

Effects of a single treatment with two nonthermal laser wavelengths on chronic neck and shoulder pain

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Robert G Silverman¹
Albert Comey²
Travis Sammons³

¹Clinical Study Site, New York
ChiroCare, White Plains, NY, USA;

²Clinical Study Site, Comey Chiropractic
Clinic, Largo, FL, USA; ³Erchonia
Corporation, Melbourne, FL, USA

Introduction: Nonthermal lasers provide pain relief for a variety of musculoskeletal disorders and improve physical functioning. A nonthermal laser that employs a 635 nm red diode is cleared for the temporary reduction of neck and shoulder pain of musculoskeletal origin. As a 405 nm violet laser has shown synergy with the 635 nm red laser when used together for treating other conditions, the objective of this study was to compare the efficacy of 635 nm red and 405 nm violet lasers vs the 635 nm red laser for treating neck and shoulder pain of musculoskeletal origin.

Materials and methods: Otherwise healthy adult subjects with chronic neck or shoulder pain for ≥ 30 days were enrolled and randomized to receive a single 13-min treatment with combined red and violet lasers (n=44) or the red laser alone (n=43). The primary efficacy measure was change in baseline VAS pain scores 3 mins after treatment. Subject success was predefined as a $\geq 30\%$ decrease in VAS scores and study success was predefined as $65 \pm 5\%$ individual subject successes.

Results: Among subjects treated with the red and violet lasers, mean VAS neck and shoulder pain scores decreased from 65.0 to 35.2 ($p < 0.0001$). Most subjects in the study (75%) achieved $\geq 30\%$ decrease in VAS scores. The decreased mean (SD) VAS scores remained 29.6 (16.7) and 29.3 (19.2) after 24 and 48 hrs, respectively. The secondary efficacy measures of change in range of motion (ROM) and patient satisfaction also improved. There were no adverse events.

Conclusion: Overall, treatment with the red and violet lasers outperformed the FDA-approved red laser with respect to change in pain scores and improvement in shoulder ROM.

Keywords: nonthermal laser, low-level laser, chronic pain, randomized trial

Introduction

Nonthermal or low-level lasers can be used to stimulate mitochondrial chromophores – specifically cytochrome C oxidase – to achieve a therapeutic effect.^{1,2} Nonthermal lasers have been shown to enhance the healing of bone fractures,^{3,4} burns^{5,6} and diabetic ulcers,^{7,8} stimulate nerve regeneration⁹ and even treat acne vulgaris by its effect on *Propionibacterium acnes*.¹⁰ Nonthermal lasers have also been shown to treat a variety of painful musculoskeletal disorders¹¹ including neck and shoulder pain^{12,13} and can provide relief from pain for 2–6 months after treatment.¹⁴ In one study, relief from plantar fasciitis persisted for 12 months.¹⁵

Correspondence: Travis Sammons
Erchonia Corporation, 650 Atlantis Road,
Melbourne, FL 32904, USA
Tel +1 321 473 1251
Fax +1 321 473 1608
Email TSammons@erchonia.com

A systematic review and meta-regression analysis found treatment with nonthermal lasers to be more beneficial than placebo for chronic neck pain¹⁶ and improving physical functioning and quality of life.¹⁷

A randomized, double-blind, sham-controlled trial assessed the efficacy of a 635 nm red nonthermal laser for treating subjects with chronic shoulder and neck pain ($N=86$).¹³ A single 1 min treatment was applied to 12 sites on the neck and shoulders. A VAS was used to measure changes in pain perception immediately after treatment. Among laser-treated subjects, 65.1% met the criteria for treatment success, defined as a 30% decrease in VAS pain scores vs 11.6% among sham-treated subjects ($p<0.0001$). Mean VAS scores decreased from 60.2 to 31.2 ($p<0.0001$) for Low-level laser (light) therapy (LLLT)-treated subjects vs 60.0–55.1 for sham-treated subjects ($p=NS$). The mean between-group difference in post-treatment VAS scores was 24.1 points ($p<0.005$). There was also a significant improvement in range of motion (ROM) among laser-treated subjects but not sham-treated subjects. These results supported the 510(k) clearance of this 635 nm red diode device for the temporary reduction of neck and shoulder pain of musculoskeletal origin.¹⁸

