The Effectiveness of Low-Level Laser Therapy in Patients with Drug-Induced Hyposalivation: A Pilot Study

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Abstract

Objective: The aim of this study was to compare switched on and switched off (sham) low-level laser therapy (LLLT) in the treatment of drug-induced hyposalivation. Background Data: Hyposalivation is decreased salivary flow rate most frequently present in patients who take a lot of medication, suffer from Sjögren’s syndrome, or were irradiated. Available therapies provide only short-term relief. Materials and Methods: Forty-three participants (40 females and 3 males, average age 72.3–8.9) participated in the study. Either before therapy or after therapy, every participant fulfilled quality-of-life assessment scale (OHIP-CRO). Unstimulated and stimulated salivary flow rates were measured before and after treatment. LLLT was performed by the use of gallium-aluminum-arsenide (GaAlAs) laser (830 nm) on parotid, submandibular, and sublingual glands every day except during weekends for 14 days. Results: Significant difference in unstimulated salivary flow rate after the treatment was found in the study group (p = 0.002) compared with the sham group. No significant difference in stimulated salivary flow rate after treatment was found in the laser group (p = 0.626) nor in the sham laser group (p = 0.233). No significant difference in patient’s quality-of-life score was found after both treatments. Conclusions: The results of this study showed that the LLLT increased unstimulated salivary flow rate significantly. However, stimulated salivary flow rate did not increase significantly after the LLLT. In patients who underwent sham laser therapy, neither unstimulated nor stimulated salivary flow rate increased significantly.

Introduction

HYPOSALIVATION IS A common disturbance in patients who take a number of medications, suffer from Sjögren’s syndrome, or are irradiated. It impairs the patient’s quality of life because it is associated with difficulties in chewing, swallowing, tasting, or speaking. Further, hyposalivation influences oral health, leading to cervical caries, gingivitis, candidal infection, and salivary gland infections. The treatment is aimed at increasing the salivary flow by chewing hard food and gum, the use of systemic sialogogues, electrical stimulation, acupuncture, and the use of salivary substitutes. However, most of these therapies provide only short-term effect.

Another possible effective treatment approach of hyposalivation could be low-level laser therapy (LLLT). The low-level (gallium-aluminum-arsenide [GaAlAs] diode) laser therapy is known for its high penetration into tissues and action on mitochondrial membranes by the increase in the ATP production and reactive oxygen species, which play a significant role in cell activation. The laser photobiomodulation influences protein synthesis, growth, differentiation, and cell proliferation. Although many in vitro studies have investigated the influence of the LLLT on the action of salivary gland cells, there are only few clinical studies published so far on the effect of the LLLT on the salivary flow rate in patients with hyposalivation, yielding contradictory results.

The aim of this study was to evaluate the efficacy of the LLLT in the treatment of patients with drug-induced hyposalivation.

Materials and Methods

Selection of patients

The clinical study was conducted at the Department of Oral Medicine, School of Dental Medicine, University of Zagreb. The study protocol was approved by the Local...
Table 1. Laser Specifications

<table>
<thead>
<tr>
<th>Specification</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model</td>
<td>BTL–5000 Laser</td>
</tr>
<tr>
<td>Type</td>
<td>GaAlAs</td>
</tr>
<tr>
<td>Wavelength</td>
<td>830 nm</td>
</tr>
<tr>
<td>Repetition frequency</td>
<td>0.1–10,000 Hz</td>
</tr>
<tr>
<td>Dosage</td>
<td>0.1–100 J/cm²</td>
</tr>
<tr>
<td>Duty factor</td>
<td>5–100%</td>
</tr>
<tr>
<td>Average power</td>
<td>35 mW</td>
</tr>
<tr>
<td>Emission mode (on/off)</td>
<td>800 msec/1 msec</td>
</tr>
<tr>
<td>Fluence</td>
<td>1.60 J/cm²</td>
</tr>
<tr>
<td>Duty factor</td>
<td>80%</td>
</tr>
<tr>
<td>Exposure time (duration of treatment)</td>
<td>120 sec</td>
</tr>
<tr>
<td>Number of exposures</td>
<td>10</td>
</tr>
<tr>
<td>Delivered energy per exposure</td>
<td>4.2 J</td>
</tr>
<tr>
<td>Total exposure</td>
<td>1200 sec</td>
</tr>
<tr>
<td>Total energy of the whole treatment</td>
<td>42 J</td>
</tr>
</tbody>
</table>

GaAlAs, gallium-aluminum-arsenide.

