Clinical Efficiency of Nd:YAG Laser in Reducing Orthodontic Pain

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Abstract
Orthodontic treatment not only improves the malocclusion, but also brings beauty and confidence to patients. However, we can’t ignore the accompanying orthodontic pain that gives rise to the inconvenience to patients. Therefore, the effective method of relieving orthodontic pain has become a hot issue recently. The present study aimed to clinically evaluate whether Low-Level Laser Therapy (LLLT) via Nd:YAG laser could reduce pain caused by orthodontic treatment. One hundred and fifty orthodontic patients who had fixed orthodontic placements in the maxillary arch for the first time were recruited. They were averagely and randomly assigned to the LLLT group, placebo group, and control group. The Nd:YAG laser irradiation was exerted to the buccal and lingual sides of the maxillary teeth of LLLT group every day for the first week. The placebo group had the laser fiber positioned into the mouth at the same areas without laser irradiation. The control group had no laser intervention. All patients received the survey to describe their pain within the period. Also, the Gingival Crevicular Fluid (GCF) was collected to measure the contents of IL-1β, TNF-α and PGE2 by ELISA. The results showed that LLLT did not affect the start of pain perception or the most painful day. However, LLLT significantly ceased the pain sooner. Also, comparing with the placebo group and control group, the patients in the LLLT group had lower mean scores for pain on each day as well as intensity of pain on the most painful day. In addition, the IL-1β, TNF-α and PGE2 levels in GCF decreased significantly by LLLT. Moreover, the patients showed better satisfaction to the LLLT treatment. These results hint us that LLLT could efficiently alleviate the pain and shorten the pain span caused by orthodontic treatment. It also could improve the patients’ acceptance to orthodontic treatment.

Keywords: Low-level laser therapy; Orthodontic treatment; Pain; Visual analog scale; Gingival crevicular fluid

Introduction
Orthodontics is to achieve the physiological reconstruction of the surrounding tissues of teeth by means of biomechanical principles, consequently resulting into the teeth displacement. It plays an important role in improving oral and overall health and achieving balance and harmony between the face and teeth for a healthy smile, which may enhance one’s self esteem. More and more people have started opting to receive orthodontic treatment in the modern society [1].

In the process of periodontal reconstruction, the periodontal membrane between teeth and alveolar bone will deform under the tension, which will hinder the blood flow in the periodontal membrane. At this time, an ischemic area will be generated in the periodontal membrane and cause anoxic state, which results in the release of certain nerve transmitters to excite nociceptors. Meanwhile, the nerve terminal in the periodontal membrane are also subjected to harmful mechanical stimulation, and mast cells in the periodontal membrane will synthesize and release chemical transmitters and enzymes related to inflammation, causing orthodontic pain [2]. The pain during the treatment process brings lots of inconveniences to patients, and even causes their difficulty in chewing and eating [3] or give up because of the intolerability [4]. This has led orthodontists to pay lots of attentions to the pain management.
In recent years, Low-Level Laser Therapy (LLLT) has been introduced into oral therapy [5-7], and has been proved to be effective in promoting a reduction in spontaneous and chewing pain after the application of orthodontic force [8]. Nd:YAG laser has been used widely because of its ability to penetrate into the tissue deeply which makes it ideal for soft-tissue procedures [9] as well as reduction in postoperative pain [10]. However, the evidence about its efficacy of alleviating orthodontic pain is still weak, and its specific prescription is also lack of research foundation.

Therefore, in this study, LLLT via pulsed Nd:YAG laser was introduced so as to clarify its clinical efficacy in relieving pain during orthodontic process, and evaluate the time pattern of orthodontic pain. Moreover, the effects of Nd:YAG laser on the expressions of proinflammatory factors and pain related substances in Gingival Crevicular Fluid (GCF) of orthodontic patients were investigated.

