Pain Medicine

Pain Medicine 2010; 11: 1169–1178
Wiley Periodicals, Inc.

Low-Level Laser Therapy for Acute Neck Pain with Radiculopathy: A Double-Blind Placebo-Controlled Randomized Study

Ljubica M. Konstantinovic, MD, PhD,*
Milisav R. Cutovic, MD, PhD,*
Aleksandar N. Milovanovic, MD, PhD,†
Stevan J. Jovic, MD, PhD,* Aleksandra S. Dragin, MS,* Milica Dj. Letic, MS,‡ and Vera M. Miler, MS§

*Clinic for Rehabilitation,

†Institute for Occupational Medicine and

‡Institute for Rehabilitation, Medical School, University of Belgrade, Belgrade, Serbia;

§High School dr Djordje Natosevic, Indjija, Serbia

Reprint requests to: Ljubica M. Konstantinovic, MD, PhD, Clinic for Rehabilitation dr Miroslav Zotovic, Medical School, University of Belgrade, Sokobanjska 13, Belgrade, Serbia. Tel: +3812602541; Fax: +381112667623; E-mail: ljkonstantinovic@yahoo.com.

Abstract

Objective. The objective of the study was to investigate clinical effects of low-level laser therapy (LLLT) in patients with acute neck pain with radiculopathy.

Design. Double-blind, randomized, placebo-controlled study.

Setting. The study was carried out between January 2005 and September 2007 at the Clinic for Rehabilitation at the Medical School, University of Belgrade, Serbia.

Patients and Intervention. Sixty subjects received a course of 15 treatments over 3 weeks with active or an inactivated laser as a placebo procedure. LLLT was applied to the skin projection at the anatomical site of the spinal segment involved with the following parameters: wavelength 905 nm, frequency 5,000 Hz, power density of 12 mW/cm^2, and dose of 2 J/cm^2, treatment time 120 seconds, at whole doses 12 J/cm^2.

Outcome measures. The primary outcome measure was pain intensity as measured by a visual analog scale. Secondary outcome measures were neck movement, neck disability index, and quality of life. Measurements were taken before treatment and at the end of the 3-week treatment period.

Results. Statistically significant differences between groups were found for intensity of arm pain ($P = 0.003$, with high effect size $d = 0.92$) and for neck extension ($P = 0.003$ with high effect size $d = 0.94$).

Conclusion. LLLT gave more effective short-term relief of arm pain and increased range of neck extension in patients with acute neck pain with radiculopathy in comparison to the placebo procedure.

Key Words. Low-Level Laser Therapy (LLLT); Acute Neck Pain

Introduction

Acute neck pain with cervical radiculopathy is a common condition with a reported annual incidence of approximately 83 per 100,000 and an increased prevalence in the fifth decade of life (203 per 100,000) [1,2]. The most common causes of compression of the cervical level nerve root are stenosis of the lateral canal secondary to spondylarthrosis [3] and a prolapsed intervertebral disk (PID) [1]. However, nerve root pain can occur in the absence of visible compression [4,5]. The main clinical features of the condition are pain and functional disability, which have a considerable impact on overall health [6]. Clinical diagnosis of cervical radiculopathy is hindered by a lack of well-defined clinical criteria [7–9]. The scientific evidence supports the use of manual provocative tests in patients with neck pain and suspected radiculopathy and together with a combination of patient history, physical examination, imaging techniques, and needle electromyography (EMG) to diagnose the cause and site of cervical radiculopathy. Patient self-reported assessment is useful to evaluate perceived pain, function, disability, and psychosocial status [10]. The natural course of spondylotic and discogenic cervical radiculopathy is generally favorable; however, the percentage of spontaneous recovery is unknown [11,12]. Several intervention strategies are commonly used in the management of cervical radiculopathy. These range from conservative approaches to surgical intervention [13]. Conservative treatments have shown positive results in patients with severe pain and neurological lesions [14]. However, it was found that a lower

percentage of patients underwent conservative treatment as compared to surgery [15], in spite of the fact that no advantage of surgery has been demonstrated [16]. For many of the treatment modalities that are used widely in practice, insufficient evidence supports their use [17,18].

Increasing evidence suggests that inflammation alone or in association with root compression is the main pathological factor that is responsible for radiculopathy that is associated with disk herniation [19]. Disk herniation may cause pain by mechanical compression of the nerve root. Cervical nerve roots can also be at risk of injury due to foraminal impingement and mechanical compression, which lead to endoneurial edema, neuronal damage, and decreased axonal conduction velocity, and these in turn are strongly related to pain [20,21]. Data strongly support the role of proinflammatory cytokines in pain that is associated with herniated disks. Cytokines, such as interleukin 3 (IL-3), IL-6, and IL-8, cause hyperalgesia in animals [22] and may play a role in the physiopathology of radiculopathy. The interactions of axons with proinflammatory cytokines could increase electrical conductivity. Recently, a study demonstrated the effect of cyclic mechanical stress on the production of inflammatory agents and postulated a possible synergistic effect of simultaneous mechanical and chemical irritation of the annulus fibrosus cells on the production of pain mediators, such as prostaglandin E2 [23].

Many experimental and clinical studies have shown analgesic and anti-inflammatory potential of low-level laser therapy (LLLT) in a dose-dependent manner [24,25]. It has been shown to be a low risk and safe treatment, but its true efficacy is controversial. LLLT was demonstrated to modulate the inflammatory, proliferative, and remodeling phases of the healing process [26,27]. Important additional effects appear to include a direct influence on neural structures that are damaged by compression or inflammation, and this significantly improves nerve recovery [28–30].

