■ LITERATURE REVIEW

Low Level Laser Therapy for the Treatment of Temporomandibular Disorders: A Systematic Review of the Literature

Marcello Melis, D.M.D., R.Pharm.; Massimiliano Di Giosia, D.D.S.; Khalid H. Zawawi, B.D.S., D.Sc.

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Address for correspondence:
Dr. Marcello Melis
Via Roma 130
09047 Selargius (CA)
Italy
Email:
marcellomelis01@libero.it

ABSTRACT: The authors performed a review of the literature to evaluate the efficacy of low level laser therapy (LLLT) for the treatment of temporomandibular disorders (TMD). Selection criteria included: 1) human subjects, 2) articles written in English, and 3) randomized placebo-controlled trials. Evaluation was performed according to the CONSORT 2010 criteria. A total of 14 articles were included in the review. Studies varied considerably in terms of methodological design, particularly regarding the site of application of the laser beam, the number of applications performed, their duration, the laser beam features (wavelength, frequency, output, dosage), and outcome measures. The outcome of the trials was controversial and not particularly related to any features of the laser beam, to the number of laser applications, and their duration. Based on the results of this review no definitive conclusions can be drawn on the efficacy of LLLT for the treatment of TMD. Many methodological differences among the studies, especially regarding the number and duration of laser applications and characteristics of the laser beam (wavelength, frequency, output), do not allow for standardized guidelines for effective treatment with LLLT. The only indication seems to be that LLLT is probably more effective for the treatment of TMJ disorders, and less effective for the treatment of masticatory muscle disorders.

Dr. Marcello Melis *received his pharmacy degree from the University of Cagliari (Italy) in 1990 and his D.M.D. degree from the Dental School of the same university in 1998. He was a resident at the Gelb Orofacial Pain Center at Tufts University, Boston from 1998 to 2000 when he completed the Fellowship Certification Program in Temporomandibular Disorders and Orofacial Pain. Currently, Dr. Melis practices in Cagliari in the field of temporomandibular disorders and orofacial pain and is an adjunct clinical instructor in the Craniomandibular Pain Center at Tufts University. He has been involved in several international research activities focusing on temporomandibular disorders and orofacial pain, occlusion, and muscle function.*

Temporomandibular disorders (TMD) is a collective term that embraces a number of clinical problems involving the masticatory muscles, the temporomandibular joint (TMJ), and the associated structures.[1] Such disorders are a major cause of non-dental pain in the orofacial region, with 40% to 75% of nonpatient adult populations displaying at least one sign, and approximately 33% reporting at least one symptom of TMJ dysfunction.[1]

Management of TMD is based mainly on conservative and reversible treatment modalities such as self-management, behavioral modification, physical therapy, medications, and orthopedic appliances.[1] More aggressive and irreversible therapies such as complex occlusal therapy or surgery should be avoided and limited to few selected cases.[1]

Among physical therapy procedures, low level laser therapy (LLLT) has recently been proposed to reduce symptoms and improve function in TMD patients.[2,3]

Lasers can be divided into "hard lasers" and "soft lasers" according to their energy output.[4] The former have higher energy output and are used to cut tissues, especially during surgical procedures.[4] The latter, also

called LLLT, have lower energy output and do not increase skin temperature; their main effect is based on light absorption rather than thermal effect.[5] They typically use light with a wavelength ranging between 630 nm and 1300 nm.[6]

Despite the fact that the precise mechanism of LLLT is not clear, it seems to have a biostimulating, anti-inflammatory, and analgesic effect through direct irradiation, without causing a thermal response.[7] Biostimulation occurs through metabolic activation, stimulation of the cellular respiratory chain in the mitochondria, and increasing vascularization and fibroblast formation.[8-10] The anti-inflammatory and analgesic effects of LLLT are probably due to multiple actions. It increases the beta-endorphin level in the spinal liquor and increases the urinary excretion of glucocorticoids, which are inhibitors of the synthesis of beta-endorphins.[11,12] It also increases the pressure pain threshold through a complex electrolytic nerve fiber blocking mechanism, and causes a decrease of the release of histamine and acetylcholine, and a reduction of the synthesis of bradykinin.[11,12] LLLT also produces an increase of ATP production, improvement of local blood microcirculation, reduction of edema through an increase of lymphatic flow, and reduction of prostaglandin E2 and cyclooxygenase-2 levels.[10-14]

Different studies report contrasting results in terms of pain reduction and improvement of mandibular function after LLLT in TMD patients. Thus, the aim of this study was to conduct a systematic review of randomized controlled trials to evaluate the efficacy of LLLT as a treatment modality for TMD.