**Materials and Methods**

**Study population**

One hundred and fifty orthodontic patients (88 males and 72 females, 21.7 ± 3.2 years) wearing maxillary arch wire for the first time were selected from the Department of Orthodontics, School of Stomatology, the Fourth Military Medical University (2016.12-2019.04). The inclusion criteria were as follows: Good physical condition without any systemic diseases, permanent teeth with completely erupted second molar, malocclusion is characterized by mild to moderate crowding with good periodontal health, no previous orthodontic treatment, and no use of any medication. All patients were treated with standard MBT straight wire technique without extraction, and had their fixed orthodontic appliances placed in maxillary arch from the left first molar to the right first molar with 0.014-inch nickel-titanium arch wire. This aligning arch was fully engaged with elastomeric ties and was bent according to the crowding to be as inactive as possible. All the patients were randomly divided into LLLT group (21.5 ± 3.5 years, n=50), placebo group (21.4 ± 3.3 years, n=50) and control group (22.3 ± 2.1 years, n=50). The patients were informed about the risks and benefits of the procedures performed, and informed consent was obtained from each patient or parent (for patients less than 18 years old) for laser irradiation. This study was approved by the Ethics Committee of School of Stomatology, the Fourth Military Medical University, and the experiments were performed in accordance with the Declaration of Helsinki for humans.

**Laser performance**

The LLLT patients received 1,064 nm Nd:YAG laser (Fotona, Slovenia) irradiation immediately after wearing the orthodontic arch wire for the first time. The LLLT was performed every day for the first week. The laser fiber was applied to six areas of the maxillary canines, i.e. the mucosa overlying the cervical third, middle third and apical third of the root on the buccal and lingual side. Each area was exposed to LLLT for 20s. Patients in the placebo group received the treatment with the laser fiber on the corresponding mucosa of the maxillary teeth for the same amount of time without activating the laser. The control group did not receive laser treatment. Protection glasses provided by the manufacturer were worn by both the operators and the patients.

**Determination of IL-1β, TNF-α and PGE2 in gingival crevicular fluid**

Before collecting the GCF, the supragingival plaque around the teeth was removed carefully without touching the marginal gingiva, and the crevicular site was gently washed with water and dried with an air syringe. GCF was collected at four time points, i.e. day 0, day 1, day 2 and day 7, from the mesiobuccal-palatal, distobuccal-palatal areas of the maxillary canine [11] with Periopaper® strips (ProFlow Inc., Amityville, New York, USA). Care was taken to avoid mechanical injury to the periodontal tissue. Strips contaminated with blood or exudates were discarded. Immediately after collection, two millimeters of the wetted area of the strips were cut and transferred to microcentrifuge tubes. All strips were stored at -80°C until further biochemical analysis. The levels of Interleukin-1β (IL-1β), Tumor Necrosis Factor-α (TNF-α), and Prostaglandin E2 (PGE2) in GCF were determined by Enzyme-Linked Immunosorbent Assay (ELISA, Jingmei Biotechnology, Beijing, China) specific for each compound. The assays were carried out in accordance with the manufacturer’s instructions, and the levels of the biochemical compounds were reported as the total amount (ng/ml).

**Orthodontic pain assessment and satisfaction evaluation**

All patients were instructed to complete a survey over the next 7 days, and they were told to not take any analgesics. The pain onset time, the occurrence time of the most severe pain, the pain offset time, and the pain duration were recorded. Additionally, the pain score on the most painful day and the pain score of each day during the observation time were evaluated by a 10 cm Visual Analog Scale (VAS) [12], with 0 for painlessness and 10 for excruciating pain. The patient was asked to mark the appropriate scale on the ruler that represented his pain level. Finally, each patient was asked to report his/her feeling, i.e. very satisfied, satisfaction, somewhat satisfied and dissatisfaction, to the operator. This trial was conducted in a double-blind manner. All patients were not aware which group they were randomly assigned to, and the evaluator was not clear about the meanings of the data and scores recorded in the study.

**Statistical analysis**

All the data were analyzed with SPSS 17.0 software (SPSS Inc., Chicago, IL, USA). The chi-square test was used to test the consistency of gender and degree of malocclusion, and one-way Analysis of Variance (ANOVA) was used to test the age consistency of patients, respectively. The homogeneity of variance of all the recorded data was tested by the Bartlett test. The results of measurement data were expressed as the mean ± Standard Deviation (SD), and the LSD test was used for comparison among the groups, while the results of counting data were expressed by rate (%), and comparison among groups was conducted by the χ² test. The statistical significance was set at p<0.05.

**Results**

**Pain temporal sequence**

The pain temporal sequence was shown in Table 1. There were no statistical differences for the pain onset time and the occurrence time of the most severe pain among the three groups (p>0.05). Compared with the placebo group and the control group, the pain of LLLT group disappeared earlier (p<0.05), and LLLT significantly shortened the pain duration (p<0.05).

