Effects of Superpulsed Low-level Laser Therapy on Temporomandibular Joint Pain

Ida Marini, MD, DDS, Maria Rosaria Gatto, PhD,† and Giulio Alessandri Bonetti, MD, DDS**

Objectives: A randomized double-blind study was conducted to compare the efficacy of superpulsed low-level laser therapy (SLLLT) with nonsteroidal anti-inflammatory drugs in the treatment of pain caused by temporomandibular joint disorders.

Methods: A total of 99 patients with temporomandibular joint disorders, secondary to disc displacement without reduction or osteoarthritis were randomly divided into 3 groups. Thirty-nine patients received SLLLT in 10 sessions over 2 weeks, 30 patients received ibuprofen 800 mg twice a day for 10 days, and 30 patients received sham laser as placebo in 10 sessions over 2 weeks. Pain intensity was measured by visual analog scale at baseline, 2, 5, 10, and 15 days of treatment. Mandibular function was evaluated by monitoring active and passive mouth openings and right and left lateral motions at baseline, 15 days, and 1 month of treatment. Magnetic resonance imaging was performed at baseline and the end of therapy.

Results: Mean visual analog scale pain scores in SLLLT group was significantly lower than in nonsteroidal anti-inflammatory drug group and control group ($P = 0.0001$) from fifth day up to the end of the observation period. As for active and passive mouth openings and right and left lateral motions, superiority of SLLLT was evident 1 month after treatment (interaction time treatment, $P = 0.0001$).

Discussion: Mandibular function improved in all SLLLT patients proving the effectiveness in the treatment of pain, as demonstrated by a significant improvement in clinical signs and symptoms of temporomandibular joint disc displacement without reduction and osteoarthritis at the end of treatment and stability over a period of 1 month.

Key Words: RCT, temporomandibular joint pain, pulsed low-level laser therapy, osteoarthritis.

(*Clin J Pain* 2010;00:000–000)

Temporomandibular disorder (TMD) is a collective term for a number of clinical signs and symptoms involving the masticatory muscles, the temporomandibular joint (TMJ), and associated structures.[1]

Temporomandibular pain is typically located in the preauricular area, the muscles of mastication, or the TMJ. However, patients may also report other facial pain, headache, and neck pain. In addition, TMD patients may report a variety of jaw problems other than pain, including difficulty in maximal opening of the jaw, locking in the open or closed position and clicking, popping, or grating sounds.

For TMD-involving joint disorders, TMJ disc displacement (TMJ DD) without reduction refers to any abnormality within the TMJ that denotes an abnormal position of the articular disc relative to the mandibular condyle and articular eminence. Early stage TMJ DD, referred to as TMJ DD with reduction is quite common and characterized by joint noise or clicking of the joint or opening and classing due to the impaired gliding function of the articular disc.

Pain can be present at any stage of TMD and is a significant part of symptoms that prompt patients to request treatment.[2] Pain is a common symptom of conditions affecting the TMJ, thus representing an important source of disability and considerable socioeconomic costs as a result of medical treatments, surgical interventions, and frequent absences from work.[3] Chronic joint disorders represent some of the most prevalent pain conditions treated in primary care.[4]

Anti-inflammatory, analgesic medication, occlusal splint, and physical therapy are often prescribed in the attempt to decrease the pain associated with TMD[5]; physical agents for TMD treatment include electrotherapy, ultrasound, acupuncture, and laser. Superpulsed low-level laser therapy (SLLLT) seems to be a good choice as a noninvasive treatment for TMJ pain while exhibiting a low cost for the patient. Many authors have reported significant pain reduction with LLLT in acute and chronic musculoskeletal pain conditions[4,6–14] for the pain of TMD[15–19] and chronic orofacial pain.[20]

The biologic effects of LLLT are basically unknown, but they have been suggested to influence pathobiologic processes only.[21] Suggested effects include increased vascularization as well as stimulated collagen production and fibroblast activity,[22,23] photochemical effects,[24] and improved microcirculation,[10,12,25,26] unrelated to the increased temperature in the irrigated tissue.[27,28] Increased superficial blood flow in the foot has also been reported after laser therapy of healthy individuals[29] and in patients with Raynaud phenomenon.[30] SLLLT is a new approach increasingly used in medicine, which has been shown to have several effects on the management of pain, nerve regeneration, bone production, and bone-implant interaction.[31,32]

The aim of this randomized double-blind clinical trial is to investigate the efficacy of the new SLLLT versus anti-inflammatory and placebo therapy in the treatment of TMD, and to determine the optimal time and exposure application to the SLLLT for treating TMJ DD without reduction and osteoarthritis of TMJ with pain.

