

Efficacy of 904 nm Gallium Arsenide Low Level Laser Therapy in the Management of Chronic Myofascial Pain in the Neck: A Double-Blind and Randomize-Controlled Trial

Ali Gur, MD,* Aysegul Jale Sarac,¹ Renzi Cevik,¹ Ozlem Altindag,¹ and Serdar Sarac²

¹Physical Medicine and Rehabilitation, School of Medicine, Dicle University, Diyarbakir, Turkey

²Physical Medicine and Rehabilitation, Kartal State Hospital, Istanbul, Turkey

Background and Objectives: A prospective, doubleblind, randomized, and controlled trial was conducted in patients with chronic myofascial pain syndrome (MPS) in the neck to evaluate the effects of infrared low level 904 nm Gallium-Arsenide (Ga-As) laser therapy (LLLT) on clinical and quality of life (QoL).

Study Design/Patients and Methods: The study group consisted of 60 MPS patients. Patients were randomly assigned to two treatment groups: Group I (actual laser; 30 patients) and Group II (placebo laser; 30 patients). LLLT continued daily for 2 weeks except weekends. Follow-up measures were evaluated at baseline, 2, 3, and 12 weeks. All patients were evaluated with respect to pain at rest, pain at movement, number of trigger points (TP), the Neck Pain and Disability Visual Analog Scale (NPAD), Beck depression Inventory (BDI), and the Nottingham Health Profile (NHP).

Results: In active laser group, statistically significant improvements were detected in all outcome measures compared with baseline ($P < 0.01$) while in the placebo laser group, significant improvements were detected in only pain score at rest at the 1 week later of the end of treatment. The score for self-assessed improvement of pain was significantly different between the active and placebo laser groups (63 vs. 19%) ($P < 0.01$).

Conclusion: This study revealed that short-period application of LLLT is effective in pain relief and in the improvement of functional ability and QoL in patients with MPS. *Lasers Surg. Med.* 35:229-235, 2004.

© 2004 Wiley-Liss, Inc.

Key words: gallium arsenide; low level laser therapy; myofascial pain syndrome; neck pain; quality of life; depression

INTRODUCTION

Myofascial pain syndrome (MPS) is a common cause of pain in clinical practice. MPS is characterized by acute or chronic specific pain affecting a small number of muscles and involving single or multiple "trigger points" that are usually located in tight bands within the affected muscles [1]. These trigger points (TP) are hypersensitive to pressure and produce a local twitch and referred pain within a defined reference area [2,3]. It has been proposed that acute or chronic muscle stress may be an initiating factor in MPS.

MPS was shown the most common in neck or shoulder and it is one of the most common of neck or shoulder pain in our population. Neck pain is a common complaint with a point prevalence from 10 to 18% and lifetime prevalence from 30 to 50%. Chronic neck pain has a high prevalence in the community and is responsible for significant loss of work-days and a reduction in quality of life for individuals [4,5].

Common treatment consists of drugs, massage, and other physiotherapy, local and epidural injections. Non-steroidal anti-inflammatory drugs are commonly used for this condition but have significant side-effects, and pain modulating therapies, such as anti-epileptic medication, are not well tolerated. Thus, there is a need for non-drug, and non-invasive therapies for chronic neck pain related with MPS which can be used as a first-line therapy in practice [6]. Current treatment increasingly includes complementary methods, of which low level laser therapy (LLLT) is one of the most commons.

LLLT was introduced in a clinical randomized controlled trial on musculoskeletal pain as early as in 1980 [7]. In the past two decades, a number of clinical randomized controlled trials have been performed with LLLT to treat a variety of musculoskeletal and neurogenic pain conditions. Clinical applications of LLLT have been performed either by direct exposure of the skin overlying the injury, exposure of TP or acupuncture points, or of nerves inside or outside the painful area. A broad range of doses (0.0001-38 J/cm² [8] has been reported to produce significant effects on musculoskeletal disorders in about one third of the LLLT trials. Thus the rationale behind the selection of application technique and treatment parameters like power density, size of exposure area, timing or treatment frequency often remains unclear. Recent review articles have concluded that there is a little-if any-in evidence favor of LLLT for the treatment of musculoskeletal pain [9,10]. Several editorials in medical journals have supported the criticism on the clinical use of LLLT [11]. Still the amount of rando-

*Correspondence to: Ali Gur, MD, Physical Medicine and Rehabilitation, Dicle University School of Medicine, Diyarbakir, Turkey. E-mail: alig@dicle.edu.tr

Accepted 11 June 2004

Published online in Wiley InterScience

(www.interscience.wiley.com).

DOI 10.1002/1sm.20082

mined controlled trials with results in favor of LLLT is by far too large to be explained by random chance alone [10].

