Title:

Pain in fixed orthodontic treatment. Role of photobiomodulation: dream or reality?

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Abstract:

Pain is an unpleasant emotional and sensory experience. For many years orthodontists have been looking for an effective method of reducing this feeling of discomfort. In recent years, low-level laser therapy (LLLT) has taken hold in the orthodontic field. Among the countless advantages it can modulate the painful feeling. The aim of this research is to identify the use of photobiomodulation in subjects undergoing fixed orthodontic treatment, to reduce the pain and discomfort that it causes. The research was conducted from the Web of Science, Pubmed and Scopus databases. Only 14 of all articles met the inclusion and exclusion criteria and were therefore used to conduct the research. The different studies compared, in most cases, patients whose mouth was divided into a part treated with laser therapy and a placebo part. The results show a statistically significant difference in perceived pain between the irradiated arch and the non-irradiated arch. Three authors didn't find statistically significant results in favour of low-laser therapy, but it is important to remember that they used different parameters. To obtain generally valid studies, with consistent and reproducible results, it is necessary to standardize the different parameters used that are independent by operator performing the procedure.

Keywords: Photobiomodulation, Low-level laser therapy, Pain, Orthodontic treatment.

INTRODUCTION

Pain is an unpleasant emotional and sensory experience. It is known that it is one of the negative aspects of a fixed orthodontic treatment. It is perceived as discomfort, dull pain, hypersensitivity in affected teeth [1,2] and it is present in most procedures: separator placement, banding, initial wire engagement, wearing elastics and debonding [3,4,5].
About 90% of patients undergoing orthodontic treatment experience the painful sensation [6] and, according to O'Connor, it is considered the fourth most frequent reason for apprehension and fear in patients who need to start any fixed treatment [7].
For the patient, the pain associated with orthodontic appliance is a real problem since it interferes with chewing performance and speech [8].
For many years orthodontists have been looking for an effective method of reducing this feeling of discomfort perceived by their patients because it is often determined to continue or not the therapy [9].
In recent years, low-level laser therapy (LLLT) has taken hold in the orthodontic field for the countless advantages it brings: it can, induce the activation and proliferation of osteoblasts and osteoclasts, accelerating the remodelling of bone, increasing the velocity of orthodontic tooth movement [10,11,12] and the efficiency of orthodontic treatment during dental alignment [13]; it can also be used to enhance keratin synthesis [14,15], in case of hypersensitivity, analgesia and inflammatory processes in periodontal tissues [16], but above all it can modulate the painful feeling as a non-invasive, non-thermal and inexpensive technique without significant adverse effects [17,18].
The analgesic and anti-inflammatory properties of LLLT are attributed to increased blood flow, decreased levels of prostaglandin E2 and inhibiting COX-2 enzyme secretion [19,20].
The aim of this research is to identify in literature the use of photobiomodulation in subjects undergoing fixed orthodontic treatment, to reduce the painful perception and discomfort that it causes.

MATERIALS AND METHODS

The research was conducted from the Web of Science, Pubmed and Scopus databases. Hand-searching was not performed.
Keywords used were “photobiomodulation”, “laser”, “orthodontic”, “dental movement”, “tooth movement” and “pain”.
Inclusion and exclusion criteria were determined prior to reading the retrieved abstracts.

Inclusion criteria were as follows:
- Articles published in the last 10 years,
- Studies published in English language,
- Studies conducted on human species,
- Participants that underwent fixed orthodontic treatment without limitation in gender, age, race and social economic status,
- Randomized clinical trials which analysed the effectiveness of LLLT in reducing orthodontic pain compared with placebo group (simulated pain treatment) and/or a control group (no treatment of any kind),
- Studies that used the analogue visual scale (SEA), the numerical scale of evaluation or another type of questionnaire to evaluate the duration and intensity of pain.

Exclusion criteria were as follows:
- Articles not written in English language,
- Studies were cases or letter reports, review articles, cohort studies, opinion articles, abstract and descriptive,
- Studies in vitro studies or animal,

- Participants had pain caused by acute or chronic dental, periodontal or gum disorders,
- Studies of patients compromised by neurological and psychiatric disorders, systemic diseases or chronic pain,
- Participants not subjected to fixed orthodontic treatment such as studies on orthodontic elastomeric separation or similar.

