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The effect of laser and botulinum toxin in the treatment of myofascial pain and mouth opening: A randomized clinical trial☆,☆☆,★,★★

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ABSTRACT

This study conducted a randomized clinical trial in 15 patients, who sought care at the Dental Clinic of the University of Passo Fundo, in order to compare the use of low-level laser and botulinum toxin in the treatment of myofascial pain and whether they alter the mouth opening of patients with temporomandibular disorder. The patients were divided into two groups: the Laser group received low-level GaAlAs laser, 100 mW of power at a wavelength of 830 nm in continuous light emission; and the Toxin group received 30 U of botulinum toxin type A (BTX-A) in the first session, and 15 U after fifteen days. The assessments were performed by measuring pain with Visual Analogue Scale (VAS), and mouth opening with a digital caliper. Data were submitted to Student's t test at 5% significance level. Regarding pain symptoms, the results indicate that groups treated with laser and toxin registered 7 U in VAS, at day 5 the scores were 4.75 and 4.86 U, respectively. The laser worked faster (day 12) at 2.75 U, and the group treated with BTX-A registered 2.86 U at day 30. Both therapies investigated were effective in reducing pain, but the effect of low-level laser was faster than the use of BTX-A. Both treatments showed no statistically significant improvement in mouth opening.

1. Introduction

Temporomandibular disorder (TMD) is characterized by pain and disorders in joints and/or muscles and associated structures [1]. Its etiology is currently known to be multifactorial [2], including psychological factors, unbalanced occlusion, parafunctional habits, and hereditary and psychological systemic factors [3]. TMD is considered a major cause of non-dental pain in the orofacial region [4]. Patients present several signs and symptoms, such as headaches, pain in the face and neck, joint noise, and limited mouth opening [5].

The collection of information about the potential etiological factors, signs, and symptoms must be done carefully for correct diagnosis. Early diagnosis may avoid complex treatments, such as surgery and invasive occlusal therapy [6,7].

Several treatments are suggested for TMD. Indications are the use of anti-inflammatory drugs, intake of soft food, physiotherapy, occlusal splints, and acupuncture [1,8]. In addition, there are several evidences of the reduction of myofascial pain symptoms with the application of low-level laser [1], and more recently, with the use of botulinum toxin type A [9].

The use of laser has grown extensively in all areas of dentistry because of its therapeutic properties, such as tissue repair and improvement of local microcirculation, besides the positive psychological effect, especially in patients with chronic pain [10]. Low-level laser is a non-thermal treatment that aims to reduce the pain of TMD through its anti-inflammatory, analgesic, and biostimulant effects [2,5]. Biostimulation occurs through metabolic activation, such as formation of fibroblasts, increased vascularization, and mitochondrial activity [11,12].

Botulinum toxin type A is a neurotoxin synthesized by *Clostridium botulinum* bacteria, which acts efficiently in myofascial pain and headache [13,14,15]. It is classified as a zinc endopeptidase that cleaves one or more proteins at the union of acetylcholine with the presynaptic

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membrane. This results in local chemodenervation with loss of muscle tone, promoting reduction in contractility [16].

Seeking better treatments to improve the quality of life of patients with myofascial pain, this study compares the effectiveness between low-level laser and botulinum toxin type A, testing the following null hypotheses: (1) there is no difference between both treatments for myofascial pain, and (2) the different techniques do not change the mouth opening of patients with TMD.

2. Material and Methods

2.1. Research Ethics Criteria

This study was approved by the Research Ethics Committee according to normative act n. 570/2011 (CAAE: 0312.0.398.000–11).

2.2. Type of Study and Sample Qualification

It is a randomized clinical trial with 25 patients who sought care at the Dental Clinic of the University of Passo Fundo. For the selection of individuals, the following criteria were used:

Inclusion criteria: unilateral or bilateral myofascial pain lasting more than a month; complaint of pain in mouth opening; bruxism, clenching or tooth wear.