Recently, in a systematic review by Bjordal et al. [12], they stated that the results are conflicting in different studies and may depend on the method of application and other features of the LPLT application in chronic joint disorders. Authors, in their review, stated that LLLT with the suggested dose range significantly reduces pain and improved health status in chronic joint disorders, but the heterogeneity in patient samples, treatment procedures, and trial design calls for cautious interpretation of the results.

In recent studies, many authors have reported significant pain reduction with LLLT in acute and chronic painful conditions such as rheumatoid arthritis (830 nm Ga-As-Al) [13], cervical osteoarthritis (830 nm Ga-As-Al) [14], knee osteoarthritis (904 nm Ga-As) [15], fibromyalgia (904 nm Ga-As) [16,17], postoperative pain (low intensity 1.06 microm neodymium: yttrium-aluminum-garnet laser emitted 542 mW/cm²) [18], and low-back pain (904 nm Ga-As) [19]. However, some have failed to show such an effect in painful musculoskeletal pathologies such as epicondylitis (830 nm Ga-Al-As) [20], plantar fasciitis (830 nm Ga-Al-As) [21], and myofascial pain in the neck (830 nm Ga-Al-As) [22]. The equipment, experimental designs, and techniques used in the low-energy laser literature are highly variable, and close attention should be paid to therapy parameters when reviewing and comparing these studies. Still, the efficacy of this therapy method is controversial.

There are few studies of LLLT for neck pain. Those that exist describe the use of different wavelengths such as 830 nm. Ga-Al-As [14], Cecherelli (pulsed infrared diode laser) [23] and 630 nm He-Ne [24] in the management of chronic pain and describe treatment of acute rather than chronic pain (904 nm Ga-As) [25].

Thus, a prospective, double-blind, randomized, and controlled trial was conducted in patients with MPS in the neck to evaluate the effects of LLLT on clinical and QoL.

SUBJECTS AND METHODS

Subjects

Of the total 148 patients referred for the first assessment, 69 did not meet the inclusion criteria and 19 subjects refused to participate; 60 patients were included in the trial (Fig. 1).

The diagnosis of MPS was based on the following criteria: (1) presence of a tender spot characterized by spontaneous pain or associated with movement of the right or left superior trapezius muscle; (2) reproduction or enhancement of the clinical symptoms by compression of the active TP; (3) presence of a palpable taut band peripherally to the TP. Non-essential criteria considered in diagnosis were: presence of spontaneous referred pain in parts of the body other than the superior trapezius muscle; elicitation of referred pain by compression of the active TP; weakness of the trapezius muscle; restricted range of motion of the cervical spine; palpable or local twitch response upon

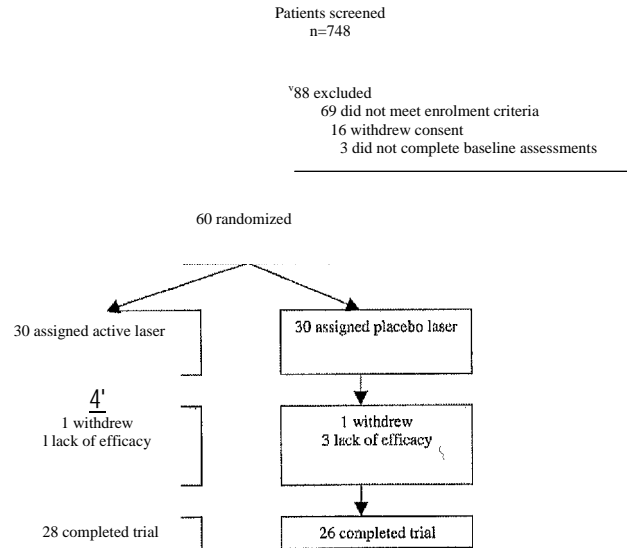


Fig. 1. Trial profile,

snapping palpation of the most sensitive spot in the taut band.

After an examination by a physician, the patients were included in the study if they fulfilled the following criteria: (1) age 17-55 years; (2) pain from the neck and shoulder-girdle lasting at least 1 year, affecting the quality of work or daily living; (3) between one and ten tender points in the shoulder-girdle, tender points that on palpation induced reproduction of the reported symptoms.

Major clinical conditions other than MPS were excluded by physical examination and routine whole blood cells counting, hematocrit, hemoglobin, baseline thyroid-stimulating hormone, and antinuclear autoantibodies studies. The following patients were excluded from the study: (1) patients with signs and symptoms of fibromyalgia; (2) patients aged below 17 or above 55 years; (3) patients with mental retardation; (4) patients with neurological deficits involving the upper limbs; (5) patients with advanced osteopathic or arthropathic disorder of the cervical spine or the shoulder of the investigated side. Furthermore, we excluded patients presenting contraindications for the administered therapies, namely, patients suffering from cardiovascular disease, hypertension, coagulopathy, ulcer, recent severe hemorrhage, renal insufficiency, severe hepatic disease, neoplasia, epilepsy, cutaneous pathology or pain of central origin, and pregnant women.