The 405 nm violet laser has also demonstrated a variety of beneficial effects, such as wound healing^{19–21} and antimicrobial effects.^{22–25} Although it has not been previously studied for painful conditions, the 405 nm violet laser has shown synergy with the therapeutic effects of a 635 nm red laser when the two diodes are used simultaneously.²⁶ The objective of this nonrandomized noninferiority design was to compare the efficacy of combining 635 nm red- and 405 nm violet-emitting diodes for treating neck and shoulder pain of musculoskeletal origin versus treatment with the 635 nm red diode alone.

Methods

Study subjects

Study subjects ≥ 18 years old were recruited from among the investigators' pool of patients seeking treatment for neck and shoulder pain, and from among individuals responding to locally placed recruitment flyers and print ads. Each subject provided written informed consent prior to participating in any study-related activities. This study was conducted in accordance with the Declaration of Helsinki. Subjects received no compensation for their participation.

Subjects were required to have symptoms of chronic neck or shoulder pain caused by osteoarthritic degenerative joint disorder, chronic muscle spasms, cervical and thoracic spine sprain strain based on medication use history, medical records including x-ray, magnetic resonance imaging and CAT scan reports and physical examination. Symptoms were considered chronic if they persisted for ≥ 30 days.

Subjects expressed their willingness to refrain from using over-the-counter (OTC) or prescription medication or herbal supplements intended for the relief of pain or inflammation, including muscle relaxants, for the duration of the study and refrain from other therapies for neck or shoulder pain including physical therapy, occupational therapy, hot or cold packs or alternative therapies, such as chiropractic care and acupuncture for the duration of the study.

Subjects were excluded from participation if they presented with primary pain located outside or in addition to the region of the neck or the shoulder; the etiology of neck or shoulder pain could not be definitively diagnosed or was due to other than osteoarthritis, chronic muscle spasms or cervical and thoracic spine sprain strain, or if other potential contributing etiologies could not be satisfactorily ruled out; acute pain symptoms; active chronic pain disease such as chronic fatigue syndrome or fibromyalgia; analgesic or muscle relaxant use within 7 days prior to study treatment; use of systemic corticosteroids not including inhaled and topical products; use of narcotics or botulinum toxin injection in the neck or shoulder within 30 days prior to study treatment; cancer or treatment for cancer within the last 6 months; unstable cardiac disease, such as cardiac arrhythmia, congestive heart failure or myocardial infarction; prior neck or shoulder surgery or herniated disc injury; active infection, wound or other external trauma in the planned treatment area; any medical or physical contraindications to light therapy; serious mental health illness such as dementia, schizophrenia or psychiatric hospitalization in the past 2 years; pregnancy, breastfeeding or planned pregnancy; participation in a research study within the past 30 days.

Study device

The device used in this study was a hand-held, low-level nonthermal laser that uses a 635 nm semiconductor diode (visible red light) and a 405 nm semiconductor diode (visible violet light), each emitting its respective wavelength with a tolerance of ± 10 nm (Erchonia[®] Model

EVRL).²⁷ The device is configured with one 7.5 mW line-generated red laser diode and one <5 mW line-generated violet laser diode with patented optics. The total amount of applied energy was 4.68 J. Safety glasses were provided to subjects and investigators for use during all treatment procedures (C22-KMT-6101 laser safety glasses; Kentek Corporation, Pittsfield, NH, USA).

Study procedure

Subjects received a single 13-min treatment with the non-thermal laser device on the day of study enrollment. Overall, the treatment protocol was identical to the protocol previously used with the single red 635 nm diode.¹³

Study endpoints

Baseline evaluation of each subject was performed on the day of study enrollment and included demographics, neck and shoulder VAS pain scores and linear ROM measurements. The VAS is a 100 mm horizontal line on which the patient's pain intensity is represented by a point between the extremes of "no pain at all" and "worst pain imaginable" which is sensitive to treatment effects.²⁸ Evaluation was repeated 3 mins, 24- and 48 hrs following administration of the laser treatment.

