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ORIGINAL ARTICLE

Yahya Ceylan · Sami Hizmetli · Yavuz Siliğ

The effects of infrared laser and medical treatments on pain and serotonin degradation products in patients with myofascial pain syndrome. A controlled trial

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Abstract In this controlled study of 46 patients with myofascial pain syndrome, we investigated the effects of infrared (IR) laser application to trigger points and medical treatment on pain reduction and serotonin and its degradation products. Retaining double-blind trial principles, the patients were randomly assigned to two groups. The treatment group received IR laser treatment, whereas the control group received sham laser. However, both groups received medical treatment. In the treatment group, laser was applied once a day for 10 consecutive days at a dose of 1.44 J/cm^2. The effect of the laser treatment on pain was evaluated by visual analog scale. Urinary excretion of 5-hydroxy indole acetic acid (5-HIAA) and serotonin + 5-hydroxy tryptophan (5-HT + 5-HTP) was studied by column chromatography. At the end of the treatment, there was a statistically significant difference between the VAS values of the treatment and control groups. The 24-h urinary excretion of the 5-HIAA and 5-HT + 5-HTP was significantly higher in the laser treatment group than in the placebo group. In conclusion, IR laser is an effective modality in the treatment of MPS which increases an important mediator of pain inhibition, serotonin.

Keywords Laser therapy · Myofascial pain · Seratonin

Y. Ceylan · S. Hizmetli (✉)
Department of Physical Medicine and Rehabilitation,
Cumhuriyet University Medical Faculty,
58140 Sivas, Turkey
E-mail: hizmetli@cumhuriyet.edu.tr
Tel.: +90-346-2191310
Fax: +90-346-2191284

Y. Siliğ
Department of Biochemistry,
Cumhuriyet University Medical Faculty,
Sivas, Turkey

Introduction

Though myofascial pain syndrome (MPS) is one of the most important diseases causing chronic and widespread pain, it is hardly ever diagnosed, and proper treatment is often missed [1]. The prevalence of MPS is predicted to be 12% in the population, and it is probably the most common cause of musculoskeletal pain [2].

Myofascial pain syndrome is a muscle pain characterized by referred pain radiating to a specific region by stimulation of the myofascial trigger points. Micro- and macrotraumas, excessive tension in the muscles, tiredness, psychological stress, and genetic factors are thought to be related to the disease. However, its etiology has not been clarified yet [3, 4]. On the other hand, some studies suggest that there are some features common to MPS and chronic fatigue syndrome such as sleep disorders and depression [2]. Taut bands and trigger points within these bands and the referred pain caused by palpation of these trigger points, together with regional pain symptom, are the leading factors for clinical diagnosis [1, 4].

Cold laser has been recently used for treatment of various disorders such as wound healing, edema, and pain. The mechanism of pain reduction is not completely understood. Some researchers have suggested that the cold laser changes the neuronal activity which, in turn, causes photochemical reactions [5]. Some studies report that cold laser application to trigger points in MPS decreases pain and tenderness and increases skin impedance [5, 6, 7, 8]. Walker et al. reported that cold laser application decreases pain and increases excretion of serotonin and its degradation products such as 5-hydroxy indole acetic acid (5-HIAA) in urine [9]. Jorgen et al. also examined the effectiveness of cold laser in patients with chronic orofacial pain and concluded that it is not very effective in these patients. However, in the same study there was also an increase in the urinary excretion of 5-HIAA in patients with reduced pain [10].

Excretion of 24-h urinary 5-HIAA is a measure of serotonin synthesis and degradation in the body. The

Table 1 Demographic variables, mean trigger point counts, and mean treatment duration in the treatment and control groups

Group	Number	Age	Males:females	Trigger point count	Duration of treatment
Treatment	19	34.05 ± 8.25	6:13	4.32 ± 0.75	12.96 ± 2.25 dk
Control	20	36.6 ± 6.36	2:18	4.55 ± 0.76	13.65 ± 2.28 dk

change in its amount is thought to reflect fluctuations in the serotonin metabolism, also in the central nervous system [2, 14]. Regulation of the circadian rhythm of serotonin is very important for normal sleep patterns and analgesia systems [10, 11].

In this study we aimed to study the effect of IR laser application to the trigger points in patients with MPS on pain and the 24-h urinary excretion of serotonin and its degradation products, which has a very important role in pain inhibition.

Materials and methods

This study was conducted on 46 patients diagnosed as having MPS according to the American College of Rheumatology criteria and recruited from the Cumhuriyet University Physical Therapy and Rehabilitation Outpatient Department in Sivas, Turkey.