Materials and Methods

Literature Search

A literature search of the published articles was performed using Pubmed and combining the terms: *temporomandibular disorders*, *temporomandibular joint disorders*, *temporomandibular joint dysfunction*, *temporomandibular joint dysfunction syndrome*, *temporomandibular joint disc*, *TMD*, *TMJ*, *craniomandibular disorders*, *myofascial pain*, *myofascial pain syndrome*, *face pain*, *facial pain*, on one side; and the terms: *laser*, *laser therapy*, *low level laser therapy*, *low intensity laser therapy*, *soft laser*, *LLLT*, *LILT*, on the other side. The selection was limited to articles written in English and experiments conducted on humans.

Titles and abstracts were evaluated in order to select the articles relevant to the topic, and the full text of these was obtained. The references of the articles were hand-searched in order to look for other relevant articles. Based on the trial design of the studies, only randomized controlled trials (RCTs) and only studies where laser therapy was compared to a placebo treatment were selected. A flow chart of the literature review is shown in **Table 1**.

After deciding the key words, two different authors ran the search independently. In case of disagreement, inclusion of the selected articles was discussed and a decision was made by consensus.

Quality Assessment of the Studies

Evaluation of the selected RCTs was carried out using the 2010 CONSORT criteria as modified by Fricton, et al.[15,16] The CONSORT criteria consist of a checklist and a flow chart with a list of requirements to help authors perform high-quality RCTs. For this reason, fulfillment of such requirements can also be used for the assessment of those studies. As proposed by Fricton, et al.,[16] the authors eliminated from the criteria those that do not affect the results of the studies and grouped some of them together to simplify the assessment of the studies (**Table 2**). All criteria divided into criterion **a** and criterion **b** were grouped together and evaluated as one (for example **1a** and **1b**). Then, criteria **8a**, **8b**, **9** and **10**, and criteria **12a**, **12b**, **17a**, **17b** and **18** were also grouped together and evaluated as one. The criteria listed by Fricton, et al.[16] are slightly different from the ones of the present study because recently the latest version of the CONSORT criteria became available.[15] For each point, a score of 0 was given if the criterion was not fulfilled, and a score of 1 was given if the criterion was fulfilled. This leads to a total score ranging from 0 to 12. As in Fricton, at al.,[16] the level I criteria for minimizing systematic bias were first determined by evaluating CONSORT points 8, 9, 10, 11, 15, and 16. Then, all CONSORT criteria were considered. Evaluation of the studies was carried out by two independent au-thors, except for the assessment of the statistical analysis, which was performed by an expert in statistics. In case of disagreement between the evaluators, differences were discussed and a decision was made by consensus.

Results

A total of 35 articles were first identified through the Pubmed search, and two more studies were found by hand-searching the references of the original articles. Only 17 were RCTs, and only 14 of them[17-30] included a placebo-controlled group in their study design (**Table 1**).

The studies selected for the review differed considerably in terms of methodological design, particularly regarding the site of application of the laser beam, the number of applications performed, their duration, the

Table 1
Literature Review Search Flow Chart

	Key words	Selections
1	"Temporomandibular Joint Disorders" [Mesh] OR "Temporomandibular Joint Disk" [Mesh] OR "Temporomandibular Joint Dysfunction Syndrome" [Mesh] OR "Temporomandibular Joint" [Mesh] OR "Craniomandibular Disorders" [Mesh] OR "Myofascial Pain Syndromes" [Mesh] OR "Face Pain" [Mesh] OR "Temporomandibular disorders" [All] OR "Temporomandibular joint disorders" [All] OR "Temporomandibular joint" [All] OR "Temporomandibular joint dysfunction syndrome" [All] OR "TMD" [All] OR "TMJ" [All] OR "Craniomandibular disorders" [All] OR "Myofascial pain" [All] OR "Myofascial pain syndrome" [All] OR "Face pain" [All] OR "Facial pain" [All].	28824
2	"Laser Therapy, Low-Level" [Mesh] OR "Laser Therapy" [Mesh] OR "Lasers" [Mesh] OR "Low level laser therapy" [All] OR "Laser therapy" [All] OR "Low intensity laser therapy" [All] OR "LLLT" [All] OR "LILT" [All] OR "Soft laser" [All].	180728
3	Combining 1 and 2	291
4	3 Limited to English and human	204
5	4 Title and abstract based selection (topic, original studies)	35
6	5 Hand search	+2
7	Randomized control trials	17
8	Studies with placebo control	14

laser beam features (wavelength, frequency, output, dosage), and outcome measures. All data are summarized in **Table 3**.