The primary measure of efficacy was the change in baseline neck and shoulder VAS pain scores within 3 mins after treatment. Subject treatment success was predefined as a $\geq 30\%$ decrease in VAS scores. Overall study success was predefined as $65 \pm 5\%$ individual subject successes. As this was a noninferiority study, the efficacy of the red/violet diode device was compared with the prior red 635 nm diode device. Change in mean neck and shoulder VAS pain scores was assessed using a two-sample *t*-test for correlated samples.

Subject satisfaction was assessed using a 5-point Likert scale ranging from "Very Satisfied" to "Not at All Satisfied" in response to the question "Overall, how satisfied or dissatisfied are you with any change in the pain in your neck and/or shoulder following the study procedure with the study laser device?" at the 24- and 48-hr assessments.

The primary safety endpoint was reports of adverse events at any time during the study.

Ethics

The protocol used in this study was approved by a commercial institutional review board (Western Institutional

Review Board[®], Puyallup, WA; Study Numbers 1,184,868 [Silverman] and 1,185,325 [Comey]).

Results

Subject demographics and clinical characteristics

Forty-four (44) subjects were enrolled and completed the study. Subjects were male (n=17; 39%) and female (n=27; 61%) with a mean (SD) age of 54.1 (14.3) years (range, 27–82 years). Subjects described themselves as Caucasian (n=36; 82%), Hispanic (n=2; 4.5%), Asian (n=2; 4.5%), African-American (n=1; 2%) or other (n=3; 7%).

Pain location on the neck was on the right side (n=29, 66%), left side (n=29, 66%), or back (n=26, 57%) and shoulder pain was right (n=27, 61%) and left (n=20, 45%) which were all of musculoskeletal origin. Duration of neck and shoulder pain was 76.6 (110.8) months (range, 1.5–468 months). Mean VAS pain rating at study entry was 65.0 on the 100-point VAS. Prior OTC and/or prescription analgesic use (n=23, 52%) to relieve neck/shoulder pain consisted of one (n=16), two (n=4) or three (n=2) medications (Table 1).

Efficacy

The primary efficacy measure, mean VAS neck and shoulder pain scores, decreased from 65.0 to 35.2. A *t*-test for correlated samples showed a mean decrease of 29.8 points to be significant ($p < 0.0001$). Most subjects in the study (75%) achieved $\geq 30\%$ decrease in VAS scores, exceeding the overall study success criteria by 5% (Table 2). Among subjects achieving individual treatment success (n=33), the mean baseline VAS scores decreased from 63.9 (8.7) to 27.5 (10.9) a mean decrease of 36.4 (13.4) points, or 56.4 (17.2)% ($p < 0.0001$). The reduced mean VAS scores remained 29.6 (16.7) and 29.3 (19.2)

Table 1 Prescription and over-the-counter analgesics

| Medication | n (%) ^a |
|------------------|--------------------|
| Ibuprofen | 13 (43) |
| Naproxen | 11 (37) |
| Aspirin | 1 (3.3) |
| Aspirin/caffeine | 1 (3.3) |
| Capsaicin patch | 1 (3.3) |
| Celecoxib | 1 (3.3) |
| Tramadol | 1 (3.3) |
| Diclofenac gel | 1 (3.3) |

Note: ^aSome subjects used more than one medication.

Table 2 Change in visual analog pain scores

| Timepoint | Dual diode, N=44 | Single diode, N=43 |
|-----------------------|------------------|--------------------------|
| | Mean (SD) | Mean (SD) |
| Pretreatment | 65.0 (8.4) | 60.2 (9.8) |
| 3 mins post-treatment | 35.2 (17.0) | 31.2 (18.7) |
| 24 hrs post-treatment | 34.6 (17.6) | 34.0 (24.6) ^a |
| 48 hrs post-treatment | 32.3 (19.9) | 34.2 (23.9) ^a |

Note: ^aN=34.

after 24 and 48 hrs, respectively (Figure 1). With only one subject failing to respond to treatment, the overall response rate was 97.7%.