Ethics Committee (1605/2015). Standards of the Helsinki Declaration were followed.16

The study sample consisted of 43 patients (40 females and 3 males, average age 72.3±8.9 years), who were randomly selected from a group of patients who had been referred to the Department of Oral Medicine, School of Dental Medicine, University of Zagreb, because of hyposalivation. The inclusion criteria for all patients were hyposalivation only because of drug intake. Subjects with clinical signs and symptoms of oral disease and hyposalivation because of other conditions (Sjögren syndrome) and irradiation were not included in this study. Hyposalivation was diagnosed when subjects produced less than 1 mL of the whole unstimulated saliva during the period of 5 min.17 Stimulated salivary flow rate was measured after participants rinsed their mouth and swallowed 3% citric acid solution. All selected patients signed an informed consent before undergoing the research procedure, agreeing to their participation in the study.

LLLT procedure

The participants were randomly distributed into the low-level laser study group (switched on; 28 participants) or the sham laser group (control; 15 participants). The randomization was performed by a simple method of flipping a coin after including the patient into the study. The participants did not know into which group they had been assigned.

LLLT was performed by the GaAlAs laser (BTL, Prague, Czech Republic) with wavelength of 830 nm. Laser parameters were set at average power of 35 mW, frequency of 5.2 Hz, chopped mode (switched on: 800 msec, switched off: 1 msec), fluence of 1.60 J/cm², and duty factor of 80%. Other parameters are presented in Table 1. The laser irradiation was applied bilaterally in noncontact mode on parotid, submandibular glands, and intraorally to the sublingual gland. The distance between the probe and the irradiated area was kept constant at ~5 mm throughout the treatment protocol. To cover the whole area of the glands treated, slow circulation movements were performed during the treatment. The LLLT was repeated every day except during weekends for 14 days (10 sessions). Every session lasted 20 min, 10 min per side (5 min for parotid gland and 5 min for both submandibular and sublingual glands; total 120 sec of irradiation per session).

Every participant fulfilled quality-of-life assessment scale (OHIP-CRO14) before and after either therapy.18 Unstimulated and stimulated salivary flow rates were measured before and after finishing either treatment. Participants collected saliva into calibrated test tubes for 5 min between 8 and 11 a.m. according to Wu-Wang et al.19

Statistical analysis

Normality of distribution was assessed by Kolmogorov–Smirnov test. Due to normal distribution of the variables, parametric statistics was used. Data were displayed as mean±standard deviation. Differences between groups were assessed by Student’s t-test for independent samples. Difference between before and after treatment in each group was assessed by paired samples t-test. Values lower than 0.05 (p<0.05) were considered statistically significant.

Results

Baseline characteristics of the participants are displayed in Table 2.

No significant difference in gender, age, duration, baseline salivary flow rate (both unstimulated and stimulated), and baseline quality of life was found between the groups (Table 2).

There was significant increase in unstimulated salivary flow rate after the LLLT (p=0.002). No significant difference in unstimulated salivary flow was found in the sham laser group (p=0.253; Fig. 1). No significant difference in stimulated salivary flow rate was found in the laser group (p=0.626), nor in the sham laser group (p=0.233; Fig. 2).

Table 2. Baseline Characteristics of the Participants

<table>
<thead>
<tr>
<th></th>
<th>Laser</th>
<th>Sham laser</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>Gender, N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>27 (96.4)</td>
<td>13 (86.7)</td>
<td>0.281</td>
</tr>
<tr>
<td>Male</td>
<td>1 (3.6)</td>
<td>2 (13.3)</td>
<td></td>
</tr>
<tr>
<td>Age, mean±SD</td>
<td>71.3±7.6</td>
<td>74±7</td>
<td>0.118</td>
</tr>
<tr>
<td>Duration of hyposalivation, months, mean±SD</td>
<td>14.3±11.7</td>
<td>15.5±7.1</td>
<td>0.330</td>
</tr>
<tr>
<td>Unstimulated salivary flow rate, mL/min, mean±SD</td>
<td>0.12±0.09</td>
<td>0.17±0.10</td>
<td>0.286</td>
</tr>
<tr>
<td>Stimulated salivary flow rate, mL/min, mean±SD</td>
<td>0.53±0.39</td>
<td>0.33±0.17</td>
<td>0.083</td>
</tr>
<tr>
<td>Quality of life, OHIP score</td>
<td>22.9±12.6</td>
<td>20.1±13.9</td>
<td>0.523</td>
</tr>
</tbody>
</table>