Of the 14 studies selected for the review, laser therapy was applied to the TMJ in eight studies, to the masticatory muscles in three studies, and to both the TMJ and the masticatory muscles in three studies. The number of laser applications varied between three (one application per week, for three weeks) and 20 (2-3 applications per week, for eight weeks), and their duration varied between 10 seconds and 10 minutes for each application. The characteristics of the laser beam are defined by the laser output, the frequency and wavelength of the laser beam, and these parameters, together with the area of the beam spot, result in the dosage density administered to the skin. These variables were very different in the studies examined. Output varied between 17 mW and 27 W, frequency varied between 0 Hz and 1,500 Hz, wavelength varied between 632.8 nm and 910 nm, and density dosage varied between 1 J/cm^2 and 105 J/cm^2. Also, outcome measures varied among the studies. They addressed pain intensity and mandibular function. Pain intensity was assessed using visual analog scales to indicate either spontaneous pain or pain on palpation, number of tender points, or by using the craniomandibular index. Mandibular function was assessed by measuring mouth opening, lateral mandibular movements, mandibular protrusion, presence of TMJ sounds, masticatory efficiency, and muscle activity through electromyography. Due to such great variability, quantitative data synthesis and evaluation in a meta-analysis was not possible.

Only the study by Emshoff, et al.[25] fulfilled the four required level I criteria for minimizing systematic bias. Most of the other studies failed to describe in detail the method used to generate and conceal the random allocation of the subjects in the groups (points 8-10), and to show a table with baseline demographic and clinical characteristics of each group (point 15).

Table 2
CONSORT Criteria

Section	No.	Explanation
Title and abstract	1a	Identification as a randomized trial in the title.*
	1b	Structured summary of trial design, methods, results and conclusions.*
Background and objectives	2a	Scientific background and explanation of rationale.*
	2b	Specific objectives or hypotheses.*
Trial design	3a	Description of trial design (such as parallel, factorial), including allocation ratio.
	3b	When applicable, important changes to methods after trial commencement (such as eligibility criteria), with reasons.
Participants	4a	Eligibility criteria for participants.
	4b	Settings and locations where the data was collected.
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered.
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed.
	6b	When applicable, any changes to trial outcomes after the trial commenced, with reasons.
Sample size	7a	How sample size was determined.
	7b	When applicable, explanation of any interim analyses and stopping guidelines.
Randomization sequence generation	8a	Method used to generate the random allocation sequence.**
Randomization/type	8b	Type of randomization; details of any restriction (such as blocking and block size).**
Randomization/ allocation	9	Mechanism used to implement the random allocation sequence allocation (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned.**
Randomization/ implementation	10	Who generated the random allocation sequence, who enrolled participants to interventions, and who assigned participants to interventions.**
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how.**
	11b	If relevant, description of the similarity of interventions.**
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes.
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses.
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval).
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended.

(Table 2 cont. on next page)

Table 2 (cont.)
CONSORT Criteria

Section	No.	Explanation
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory.
Participant flow	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome.
Losses and exclusions	13b	When applicable, for each group, losses and exclusions after randomization, together with reasons.
Recruitment	14a	Dates defining the periods of recruitment and follow-up.
Reason for stopped trial	14b	When applicable, why the trial ended or was stopped.
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group.**
Numbers analyzed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups.**
Harms	19	All important harms or unintended effects in each group.*
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses.*
Generalizability	21	Generalizability (external validity, applicability) of the trial findings.*
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence.*
Registration	23	Registration number and name of trial registry.*
Protocol	24	Where the full trial protocol can be accessed, if available.*
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders.*

*CONSORT 2010 criteria not evaluated in this study.
**Level I criteria for minimizing systematic bias.

The overall score of the studies varied from a minimum of six to a maximum of 12. Most of the studies failed to calculate the sample size of each group (point 7), and to define the period of recruitment and follow-up of the subjects (point 14). Interestingly, the quality of the studies tends to improve going from the oldest to the most recent.