Received for publication October 15, 2009; accepted March 19, 2010.
From the *Department of Orthodontics and Gnathology; and †School of Dentistry, Alma Mater Studiorum University of Bologna, Bologna, Italy.
Reprints: Maria Rosaria Gatto, PhD, School of Dentistry, Alma Mater Studiorum, University of Bologna, Via San Vitale, 59 40125, Bologna, Italy (e-mail: mariarosaria.gatto@unibo.it).

MATERIALS AND METHODS

Participants

Participants recruited for the study were patients referred to the Department of Oral-facial Pain of University of Bologna for specialist treatment because of TMJ pain. In a group of 120 patients, 99 patients (74 females and 25 males) aged between 15 and 50 years were recruited. Inclusion criteria were clinical diagnoses of TMJ DD without reduction and osteoarthritis, pain for more than 6 months of similar intensity. TMD diagnosis was classified using axis I of the Research Diagnostic Criteria for TMDs (RDC/TMD).[33] The RDC diagnosis consists of joint pain at rest (spontaneous pain) and evoked pain on palpation of the TMJ; TMJ reduction consists of limitation in mouth opening, reciprocal clicking, or joint noise with mandibular movement examination.

Patients were screened by an experienced and RDC/TMD calibrated oral facial pain specialist (M.I.) and referred to the clinical investigator (A.B.G.). Exclusion criteria for the study were patients with myogenic pain, musculoskeletal pain based on the RDC/TMJ, depressive disorder, dental diseases, pregnancy, malignancy, and other systemic rheumatologic diseases such as rheumatoid arthritis. The study was approved by the local Ethics Committee and an informed consent was obtained in accordance with the guidelines of the Helsinki Declaration.

Experimental

A superiority trial with parallel design was carried out. A small pilot study was performed to determine the estimated effect size as mean of the differences between visual analog scale (VAS) at baseline and at 2 days; for a 2-sided significance level of 5% and a power of 80%, the number required in each group was 33. Ninety-nine patients were randomly assigned to 3 groups:

Group L (39 patients, 11 males and 28 females) received laser treatment;

Group D (30 patients, 6 males and 24 females) received anti-inflammatory drugs;

Group C (30 patients, 8 males and 22 females) received no treatment (control).

The initial random allocation provided an equal number of patients in each group (n = 39); however, the withdrawal was present in D and C groups [an equal number of patients (n = 9) withdrawals from the arm of treatment in both the groups]. At the end of the treatment, a degree of acceptance was requested. In our opinion, the greatest acceptability of the laser treatment by the patients was due to the inclusion criteria that requested patients with a very high pain level, and who have had pain for a long time. Almost all our patients had an effusion in temporal-mandible joint and it is known that it does not stop with placebo effect only.

The results of the intention-to-treat analyses confirmed the findings presented in the paper; consequently, we decided to report only the results referred to the patients who completed the initial protocol they were randomly assigned.

Group L: 39 patients. Each patient received laser therapy, gallium-arsenide diode superpulsed laser, (LUMIX 2 HFPL Fisioline, Verduno, Italy) with time pulsation < 200 ns; frequency range 1 to 50 kHz, wave length 910 nm, mean power 400 mW, and peak power 45W. The affected TMJ areas of these patients were treated daily in 3 steps:

1. 20 kHz for 10 minutes
2. 18 kHz for 5 minutes
3. 16 kHz for 5 minutes

All patients were treated for 10 consecutive days (5 d/wk) in right and left TMJ, by the same operator.

Laser test was performed at the end of every application to measure the laser output. The laser parameters selected were based pragmatically on those used in everyday practice by a principal author, which had been formally piloted in previous studies.[34]

Group D: 30 patients. These patients underwent pharmacology therapy with nonsteroidal anti-inflammatory drugs (NSAIDs), 800 mg twice a day of ibuprofen for 10 days.

Group C: 30 patients. Each patient underwent a daily regimen of laser treatment simulation, using only red light of the laser without energy for 20 minutes. They also were treated for 10 days (5 d/wk).

The patients and operators of L and C groups put on protective glasses specific for this diode laser. When the assignment was made, the patients belonging to L and C groups did not know whether they received laser treatment or laser treatment simulation; neither the operator knew whether the laser treatment he was applying was true or simulation.