Exclusion criteria: pregnancy and breastfeeding; heart disease and pacemaker; malignant tumors; degenerative joint diseases, psoriasis, and rheumatoid arthritis; myasthenia gravis and Lambert Eaton's syndrome; congenital abnormalities; recent history of trauma; treatment for pain in the month prior to the study; psychic disorders; dental diseases such as caries or pulpitis; epilepsy; use of chronic medication, occlusal splint or other treatment for pain control; use of aminoglycosides; allergy to lactose; tetanus vaccine in the last 12 months.

Therefore, after analyzing inclusion and exclusion criteria, 18 patients were able for treatment. Randomization was performed through an online program (www.random.org) so it would be as impartial as possible. After this initial step, only 16 patients showed up at the place indicated for the research, and one patient quit treatment during the experiment. For the purpose of results, a sample of 15 patients (8 from the Laser group and 7 from the BTX group) was considered.

2.3. Methodology

For the Laser group, a low-level device (Photon Lase III, DMC equipment, São Carlos, SP, Brazil) was used with GaAlAs (Gallium Arsenide and Aluminum) active medium, 100 mW of power, at a continuous emission mode, wavelength of 830 nm, and dose of 80 J/cm^2 per application point. This dose appears calibrated on the device display when the TMD function is selected. The laser light was applied with the tip of the device perpendicular to and in contact with the tissue to be irradiated, in two points of the superficial bundle of the masseter muscle (in the upper portion and the lower portion), and in one point of the temporal muscle (central portion). Applications were performed in the endplate of muscles, and they were always bilateral.

Seven applications were performed at 48-h intervals between each application (session), excluding weekends. Laser dose was determined according to the manufacturer's protocol (DMC).

For the Toxin group, 500 U of botulinum toxin type A was used. In the first session, 30 U were applied per point, in two points of the superficial bundle of the masseter muscle (in the upper portion and the lower portion), and in one point of the temporal muscle (central portion). Fifteen days later, 15 U were applied per point, likewise the first session. Applications were performed in the endplate of muscles, and they were always bilateral. For the purpose of application, the botulinum toxin type A was reconstituted with a 10 ml luer syringe containing 1.1 ml of 0.9% saline solution, which was introduced into the vial containing the botulinum toxin type A, so the toxin may be stored and refrigerated (from +2 °C to +8 °C) inside its container. Upon reconstitution, the central portion of the exposed rubber stopper was cleaned with alcohol, immediately prior to piercing the septum. A ratio of 5:1 U was used because there is no specific syringe to apply the toxin. Thus, for 30 U of toxin, 6 strokes of the syringe were determined for 30-unit insulin, and 3 strokes for 15 U. Two syringes were used per patient in each application.

Prior to application, the muscles were sterilized with 2% chlorhexidine solution with no alcohol and soaked in gauze. Application points were determined with a marker where topical anesthetic cream was applied with a stick spreader, and there was a 30-min wait until the botulinum toxin type A was applied.

Next, the aforementioned muscles were pressed by the index finger and thumb for needle insertion perpendicular to the tissue. Toxin injection proceeded with the insulin syringe of ultrathin, sterile, 23-gauge, and 12-mm length needle.

Mouth opening assessment for both groups was performed in patients with orofacial pain, evaluating the interincisal distance (in millimeters) at pre- and post-treatment with a digital caliper (Mitutoyo — Japan), and pain was measured with the Visual Analogue Scale (VAS) before the first application and prior to the following applications.

The experiment was performed by an evaluator who measured mouth opening and pain, and by two applicators - one for the laser and one for the botulinum toxin type A. All operators were previously trained.

2.4. Statistical Analysis

Data were subjected to Student's t test to assess the experimental groups at 5% significance level.

3. Results

We observed 15 patients — thirteen women and two men. The average age was thirty-eight years.

Regarding pain symptoms reported by the patients of the groups assessed, we found that in the Laser group there was statistically significant reduction of pain after 12 days of irradiation ($p = 0.019$). On the other hand, in the Toxin group, we found that the reduction of symptoms only occurred 30 days after the first application ($p = 0.043$). However, there was no statistically significant difference between both groups studied regarding the reduction of pain symptoms 30 days after starting the treatment ($p = 0.985$) (Fig. 1).