As shown in **Table 3**, LLLT was found to be superior to placebo in improving pain intensity (either spontaneous or elicited by palpation), increasing mouth opening and lateral movements of the mandible, reducing the number of tender points, and decreasing TMJ effusion in eight studies. Conversely, no significant difference between the two groups was reported for pain intensity (either spontaneous or elicited by palpation), mouth opening, lateral movements of the mandible, mandibular protrusion, presence of TMJ sounds, pressure pain threshold over the TMJ, masticatory efficiency, craniomandibular index score, and electromyographic measurements in eight studies. In two studies, LLLT was also found to be superior to microcurrent electric neuromuscular stimulation in improving pain intensity and mouth opening, and to administration of ibuprofen in improving pain intensity, increasing mouth opening and lateral move-

Table 3
Selected RCTs from PubMed Search

Author	Site	Subjects	Timing	Duration	Wavelength	Frequency	Output	Dosage	Measure	Outcome	Score
Bertolucci LE, et al. 1995-1[17]	TMJ	32 (16+16)	3 apps/wk for 3 wks	9 min	904 nm	700 Hz	27 W		PI, MO, LM	LLLT>placebo	8
Bertolucci LE et al.-1995-2[18]	TMJ	48 (16+16+16)	3 apps/wk for 3 wks	9 min	904 nm	700 Hz	27 W		PI, MO, LM	LLLT>placebo LLLT>MENS* (PI, MO) LLLT=MENS (LM)	7
Conti PCR 1997[19]	TMJ Muscles	20 (5/5+5/5)	1 app/wk for 3 wks	40 sec	830 nm		100 mW		PI, MO LM, PR	LLLT=placebo	8
Kulekcioglu S et al. 2003[20]	TMJ Muscles	35 (20+15)	15 apps	3 min	904 nm	1000 Hz	17 mW	3 J/ cm^2	PI, TP, TMJ sounds, MO, LM	LLLT>placebo (TP, MO, LM) LLLT=placebo (PI, TMJ sounds)	8
de Abreu Venancio R et al. 2005[21]	TMJ	30 (15+15)	2 apps/wk for 3 wks	10 sec x 3	780 nm		30 mW	6.3 J/ cm^2	PI, MO LM, PR, TMJ PPT	LLLT=placebo	9
Mazzetto MO et al. 2007[22]	TMJ	48 (24+24)	2 apps/wk for 4 wks	10 sec	780 nm		70 mW	89.7 J/ cm^2	PI on palpation	LLLT>placebo	8
Carrasco TG et al. 2008[23]	TMJ	14 (7+7)	2 apps/wk for 4 wks	60 sec	780 nm		70 mW	105 J/ cm^2	PI on palpation, ME	LLLT>placebo (PI on palpation) LLLT=placebo (ME)	8
da Cunha LA et al. 2008[24]	TMJ Muscles	40 (20+20)	1 app/wk for 4 wks	20 sec	830 nm		500 mW	100 J/ cm^2	PI, CMI	LLLT=placebo	8
Emshoff R et al. 2008[25]	TMJ	52 (26+26)	2-3 apps/ for 8 wks	2+2 min	632.8 nm		30 mW	1.5 J/ cm^2	PI	LLLT=placebo	12
Carrasco TG et al. 2009[26]	Muscles	60 (10+10+10+ 10+10+10)	2 apps/wk for 4 wks		780 nm		50/60/ 70 mW	25/60/ 105 J/cm^2	PI on palpation	LLLT=placebo	7

(Table cont. next page)

Table 3 (cont.)
Selected RCTs from PubMed Search

Author	Site	Subjects	Timing	Duration	Wavelength	Frequency	Output	Dosage	Measure	Outcome	Score
Shirani AM et al. 2009[27]	Muscles	16 (8+8)	2 apps/wk for 3 wks	6 min 10 min	660 nm 890 nm	0 Hz 1,500 Hz	17.3 mW 9.8 W	6.2 J/cm^2 1.0 J/cm^2	PI	LLLT>placebo	9
Marini I et al. 2010[28]	TMJ	99 (39+33+33)	5 apps/wk for 2 wks	10+5+5 min	910 nm	1-50 Hz	400 mW -45W		PI, MO, LM, MRI	LLLT>placebo LLLT>ibuprophen	9
Mazzetto MO et al. 2010[29]	TMJ	40 (20+20)	2 apps/wk for 4 wks	10 sec x 4	830 nm		40 mW	5 J/cm^2	PI on palpation MO, LM	LLLT>placebo	6
Venezian GC et al. 2010[20]	Muscles	48 (12+12+ 12+12)	2 apps/wk for 4 wks	20/40 sec	780 nm		50/60 mW	20/60 J/ cm^2	PI on palpation, EMG	LLLT=placebo	9