The articles found in the search were selected based on the relevance of their abstract, title and keywords. Publications addressing questions which seemed relevant to the specifications of the problem, were read in full and either included for further analysis or excluded.

RESULTS

321 results have been identified through database searching: 164 on Web of Science, 71 on Pubmed and 86 on Scopus. The filters "last 10 years" and "human species" have been applied, finding the following articles: 136 on Web of Science, 52 on Pubmed and 63 on Scopus. After excluding duplicates and reviewing titles and abstracts, 52 articles were evaluated in full text.
Only 14 of all articles met the inclusion and exclusion criteria and were therefore used to conduct the research.
The selected studies that evaluated the effectiveness of LLLT for orthodontic pain used different parameters, such as wavelength, power output, energy dose, exposure duration, focal spot area, power density, energy density, and frequency of treatment.
Moreover, the subjects examined differ in age, sex, cultural difference, malocclusion and more.
Table 1 shows the different parameters of each study.

DISCUSSION

For years orthodontic treatment has been accompanied by pain and this concept is considered natural and negligible compared to possible problems such as prolonged treatment time, periodontal problems and root resorption [21].
To date, more and more orthodontists are looking for a way to relieve patients' pain. There are several ways to decrease this discomfort such as using drugs, chewing plastic wafers or gum, a diet of softer foods, vibratory and transcutaneous electrical stimulation [22,23].
LLLT is one of the latest methods to relieve orthodontic pain.
Although the mechanisms of action are not yet clear [16], low-laser therapy has been shown to have neural and anti-inflammatory periodontal regenerative properties. The use of diode laser in a continuous wave can produce a significant pain reduction after tooth movement in the first three days [24,25].

Orthodontic treatment:
In this research, studies using elastomeric separators or bands [26], maxillary orthodontic expansion [27,28], invisible removal aligners [29,30] or agenesis cases [31] were excluded because the forces used and the perception of pain could be very different from a fixed orthodontic treatment.
On the contrary, all studies of patients with each fixed orthodontic treatment have been included.
In one of these studies, patients treated by straight-wire technique with Equilibrium brackets (Dentaurum, Ispringen, Ger many) or with In-Ovation C (GAC/Dentsply, Tokyo, Japan) self-ligating brackets [32] were compared. The results show that there is not a significant difference of average pain between bracket groups during the first week of active orthodontic treatment ($p > 0.05$) [33].
The level of dental crowding of treated patients was also not the same. Some patients had slight crowding [34] or level up to 5 mm [33]. Other subjects had 3-5 mm maxillary dental crowding [21,35].

In the study of Lo Giudice et al. 90 subjects were divided into three groups with different crowding: mild (3-5 mm), moderate (5-7 mm), and severe (>7 mm). Authors didn't find differences in the pain perceived among examined patients with mild, moderate and severe mandibular anterior crowding. However, there is no specific indication for the usage of LLLT according to the amount of crowding [36].
But not only that, in some treatments the subjects were subjected to bilateral extraction of the first upper premolars and retraction of the canines to correct protrusion and dental crowding. This means that greater forces have been used to get more displacement of some teeth, using springs and to obtain a good posterior anchorage transpalatal bars, banding and Nance button were used [35,37,38,39,40,41,42,43,44].

Laser procedures:
In most studies, the procedure was carried out in an isolated room, using protective glasses for the operator, patient and dental assistant [39]. To confuse the patient and allow the placebo effect, the non-irradiated side was treated in the same way but with the machine turned off. To prevent the perception of the beeping emitted by the laser, music was played at a high volume [39,41].
So patients could not distinguish the placebo and experimental sides [37].
An article indicates a beneficial effect even on the side not treated with lasers, indicating that there is a generalized effect within the trigeminal system. However, there have been no effects on extra-trigeminal sensitivity. The authors hypothesize that LLLT may have reduced peripheral sensitization of Aδ fibers and C-related nerve fibers [34].
One of the effects of laser therapy with split mouth is the probability of carry-across effects of the laser beam from one side to the other [45]. Many authors used a plastic shield like a barrier at the midline to limit the laser beam's penetration and, perchance, alter the results [39,41].
The lasers used had different type, wavelength and power. The irradiated dosimetry, energy density, timing, points on each side and number of monthly applications were also not the same. For example, in one of this studies, patients were first subjected to the alignment and leveling stages with nickel titanium archwires, then when the canine retraction began, with 0.018-in-stainless steel wires, laser therapy was used [37].
In the Domìnguez and Velàsquez study laser treatment was carried out during the final stage of orthodontic treatment, when stainless steel archwires 0.019x0.025 inch are used [33]. These results, in addition to the other studies, make us think that LLLT is effective in modulating painful sensation at all stages of orthodontic treatment.
Or a 3-week low-laser therapy model can be convenient in clinical practice as it coincides with conventional orthodontic appointments [39].