An orthopaedic surgeon, who had excluded orthopaedic disease as a cause of the pain, had examined all patients. Rheumatic or other inflammatory diseases had been excluded by laboratory test procedures and clinical examination. All subjects were free of any infections, inflammatory or allergic reactions for at least 2 weeks prior to the blood sampling and free of drugs known to affect immune or endocrine functions and of hormonal preparations. Each patient had normal findings on radiographs of the chest, hands, feet, and sacroiliac joints. Each patient had been

examined by a physician to ensure that they met the criteria for MPS and to rule out the presence of any other rheumatic disorder, including chronic fatigue syndrome and fibromyalgia syndrome. Thus, the patients' symptoms could be attributed solely to MPS. The Human Studies Research Committee of the University of Dicle, Diyarbakir, approved all procedures, and written informed consent was obtained from each subject prior to inclusion in the study.

Sixty patients of whom 11 were men and 59 were women, mean age was 31.72 ± 9.25 years (range 18-53), were included. No drop-out was reported after inclusion and randomization due to complications.

Equipment

The active laser was a Ga-As infrared laser, class III b Laser Product, with a wavelength of 904 nm, Frank Line IR 30, Fysiorned Belgium. The same unit was used for the placebo treatment, for which no laser beam was emitted. Laser units were checked by the manufacturer just before the first patient started and after patient no. 15 of the study. After patients 30 and 45, the technical medical department at Dicle University checked the units.

Study Design, Randomization, and Blinding

Sixty patients were randomly assigned to two treatment groups by one of the non-treating authors by drawing 1 of 60 envelopes labeled 'A' (Group I: actual laser; 30 patients) and 'B' (Group II: placebo laser; 30 patients).

Before each treatment session the physiotherapist palpated the TP (up to ten). The probe was in contact with the skin at a right angle. The patients were treated for 3 minutes at each trigger point daily for 2 weeks, except weekends, at the same time in the afternoon in a sitting position, and at a temperature of 20°C. LLLT was used at each trigger point, producing an energy density (radiant exposure) at each point of approximately 2 J/cm² (maximum 20 J/cm²). The physical therapist investigator used a standard technique, with a GasAs laser (20 W maximum output per pulse, 904 nm, 200 nanoseconds maximum pulse duration, 2.8 kHz pulse frequency, 11.2 mW average power, and 1 cm² surface). The same unit was used for the placebo treatment, for which no laser beam was emitted. The study was conducted in a double-blind fashion. Subjects and physician were unaware of the code for active or placebo laser until the data analysis was complete but therapist was aware of the code for active or placebo laser. The patients, who were eligible and willing to participate in the study, were assessed by an independent examiner.

The blind settings for patients and the physician were maintained until the last patient had completed the study but therapists were not blind. As a rule, the same therapist gave all the laser treatments for each patient. Upon arrival to the first and follow-up appointments, patient characteristics and health information and baseline measures such as demographic characteristics, functioning, pain, and quality of life scores were recorded.

The Human Studies Research Committee of the University of Dicle, Diyarbakir, approved all procedures, and written informed consent was obtained from each subject prior to inclusion in the study.

Follow-Up Measures

Active and placebo Laser therapies continued daily for 2 weeks except weekends (ten treatments for each group). Follow-up measures were evaluated at baseline, 2, 3, and 12 weeks. Study was completed at 12 weeks. All patients were evaluated with respect to pain at rest, pain at movement, self-assessed improvement of pain, number of TP, and the Neck Pain and Disability Scale (NPDS). Depression was evaluated according to Beck depression Inventory (BDI). QoL of the MPS patients was assessed according to the Nottingham Health Profile (NHP).

Each patient was asked to point with his finger to the most painful zone in the affected trapezius. All areas of tenderness were marked with a pen. Subsequently, the characteristics of the trigger point were evaluated by the examiner through palpation of the zone pointed out by the patient. Zero point were assigned when the examiner noticed an increased consistency of the TP in absence of pain; one point when the consistency was increased but the patient reported pain only after an explicit question from the doctor; two points when the consistency was increased and the patient spontaneously reported pain; three points when the consistency was increased and the patient manifested withdrawal from palpation. Pain degree at rest and movement was measured by visual analogue scale (VAS). In order to accommodate, we also asked patients to record their perceived improvement of their pain as a VAS score, allowing them to indicate a worsening, as well as an improvement, in symptoms. The VAS for self-assessed improvement, which rated global improvement, included a negative arm to indicate worsening of symptoms. This was completed at the end of treatment. A derived score based on the difference between the final VAS and the initial VAS, expressed as a percentage of the initial VAS, was used for statistical analysis of the overall response to treatment. Patients were instructed to avoid any activity which exacerbated the pain between treatments. General advice was given with regard to maintaining correct posture and attending to ergonomic factors in the work place or the home environment. These strategies were utilized to assist in the overall management of the patient's pain.