The aim of this study was to investigate the clinical effects of LLLT in patients with acute neck pain with radiculopathy. We hypothesize that LLLT would provide a clinically and statistically significant benefit over a placebo for patients with acute neck pain with radiculopathy.

Materials and Methods

Patients

The study was carried out between January 2005 and September 2007 at the Clinic for Rehabilitation at the Medical School, University of Belgrade, Serbia. During this period, 285 patients with acute neck pain with radiating arm pain were admitted to the clinic. The prospective double-blind randomized study included 60 patients with acute neck pain with unilateral radiculopathy (Figure 1). Clinical characteristics for inclusion in the study were: neck and/or unilateral arm pain; clinical signs of radicular lesion in a dermatomal distribution and/or myotomal muscle weakness (graded less than 4/5) and/or diminished reflexes in the upper extremities; disability evaluated as moderate to severe; absence of symptoms and signs of myelopathy; duration of symptoms less than 4 weeks; absence of symptoms or signs of other similar neck and arm diseases; no more than three previous episodes [31]; and evidence from magnetic resonance imaging (MRI) of a PID or spondylotic degenerative changes. In the study, 225 patients were not included because they failed to meet inclusion criteria, were unresponsive to initial contact, or had red flag symptoms [32], such as neck trauma, diabetes mellitus, inflammatory arthritis, neurological disease, or cancer disease. In addition, pregnant patients and patients that had been treated surgically for the same problem or treated with oral corticosteroids and steroid injections for any reason in the previous month were not included [33].

Diagnosis was made by a combination of clinical musculoskeletal and neurological examinations of the neck and upper extremities [34]; provocative tests: upper limb tension test and Spurling's test [35]; and additional neuroradiological and neurophysiological examinations. MRI was done before the treatment and was a requirement for inclusion the trial. Conventional needle myography (EMG) was performed after 3 to 4 weeks from the beginning of symptoms; only observations of signs of acute denervation were considered to be consistent findings, but the observation of acute denervation was not required for inclusion in the study.

During the study, two patients dropped out; one due to nausea and the other due to an increase in blood pressure. However, the last recorded parameters for these patients were included in the analysis. Withdrawal of the subjects was not registered.

All patients gave informed written consent to participate in the study. The study was approved by the Ethics Committee of the Clinic for Rehabilitation at the Medical School, University of Belgrade.

Blinding

The patients were allocated randomly into two groups using 60 sequentially numbered, opaque, sealed envelopes that had been prepared earlier, using a computerized table of random numbers and balanced to ensure equal numbers in each group. The allocations were concealed from the statistician (GH) until the statistical analysis had been completed.

Treatment

The patients were allocated randomly to one of two treatment groups: Group A (n = 30) was treated with local active LLLT and group B (n = 30) was treated with local placebo LLLT. Laser units were manufactured by Enraf Nonius. The devices for LLLT were assigned as device A for active LLLT and device B for placebo LLLT. The patients did not know which unit was active. Patients were

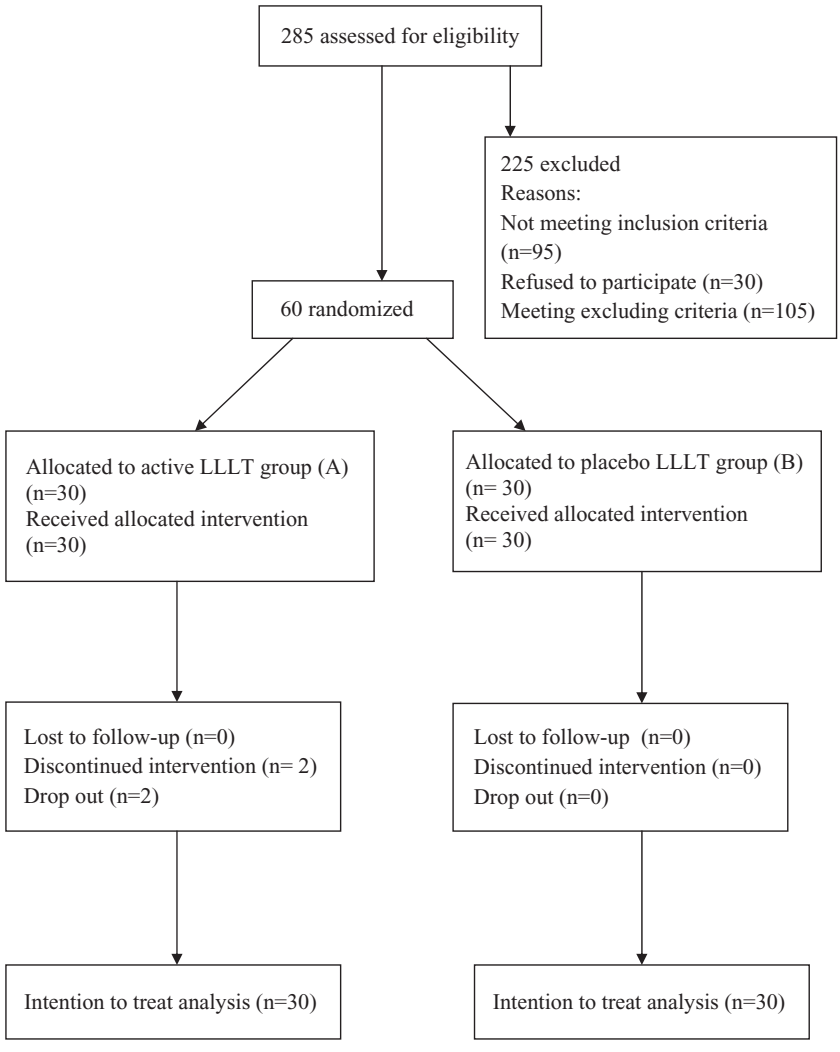

Figure 1 Flowchart of patients recruitment. LLLT = low-level laser therapy.