Dosages and ways of energy distribution:
Low-level laser therapy usually uses the following parameters: a power density between 5 and 150 mW x cm-2, red and NIR wavelength range of 600-1000 nanometers, applied for 30 to 60s per point. The resulting therapeutic effect depends on energy density measured in joules (J) per cm2 [46,47].
The effects of LLLT depend upon the different tissues, cell type, irradiation parameters, time of exposure and redox state of the cell [48].
There is a biphasic dose response which underlines the existence of optimal irradiation and dose parameters.
To make laser therapy effective, the parameters need to be within the biostimulatory dose windows [49].
It is important to remember a higher dosage than optimal can have negative therapeutic outcomes, on the contrary, a lower dosage than the optimal value might have a diminished effect [50].
For the success of the treatment are necessary in particular the wavelength and energy (in J), energy density (J/cm2), but also the original power, power density and duration parameters [49,51].

In the studies examined in this research the wavelength is between 632 and 980 nm, the energy varies between 0.7 and 400 mW and the total energy is not indicated in all studies. All studies indicating the amount of energy are within the efficacy window. These different protocols make it difficult to compare and quantify the beneficial effects on patients [52].

Statistically significant results:
The different studies compared, in most cases, patients whose mouth was divided into a part treated with laser therapy and a placebo part. The results show a statistically significant difference in perceived pain between the irradiated arch and the non-irradiated arch [33,34,41,44].
In Sobouti et al. study, LLLT contributed to about 12.1 % reduction of painful sensation in the laser side compared with the matched placebo side [37].
Another study shows that the irradiated side had a significant reduction in the average range of dental pain at 3, 7, and 14 days after laser treatment [38,42].
In the study of Dominguez et al. results show that the highest pain intensity takes place at the first 48 h in treatmented side and not, then a slight pain reduction in the laser group was observed [40].
In study of Alam et al. all patients are randomly divided into 4 groups: LLLT + self-ligating bracket, LLLT + conventional bracket, non-LLLT + self-ligating bracket, and non-LLLT + conventional bracket function. Authors revealed LLLT + self-ligating results as the best and LLLT + conventional as the 2nd best in lessened pain perception [53].
In another study, a statistically significant difference between the placebo/control groups and the irradiated group was found. In the first case the peak of pain appeared on the 2nd day ending around day 6-7. In the second case the peak of pain came after 6 hours and disappeared on day 4, patients then found a reduced duration of pain [36].
In three studies the results do not show a statistically significant difference for relieving orthodontic pain sensation following the use of laser therapy [21,43,35].
In study of AlSyed et al, however, the mean pain scores found in the laser group were less than those of the placebo group in all studied time points. This indicates some clinical efficiency of LLL despite the absence of statistical significance [35].

Appearance of pain:
All articles used for this research agree on the onset of pain in about 2-4 hours after the arch wire was activated insertion, up to a peak at 24 hours. Then the painful sensation decreases and disappears within 7 days [21,33,34,39,41]. In according to Koritsanszky et al. [52].

Age and sex difference:
It is known that pain perception can be affected by different individual parameters, such as age, sex, pain threshold, magnitude of the applied force, emotional status, cultural differences, and previous pain experiences [53,54,55].
In several studies, however, no significant difference was found in the pain sensation between males and females, nor between adolescents and adults [39,41].
The inclusion of both genders and different ages favor the generalizability, but it is also important to remember that the most sensitive age might be between 13 and 16 years old [6].
Since, in these split-mouth designs each patient was matched with himself/herself, such variations in the subject's demographics less confound the results [37].