Depression evaluated by psychiatrist according to BDI scale and DSM IV criteria.

Functional status was assessed by the Neck Pain and Disability Scale (NPDS) [26]. The NPDS was the primary outcome measure. It consists of 20 items that use a visual analog scale to measure neck pain and associated problems. Scoring on each item ranges from 0 to 5, and NPDS score is produced by summing the item scores. Scores above 23 indicate clinically significant neck pain and the higher the score, the greater the degree of pain and disability. The NPDS has been shown to be an internally consistent instrument that measures four underlying factors—problems with the neck, intensity of pain, interference

with functional aspects of living, and the presence of associated emotional factors. It was used because it incorporates the visual analog scale used in previous research and it provides a comprehensive measure of neck pain and disability.

Health status and QoL of the MPS patients was assessed by NHP [27]. At the end of the trigger point examination, each subject was given a copy of the forms,

The NHP [28] is one of the generic health status instruments that have been used in a wide range of diseases to assess subjective perception of physical, emotional, and social aspects of the illnesses and to monitor the progress of the diseases and impact of therapy. It is a self-administered questionnaire containing 38 items (answered yes or no), that measure six dimensions; energy (3 items), pain (8 items), physical mobility (8 items), emotional reactions (9 items), sleep (5 items), and social isolation (5 items). Scores for each section can range from 0 to 100 with a higher score indicating more severely compromised quality of life. Each item had a weighted score but the authors of the instrument had reported that their use was equivalent to reporting the percentage of items affirmed in each section [28]. It is most effective and easy to use in clinical practice.

Statistics

The data obtained were analyzed using the Statistical Package for the Social Sciences (SPSS 10.0). The sample size was calculated to detect a 20% difference between treatment groups in the primary effectiveness measure. Using a power of 78 and $\alpha = 0.05$, the required sample size was 30 patients per group. The results are expressed as means \pm standard deviations. Statistical significance was tested using the paired *t* test for repeated measures of the same group and was tested independent Student's *t* test for between group comparisons. In addition, Chi-square test or Fisher's exact test when the cell number is small were used for categorical variables. The level of statistical significance was set at a two-tailed *P*-value of 0.05.

RESULTS

The mean age of active and placebo laser groups were 32.24 \pm 8.43 and 30.92 \pm 9.37 years. Many of the patients had a low educational level. Active laser group consisted of 23 females and 7 males and there were 24 females and 6 males in placebo group. In both groups, mean body mass index and duration of MPS were approximately the same. There was no statistically significant difference in any baseline characteristics between the groups ($P > 0.05$) (Table 1).

All scores in both the active and placebo laser groups were compared at baseline, at the completion of treatment (second week of study period), 1 week (third week of study period) and 10 week (twelfth week of study period).

In active laser group, statistically significant improvements were detected in mean number of TP at all follow-up measures compared with baseline ($P < 0.01$) while there was no statistically significant difference at any follow-

TABLE 1. Baseline Characteristics for Both Active and Placebo Laser Groups

Variables	Active laser	Placebo laser
Age (year)	32.24 \pm 8.43	30.92 \pm 9.37
Disease duration (month)	43.38 \pm 24.42	42.55 \pm 26.31
Body mass index (kg/m ²)	28.19 \pm 5.27	27.22 \pm 5.69
Marital status (n/%)		
Married	12(40)	11 (37)
Single	13(43)	14 (46)
Divorced	5(17)	5 (17)
Educational status (n/%)		
Elementary school	14(46)	16 (53)
Secondary school	8(27)	6 (20)
University/high school	8(27)	8 (27)
Employment status (n/%)		
Employed	4(12)	5 (17)
Homemaker	17(57)	14 (46)
Student	6(21)	7 (25)
Others	3(10)	4 (12)

Figures represent mean (and standard deviations), unless stated to be a percentage of the group. Statistically no significant difference between groups (independent Student's *t* test, Chi-Square test, or Fisher's exact test when the cell number is small).

up measures in placebo group compared with baseline (Table 2). There was no significant difference between two groups in the mean numbers of TP prior to treatment. However, there were significant improvements in the active laser group compared with placebo group at the end of the treatment, and at 1 and 10 weeks after completion of treatment ($P < 0.01$).