Pain Severity and Mandibular Function

Spontaneous pain intensity was measured by a VAS. The VAS consists of a 10 cm straight line on which the patients marked their pain intensity where 0 corresponds to no pain and 10 the worst imaginable pain.[35]

The patient was asked to open his/her mouth as much as possible for the measurement of maximal active mouth opening. Maximal passive mouth opening was measured after the application of downward pressure on the mandible by the second and third fingers of the patient. The vertical distance between upper and lower teeth was measured by a ruler and recorded in millimeters for these parameters. Lateral jaw motion was assessed by measurement of the horizontal distance between the midpoints of upper and lower incisors in millimeters.

Active and passive mouth openings and right and left lateral motions were monitored for all the patients at baseline, at 15 days, and after 1 month of treatment for mandibular functions. The investigator was not aware of the treatment (L, D, or C) to which every single patient had been assigned, when checked for pain and mandibular function.

TABLE 1. Visual Analog Score at Baseline, 2, 5, 10, and 15 Days (d)

Groups	Baseline Mean ± SD	2 d Mean ± SD	5 d Mean ± SD	10 d Mean ± SD	15 d Mean ± SD
L	7.72 ± 0.41	8.15 ± 0.42	0.76 ± 0.70	0.24 ± 0.35	0.07 ± 0.13
D	7.42 ± 0.51	6.47 ± 0.80	4.37 ± 1.54	4.98 ± 1.60	6.36 ± 1.16
C	7.13 ± 0.88	6.59 ± 0.91	6.22 ± 0.92	6.14 ± 0.91	6.09 ± 0.94

TABLE 2. Significance of the Comparisons of Visual Analog Score Between the Groups

Groups	Baseline, *P*	2 d, *P*	5 d, *P*	10 d, *P*	15 d, *P*
L vs. D	0.008	0.0001	0.0001	0.0001	0.0001
L vs. C	0.001	0.0001	0.0001	0.0001	0.0001
D vs. C	0.125	0.568	0.0001	0.005	0.169

$\alpha = 0.02$.
d indicates days.

TABLE 3. Covariance Analysis (Adjusting for Visual Analog Score at Baseline and Age) Among the 3 Groups

Comparison Among L, D, and C Groups	*P*	R^2
VAS at 2 d	0.0001	0.82
VAS at 5 d	0.0001	0.87
VAS at 10 d	0.0001	0.90
VAS at 15 d	0.0001	0.96

Imaging

Magnetic resonance imaging (MRI) is considered the most accurate diagnostic method for evolution of soft tissues of the TMJ, especially in cases suspected of disc disorder.[36,37] MRI was performed on each patient to analyze disc and condyle position in the glenoid cavity, if the disc is displaced on the osseous, detect changes of the condyle such as flattening and erosion of the articular surfaces, and to detect possible intra-articular effusions. The radiologist has investigated in particular:

1. Morphologic structural analysis of hard tissues (tuberculus, glenoid fossa, etc).
2. Condyle position
3. Static and dynamic position and morphology of the disc
4. Eventual intrachamber effusions
5. Muscle morphology

MRI was performed on each patient at baseline and at the end of the treatment. One blinded radiologist reviewed the MRI.

Statistical Analysis

Mean age was significantly higher in group L (F = 3.42, $P = 0.04$), that is, 41.93 ± 11.51 versus 36.23 ± 11.30 in group D and 35.90 ± 6.84 in group C. Mean ± standard deviation was used to describe: (i) age and VAS at baseline, 2, 5, 10, and 15 days; (ii) active and passive mouth openings and right and left lateral motions at baseline, immediately after treatment, and 1 month after treatment. Analysis of variance was used to compare the ages of the 3 groups. Kolmogorov-Smirnov test with Lilliefors correction for significance was carried out to evaluate the fitting of the VAS, active and passive mouth openings, and right and left lateral motions to the Gaussian distribution. The distribution of VAS at 5 ($P = 0.04$), 10 ($P = 0.001$), and 15 days ($P = 0.0001$) significantly differ from the Gaussian distribution. Consequently, *t* test for independent samples and Mann-Whitney *U* test were used to compare VAS and active and passive mouth openings and right and left lateral motions at different times between each pair of the 3 groups. Analysis of covariance (adjusting for VAS at baseline and age) was used to compare VAS at different times among the 3 groups. Analysis of variance for repeated measures was finally carried out by using covariate time (5 modalities for VAS and 3 modalities for active and passive mouth openings and right and left lateral motions), sex (2 modalities), age in years, and groups (3 modalities of treatment). Alpha level was set at 0.05 and Bonferroni correction was applied for multiple comparisons where α level was set at 0.02.