Regarding mouth opening, we found no significant statistical difference between the Laser group and the Toxin group, considering that both groups showed no significant increase in mouth opening during treatment ($p = 0.272$) (Fig. 2).

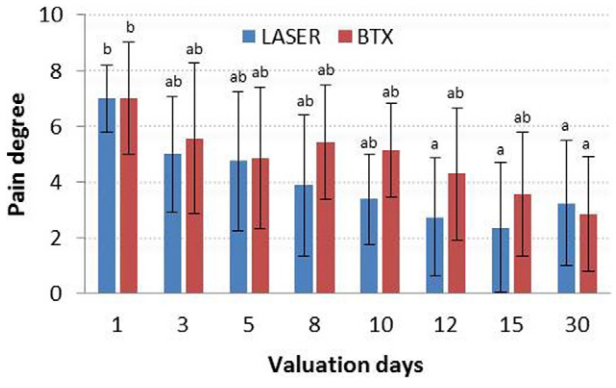

Fig. 1. Degree of pain (VAS scale) in the groups studied in relation to the assessment days. Same letters indicate no statistical differences between groups.

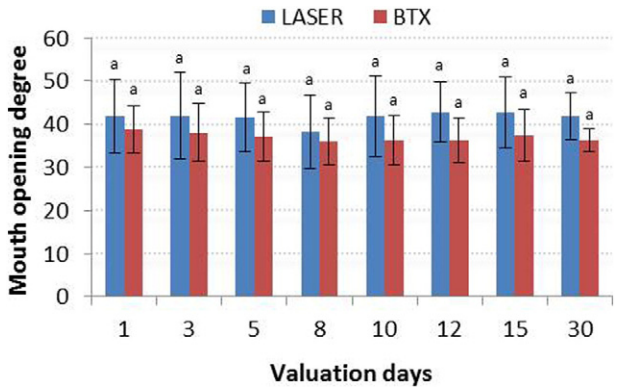

Fig. 2. Mouth opening degree in the groups studied in relation to the assessment days. Same letters indicate no statistical differences between groups.

4. Discussion

In the present clinical, randomized, and blind study, we assessed the effect of low-level laser and botulinum toxin type A on patients with myofascial pain. The evolution of pain symptoms was observed by the Visual Analogue Scale, and mouth opening was measured with a digital caliper, in both therapies.

The results obtained in this study indicate that there was a statistically significant reduction of pain with no statistically significant improvement of mouth opening, in both therapies. Thus, both null hypotheses tested in this study should be accepted.

The prevalent symptom in a patient with TMD is pain followed by spasms of masticatory muscles, because they are fatigued or in continuous contraction [17]. Supported by this theory, scholars have found, in low-level laser therapy (LLLT) and botulinum toxin type A (BTX-A), ideal treatments to reduce pain. The success of TMD treatment with both techniques is due to its myorelaxant effect, thereby reducing pain and improving the balance of mandibular functions [18,19,20].

The Laser group showed a statistically significant improvement (reduction of pain) after 12 days when compared to the first application; such results agree with those found by Kulekcioglu et al. [21], who observed significant improvement in the pain treatment group; they addressed this analgesic and biostimulator effect to laser therapy. Ficacková et al. [22] observed a significant improvement in patients treated with infrared laser compared to those receiving zero dose, and pain reduction occurred in 82% of patients presenting myofascial pain. Carrasco et al. [24] noted significant improvement in pain parameters in the treatment group, which was not observed in the placebo group. Sancakli et al. [20] reported an improvement of pain in patients with TMD because of the analgesic and myorelaxant effect of the low-level laser. Pain reduction may be attributed to decreased contraction and inflammation of muscles by the effect of the laser and secondary muscle inhibition, which occurs in the sensory hyperactivity of joint receptors. Hotta et al. [24] showed statistically significant improvement in pain symptoms and electromyographic activity of the superficial bundle of masseter muscles in normal occlusion after applying light once a week for ten sessions. One theory holds that LLLT reduces inflammation by decreasing the levels of prostaglandin 2 (PGE 2).