In active laser group, statistically significant improvements were detected in pain measures such as pain levels at rest and at movement at the end of treatment (51%), 1 week (66%) and 10 weeks (36%) later compared with baseline ($P < 0.01$). In the placebo laser group, statistically significant improvements were detected in only pain levels at rest at the 1 week later (23%) of the end of treatment compared with baseline. At baseline, there was no significant difference between both the mean pain scores at rest and at movement of the two groups. However, at the end of treatment and 1 week later there was a significantly greater improvement in the active laser group compared with placebo group but was not 10 week later ($P < 0.01$). The score for self-assessed improvement of pain was significantly different between the active and placebo laser groups (63 vs. 19%) ($P < 0.01$) (Fig. 2).

With regard to the NPDS, NHP, BDI scores in active laser group there was a statistically greater improvement in all follow-up measures ($P < 0.01$), except in NHP at 10 weeks later compared with placebo group whereas at baseline there was no significant difference between two groups (Table 2).

Generally, no side effects were observed in patients. Tiredness was seen within the first 5 days of active laser treatment in only one patient.

Placebo laser		Active Laser	
Parameter	Mean ± SD	Mean ± SD	Significance
NHP score	4.83 ± 4.59	5.68 ± 3.56	ns
PS score	5.79 ± 3.12	6.87 ± 1.96	ns
BDI score	6.62 ± 3.09	7.19 ± 2.52	ns
VAS	61.87 ± 26.73	68.52 ± 28.39	ns
NPDS	69.61 ± 27.92	75.47 ± 26.15	ns
Disability	19.56 ± 12.07	20.81 ± 12.25	ns
TP	3.25 ± 2.21 ^{ce}	4.18 ± 2.65 ^c	ns
Quality of life	4.18 ± 2.65 ^c	5.26 ± 1.49 ^c	ns
Functioning	41.14 ± 28.34 ^{ae}	56.41 ± 29.18 ^c	ns
Pain at rest	14.72 ± 13.19 ^c	14.55 ± 10.47 ^{ae}	ns

Values are mean ± standard deviation for all variables; where no superscript appears, there is no significant difference.

^aSecond week.
^bThird week.
^cTwelfth week values of Active Laser Group are significantly different from values before therapy of the same group by paired *t* test ($P < 0.01$).
^dThird week values of Placebo Laser Group are significantly different from values before therapy of the same group by paired *t* test ($P < 0.01$).
^eFollow-up values of Active Laser Group are significantly different from the values in the corresponding week of the Placebo Laser Group by Independent Student's *t* test ($P < 0.01$).

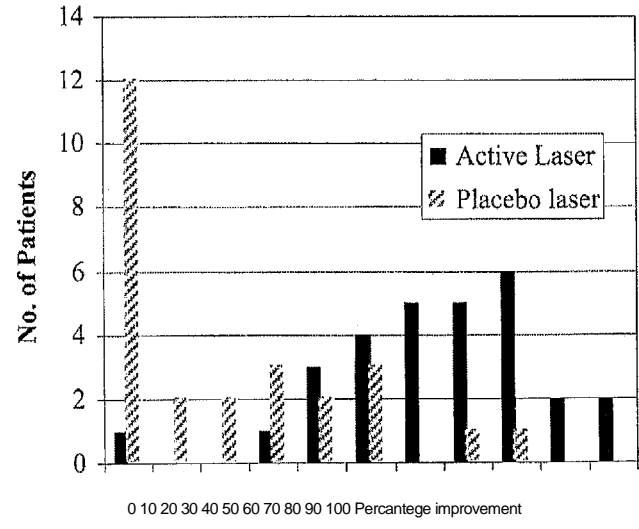


Fig. 2. Perceived percentage improvement in pain at the end of treatment in both actual and placebo laser groups.

DISCUSSION

We found significant improvements in patients in active therapy group with respect to all of the parameters such as pain, number of TP, depression score, functioning, and quality of life measures, whereas there were significant improvements in patients in the placebo laser group with respect to only pain levels at rest at the 1 week later of the end of treatment. Our study revealed a statistically significant and clinically useful effect in management of chronic neck pain related with MPS. Additionally, the score for self-assessed improvement of pain was significantly different between the active and placebo laser groups (63 vs. 19%).

There are reports in the literature in which 'trigger points' are treated with laser [29], and a reduction in local tenderness occurs though significant controversy exists as to the nature and even the existence of TP in the neck [30]. In our study, we determined statistically significant reduction in numbers of TP in active therapy group.

In our study, in active laser group, statistically significant improvements were detected in pain measures at the end of treatment (51%), 1 week (66%) and 10 weeks (36%) later compared with baseline whereas in the placebo laser group, statistically significant improvements were detected in only pain levels at rest at the 1 week later (23%) at the end of treatment compared with baseline.

LLLT is reported as being side effect free and studies rarely report any systematic recording of side-effects. Kert and Rose [31] are the only authors who have described in detail several possible patterns of increased pain as a reaction to treatment. In our study, no serious side effect was observed in patients. Tiredness was seen within the first 5 days of active laser treatment in only one patient.