The secondary efficacy measure, neck and shoulder ROM, also showed improvement. Mean seated passive abduction improved 27.9 degrees on both sides, mean shoulder measurements in relaxed position improved 30.1 degrees on the right side and 28.5 degrees on the left side and mean neck ROM measurements improved 22.7 and 23.4 degrees for the right and left sides, respectively (Table 3). Overall, subjects achieved a mean 29.07% improvement in neck and shoulder ROM. Among subjects achieving individual treatment success, there was no additional improvement in ROM outcomes. A comparison of clinical outcomes following treatment with the violet and red lasers vs the red laser alone is summarized in Table 4.

The proportion of subjects who were “Very Satisfied” with an overall change in neck and shoulder pain increased from 41% at endpoint evaluation to 46% at 48 hrs post-procedure evaluation and 71% of subjects were “Very Satisfied” or “Somewhat Satisfied” (Table 5). One subject who did not achieve a $\geq 30\%$ decrease in VAS scores

remained “Very Satisfied” with treatment outcome at 48 hrs.

Safety

No adverse events were reported by any subject throughout the study duration.

Discussion

The process of LLLT is based on a photochemical reaction with light in the visible spectrum (380–700 nm) to achieve therapeutic effects. This occurs when a suitable chromophore absorbs a photon of light and an electron is elevated to an excited state.³⁰ One such chromophore is the enzyme cytochrome C oxidase in the mitochondrial respiratory chain, with peak absorption found in the red to near-infrared spectrum.²⁹ The therapeutic effects of LLLT occur when the inhibitory signaling molecule nitric oxide becomes dissociated from cytochrome C oxidase. This results in increased electron transport, mitochondrial membrane potentials and production of mitochondrial ATP, NADH, RNA and cellular respiration.^{31,32}

The objective of this study was to determine whether combining 405 nm violet and 635 nm red lasers are equivalent or superior to the 635 nm red laser alone for the treatment of chronic neck and shoulder pain. The 635 nm device was previously FDA cleared for the temporary reduction of neck and shoulder pain of musculoskeletal origin; however, this is the first clinical study to demonstrate the effectiveness of a wavelength lower than 635 nm for treating musculoskeletal pain. Overall, the violet and red laser combination was superior to the red laser in most clinical measures. Although subjects treated with violet and red laser device had higher baseline pain scores, they

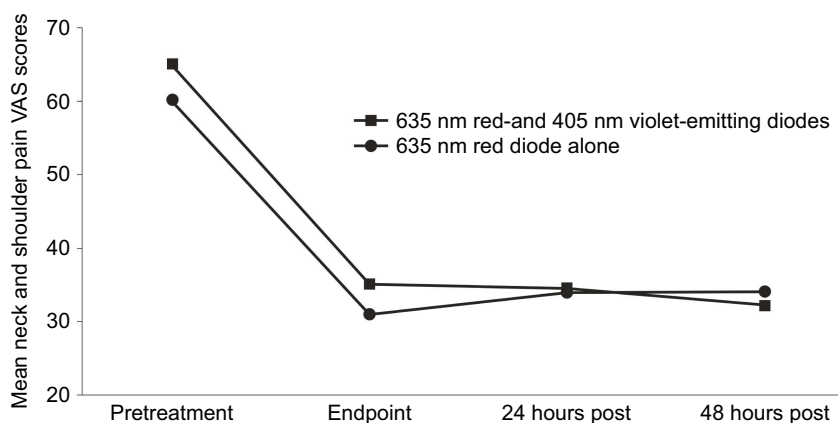


Figure 1 Change in VAS pain scores following treatment. Following treatment with 635 nm red- and 405 nm violet-emitting diodes, the neck and shoulder VAS scores decreased from 65.0 to 35 ($p < 0.0001$), a decrease of 29.8 points vs a decrease of 29.0 points for the 635 nm red diode alone.