On the other hand, for the group using BTX-A, pain reduction was noted at day 30 due to an activity peak that occurred after 15 days with the application of the supplementary dose of 15 U (last day of application). This study showed a reduction of pain symptoms at day 30 of the assessment with the use of BTX-A, which is consistent with the results by Schwartz & Freund [16], who said that several TMD groups involving orofacial muscles have shown clear reduction of pain symptoms by applying BTX-A. Furthermore, Von Lindern et al. [25] found improvement of pain symptoms in 91% of patients in the group treated with BTX-A. Following toxin injection, there is an improvement in the aerobic metabolism with increased oxygen generation. There are also changes in the area of myofibrils, muscle cells, and the neuromuscular junction. Ihde & Konstantinovic [26] reported that patients with chronic myofascial pain were treated with BTX-A and presented significant improvement of pain symptoms. This may be explained by the fact that BTX-A cleaves 25-kD protein synapsis in different locations, likewise BTX-E. The light chain molecules induce the proteolytic cleavage of SNARE proteins and inhibit the release of acetylcholine to the nerve terminal surface, which consequently prevents vesicular fusion. When the structure is a muscle, paralysis with chemodenervation occurs. Between two and five days after BTX muscle injection, paralysis occurs for up to three months before regeneration gradually starts. The duration of this mechanism may vary for each individual [27].

Regarding the improvement of mouth opening, the results of this study are consistent with those by Carrasco et al. [23], which found no statistically significant improvement of mandibular movements after LLLT in patients with TMD. On the other hand, Mazzetto et al. [19] observed a statistically significant improvement in mouth opening after applying laser twice a week for two weeks. Accordingly, Kato et al. [3] observed an improvement in mouth opening using laser three times a week for 10 sessions, supporting the results with the cumulative effect of the laser. Sancakli et al. [20] also reported an improvement in mouth opening by using laser three time a week for twelve sessions, addressing this result to the analgesic and myorelaxant effect of the laser. Cetiner et al. [28] observed improvement in mouth opening of patients irradiated with LLLT for 10 sessions twice a week. The different results found in this work and the experiences reported may be explained by the different rate of application: patients had 7 irradiation sessions with a 48-h interval (except weekends), while other studies had more days of application. Therefore, our rate of application was not efficient to promote muscle relaxation, which would allow greater mouth opening within the timeframe proposed in the study.

Furthermore, Rudzinska et al. [29] reported that three months after BTX-A injection, nine out of fifty-six patients still had a significant improvement in the contraction of facial muscles. Similarly, Tan and Jankovic [30] observed relief of teeth grinding and improvement in chewing for patients with bruxism treated with BTX-A. Guardanardini et al. [31] found a significant improvement in jaw movements, including mouth opening, after botulinum toxin (BTX) injection in patients with myofascial pain. The benefit observed continued after three months of treatment. In this study, the last assessment was performed at day 30, and several reports claim that the BTX effect started after a few weeks of application. As the last application occurred 15 days after starting the treatment, perhaps it was still not long enough for a change in mouth opening to show a significant effect. The improved mouth opening reported in the literature may be explained by the fact that BTX prevents the release of the mediator, acetylcholine, promoting lower muscle contraction hence the improvement of mouth opening. Although the treatments performed showed no increase in mouth opening, patients reported improvement in comfort when chewing, less muscle fatigue when opening and closing the mouth, such as for chewing and speech. According to Chang et al. [5], this probably occurs because of the analgesic and photobiomodulation action of the laser that reduces inflammatory mediators. Moreover, nervous stimulation caused by the laser improves the activity of masticatory muscles, making them more functionally effective.

Further studies are necessary to establish the efficacy of LLLT and BTX-A for chronic pain disorders and their particular action mechanisms, as well as their potential for multifactorial treatments.

5. Conclusion

Based on the analysis and results of this clinical trial, both therapies investigated were effective in reducing pain during the observation period employed, however the effect of low-level laser was faster than the

use of BTX-A. Both treatments showed no statistically significant improvement in mouth opening.

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