The exact mechanism of pain reduction by LLLT is not completely understood although a number have been postulated. While the underlying mechanism is unknown,

it has been demonstrated in animal studies that pulsed Nd-Yag laser therapy results in a selective reduction of A S and C fiber activity [32],

Anti-inflammatory effects have been demonstrated both in-vitro (820 nm Ga-Al-As) [33] and in-vivo (632.8 nm He-Ne) [34] and a direct effect on motoricity of lymph vessels (630 nm He-Ne) [35], reducing interstitial fluid at the site of inflammation, has been described. Many investigators have observed an anti-inflammatory effect of LLLT in studies conducted in patients with rheumatoid arthritis by 10 Hz Q-switch neodymium laser (1.06 urn with an output of 15 J/cm² per 30 nanoseconds) [36] and by 630 nm He-Ne laser [37]. A histochemical study has shown a marked increase of prostaglandin I₂ following LLLT, and consequently inhibition of platelet aggregation and vasodilatation [38]. Improvement of local circulation leads to reduction of edema and better oxygenation of tissues and thus may result in reduction of pain. In addition, increased fibroblast activity and lying down of collagen in damaged ligaments may also contribute to long-term pain relief associated with laser therapy (632.8 nm He-Ne) [39].

Lack of Na-K-ATP ase activity seems to increase nociceptive impulse transmission; an increase in Na-KATP ase following LLLT may be a factor in pain attenuation [40-42]. Kudoh et al [41] reported a charge of Na-K-ATP ase in rat saphenous nerve alter LLLT treatment (830 nm Ga-Al-As). Synder-Mackler and Bork [43] reported a statistically significant increase in the latency of the superficial radial nerve in healthy subjects that corresponded to a decrease in sensory nerve conduction velocity after application of LLLT (630 nm He-Ne).

Thus, LLLT could produce pain relief by one or a combination of these mechanisms: collagen proliferation, anti-inflammatory effect, circulation enhancement, peripheral nerve stimulation, and analgesic effect.

In a systematic review by Bjordal et al [10], the results from some in vitro trials on fibroblast cell cultures [44,45], showed that optimal power density and dose for increasing collagen production by 34-37% were 4.5-7.5 mW/cm² and 0.45-0.6 J/cm² for continuous 632.8 nm He-Ne laser and 820 nm Ga.-Al-As laser respectively. In vivo trials on sutured soft tissue injuries produced similar results on collagen production with slightly higher doses (1-3.6 J/cm²) of continuous 632.8 nm He-Ne laser, and the same power density [46,47]. One in vivo trial suggested that pulsed 904 nm GaAs laser only needed 0.4 J/cm² to increase fibroblast metabolism [48]. In in vitro trials higher energy doses have been reported to suppress inflammation [49,50]. This effect was also reported to be dose-dependent with an optimal range of 1.9-6.3 J/cm² and power density of 21.2 mW/cm².

In the planning stage of this study, we had difficulty in finding readings in the literature related to the use of laser therapy in MPS. We found that there were no standard therapy programs regarding the dose and duration of the laser, and the current publications revealed various results. These varieties in the literature may have arisen from the selection of patients, application of the therapy, and dose, period, and type of laser.

There are many open questions. What is the real mechanism of the therapy? What is the correct dosage per point? We know that the penetration of the skin differed between Ga-As and He-Ne lasers. Most of the energy is absorbed in the first 2 mm. Also there are differences in the technology and in the devices, and differences between the geometry of the laser beam, the divergence of the beam, and the system of collimation of the diode laser equipment. Because of the large number of positive reports and the innocuous nature of the therapies, further clinical evaluation of laser therapy is warranted.

In conclusion, this study revealed that short-period application of LLLT is more effective in pain relief and in the improvement of functional ability and quality of life than that of placebo laser in patients with MPS patients. Chronic neck pain related with MPS is a common clinical condition and LLLT with Ga-As may offer an additional, non-drug option in general practices. Thus, LLLT can be an important adjunct in the treatment of MPS patients, especially in patients with adverse side effects to drug and invasive treatment.