Different method of measuring pain:
The recording of the painful sensation was done with different parameters. Some studies have used the Visual Analogue Scale (VAS). It is a widely accepted method for measuring and showing differences in pain

reported by patients, it is reliable, understandable by patients, sensitive, and reproducible. Although it is a subjective method, it is one of the best methods because of its reliability in scoring pain in different time points when a big difference among participants is expected [56,57].
Other articles used a questionnaire based on a numeric rating scale (NRS) of evaluation to investigate the effects of laser therapy on pain sensation. It is highly correlated with VAS [58]. This choice was also made to allow younger patients to comprehend the method of data collection [59]. Additionally, NRS can be administered verbally during a phone call [60].

Type of machinery and employee operator:
Often the method of administration of laser therapy is unclear but above all not reproducible. In many studies the protocol involves the use of the device in different points of the mouth and for a variable period of time. To increase the reliability of the method, many authors had orthodontic treatment and laser applications performed by the same operator [21,33,34,36,38,43].
Unfortunately, even the individual operator is not able to reproduce his work in the same way over time. It is difficult to use in the repeatable way the hand-piece at each session (Figure 1).

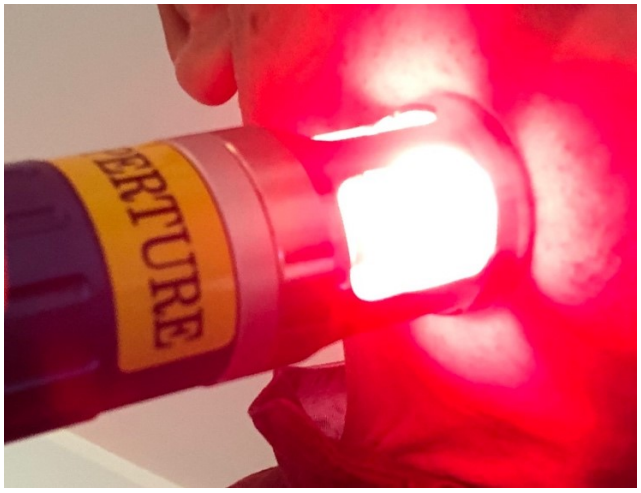

Figure 1: It is difficult to use in the repeatable way the hand-piece at each session.

In a recent study by Lo Giudice in 2020 ATP38 was used. This device is equipped with a multi-panel system with a combination of wavelengths from 450 to 835 nm depending on therapeutic indication. One of the advantages of using a static device is that the session is independent by the operator; this can enhance the standardization of the dosage administered since the operator error is eliminated and it can make the effect reproducible (Figure 2) [60].

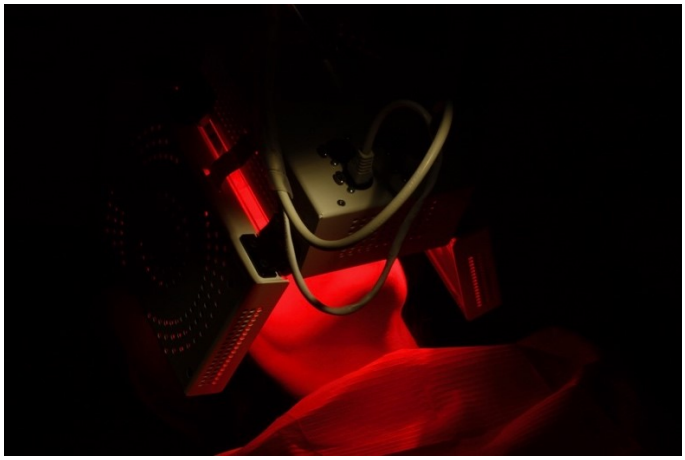

Figure 2: ATP38 in use

CONCLUSIONS

This search shows that most authors observed that reduction of pain cannot be attributed to placebo-based mechanisms. They said that laser therapy is effective in reducing painful sensation during different stages of orthodontic treatment. Other authors showed that there weren't statistically significant results in favour of low-laser therapy, but it is important to remember that they used different parameters, including technical specifications and application modes. In this regard, even just one parameter can influence the effect of LLLT. Additionally, results depend also on the participants' individual variability.
To obtain generally valid studies, with consistent and reproducible results, it is necessary to standardize the different parameters used that are independent by operator performing the procedure.
Hopefully, suggesting the spread of devices similar to ATP38, the scientific validity of PBM research in orthodontia will increase.

Supplementary Materials: Figure 1, Figure 2, Table 1

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