PI: pain intensity; **MO**: mouth opening; **LM**: lateral movements; **LLLT**: low-level laser therapy; **MENS**: microcurrent electric neuromuscular stimulation; **TP**: tender points; **CMI**: craniomandibular index; **PR**: protrusion; **TMJ PPT**: temporomandibular joint pressure pain threshold; **ME**: masticatory efficiency; **EMG**: electromyography

ments of the mandible, and decreasing TMJ effusion.

Considering the studies separately, where LLLT was applied on the TMJs, six out of eight articles reported LLLT to be superior to placebo, except for masticatory efficiency. Considering the studies where LLLT was applied on the masticatory muscles, one out of three articles reported LLLT to be superior to placebo. Considering the studies where LLLT was applied both on the TMJ and the masticatory muscles, one out of three articles reported LLLT to be superior to placebo, but only for increasing mouth opening and lateral movements of the mandible and reducing the number of tender points.

Discussion

Site of Laser Application

The site of application of the laser beam was the first characteristic that differed between the studies. As already mentioned, laser therapy was applied to the TMJ in eight studies,[17,18,21-23,25,28,29] to the masticatory muscles in three studies,[26,27,30] and to both the TMJ and the masticatory muscles in three studies.[19,20,24] Considering the studies separately, where LLLT was applied on the TMJs, six out of eight articles reported LLLT to be superior to placebo, except for masticatory efficiency (**Table 3**). In the studies where LLLT was applied on the masticatory muscles, one out of three articles reported LLLT to be superior to placebo. In the studies where LLLT was applied both on the TMJ and the masticatory muscles, one out of three articles reported LLLT to be superior to placebo, but only for increasing mouth opening and lateral movements of the mandible and reducing the number of tender points. Based on these results, LLLT seems to be more effective when applied on the TMJ than when applied on the masticatory muscles. However, the study by Emshoff, et al.,[25] which obtained the highest score from both reviewers because of excellent methodological design, and therefore should be the most reliable study, together with the study by De Abreu Venancio, et al.,[21] showed a similar effect between LLLT and placebo when applied on the TMJ, contradicting the results of the rest of the studies. Still, it must be noted that in the study by Emshoff, et al.,[25] the patients treated with LLLT were all subjects who had already failed to respond to conventional therapy for TMD (self-care including soft diet, cold/hot packs, topical 3% diclofenac gel, occlusal appliance); therefore, they could be more resistant to any type of therapy.

Number and Duration of Laser Applications

The number of applications performed differed considerably, ranging from three (one application per week, for

three weeks) to 20 (2-3 applications per week, for eight weeks), and their duration varied from 10 seconds to 10 minutes for each application. Nevertheless, increasing the number of laser applications did not improve LLLT efficacy. In fact, the highest number of laser applications was used by Emshoff, et al.,[25] who reported analogous results between LLLT and placebo. Also, increasing the duration of laser applications did not improve LLLT efficacy when the laser is applied on the TMJ or on both the TMJ and the masticatory muscles, but when the laser is applied on the masticatory muscles only, a duration of 360 seconds or more was necessary to achieve positive results.

When combining the number and the duration of laser applications, the results remained similar.

Characteristics of the Laser Beam

The characteristics of the laser beam (i.e., wavelength, frequency, output) were dissimilar among the studies as well, leading to a different dosage of energy applied on the target site. When assessed separately, neither a particular wavelength, nor a frequency, nor an output of the laser beam were associated with a positive effect of LLLT, although frequency was rarely reported. However, these parameters, together with the area of the beam spot, define the dosage density administered to the skin, and such variable, although not always reported, ranged from 1 J/cm^2 to 105 J/cm^2. Even in this case, a different density dosage does not seem to affect the efficacy of the treatment. For example, in the study by Carrasco, et al.,[26] three different density dosages were used: 25 J/cm^2, 60 J/cm^2, and 105 J/cm^2, but the outcome was the same for all three trials.