REFERENCES

1. Travell JG, Simons DG. Myofascial pain and its trigger points. In: Travell JG, Simons DG, editors. Myofascial pain and dysfunction. The trigger point manual. Baltimore, MD: Williams and Wilkins; 1983. pp 5-164.
2. Fischer AA. New developments in diagnosis of myofascial pain and fibromyalgia. *Phys Med Rehab Clin North Am* 1997; 8:1-27.
3. Yunus MB, Kahan-Raman UP, Kalian-Raman K. Primary fibromyalgia syndrome and myofascial pain syndrome: Clinical features and muscle pathology. *Arch Phys Med Rehabil* 1988;69:451-454.
4. Cote P, Cassidy JD, Carroll L. The Saskatchewan health and back pain survey: The prevalence of neck pain and related disorders in Saskatchewan adults. *Spine* 1998;23:1689-1698.
5. Hoving L, Gross AR, Gasner D, et al. Critical appraisal of review articles in the effectiveness of conservative treatment for neck pain. *Spine* 2001;26(2):196-205.
6. Noes BW, Bouter LM, van Mameren H, et al. The effectiveness of manual therapy, physiotherapy, and treatment by the general practitioner for non-specific back and neck complaints: A randomized clinical trial. *Spine* 1992;17:28-35.
7. Goldman JA, Chiapella J, et al. Laser therapy of rheumatoid arthritis. *Laser Surg Med* 1980;1:93-101.
8. Basford JR. Low intensity laser therapy: Still not an established clinical tool. *Laser Surg Med* 1995;16(4):331-342.
9. de Bie RA, Verhagen A, et al. Efficacy of 904 nm laser therapy in musculoskeletal disorders. *Phys Ther Rev* 1998; 3(2):1-14.
10. Bjordal JM, Couppe C, Ljunggren AE. Low level laser therapy for tendinopathy. Evidence of a dose-response pattern. *Phys Ther Rev* 2001;6:91-99.
11. Dever M. What's in a laser beam for pain therapy? *Pain* 1990;43:139.
12. Bjordal JM, Couppe C, Chow RT, Tuner J, Ljunggren EA. A systematic review of low laser therapy with location-specific doses for pain from chronic joint disorders. *Aust J Physiother* 2003;49:107-116.
13. Johanssen B, Hauschild B, Remvig L, et al. Laser therapy of rheumatoid arthritis. *Scand J Rheumatol* 1994;23:145-147.
14. Ozdemir F, Birtane M, Kokino S. The clinical efficacy of low power laser therapy on pain and function in cervical osteoarthritis. *Clin Rheumatol* 2001;20:181-184.