**The alterations of pain scores**

The alterations of pain scores were shown in Table 2. The pain scores of the patients in either group showed a similar trend of rapid increase followed by gradual decrease during the observation period. Specifically, the pain score peaked on the second day, and gradually
decreased over time until zero on day 7. In addition, except for day 7, the pain scores of LLLT group patients at all-time points were significantly lower than those of placebo group (p<0.05) and control group (p<0.05). The pain score on the most painful day in the LLLT patients was 3.29 ± 1.04, which was significantly different from that of the placebo group (7.23 ± 2.01) and the control group (7.44 ± 1.57) (p<0.05). The alterations of the mean pain score within the observation period.

<table>
<thead>
<tr>
<th>Group</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
<th>Day 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>3.10 ± 1.51</td>
<td>6.14 ± 1.33*</td>
<td>2.04 ± 1.02</td>
<td>5.54 ± 1.24*</td>
<td>0.44 ± 0.62*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>3.07 ± 1.45</td>
<td>5.97 ± 1.31*</td>
<td>2.21 ± 1.32</td>
<td>5.76 ± 1.28*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LLLT</td>
<td>2.98 ± 1.23</td>
<td>4.01 ± 1.25</td>
<td>2.18 ± 1.16</td>
<td>3.39 ± 1.12*</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*p<0.05; vs. LLLT group

Table 2: The alterations of the mean pain score within the observation period.

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
<th>Day 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>5.46 ± 1.75*</td>
<td>7.24 ± 1.45</td>
<td>5.36 ± 1.51*</td>
<td>4.73 ± 1.11*</td>
<td>3.23 ± 1.11*</td>
<td>1.54 ± 1.20*</td>
</tr>
<tr>
<td>Placebo</td>
<td>5.23 ± 1.57*</td>
<td>7.47 ± 2.48*</td>
<td>5.67 ± 1.55*</td>
<td>4.85 ± 2.10*</td>
<td>3.36 ± 1.45*</td>
<td>1.46 ± 1.04*</td>
</tr>
<tr>
<td>LLLT</td>
<td>2.78 ± 1.02</td>
<td>3.58 ± 1.29</td>
<td>2.82 ± 1.06</td>
<td>1.22±0.35</td>
<td>0.84 ± 0.61</td>
<td>0.53 ± 0.23</td>
</tr>
</tbody>
</table>

*p<0.05; vs. LLLT group

Table 3: The IL-1β, TNF-α and PGE2 levels in GCF (ng/ml).

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-1β</td>
<td>33.24 ± 8.84</td>
<td>83.11 ± 8.49*</td>
<td>86.57 ± 7.74*</td>
<td>59.88 ± 5.37*</td>
</tr>
<tr>
<td>TNF-α</td>
<td>10.97 ± 3.28</td>
<td>39.87 ± 6.01*</td>
<td>41.07 ± 8.05*</td>
<td>27.55 ± 4.00*</td>
</tr>
<tr>
<td>PGE2</td>
<td>104.28 ± 9.58</td>
<td>114.15 ± 19.33*</td>
<td>108.58 ± 10.64*</td>
<td>89.77 ± 9.62*</td>
</tr>
</tbody>
</table>

*p<0.05; vs. baseline; # p<0.05; vs. LLLT group

Table 4: The satisfaction comparison among groups (Rate (N)).

<table>
<thead>
<tr>
<th>Satisfaction</th>
<th>Group</th>
<th>Very satisfied</th>
<th>Satisfied</th>
<th>Somewhat satisfied</th>
<th>Dissatisfied</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LLLT</td>
<td>84% (42)</td>
<td>10% (5)</td>
<td>6% (3)</td>
<td>0% (0)</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>12% (6) *</td>
<td>28% (14) *</td>
<td>40% (20) *</td>
<td>20% (10) *</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>10% (5) *</td>
<td>26% (13) *</td>
<td>50% (25) *</td>
<td>14% (7) *</td>
</tr>
</tbody>
</table>