Table 3 Change in range of motion

| Seated passive shoulder abduction | Right side | Left side |
|-----------------------------------|--------------------|--------------------|
| | Degrees, mean (SD) | Degrees, mean (SD) |
| Pretreatment | 134.7 (26.4) | 137.6 (24.7) |
| Endpoint (3 mins) | 162.6 (16.1) | 165.6 (13.9) |
| Change | 27.9 (16.9) | 27.9 (17.3) |
| Relaxed shoulder position | Mean (SD) | Mean (SD) |
| Pretreatment | 131.0 (26.6) | 135.2 (24.3) |
| Endpoint (3 mins) | 161.1 (21.0) | 163.8 (18.1) |
| Change | 30.1 (14.6) | 28.5 (15.2) |
| Neck | Mean (SD) | Mean (SD) |
| Pretreatment | 52.6 (13.1) | 51.1 (14.9) |
| Endpoint (3 mins) | 75.2 (9.6) | 74.4 (12.0) |
| Change | 22.7 (9.6) | 23.4 (9.2) |

Table 4 Clinical outcomes of violet and red lasers versus red laser only

| | Violet and red lasers | Red laser only | Difference |
|--|-----------------------|----------------|------------|
| | N=44 | N=43 | |
| Duration of pain, months | 110.8 | 61.7 | 49.1 |
| Change in shoulder range of motion, degrees | 29.3° | 14.4° | 14.9° |
| Change in VAS immediately after treatment | 29.8 | 29.0 | 0.8 |
| Subjects meeting study success criteria, ≥30% pain reduction | 75% | 65% | 10% |
| Percent improvement from study endpoint to 48 hrs post-treatment | +8.13% | -9.01% | 17.14% |

Table 5 Subject post-treatment satisfaction

| Satisfaction | 3 mins n (%) | 24 hrs n (%) | 48 hrs n (%) |
|------------------------------------|--------------|--------------|--------------|
| Very satisfied | 18 (41) | 17 (39) | 20 (46) |
| Somewhat satisfied | 21 (48) | 14 (32) | 11 (25) |
| Neither satisfied nor dissatisfied | 9 (11) | 8 (18) | 5 (11) |
| Not very satisfied | – | 3 (7) | 6 (14) |
| Not at all satisfied | – | 2 (4) | 2 (4) |

achieved a greater reduction in pain scores and improved ROM.

In a previous study, a 635 nm laser device significantly reduced plantar fasciitis pain following two weekly

treatments for 3 weeks.³³ In the present study, therapeutic benefit was achieved with a single treatment session. Mean neck and shoulder VAS pain scores decreased from 65.0 to 35.2, a mean decrease of 29.8 points ($p<0.0001$). Most subjects in the study (75%) achieved $\geq 30\%$ decrease in VAS scores, exceeding the overall study success criteria. In the previous 635 nm study, sham-controlled study, mean VAS neck and shoulder pain scores decreased from 60.2 to 31.2, a mean 29.0-point decrease ($p<0.0001$).¹³ In that study, 65.1% of the treated subjects achieved $\geq 30\%$ decrease in VAS scores (Table 2). Overall, the violet and red laser combination was superior to the red laser in every clinical measure.

These data were used to support the 510(k) clearance of a 405 nm violet/635 nm red laser device for the temporary reduction of neck and shoulder pain of musculoskeletal origin.²⁷

The results of this single treatment clinical trial add to the existing body of data demonstrating the ability of nonthermal lasers to alleviate pain associated with chronic joint disorders,³⁴ chronic low back pain,³⁵ neck pain,^{16,17} adhesive capsulitis (frozen shoulder)³⁶ and pain from a variety of musculoskeletal and orthopedic injuries and procedures.^{25,31,37}

As nonthermal lasers have demonstrated efficacy without any known adverse effects, and there is little evidence supporting the long-term use of opioids for chronic pain,³⁸ lasers should be considered as a first step for treating chronic musculoskeletal pain.

Conclusion

A novel, low-level nonthermal laser that combines red 635 nm and violet 405 nm semiconductor diodes was used to treat subjects with neck and shoulder pain of musculoskeletal origin. A single treatment resulted in diminished pain scores in 75% of subjects with increased ROM and overall subject satisfaction. Treatment with the red and violet lasers outperformed the FDA-approved red laser with respect to pain scores and improvement in shoulder ROM.

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Disclosure

Mr Travis Sammons is an employee of Erchonia Corporation. The authors report no other conflicts of interest in this work.

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