treated five times weekly for a total of 15 treatments. All patients were instructed to perform restricted and allowed activity (low aerobic activity). Both treatments were applied by the same therapist, who was also unaware which unit was active.

Active LLLT Treatment

The parameters of the laser beams are shown in Table 1. The parameters were chosen on the basis of preliminary results and previous studies [18,19]. The optical output was tested before and after the end of the trial.

Placebo LLLT Treatment

Placebo LLLT was applied in the same manner, but using a unit that had been deactivated by a member of the Institute for Physics, Belgrade. The physicians and the patients were unable to distinguish between the active and placebo units.

Table 1 Characteristics of the laser beams

Parameters	Value used
Wavelength	905 nm (red)
Laser frequency	5,000 Hz
Maximum power output	25 mW
Diode surface	1 cm^2
Power density	12 mW/cm^2
Energy	2 J/point
Energy density	2 J/cm^2 at each point
Treatment time	120 seconds at each point
Number of points	6
Daily energy delivered	12 J
Total energy delivered	180 J
Application mode	Probe held stationary in contact with skin
Anatomical site	Local transforaminal*

* 2.5 cm and 3.5 cm laterally from process spinosus of involved (C6, C7, or C8) and the two next distal spinal segment.

Outcomes

The primary outcome measure was intensity of pain. The secondary outcome measures were: neck mobility, neck disability index (NDI), and a 12-item short-form health survey (SF-12). Intensity of pain was measured using a visual analog scale (VAS), either for neck (VAS-neck) or for arm (VAS-arm) pain. The VAS corresponded to a 100-mm horizontal scale, that was graded from zero, which represented no pain, to 100, which represented the worst imaginable pain [36,37]. We classified the changes in VAS scores into bands and analyzed the resulting data as an ordinal response. Severity of pain was graded into four groups according to the range of VAS scores: none to mild (0–30 mm); moderate (30–60 mm); moderately severe (60–80 mm); and severe (80–100 mm) [38]. Neck mobility was measured by assessment of flexion and extension. Flexion was expressed as the distance in millimeters from the midpoint of the chin to the apex of the sternal manubrium. Extension range was evaluated as the distance in millimeters from the occipital tuberosities to the spinous process of C7. NDI consists of a 10-item questionnaire that assesses the impact of pain on daily activities using a score from 0 to 5 for each section, with higher values indicating more severe impact [39]. NDI was represented as percentage disability, which was calculated from the measured values (measured sum/50 × 100). The SF-12 consists of 12 questions that concern general health and can be divided into two aggregate summary measures: the physical component summary (PCS) and the mental component summary [40].

Subjects were evaluated before and at 3 weeks after by independent physicians, who performed the diagnostic assessment and were blind to the type of treatment.

To identify any adverse effects of treatment in a systematic manner, subjects were asked to record any new symptoms.

Statistics

The analysis was conducted on an "intention to treat" basis. SPSS 11.5 (SPSS Inc., Chicago, IL) was used for analysis. The results were expressed as the mean ± standard deviation (SD) for data that had a normal distribution, or as median (25% and 75% percentiles) for data that were not distributed normally. We present two types of comparison: 1) comparison of means obtained prior to therapy and at the end of therapy for each measured outcome in both groups; and 2) comparison between groups of differences in scores obtained prior therapy and at the end of therapy for each measured outcome. For (1), statistically significant differences were tested using both the paired *t*-test and the Wilcoxon signed-ranks test for paired observations. For (2), statistically significant differences were tested using the independent *t*-test or Wilcoxon–Mann–Whitney test for two independent groups or the chi-square test, depending on type of outcome variable. The level of statistical significance was set at a two-tailed alpha level of 0.05. *Post hoc* power analysis was used to analyze the effect size in order to evaluate the importance of measured changes. An ordinal regression analysis was performed for changes in pain severity.

Results

Baseline characteristics are presented in Table 2. Intergroup baseline statistics were determined with respect to sex by the chi-square test and *t*-test and with respect to age and duration by the independent sample *t*-test. A statistically significant difference between the groups was only verified for duration of symptoms ($t = -2.016$, $P = 0.048$); however, this was without clinical significance in relation to duration of the acute phase. Most of the other characteristics were evaluated as outcomes, and some of those presented are only descriptive.