Whole blood count, urinary tests, erythrocyte sedimentation rate, and biochemical tests were performed in all patients. Patients with systemic disorders or using any medications and those with abnormal laboratory results were not included in the study. Treatment and placebo groups were established by using a randomized method for those patients receiving MPS diagnoses. Twenty-three patients in the first group received IR laser and medical treatment, and 23 in the second group received sham laser and medical treatment. Medical treatment was given to both groups in order not to leave the second (sham laser) group untreated. The patients were given a banana, pineapple, walnut, tomato, and eggplant-free diet and told to collect 24-h urine on the 4th day [11].

On the 5th day, laser, sham laser, and medical treatment were started. All patients were given NSAID (500 mg naproxene sodium b.i.d.) and a muscle relaxing agent (400 mg phenbrobomat t.i.d.). Pain was evaluated pre- and post-treatment on a 100-mm visual analog scale (VAS) for each trigger point by digital palpation by the same physician. The VAS values were recorded for each patient, and the values of pain experienced were written on a scale divided into ten equal parts. All of these procedures were done by an observer physician who was at the same time the coordinator of the control groups.

The 24-h urine volumes collected from the patients were measured in the clinic, and 10-cc specimens were sent to the biochemistry metabolism laboratory. For detection of 5-HIAA and serotonin + 5-hydroxy tryptophan (5-HT + 5-HTP), a 5-HIAA colon kit (Sibar) was used. The results of 24-h urinary excretion of 5-HT + 5HTP and 5-HIAA were given in mg/day.

The IR laser therapy was performed once a day for 10 consecutive days. A Gymna 200 laser with a wavelength of 904 nm was used 3 min for each trigger point at a frequency of 4 kHz. The amount of energy given to each trigger point was 1.44 J. The length of the laser probe tip was 5 mm, and the duration of current was 200 ns. On the 9th day of treatment, 24-h urine was collected again as with the first specimens and sent to the biochemistry laboratory. For statistical evaluation of the results, Wilcoxon's signed rank test and the *t*-test were used, as appropriate.

Results

Twenty-four-hour urine could not be obtained from one of the patients in the laser treatment group. Two patients from each group had to use medication for other medical reasons, which could have affected the results. There was also an unexplainedly high excretion of 5-HIAA in two patients, one from each group. Thus these seven patients were excluded from the study. The results of the 19 patients from the first group (laser) and 20 from the second group (sham laser) were evaluated. The demographic variables, mean trigger point counts, and treatment durations of the subjects are given in Table 1.

Comparing pre- and post-treatment values of the treatment group, the decrease in VAS and increase in 5-HIAA and 5-HT + 5HTP excretion were statistically significant (Table 2). Comparing these values of the control group, there was a statistically significant decrease in VAS results but no significant change in 5-HIAA and 5-HT + 5-HTP values (Table 3).

Comparing post-treatment changes in the VAS, 5-HIAA, and 5-HT + 5-HTP values of treatment and control groups, the increase in the treatment group was greater than in the control group and statistically significant (Table 4).

Discussion

It was previously reported that cold laser is effective against pain. He-Ne, Ga-Ar, and Ga-Al-Ar lasers are the most frequently used types. There are some conflicting results about the effect on pain reduction of direct application of cold laser vs application to the acupuncture points [10, 11, 12, 13, 14, 15]. Olavi et al. applied IR laser (904 nm) to trigger points twice at

Table 2 The mean VAS, 5-HIAA and 5-HT + 5HTP values of patients in the treatment group. *VAS* visual analog scale,*5-HIAA* 5-hydroxy indole acetic acid, *5-HT + 5-HTP*serotonin + 5-hydroxy tryptophan

	VAS (mm)	5-HIAA (mg/day)	5-HT + 5-HTP (mg/day)
Pretreatment	62.47 ± 22.59	3.86 ± 1.02	4.89 ± 1.43
Post-treatment	34.54 ± 23.50	8.81 ± 4.28	7.85 ± 3.71
P value	0.0002	0.0001	0.010

Table 3 The mean VAS, 5-HIAA, and 5-HT + 5HTP values in the control group, *VAS*visual analog scale, *5-HIAA* 5-hydroxy indole acetic acid, *5-HT + 5-HTP* serotonin + 5-hydroxy tryptophan