RESULTS

Baseline VAS was significantly higher in the L group (F = 7.9, $P = 0.001$) and it remained higher than in the other groups at day 2 also; however from day 5 to the end of the study, it dramatically decreased with respect to D and C groups (Table 1). VAS at baseline and at 2 days was not significantly different in the D group with respect to the C group (Table 2). To control the effect of the age and VAS at baseline, analysis of covariance was carried out (Table 3). It reinforced previous results confirming the major efficacy of laser in comparison with the other 2 treatments from 5 days until the end of the observation period. No significant effect of the interaction of age-VAS at baseline was observed. The effect of treatment was statistically significant (interaction time-treatment, $P = 0.0001$). (Fig. 1).

Mean values of active and passive mouth openings and of right and left lateral motions are generally higher in the L group after treatment and 1 month later (Table 4). These parameters are always significantly different between L and D groups (Table 5). Superiority of laser is mostly evident 1 month after the treatment (interaction time-treatment, $P = 0.0001$).

MRI scans at baseline confirmed that 30 patients had TMD DD without reduction, 69 had osteoarthritis with remodeled cartilage, and 79 had intra-articular effusion, more or less abundant. At the end of the test, it was observed that the effusion disappeared only in group L patients.

DISCUSSION

In this study, we aimed to evaluate the effect of low power laser treatment in patients with TMJ with pain secondary to TMJ DD without reduction or osteoarthritis. These conditions are the most common causes of the

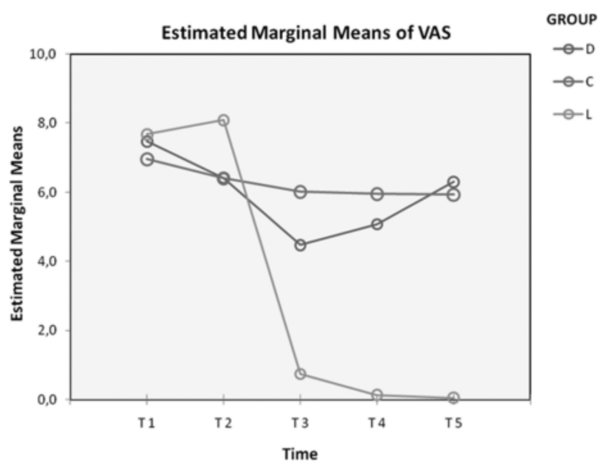

FIGURE 1. Estimated marginal means of VAS in the 3 groups at the 5 times (T1= baseline; T2=2 d; T3=5 d; T4=10 d; T5=15 d). VAS indicates visual analog score.

TABLE 4. Active and Passive Mouth Openings and Right and Left Lateral Motions at Baseline, Immediately After Treatment, and 1 Month After Treatment (mean±SD)

	Baseline	After Treatment	1 mo After Treatment
Active mouth opening (mm)	L 36.28 ± 3.44 D 39.85 ± 2.89 C 38.06 ± 3.19	L 43.24 ± 2.71 D 41.27 ± 2.49 C 39.77 ± 3.96	L 45.89 ± 2.13 D 40.90 ± 3.37 C 37.46 ± 4.94
Passive mouth opening (mm)	L 37.97 ± 3.22 D 41.68 ± 3.01 C 40.00 ± 3.21	L 45.28 ± 2.37 D 42.43 ± 2.77 C 40.77 ± 4.06	L 47.22 ± 2.31 D 42.54 ± 2.20 C 38.28 ± 4.67
Right lateral motion (mm)	L 6.37 ± 1.08 D 7.10 ± 1.28 C 6.57 ± 2.43	L 8.54 ± 1.41 D 8.63 ± 1.97 C 7.98 ± 2.20	L 12.20 ± 1.08 D 8.22 ± 1.92 C 8.04 ± 2.26
Left lateral motion (mm)	L 6.67 ± 1.14 D 6.87 ± 1.57 C 6.44 ± 2.39	L 13.01 ± 1.57 D 8.82 ± 1.78 C 8.01 ± 2.19	L 13.19 ± 1.54 D 8.43 ± 1.97 C 7.98 ± 2.21

chronic or facial pain located in the craniofacial and cervical regions.[38]

Similar to the results of various epidemiologic and clinical studies, most of the patients in our study population were female.[39] The results obtained showed that there were statistically significant differences between laser and control group. Only after the second day, a difference was noticed between the 3 groups. The control group improved, presumably for a placebo effect, the literature has associated placebo analgesia with 2 potential mechanisms: one sustained and engaged for the duration of placebo analgesia, the other transitory, that is, the feedback mechanism.[40] A number of studies have associated significant reductions in pain and pain-related neural activity during placebo analgesia.[41] The laser group showed an increase in pain, which then disappeared for a long time; the increased pain could be explained with an increased local hyperemia.