In Table 3, the mean values ± SD for outcomes are presented, except for the PCS before therapy and after

Table 2 Baseline characteristics

Characteristics	Group A (n = 30)	Group B (n = 30)
Age	41.71 ± 8.63	38.55 ± 7.86
Male	43.33	40.63
Female	56.67	59.3
Duration of symptoms (days)	17.27 ± 4.04	19.13 ± 3.14
Pain in arm and neck	16/30	18/30
Pain in arm	28/30	27/30
Number of tender points	3.2 ± 1.4	2.5 ± 1.8
Site of tender points		
Neck	16/30	17/30
Shoulder	21/30	20/30
Scapula	24/30	21/30
Decreased neck ROM	30/30	30/30
Sensitive signs	11/30	12/30
Paresthesias	27/30	25/30
Weakness	23/30	21/30
Diminished reflexes	11/30	9/30
Root level C6	18/30	19/30
Root level C7	16/30	14/30
Decreased daily activities and quality of life	30/30	30/30
MRI findings		
Protrusion of disk	18/30	16/30
Extrusion of disk	2/30	3/30
Foraminal stenosis	14/30	16/30
EMG consistent findings	19/30	18/30

Table 3 Mean and median values for outcomes

Group	Group A (n = 30)			Group B (n = 30)		
Outcomes	Pre-therapy	Post-therapy	Statistics*	Pre-therapy	Post-therapy	Statistics*
VAS-arm†	74.06 ± 4.91	44.29 ± 5.44	t = 38.12	72.52 ± 5.98	47.84 ± 7.37	t = 20.22
VAS-neck‡	56.84 ± 12.61	33.35 ± 8.73	t = 10.03	58.45 ± 11.01	39.45 ± 11.03	t = 12.67
NDI§	67.65 ± 6.0	37.81 ± 7.05	t = 21.28	66.87 ± 5.07	41.74 ± 4.25	t = 23.09
Flexion¶	31.87 ± 3.82	20.29 ± 3.44	t = 20.68	30.61 ± 4.65	21.29 ± 4.29	t = 14.17
Extension**	39.58 ± 5.11	37.68 ± 4.56	t = 18.87	26.58 ± 4.54	27.74 ± 4.16	t = 23.25
PCS††	11.09 ± 1.76	16.09 ± 1.58	t = –16.44	11.03 ± 1.14	15.13 ± 1.09	t = –26.22
MCS‡‡	10.03 ± 1.45	13.84 ± 1.19	t = –18.17	9.0 [9.0, 9.0]	12.0 [12.0, 13.0]	Z = –5.05

* $P < 0.001$ for all measured outcomes.
Values represented the mean values ± SD except for the MCS of group B, where the values represent the median [25%, 75%]; † VAS arm; ‡ VAS neck; § The NDI; ¶ flexion of neck; ** extension of neck; †† PCS; ‡‡ MCS.
VAS = visual analog scale; NDI = neck disability index; PCS = physical component summary; MCS = mental component summary.

therapy in group B, which is shown as the median [25%, 75%]. Both groups showed statistically significant values obtained after therapy in comparison with the baseline values for all investigated parameters ($P < 0.001$).

Differences between the baseline values obtained prior to therapy and those obtained at the end of the therapy for each measured outcome are compared between the two groups in Table 4. Between groups is represented on Table 4. Statistical analyses show greater improvement in group A than in group B for all measured outcomes except neck pain, with a high effect size on VAS-arm (d = 0.98) and range of extension in neck (d = 1.09).

Table 5 represents the distribution of improvement in pain scores at the end of therapy. These were defined as greatly improved (<–50 mm), much improved (–50 to –30 mm), somewhat improved (–30 to –10 mm), about the same (–10 to 1 mm), and worse (>1 mm).

Ordinal regression analyses for pain intensity in the arm and neck are presented in Table 6. The analyses show a significant relationship between the level of pain in the arm and the treatment group. After treatment, patients in group A were more likely to have lower levels of arm pain that those in group B (Odds ratio = 5.8). No effect of group was seen on pain intensity in the neck at the end of treatment ($P = 0.09$).

Systematic monitoring of adverse effects showed transitional worsening of pain in 6/30 (20%) patients, persistent nausea in 1/30 (3.33%), and an increase blood pressure in 1/30 (3.33%). All adverse effects occurred in the active laser group (group A). Transitional worsening of pain was registered immediately after the first three sessions of treatment and had a maximum duration of 6 hours. Patients with nausea or increased blood pressure were excluded from the study. The results of the monitoring of side effects show the low-risk nature of LLLT.

Table 4 Statistical analyses of measured changes

Group	A	B	A–B		
Outcomes	Mean ± SD	Mean (SD) or median (25% 75%)	t or Z	*P*	d†
VAS-arm	29.77 ± 4.35	26.68 ± 6.79	3.518	0.001*	0.98
VAS-neck	23.35 ± 11.3	19.0 ± 7.21	1.806	0.077	No
NDI	29.84 ± 7.81	25.13 ± 6.06	2.654	0.01*	0.69
flexion	11.58 ± 3.12	9.32 ± 3.66	2.613	0.011*	0.68
extension	13.06 ± 3.86	9.94 ± 2.38	3.845	0.000*	1.09
PCS	5.0 ± 1.69	4.0 [4.0, 5.0]‡	–3.17‡	0.002*	0.40
MCS	3.81 ± 1.17	3.0 [3.0, 3.0]‡	–2.28‡	0.023*	0.29

* Statistically significant values ($P > 0.05$); abbreviations of outcomes are explained in Table 3.
† d (Cohen effect size: d < 0.2 = low, 0.2 < d < 0.8 = medium, d > 0.8 = high).
‡ For outcome data that were not distributed normally (PCS and MCS group B), the median (25% 75%) and *Z* value are shown.