Outcome Measures

Outcome measures addressed pain intensity and mandibular function. Pain intensity was assessed using visual analog scales to indicate either spontaneous pain or pain on palpation, number of tender points, or by using the craniomandibular index. Mandibular function was assessed by measuring mouth opening, lateral mandibular movements, mandibular protrusion, presence of TMJ sounds, masticatory efficiency, and muscle activity through electromyography. In most of the studies that evaluated both pain intensity and mandibular function, the results for both variables were similar. One exception is the study by Carrasco, et al.,[23] where LLLT was superior to placebo for pain on palpation, but was equal to placebo for masticatory efficiency. This indicates that pain intensity directly affects mandibular function (mouth opening, lateral mandibular movements, mandibular protrusion), but masticatory efficiency can be unrelated to it.

CONSORT 2010 Score

As already mentioned, only one study fulfilled the four required level I criteria for minimizing systematic bias (Emshoff, et al.[25]). Most of the other studies failed to describe the method used to generate and conceal the random allocation of the subjects in the groups (points 8-10) and to show a table with baseline demographic and clinical characteristics of each group (point 15). Most of the studies, also failed to calculate the sample size of each group (point 7) and to define the period of recruitment and follow-up of the subjects (point 14).

Point 14a of the CONSORT 2010 specifies that the "dates defining the periods of recruitment and follow-up" of the subjects must be clearly indicated in the materials and methods section of the article. None of the studies specified those dates; however, the reviewers agreed on a less strict evaluation, assigning a one score to the study by Emshoff, et al.[25] and Shirani, et al.[27] because they indicated the duration of the study, specifying in the materials and methods section of their articles both the period over which the subjects were selected and the duration of the trial.

Point 16 of the CONSORT 2010 specifies that it must be indicated in the article whether statistical analysis was performed by originally assigned and randomized groups. This is to avoid bias due to unequal drop-outs. Only the article by Emshoff, et al.[25] clearly specified that the analysis was intention-to-treat and involved all randomly assigned patients. However, since the duration of the studies was always short (2-8 weeks), when no drop-outs were specifically reported, the reviewers assumed that statistical analysis was performed by originally assigned groups, assigning a one score to the respective articles.

General Considerations

It must be considered that TMD includes articular and muscular disorders that, even in the presence of some peculiarities, should not significantly differ from other muscular and articular disorders in the rest of the body. Several studies, many of which were also included in a recent review of the literature,[33] support the use of LLLT for the treatment of chronic joint and muscle disorders[31-33]; therefore, it is surprising that the results of the present review did not confirm such outcome. One hypothesis is that, when structural or functional problems are present (for example a displaced disc), the effects of the laser beam cannot sufficiently reduce the symptoms until the main cause is addressed, and this can be a specific feature of the TMJ.

In addition, LLLT is intended as an adjunct treatment for TMD; therefore, more positive results could probably be reached associating such therapy with standard treat-

ment modalities.

For these reasons, researchers are encouraged to further look into the potentials of LLLT in order to achieve more consistent results for the treatment of TMD.

Conclusions

Based on the results of this review, no definitive conclusions can be drawn on the efficacy of LLLT for the treatment of TMD. Many methodological differences among the studies, especially regarding the number and duration of laser applications and characteristics of the laser beam (wavelength, frequency, output), do not allow for standardized guidelines for effective treatment with LLLT.

The only indication seems to be that LLLT is probably more effective for the treatment of TMJ disorders and less effective for the treatment of masticatory muscle disorders.

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Dr. Massimiliano Di Giosia *received his D.D.S. degree from the Dental School of the University of Chieti (Italy) in 2001. He completed a three-year residency in orofacial pain at the University of Kentucky Orafacial Pain Center, directed by Dr. Jeffrey P. Okeson, in 2007. In 2008, Dr. Di Giosia completed a postgraduate course in "Headache and Cranial Neuralgias" at the University of Torino. His is a Diplomate of the American Board of Orofacial Pain. He is currently enrolled in the orthodontic residency program at the University of Cagliari. Dr. Di Giosia limits his clinical practice to the field of orofacial pain and dental sleep medicine.*

Dr. Khalid H. Zawawi *is an associate professor of orthodontics at the Faculty of Dentistry, King Abdulaziz University, Jeddah, Saudi Arabia. He received his Certificate in Orthodontics and D.D.S. degree from Boston University and completed the Fellowship Certification Program in TMD and Orofacial Pain at Tufts University School of Dental Medicine. Dr. Zawawi has been on the staff of the Faculty of Dentistry at King Abdulaziz University since 1993. He also served as a research associate at the Craniofacial Pain Center at Tufts University where he published numerous articles on TMD and orofacial pain.*