Patients treated with NSAIDs showed an improvement in pain and mandibular function during the time of treatment but returned to more or less the same level as pretreatment conditions after treatment terminated. It is hard to compare our outcomes with those of other studies that obtained similar results despite differences in design, dosage, intensity, and frequency. In Italy, administration of NSAIDs is suggested for not more than 7 to 10 days, except for rheumatoid arthritis, whereas in many countries this therapy can be prolonged to 4 to 6 weeks.

Real hazards of long-term administration of NSAIDs have been recognized lately as involving renal disease and serious toxicity to the gastrointestinal tract, as well as increasing the risks of adverse cardiovascular events. A comprehensive review of the primary literature reveals modest scientific support for the assertion that the daily use of NSAIDs offers benefits for patients with chronic TMD pain.[42]

One publication provides stronger evidence for the efficacy of NSAIDs in the treatment of arthrogenous TMJ pain.[5] The administration of naproxen resulted in a significant reduction in pain over 6 weeks in comparison to both placebo and celecoxib groups. There is a growing evidence of potential serious toxic effects of NSAIDs when administered chronically at a higher dosage[43] The lack of effectiveness of conventional approaches is further highlighted by the fact that complementary therapies are used by patients with TMJ pain more than the conventional therapy. LLLT has been used for the treatment of a broad spectrum of conditions particularly in Europe[6] and Japan.[9]

Previous studies of the analgesic effects of low-level laser applications in musculoskeletal disorders of knee, cervical, and epicondylitis have showed a conflicting result.[10,26]

In a meta-analysis study of literature from 1966 to 1990, an author[18] concluded that the efficacy of laser therapy for treating musculoskeletal pain seemed to be greater than that of a placebo treatment. In contrast, another author[44] did not support the efficacy of laser therapy for musculoskeletal pain. Finally in our opinion it is very difficult to draw conclusions because of the difference in the dosage and lasers used in the trials, as well as the outcomes, which differed widely. In a more recent study, an author[45] showed that LLLT was efficacious in providing pain relief for patients with chronic neck pain over a period of 3 months.

It is interesting to observe that patients examined with MRI at T2 showed a more or less abundant effusion within the intra-articular, which disappeared after laser therapy,

TABLE 5. Significance of the Comparisons of Active and Passive Mouth Openings and Right and Left Lateral Motions Between the Groups

	Active Mouth Opening, *P*			Passive Mouth Opening, *P*			Right Lateral Motion, *P*			Left Lateral Motion, *P*		
Groups	Baseline	15 d	1 mo	Baseline	15 d	1 mo	Baseline	15 d	1 mo	Baseline	15 d	1 mo
L vs. D	0.001	0.001	0.001	0.001	0.001	0.001	0.013	0.001	0.001	0.001	0.001	0.001
L vs. C	0.031	0.001	0.001	0.012	0.001	0.001	0.683	0.228	0.001	0.631	0.001	0.001
D vs. C	0.026	0.083	0.003	0.041	0.069	0.001	0.296	0.232	0.741	0.411	0.123	0.412

$\alpha = 0.02$.
d indicates days.

whereas it remained stable in the other 2 groups, control and patients treated with NSAIDs. This reabsorption could explain the disappearance of pain through a wash out of the algogenic metabolites and the functional improvement through the elimination of the mechanical obstacle created by the liquid. In the case of osteoarthritis, a series of pathologic phenomenon is present, which results in a synovial inflammation inducing a cascade of reactions and, in particular, prostaglandins and leukotrienes. SLLLT might act on the sinovia and to stimulate cellular energy processes that appear. It could be hypothesized that in the condyle-meniscus coordination a sinovitis could arise, even without the evident signs of osteoarthritis, which could result in osteoarthritis as indicated by an author.[46]

Our therapeutic protocol and the characteristics of SLLLT (highest peak power for a few seconds) are suggested in the treatment of painful TMD. An important adjunctive factor is the low cost of the therapy.

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