Table 5 Overall change in pain levels for VAS-arm and VAS-neck

Change in pain level	Group A (n = 30)	Group B (n = 30)
Overall change in pain level in arm		
Greatly improved	0/30 (0%)	0/30 (0%)
Much improved	18/30 (60%)	6/30 (20%)
Somewhat improved	11/30 (36.66%)	22/30 (73.33%)
About the same	0/30 (0%)	2/30 (6.66%)
Worse	1/30 (3.33%)	0/30 (0%)
Overall change in pain level in neck		
Greatly improved	1/30 (3.33%)	3/30 (10%)
Much improved	9/30 (30%)	0/30 (0%)
Somewhat improved	18/30 (60%)	26/30 (86.66%)
About the same	2/30 (6.66%)	1/30 (3.33%)
Worse	0/30 (0%)	0/30 (0%)

Discussion

The lack of evidence with regard to diagnostic procedures and treatment interventions for a condition that occurs as frequently as degenerative cervical radiculopathy is very distressing. The main characteristics of published trials are imprecise selection of patients with cervical radiculopathy non-confirmed with additional MRI and EMG investigations, with different clinical characteristics, undefined clinical stage, and usually lacking description of treatment.

This study included patients with severe pain, moderate disability, and discomfort during daily activities that were associated with acute radicular lesion caused by disk herniation or degenerative changes confirmed with MRI. Baseline demographic characteristics (Table 2) were similar to published data and showed an increased prevalence in females. Clinical examination prior to treatment revealed that lesions were predominantly at the level of the C6 root and that the patients presented frequently with tender points behind the medial border of the scapula on the involved side. These findings were particulary inconsistent with the published data [41]. The diagnoses in this study were made mainly on clinical grounds with high levels of support from consistent MRI findings. However, in the majority of cases, the neurophysiological examination did not provide consistent supporting evidence. The results showed a statistically significant improvement in the VAS score for arm pain, the parameters for neck movement, and the PCS score (Table 5) in group A in comparison with group B. Ordinal regression analyses of categorized pain intensity showed very clear differences between the groups, with greater improvement in the active laser group with respect to arm pain (odds ratio = 5.8). In a study of acute pain, the minimum clinically relevant change in pain intensity was found to be 13 mm on the VAS [42,43], and in this study, the changes in VAS for both the arm and neck were greater than this threshold value in the majority of patients in both groups (Table 5). The intensity of neck pain decreased in a statistically significant manner in both groups with no intergroup differences. Statistically significant decreases were measured for the NDI. This decrease was larger for group A, in which disability improved from moderate severe to moderate. The placebo response in this study was similar for the parameters investigated; for pain in the arm and NDI, it was approximately 30% (calculated as the difference between the values obtained prior to treatment and those obtained at the end of therapy).

The main problem in comparing the results of this study with the results of other studies of conservative treatment, particularly LLLT studies, are the differences in included patients and applied treatments [25]. The study of Soriano et al. [44], which examined the effectiveness of 10 laser treatments (wavelength 904 nm, average power 40 mW, frequency 10,000 Hz, and energy density 4 J/cm^2) was similar in design to this study and showed significant improvement in 71 patients at the end of treatment and 6 months later. Many other clinical studies have used LLLT for nonspecific chronic neck pain and myofascial neck pain [45–49]. The group of patients with nonspecific chronic neck pain is very heterogeneous, and the genesis of their pain is caused not only by pathological changes in spinal and paraspinal structures but also by complex neurophysiological and psychosocial mechanisms. In addition, well-designed trials on other conservative treatments of cervical radiculopathy have not been performed. Persson et al. [16] conducted a randomized clinical trial that compared three modes of treatment. Patients with long-lasting cervical radiculopathy were randomized for surgery, physiotherapy, or use of a cervical collar. Surgery provided superior pain relief on follow-up at 4 months. However, on follow-up at 16 months, the three groups were not different with regard to pain, muscular strength, or sensory loss. In 1966, the British Association of Physical Medicine conducted a randomized clinical trial that included 493 patients with cervical root symptoms. They were treated with traction, placebo traction, collar, placebo tablets, or placebo heat treatment [31]. Seventy-

Table 6 Ordinal regression for VAS-arm and VAS-neck

Group	Estimate coefficient	Odds ratio	Wald	*P* value	95% CI for odds ratio
	VAS-arm				
A	−1.753	5.77	9.056	0.003	(0.06, 0.54)
B*	0	1	—	—	—
	VAS-neck				
A	−1.033	2.81	2.828	0.093	(0.11, 1.19)
B*	0	1	—	—	—

* Reference group for this parameter.

five percent of patients in all treatment groups reported pain relief on follow-up at 4 weeks, and no significant difference was observed in pain or in ability to work between the five groups. A recent systematic review on exercise for patients with neck pain (with or without radicular arm pain) included specific exercises that may only be effective for mechanical neck disorders [50]. A systematic review that examined the effect of manipulation and mobilization techniques in patients with mechanical neck disorders [51] showed that manual therapy probably results in greater short-term pain relief than exercise therapy or the usual medical care that is given for atypical neck pain without radiculopathy. However, insufficient evidence was found for the beneficial effect of manipulative techniques in the subgroup with cervical radiculopathy [52]. Moreover, cervical spine manipulation carries a risk of complications, such as vertebral artery dissection and spinal cord compression due to massive disk herniation [53].