	VAS (mm)	5-HIAA (mg/day)	5-HT + 5-HTP (mg/day)
Pretreatment	66.43 ± 24.60	5.45 ± 1.87	7.12 ± 0.32
Post-treatment	54.96 ± 25.89	6.24 ± 4.07	6.64 ± 0.29
P value	0.0031	0.5755	0.4553

Table 4 The mean changes in the VAS, 5-HIAA, and 5-HT + 5-HTP values after treatment in the treatment and control groups. *VAS* visual analog scale, *5-HIAA* 5-hydroxy indole acetic acid,*5-HT + 5-HTP* serotonin + 5-hydroxy tryptophan

Group	VAS	5-HIAA (mg/day)	5-HT + 5-HTP (mg/day)
Treatment	27.41 ± 14.41	4.97 ± 4.03	1.49 ± 4.52
Control	11.44 ± 13.03	0.79 ± 3.19	0.43 ± 2.13
P value	0.0060	0.0059	0.0100

1.4 kHz frequency, with 72 W maximum energy and 150 ns current duration. Each session lasted 3 min and the total applied current was 2.7 J/point. They found the therapy to be effective [16]. Gescherelli et al. used IR laser in patients with cervical myofascial pain. They treated the patients every other day for 12 sessions with a total energy dose of 5 J. They also found the treatment effective [8].

Helen Beckerman et al. evaluated 36 studies in a meta-analysis and found extreme differences between He-Ne, IR, and combined lasers regarding duration and dose. They found no correlation between laser dose and results. They could not determine an optimal effective dose or one with minimal side effects. Though some well-designed studies had successful results, it was determined that most had methodological design errors. Cold laser therapy was shown to be effective in post-traumatic joint pain, myofascial pain, and rheumatoid arthritis; however, the degree of effectiveness was not clear [14]. We also confirmed the effectiveness of IR laser in myofascial pain by our randomized, double-blind, controlled study.

Olavi et al. determined the trigger points in patients with MPS using a device called the pain threshold meter. They defined trigger points as those with tenderness at pressure under 5 kg/cm^2 and applied laser to these points. In the placebo group, the mean threshold values were 3.58 ± 0.20 kg/cm^2 before treatment, 3.45 ± 0.21 kg/cm^2 right after treatment, and 3.75 ± 0.19 kg/cm^2 15 min after treatment. In the laser group, the mean values were 2.79 ± 0.16 kg/cm^2 before treatment, 3.76 ± 0.21 kg/cm^2 right after treatment, and 4.66 ± 0.35 kg/cm^2 15 min after treatment. These results show a 134.7% increase in pain tolerability right after treatment and a 167% increase at the 15th min after treatment. The latter increase in the placebo group was only 104% [16].

We evaluated the patients right after the last treatment session. Pressure was appplied to the trigger points until the nail bed of the 1st finger whitened [12] and measured pain at the end of the 10th session using a 100-mm VAS. The pre- and post-treatment VAS values of the placebo group were 66.43 ± 24.60 mm and 54.96 ± 25.89 mm, respectively, whereas they were 62.47 ± 22.59 mm before treatment and 34.54 ± 23.50 mm after treatment in the laser treatment group. Our results are consistent with those of Olavi et al.

Gecherelli et al. evaluated pain using VAS and the McGill pain questionnaire after 12 sessions of IR laser treatment and found that laser therapy was significantly superior to placebo. Our results are similar. However, in their study, laser treatment was applied to not only to trigger points but also to the homometameric acupuncture points [8].

Lynn Synder-Mackler et al. used a He-Ne laser with a wavelength of 632.8 nm for 3 consecutive days in 14 patients with low back and neck pain, evaluated the pain with VAS, and measured skin impedance with a dermometer. In this placebo-controlled, double-blind trial, they concluded that laser treatment decreased pain and increased skin impedance [5]. In another study with He-Ne laser, Synder-Mackler et al. also confirmed that laser treatment increases skin impedance over the trigger points by using the same device [17]. Their results show that cold laser is effective in pain reduction in trigger points and are in concordance with those of our study.

In a double-blind study with crossover technique, Waylonis et al. applied He-Ne laser (Dynatron 1120) to a total of 12 points in hands, neck, thoracic spine, and shoulders for 15 s in patients with MPS. They applied a five-session therapy, repeated it 6 weeks later, and evaluated the pain by the McGill pain questionnaire. They found no significant difference between the laser and placebo groups [18]. The treatment dosage was not stated in this study. Its methodology was poor, according to the methodological scoring prepared by Beckerman et al. [14], and the results conflict with ours. However, the region preferred for treatment was acupuncture points instead of trigger points. Also, the patients were not classified by fibromyalgia, MPS, or fibrositis—all were represented as having fibromyalgia. The laser type was also different and, moreover, the dose of the treatment was not stated. The different results in our study can be explained by these factors. Nevertheless, King et al. reported an increase in the experimental pain threshold after laser stimulation of the acupuncture points in the auricles, and they concluded that laser auriculotherapy was effective [4].