15. Gur A, Cosut A, Sarac AJ, Cevik R, Nas K. Effects of different therapy regimes of low power laser in painful osteoarthritis of the knee: A double-blind and placebo-controlled trial. *Laser Surg Med* 2003;33:330-338.
16. Gur A, Karakoc M, Nas K, et al. Efficacy of low power laser therapy in fibromyalgia: A single-blind, placebo-controlled trial. *Lasers Med Sci* 2002;17:57-61.
17. Gur A, Karakoc M, Nas K, et al. Effects of low power laser and low dose amitriptyline therapy on clinical symptoms and quality of life in fibromyalgia: A single-blind, placebo controlled trial. *Rheumatol Int* 2002;22(5):188-193.
18. Basford JR, Sheffield CG, Harmsen WS. Laser therapy: A randomized controlled trial of the effects of low-intensity Nd:YAG laser irradiation on musculoskeletal back pain. *Arch Phys Med Rehabil* 1999;80:647-652.
19. Gur A, Karakoc M, Cevik R, et al. Efficacy of low power laser therapy and exercise on pain and functions in chronic low back pain. *Lasers Surg Med* 2003;32(3):233-238.
20. Krashennikoff M, Ellitsgaard N, Rogvi-Hansen B, Zeuthen A. No effect of power laser in lateral epicondylitis. *Scand J Rheumatol* 1994;23(5):260-263.
21. Basford JR. A randomized controlled evaluation of low-intensity laser therapy: Plantar fasciitis. *Arch Phys Med Rehabil* 1998;79(3):249-254.
22. Thorsen H, Gam AN, Svensson BH, et al. Low level laser therapy for myofascial pain in the neck and shoulder girdle. A double-blind, cross-over study. *Scand J Rheumatol*. 1992;21:139-142.
23. Ceccherelli F, Altafini L, Lo castro G, et al. Diode laser in cervical myofascial pain: A double blind study versus placebo. *Clin J Pain* 1989;5(4):301-304.
24. Synder-Mackler L, Bork CE, Bourbon B. Effect of helium-neon laser on musculoskeletal trigger points. *Phys Ther* 1986;66(7):1087-1090.
25. Soriano FA, Rios R, Pedrola M, Giagnorio J, Battagliotti CR. Acute cervical pain is relieved with Gallium Arsenide (GaAs) laser radiation. A double blind preliminary study. *Laser Therapy* 1996;8:149-154.
26. Wheeler AH, Goolkasian P, Baird AC, Darden BW. The development of the neck pain and disability scale: Item analysis, face, and criterion-related validity. *Spine* 1999;24:1290-1294.
27. Hunt S, Mc Eve J, Mc Kenna S. Measuring health status: A new tool for clinician and epidemiologists. *J Roy Coll Ge Pract* 1985;35:185-188.
28. Fries JF, Spitz PW, Kraines RG, Holman R. Measurement of patient outcome in arthritis. *Arthritis Rheum* 1980;23:137-145.
29. Laasko EL, Richardson C, Cramond T. Pain scores and side effects in response to low level laser therapy (LLLT) for myofascial trigger points. *Laser Therapy* 1997;9:67-72.
30. Bogduk N, Simons DG. Neck pain: Joint pain or trigger points? Progress in fibromyalgia and myofascial pain. Elsevier; 1993.
31. Kert J, Rose L. Clinical laser therapy-low level laser therapy 1989. Copenhagen: Scandinavian Medical Laser Technology; 1989.
32. Wessselmann U, Lin SF, Rymer WZ. Selective decrease of small sensory neurons in lumbar dorsal root ganglia labeled with horseradish peroxidase after ND:YAG laser irradiation of the tibial nerve in the rat. *Exp Neurol* 1991;111:251-262.
33. Sattayut S, Hughes F, Bradley P. 820 nm gallium aluminium arsenide laser modulation of a prostaglandin E₂ production in interleukin 1 stimulated myoblasts. *Laser Ther* 1999;11(2):88-95.
34. Palma J, Juri H, Campana V, et al. Blockade of inflammatory signals by laser radiation. *Lasers Surg Med* 3(1 Suppl):11.
35. Lievens PC. The effect of a combined He-Ne and IR laser treatment on the regeneration of the lymphatic system during the process of wound healing. *Lasers Med Sci* 1991; 6:193-199.
36. Goldman JA, Chiapella J, Casey H, et al. Laser therapy of rheumatoid arthritis. *Lasers Surg Med* 1980;1:93-101.
37. Nishida J, Satoh T, Satodate R, et al. Histological evaluation of the effect of He Ne laser irradiation on the synovial membrane in rheumatoid arthritis. *Jpn J Rheumatol* 1990;2:251-260.
38. Calderhed RG. Report of Meeting of the American Society for Lasers in Medicine and Surgery: Arlington, Virginia, April 15-17, 1989.
39. Enwemeka CS, Rodriquez OO, Gall NG, Walsh NE. Morphometrics of collagen fibril populations in He-Ne laser photo-stimulated tendons. *J Clin Laser Med Surg* 1990;8:47-51.
40. Walker JB. Relief from chronic pain by low power laser irradiation. *Neurosci Lett* 1983;43(2-3):339-344.
41. Kudoh C, Inomata K, Okajima K, et al. Effects of 830 nm gallium aluminium arsenide diode laser radiation on rat saphenous nerve sodium-potassium-adenosine triphosphatase activity: A possible pain attenuation mechanism examined. *Laser Ther* 1989;1:63-67.
42. Mizokami T, Aoki K, Iwabuchi S, et al. Low reactive level laser therapy---a clinical study: Relationship between pain attenuation and the serotonergic mechanism. *Laser Ther* 1995;5:165-168.
43. Synder-Mackler L, Bork CE. Effect HeNe laser irradiation on peripheral sensory nerve latency. *Phys Ther* 1988;68:223-225.
44. Rigau J, Trelles MA, et al. Changes in fibroblast proliferation and metabolism following in vitro helium-neon laser irradiation. *Laser* 1991;4:1-9.
45. van Brengel H, Bar PR. Power density and exposure time of HeNe laser irradiation are more important than total energy dose in photobiomodulation of human fibroblast in vitro. *Lasers Med Surg* 1992;12:528-537.
46. Ghamasari SM, Acorda JA, et al. Evaluation of the wound-healing of teat with and without low level laser treatment in dairy cattle by laser Doppler flowmetry, in comparison with histopathology, tensiometry, and hydropxyproline analysis. *Br Vet J* 1996;152(5):583-592.
47. Reddy GK, Stehno-Bittel L, Enwemeka CS. Laser photostimulation of collagen production in healing rabbit Achilles tendon. *Lasers Med Surg* 1998;22:281-287.
48. van der Veen P, Lievens P. Low level laser therapy (LLLT): The influence on the proliferation of fibroblasts and the influence of the regeneration process of lymphatic, muscular, and cartilage tissue. In: Simunovic Z, editor. *Lasers in medicine and dentistry. Basic science and an up-to-date clinical application of low energy laser therapy*. Zlatko Simunovic, Locarno, Switzerland: Rijeka: Vitgraph; 2000. pp 187-217.
49. Shimizu N, Yamaguchi M, et al. Inhibition of prostaglandin E₂ and interleukin 1 beta production by low power laser irradiation in stretched human periodontal ligament cells. *J Dent Res* 1995;74:1382-1388.
50. Ozawa Y, Shimizu N, Alike Y. Low energy diode laser irradiation reduced plasminogen activator activity in human periodontal ligament cells. *Lasers Surg Med* 1997;21:456463.