Hypothetically, the biological actions of LLLT are multiple. Studies have documented changes in biochemical markers of inflammation [54], the distribution of inflammatory cells, and a reduction in the occurrence of edema, hemorrhage, and necrosis after local laser irradiation with different sources of laser beams (wavelengths of 660 and 684 nm [55], 780 nm [56], and 904 nm [57]) in experimentally induced models of inflammation. The reduction in inflammatory infiltration (approximately 30–50%) is greatest after 3 to 4 hours and correlates positively with a dose-dependent reduction in tumor necrosis factor alpha (TNFα) [58]. Effects on antioxidative enzymes could also be part of the modulation mechanism in view of the role of these enzymes in increasing the nonspecific resistance of cells to different types of damages [59]. Comparison of LLLT with anti-inflammatory drugs, such as meloxicam and indomethacin, has shown that the laser treatment has similar anti-inflammatory effects to the drugs [60]. Important additional effects may include a direct influence on neural structures that are damaged by compression or inflammation [28]. Laser phototherapy of injured peripheral nerves significantly improves nerve recovery in rat [29] and in clinical studies [30]. LLLT may have a direct effect on nerve structures, which could increase the speed of recovery of the conductive block or inhibit A-d and C fiber transmission [61,62]. It is possible that laser-induced neural blockade may then lead to a long-term alteration in nociception [63], analogous to the prolonged analgesia seen in some patients after the administration of local anesthetics [64] and changes at the endorphin level [65]. However, the neuromodulation effects of LLLT are dependent on many conditions in relation to timing and mode of irradiation and rarely have been observed for 904 nm laser sources.

The results of this study must be considered in the light of several limitations. Patients with relatively strictly defined clinical forms of the condition (severe levels of pain and moderate severe levels of disability) were selected due to the typical flow of patients to clinical treatment (selection bias). Randomization did not include initial level of disability, MRI and EMG findings, duration of symptoms, or other psychosocial characteristics that could influence the therapeutic response. The results of this study suggest only short-term effects. The identification of true positive effects and a placebo response under conditions of this study is controversial given that we had no untreated group, especially when the history, level, and percentage of spontaneous recovery were unknown.

Future studies could include patients that are randomized by levels for baseline disability, duration of symptoms, and other physical and psychosocial characteristics that could influence the response to treatment. In addition, further long-term studies could be designed that compare the use of a single type of therapy with a combined therapy approach. Further understanding of the mechanisms of the effects of LLLT could be very important for clinical recommendation.

Conclusions

The suitability of LLLT (wavelength of 905 nm and dose of 2 J per point) as a monotherapy for the treatment of acute neck pain with radiculopathy was examined. Patients treated with LLLT showed a greater improvement in local neck movements, a more significant reduction of pain intensity and related disability, and a greater improvement in quality of life, in comparison with patients treated with a placebo LLLT procedure. In addition, no major side effects were observed.

Acknowledgments

The authors would like to thank the Institute for Physics Belgrade, in particular Professor Milesa Sreckovic, for technical assistance.

Disclosure Statement

No competing financial interests exist.

References

1 Radhakrishnan K, Litchy WJ, O'Fallon WM, Kurland LT. Epidemiology of cervical radiculopathy. A population based study from Rochester, Minnesota, 1976 through 1990. Brain 1994;117:325–35.

2 Salemi G, Savattieri G, Meneghini F, et al. Prevalence of cervical spondylotic radiculopathy: A door-to-door survey in a Sicilian municipality. Acta Neurol Scand 1996;93:184–8.

3 Tanaka N, Fujimoto Y, An HS, Ikuata Y, Yasuda M. The anatomic relation among the nerve roots, intervertebral foramina, and intervertebral discs of the cervical spine. Spine 2000;25:286–91.

4 Saal JS. The role of inflammation in lumbar pain. Spine 1995;20:1821–7.

5 Grönblad M, Virri J, Tolonen J, et al. A controlled immunohistochemical study of inflammatory cells in disc herniation tissue. Spine 1994;19:2744–51.

6 Daffner SD, Hilibrand AS, Hanscom BS, et al. Impact of neck and arm pain on overall health status. Spine 2003;28:2030–5.

7 Wainner RS, Fritz JM, Irrgang JJ, et al. Reliability and diagnostic accuracy of the clinical examination and patient self-report measures for cervical radiculopathy. Spine 2003;28:52–62.

8 Rubinstein SM, Pool JJM, van Tulder MW, Riphagen II, de Vet HCW. A systematic review of the diagnostic accuracy of provocative tests of the neck for diagnosing cervical radiculopathy. Eur Spine J 2007;16:307–19.

9 Carette S, Fehlings MG. Clinical practice. Cervical radiculopathy. N Eng J Med 2005;353:392–9.

10 Nordin M, Carragee EJ, Hogg-Johnson S, et al. Assessment of neck pain and its associated disorders: Results of the Bone and Joint Decade 2000–2010 Task Force on Neck Pain and Its Associated Disorders. Spine 2008;33:S101–22.

11 Bush K, Chaudhuri R, Hillier S, Penny J. The pathomorphologic changes that accompany the resolution of cervical radiculopathy. A prospective study with repeat magnetic resonance imaging. Spine 1997;22:183–6.

12 Vinas FC, Wilner H, Rengachary S. The spontaneous resorption of herniated cervical discs. J Clin Neurosci 2001;8:542–6.