We could find no study reporting the 5-HIAA excretion in 24-h urine. There was also no information on the 5-HIAA and 5-HT + 5-HTP excretion after laser treatment in patients with MPS. Thus we could not compare results. However there were two studies measuring 5-HIAA excretion in 24-h urine after cold-laser treatment in patients with chronic pain. The first was conducted by Walker in 1983. Cold laser was applied to the involved joints or nerves in 26 patients with osteoarthritis, trigeminal neuralgia, postherpetic neuralgia, and sciatic pain. There was improvement in 19 of 26 cases. However, there was no change in patients treated by sham laser. The authors compared the 5-HIAA excretion of patients who responded well to treatment with those who responded poorly. They also compared the results of patients treated with laser and controls (sham laser) and found a significant increase in 5-HIAA excretion in the laser treatment group and in

patients responding well to treatment. They suggested that myelinated nerves in the myelin tissue with low pain threshold could have a pain-reducing effect similar to that of transcutaneous electrical nerve stimulation or acupuncture. They used a He-Ne laser, and the treatment dose was low (1 mW for 20 s three times a week) [9].

In 1989, Jorgens and coworkers treated 40 patients with 904-nm-wavelength IR laser therapy to study the effect on orofacial pain and evaluate the 5-HIAA excretion findings of Walker et al. after the laser treatment. Twenty-eight of these patients were diagnosed with oral dysthesia, five had toothache, four had trigeminal neuralgia, and three had chronic tension headache. The laser therapy was applied for eight sessions in a double-blind, placebo-controlled study with crossover design. The duration of the application was 60 s in the first two sessions and increased to 120 s in cases with poor response. The maximum energy dose for each point was 4.7 J/cm^2 for 60 s or 9.4 J/cm^2 for 120 s. The duration of radiation varied between 1 min and 18 min, depending on the radiated point count. The treatment continued for 4 weeks, two times a week. The authors evaluated the pain with VAS and found a significant decrease in the placebo group. They also measured the 5-HIAA excretion rate in 24-h urine in 36 patients [9, 10].

In the study of Jorgen et al., the decrease in pain and increase in 5-HIAA excretion was significant in the placebo group. They could not find a significant difference between placebo and laser groups. Our results differ. There was no restriction of diet or drug usage which could be related to 5-HIAA excretion in the study of Jorgen et al. However, they should have restricted the intake of serotonin and tryptophan in order to obtain healthy results in such a trial. In addition, many drugs are being used for the treatment of chronic pain which could interfere with the mechanism of serotonin and tryptophan, so these agents should be taken into consideration and stopped [10, 11, 12]. Besides the improper diet, the duration of treatment was not standard and varied to a great extent, between 1 min and 18 min. The patients were not homogenized regarding diagnosis. Because of the study's crossover design, five patients received only laser, ten received only placebo treatment, and the treatment of 21 patients was changed after four sessions [11]. These factors relating to study design can also be responsible for the different results.

When there is excessive serotonin production from tryptophan, the conversion of 5-HTP to serotonin, which is a rate-limiting step, cannot be completed, and 5-HTP is excreted in the urine. One of the markers of excessive serotonin in blood is the excreted, nonmetabolized serotonin. When there is overproduction of serotonin or when tryptophan is largely converted to serotonin (normal rate 1–3%), excretion of 5-HIAA does not reflect serotonin levels [11, 12]. However, 5-HT and 5-HTP do. We could not compare our results, as there is no study in the literature examining 5-HT + 5-HTP excretion after cold laser therapy.

We found that IR laser therapy increases 24-h urinary excretion of 5HIAA and 5-HT + 5-HTP more than placebo therapy, and this finding was statistically significant. The increase in the excretion of serotonin and 5-HTP, which is a serotonin precursor and a serotonin metabolite 5-HIAA, in 24-h urine reflects the increase in total body serotonin, including CNS serotonin [12, 13]. These results remind us that the increase in serotonin, an effective agent in pain reduction and sleep regulation, could make a partial contribution to the pain reducing effect of IR laser. Thus we conclude that IR laser radiation is significantly more effective than placebo treatment.

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