*p<0.05; vs. LLLT group

The IL-1β, TNF-α and PGE2 levels in GCF

As shown in Table 3, we found that the contents of IL-1β, TNF-α and PGE2 increased rapidly on day 1 or day 2 compared with the baseline (p<0.05), and then declined on day 7 but still was higher than the baseline data (p<0.05). No obvious differences between each group and occurred on the second day. In our study, we also showed that the onset time of the most severe pain was similar in different clinical treatment measures and included cases. Our results confirmed that the proinflammatory factors (IL-1β and TNF-α) in the normal state [13]. From the biological effect perspective, laser has been gradually favored by clinicians in recent years because it does not cause irreversible damage to biological tissue. Studies have confirmed that lasers with wavelength of 600 nm ~ 1200 nm are often used in biomedical treatment as it exerts optimal tissue permeability [14,15]. The pulsed Nd:YAG laser in this study has a wavelength of 1,024 nm, which has strong penetration ability, and is often used for alleviating pain of recurrent oral ulcer pain and myofascial pain [5,6]. Scholars have reported that the LLLT action time of each tooth position should be 2 min to 3 min in order to achieve the therapeutic effect [16]. The laser irradiation used in our study was conducted in 6 areas for maxillary canines, and each canine received laser irradiation for 2 min accumulatively, so as to achieve the experimental purpose.

Earlier clinical studies [17,18] demonstrated no difference in the onset time of initial pain in the orthodontic patients, whether LLLT was applied or not. However, some researchers believe that the application of LLLT can effectively delay the onset time of pain during the orthodontic process [16,19]. The contradiction may be related to different clinical treatment measures and included cases. Our results showed that the onset time of the most severe pain was similar in each group and occurred on the second day. In our study, we also confirmed that the proinflammatory factors (IL-1β and TNF-α) in...
GCF reached their highest level on day 1 or day 2. It was similar with the report by Ngan et al. who found the most severe inflammatory symptoms between 24 h and 48 h after orthodontic arch filaments [20]. Meanwhile, the content of PGE2 increased obviously on day 2 on which the most severe pain occurred. We supposed that the elevated IL-1β and TNF-α level were due to increased osteoclastic activity in the same region [21], and the pain of patients is related to the local inflammatory response and the release of pain related substances after orthodontic treatment [22].

Based on the statistical results, we also observed that the offset time of orthodontic pain in LLLT group was significantly earlier after the application of pulse Nd:YAG laser for LLLT, thus shortening the duration of orthodontic pain from 5 days to 3 days. In addition, according to the VAS evaluation, the pain scores at each time point as well as the pain scores at the most painful time of the LLLT group were lower, hinting us the effectiveness of LLLT in alleviating the pain caused by orthodontics. Therefore, it is not difficult to notice that LLLT can effectively control orthodontic pain. In fact, satisfaction surveys have shown that patients are more likely to use LLLT to alleviate the discomfort caused by orthodontic treatment.

LLLT has the advantages of no adverse reaction, low output energy and no local temperature rise [23]. LLLT can activate local microcirculation and cell metabolism, promote the release of endorphins, and thus achieve the same analgesic effect as anti-inflammatory and anti-pyretic drugs [13]. It has been reported that low intensity laser has strong biological effect, which could change the blood circulation in periodontal tissue and the permeability of tissue sensor membrane, lead to the bioelectricity alteration, and decreased levels of tissue endorphin and 5-hydroxytryptamine, thereby increase the threshold of pain and relieve the pain correspondingly [24]. At the same time, LLLT can accelerate the blood flow and increase the number of new blood vessels. Sonesson [25] studied the molecular mechanism of LLLT to reduce the pain of experimental tooth movement through animal experiments, and found that the mechanism may be a combination of multiple effects, includes inhibiting the release of local inflammatory factors, promoting vascular remodeling, improving blood supply, inhibiting the release of pain-causing neurotransmitters, promoting the release of endogenous analgesic neurotransmitters, and affecting ion channels.

**Conclusion**

In conclusion, this study shows that LLLT can effectively reduce the incidence of orthodontic pain, shorten the duration of orthodontic pain, relieve pain intensity, decrease the expressions of proinflammatory factors and pain related substance, and improve orthodontic patients’ satisfaction. In the future, we will further expand the sample size to refine the age range of patients, and compare the efficacy of different types of low intensity laser in alleviating orthodontic pain, so as to deepen the knowledge of the underling mechanism of relieving orthodontic pain by laser.

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**References**