13 Korthals-de Bos IBC, Hoving JL, van Tulder MW, et al. Cost effectiveness of physiotherapy, manual therapy and general practitioner care for neck pain: Economic evaluation alongside a randomised, controlled trial. BMJ 2003;326:911–4.

14 Saal JS, Saal JA, Yurth EF. Nonoperative management of herniated intervertebral cervical disc with radiculopathy. Spine 1996;21:1877–83.

15 Sampath P, Bendebba M, Davis JD, Ducker T. Outcome in patients with cervical radiculopathy: Prospective multicenter study with independent clinical review. Spine 1999;24:591–7.

16 Persson LCG, Carlsson CA, Carlsson JY. Long lasting cervical radicular pain managed with surgery, physiotherapy or a cervical collar: A prospective, randomized study. Spine 1997;22:751–8.

17 The Philadelphia Panel Members and Ottawa Methods Group. Philadelphia panel evidence-based clinical practice guidelines on selected rehabilitation interventions for neck pain. Phys Ther 2001;81:1701–17.

18 Guzman J, Haldeman S, Carroll LJ, et al. Clinical practice implications of the results of the Bone and Joint DECADE 2000–2010 Task Force on Neck Pain and its Associated Disorders: From concepts and findings to recommendations. Eur Spine J 2008;17:S199–213.

19 Autio RA, Karppinen J, Niinimäki J, et al. The effect of infliximab, a monoclonal antibody against TNF-[alpha], on disc herniation resorption: A randomized controlled study. Spine 2006;31:2641–5.

20 Hubbard RD, Quinn KP, Martínez JJ, Winkelstein BA. The role of graded nerve root compression on axonal damage, neuropeptide changes, and pain-related behaviors. Stapp Car Crash J 2008;52:33–58.

21 Hubbard RD, Winkelstein BA. Dorsal root compression produces myelinated axonal degeneration near the biomechanical thresholds for mechanical behavioral hypersensitivity. Exp Neurol 2008;212:482–9.

22 Wehling P, Cleveland SJ, Heininger K, et al. Neurophysiologic changes in lumbar nerve root inflammation in the rat after treatment with cytokine inhibitors: Evidence for a role of interleukin-1. Spine 1996;21:931–5.

23 Starkweather A, Witek-Janusek L, Mathews HL. Neural–immune interactions: Implications for management in patients with low back pain and sciatica. Biol Res Nurs 2005;6:196–206.

24 Bjordal JM, Couppé C, Ljunggren AE. Low-level laser therapy for tendinopathy. Evidence of a dose-response pattern. Phys Ther Rev 2001;6:91–9.

25 Bjordal JM, Couppé C, Chow RT, Tunér J, Ljunggren EA. A systematic review of low-level laser therapy with location specific doses for pain from chronic joint disorders. Aust J Physiother 2003;49:107–16.

26 Reis SR, Medrado AP, Marchionni AM, et al. Effect of 670-nm laser therapy and dexamethasone on tissue repair: A histological and ultrastructural study. Photomed Laser Surg 2008;26:307–13.

27 Vasheghani MM, Bayat M, Rezaei F, Bayat A, Karimipour M. Effect of low-level laser therapy on mast cells in deep second-degree burns of rats. Photomed Laser Surg 2008;26:1–5.

28 Gigo-Benato D, Geuna S, Rochkind S. Phototherapy for enhancing peripheral nerve repair: A review of the literature. Muscle Nerve 2005;31(6):694–701.

29 Rochkind S, Barrnea L, Razon N, Bartal A, Schwartz M. Stimulatory effect of He-Ne low dose laser on injured sciatic nerves of rats. Neurosurgery 1987;20: 843–7.

30 Rochkind S, Drory V, Alon M, Nissan M, Ouaknine GE. Laser phototherapy (780 nm), a new modality in treatment of long-term incomplete peripheral nerve injury: A randomized double-blind placebo-controlled study. Photomed Laser Surg 2007;25:436–42.

31 The British Association of Physical Medicine. Pain in the neck and arm: A multicentre trial of the effects of physiotherapy. BMJ 1966;1:253–8.

32 Binder AI. Cervical spondylosis and neck pain. BMJ 2007;334:527–31.

33 Lopes-Martins RA, Albertini R, Lopes-Martins PS, et al. Steroid receptor antagonist mifepristone inhibits the anti-inflammatory effects of photoradiation. Photomed Laser Surg 2006;24:197–201.

34 Magee DJ. Cervical spine. In: Magee DJ, ed. Orthopedic Physical Assessment, 3rd edition. Philadelphia, PA: W.B. Saunders; 1997:101–51.

35 Shah KC, Rajshekhar V. Reliability of diagnosis of soft cervical disc prolapse using Spurling's test. Br J Neurosurg 2004;18:4480–3.

36 Scott J, Huskisson E. Graphic representation of pain. Pain 1976;2:175–84.

37 Bijur PE, Silver W, Gallagher EJ. Reliability of the visual analog scale for measurement of acute pain. Acad Emerg Med 2001;8:1153–7.

38 Collins SL, Moore RA, McQuay HJ. The visual analogue pain intensity scale: What is moderate pain in millimetres? Pain 1997;72:95–7.

39 Vernon H, Mior S. The neck disability index: A study of reliability and validity. J Manipulative Physiol Ther 1991;14:409–15.

