to surrounding
tissue.\textsuperscript{2} The results of all three randomized control clinical trials showed that a single session of laser therapy swiftly and significantly reduces pain associated with RAS.\textsuperscript{2}

**CONCLUSION**

Laser therapy is an effective alternative for relieving pain in adult patients with recurrent aphthous stomatitis. All three studies showed evidence of rapid pain relief after therapy compared to either placebo or topical medication. Although laser therapy was not directly compared to many pain relief options used currently, laser therapy has shown to be quiet effective at relieving pain associated with recurrent aphthous stomatitis. Laser therapy has also been shown to have no concerning adverse effects noted in any of the studies reviewed.

Due to the small sample sizes and limited amount of studies, it would be beneficial to have future studies compare pain relief from laser therapy directly to pain relief from the current treatment options. Future studies should follow patients to evaluate not only pain relief from current aphthous stomatitis, but also evaluate if laser therapy is effective at reducing the amount of aphthous stomatitis that returns following laser therapy. So far, laser therapy seems to be a more effective, safer, and faster treatment at relieving pain associated with recurrent aphthous stomatitis.
References