OHIP, Oral Health Impact Profile.
There was no significant difference in OHIP-CRO14 score after treatment in both the LLLT group ($p=0.064$) and the sham LLLT group ($p=0.267$; Fig. 3).

Discussion

There are only few studies published so far on the use of LLLT in patients with hyposalivation.\textsuperscript{4,13–15} Most of the studies confirmed beneficial effect of the LLLT on salivary stimulation, no matter what the cause of hyposalivation was. According to our knowledge, this is the first study comparing the efficacy of the LLLT in switched on and switched off modes on the salivary flow in drug-induced hyposalivation. The results showed that the LLLT (1.60 J/cm\textsuperscript{2}) for 10 sessions could significantly increase salivary flow in the patients. Similar results were reported by Vidović Juras et al.\textsuperscript{13} who found increased salivary secretion in patients with dry mouth after the LLLT (GaAlAs; fluence 1.8 J/cm\textsuperscript{2}) performed for 10 sessions. Baseline salivary flow rate level was on average 0.6±0.3 mL/5 min and after 10 therapy sessions it increased to 1.1±0.8 mL/5 min. In a more recent study, Lončar et al.\textsuperscript{7} evaluated the effect of the LLLT (GaAs laser, wavelength 904 nm) in patients with xerostomia free of radiotherapy and Sjögren syndrome or xerostomic drugs. They found an increase in salivary secretion from 0.05 to 0.13 mL/1 min after 10 laser sessions when using fluence of 29.5 J/cm\textsuperscript{2} per exposure (120 sec). Simões et al.\textsuperscript{20} showed that the LLLT (wavelength 780 nm; 3.8 J/cm\textsuperscript{2}) could increase the salivary secretion in patients with Sjögren’s syndrome and reduce pain and swelling of the parotid gland when applied three times a week for the period of 8 months. In another study by Simões et al.\textsuperscript{14} laser therapy (660 nm, 6 J/cm\textsuperscript{2}) was reported as beneficial in reducing the symptoms of mucositis and xerostomia in patients undergoing radiotherapy.

In a recent study by Saleh et al.,\textsuperscript{15} the LLLT (GaAlAs laser, 830 nm, 3.57 W/cm\textsuperscript{2}, 20 sec, twice a week for 6 weeks) was not able to significantly increase the salivary flow rate after treatment.
flow rate or decrease xerostomia in patients with radiotherapy-induced hyposalivation. However, improvement was noticed at the end of therapy and authors explained it with the late effects of radiotherapy on glandular structure, such as fibrosis and acinar atrophy. Finally, Campos et al. reported in their study the beneficial effect of laser phototherapy (diode laser, 660 nm, 6 J/cm, five sessions) on the improvement of oral condition (oral mucositis, xerostomia, and severe pain) in oncological patients treated with radiotherapy. According to the mentioned studies, the LLLT provides improvement in oral symptoms in patients with xerostomia of different causes.

Conclusions

The results of this study showed improvement of the unstimulated salivary flow rate after true LLLT, however, without improvement in stimulated salivary flow rate and quality-of-life scores.

Author Disclosure Statement

No competing financial interests exist.

References

LOW-LEVEL LASER THERAPY OF HYPOSALIVATION


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AU1: Please review all authors’ surnames for accurate indexing citations. Also, mention the degrees of the author “Sanja Jurišić.”

AU2: Please confirm the correctness of authors’ affiliations. Also link affiliation footnote 6 to the author group.

AU3: Please check the edit of the sentence “Either before therapy or after therapy....”

AU4: Please check the edit of the sentence “Unstimulated and stimulated salivary flow rates....”

AU5: Please check the edit of the sentence “LLLT was performed by the use of....”

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AU8: Please confirm the address of correspondence.

AU9: The value “0,1–10 000 Hz” has been changed to “0.1–10,000 Hz.” Please confirm.