40 Ware JE, Kosinski M, Keller SD. A 12-item short form health survey. Med Care 1996;34:220–33.

41 Henderson CM, Hennessy RG, Shuey HM, Shackelford EG. Posterior-lateral foraminotomy as an exclusive operative technique for cervical radiculopathy: A review of 846 consecutively operated cases. Neurosurgery 1983;13:504–12.

42 Todd KH, Funk KG, Funk JP, Bonacci R. Clinical significance of reported changes in pain severity. Ann Emerg Med 1996;27:485–9.

43 Fejer R, Jordan A, Hartvigsen J. Categorising the severity of neck pain: Establishment of cut-points for use in clinical and epidemiological research. Pain 2005;119:176–82.

44 Soriano F, Rios R, Pedrola M, Giagnorio J, Battagliotti C. Acute cervical pain is relieved with Gallium Arsenide (GaAs) laser radiation. A double-blind preliminary study. Laser Ther 1996;8:149–54.

45 Altan L, Bingöl U, Aykaç M, Yurtkuran M. Investigation of the effect of GaAs laser therapy on cervical myofascial pain syndrom. Rheumatol Int 2005;25:23–7.

46 Ozdemir F, Birtane M, Kokino S. The clinical efficacy of low-power laser therapy on pain and function in cervical osteoarthritis. Clin Rheumatol 2001;20:181–4.

47 Chow RT, Heller GZ, Barnsley L. The effect of 300 mW, 830 nm laser on chronic neck pain: A double-blind, randomized, placebo-controlled study. Pain 2006;124:201–10.

48 Gur A, Sarac AJ, Cevik R, Altindag O, Sarac S. Efficacy of 904 nm gallium arsenide low level laser therapy in the management of chronic myofascial pain in the neck: A double-blind and randomized-controlled trial. Lasers Surg Med 2004;35:229–35.

49 Chow RT, Barnsley L. Systematic review of the literature of low-level laser therapy (LLLT) in the management of neck pain. Lasers Surg Med 2005;37:46–52.

50 Kay TM, Gross A, Goldsmith C, et al. Exercises for mechanical neck disorders. Cochrane Database Syst Rev 2005;3:CD004250.

51 Gross AR, Hoving JL, Haines TA, et al. Manipulation and mobilisation for mechanical neck disorders. Cochrane Database Syst Rev 2004;1:CD004249.

52 Hurwitz EL, Morgenstern H, Harber P, et al. A randomized trial of medical care with and without physical therapy and chiropractic care with and without physical modalities for patients with low back pain: 6-month follow-up outcomes from the UCLA low back pain study. Spine 2002;27:2193–204.

53 Di Fabio RP. Manipulation of the cervical spine: Risks and benefits. Phys Ther 1999;79:50–65.

54 Sattayut S, Hughes F, Bradley P. 820 nm gallium aluminium arsenide laser modulation of prostaglandin E2 production in interleukin-1 stimulated myoblasts. Laser Ther 1999;11:88–95.

55 Albertini R, Villaverde AB, Aimbire F, et al. Anti-inflammatory effects of low- level laser therapy (LLLT) with two different red wavelengths (660 nm and 684 nm) in carrageenan-induced rat paw edema. J Photochem Photobiol 2007;89:50–5.

56 Honmura A, Yanase M, Obata J, Haruki E. Therapeutic effects of Ga-Al-As diode laser irradiation on experimentally induced inflammation in rats. Lasers Surg Med 1992;12:441–9.

57 Correa F, Lopes-Martins RA, Correa JC, et al. Low-level laser therapy (GaAs $\lambda = 904$ nm) reduces inflammatory cell migration in mice with lipopolysaccharide-induced peritonitis. Photomed Laser Surg 2007;25:245–9.

58 Aimbire F, Albertini R, Pacheco MT, et al. Loe-level laser therapy induces dose-dependent reduction of TNF-alpha levels in acute inflammation. Photomed Laser Surg 2006;24:33–7.

59 Karu T. Primary and secondary mechanisms of action of visible to near IR radiation on cells. J Photochem Photobiol B 1999;49:1–17.

60 Campana V, Moya A, Gavotto A, et al. The relative effects of He-Ne laser and meloxicam on experimentally induced inflammation. Laser Ther 1999;11: 36–41.

61 Chow RT, David MA, Armati PJ. 830 nm laser irradiation induces varicosity formation, reduces mitochondrial membrane potential and blocks fast axonal flow in small and medium diameter rat dorsal root ganglion neurons: Implications for the analgesic effects of 830 nm laser. J Peripher Nerv Syst 2007;12:28–39.

62 Tsuchiya K, Kawatani M, Takeshige C, Sato T, Matsumoto I. Diode laser irradiation selectively diminishes slow component of axonal volleys to dorsal roots from the saphenous nerve in the rat. Neurosci Lett 1993; 161:65–8.

63 Wall PD. New horizons—An essay. In: Bridenbaugh PO, Cousins MJ, eds. Neural Blockade in Clinical Anaesthesia and Management of Pain. Philadelphia, PA: Lippincott-Raven Publishers; 1998:1135–43.

64 Arnér S, Lindblom U, Meyerson BA, Molander C. Prolonged relief of neuralgia after regional anesthetic blocks. A call for further experimental and systematic clinical studies. Pain 1990;43:287–97.

65 Laakso EL, Cramond T, Richardson C, Galligan JP. Plasma Acth and beta-endorphin levels in response to low level laser therapy (LLLT) for myofascial trigger points. Laser Ther 1994;6:133–42.