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The effect of 300 mW, 830 nm laser on chronic neck pain: A double-blind, randomized, placebo-controlled study

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Abstract

A randomized, double-blind, placebo-controlled study of low-level laser therapy (LLLT) in 90 subjects with chronic neck pain was conducted with the aim of determining the efficacy of 300 mW, 830 nm laser in the management of chronic neck pain. Subjects were randomized to receive a course of 14 treatments over 7 weeks with either active or sham laser to tender areas in the neck. The primary outcome measure was change in a 10 cm Visual Analogue Scale (VAS) for pain. Secondary outcome measures included Short-Form 36 Quality-of-Life questionnaire (SF-36), Northwick Park Neck Pain Questionnaire (NPNQ), Neck Pain and Disability Scale (NPAD), the McGill Pain Questionnaire (MPQ) and Self-Assessed Improvement (SAI) in pain measured by VAS. Measurements were taken at baseline, at the end of 7 weeks' treatment and 12 weeks from baseline. The mean VAS pain scores improved by 2.7 in the treated group and worsened by 0.3 in the control group (difference 3.0, 95% CI 3.8 2.1). Significant improvements were seen in the active group compared to placebo for SF-36-Physical Score (SF36 PCS), NPNQ, NPAD, MPQVAS and SAI. The results of the SF-36 Mental Score (SF36 MCS) and other MPQ component scores (afferent and sensory) did not differ significantly between the two groups. Low-level laser therapy (LLLT), at the parameters used in this study, was efficacious in providing pain relief for patients with chronic neck pain over a period of 3 months.

Keywords: Neck pain; GaAlAs; 830 nm; Low-level laser therapy (LLLT); RCT

1. Introduction

Despite receiving less attention than low back pain, neck pain is a highly prevalent condition, with cross-sectional studies reporting that 10–24% of the population are troubled by neck pain at any one time (Borghouts et al., 1998; Cote et al., 1998; Picavet and Schouten, 2003; Webb et al., 2003). Such common morbidity incurs significant economic costs to the community and reduced quality of life to the individual. In the Netherlands, the total cost of neck pain management has been estimated to be $US686 million in 1996 (Borghouts et al., 1999a). Between 8.8% and 11.9% of all general practitioner consultations are for neck pain (Andersson et al., 1999). Standard general practitioner-initiated treatment includes simple analgesics, anti-inflammatory medication, rest or physical therapy (Borghouts et al., 1999b; Korthals-de Bos et al., 2003).

Non-invasive techniques of treatment for neck pain lack a strong evidence base (Aker et al., 1996; Hoving et al., 2001). The lack of effectiveness of usual approaches is further highlighted by the fact that complementary therapies are used by patients with neck pain more often than conventional therapy (Wolsko et al., 2003).

In the majority of patients there is no readily demonstrable anatomical source of the neck pain, so treatment

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is necessarily pragmatic (Barnsley, 2003). A safe, convenient, readily available treatment for chronic neck pain would be a useful addition to an otherwise limited armamentarium. Low-level laser therapy (LLLT) is a potential candidate for this role.

LLLT has been used for the treatment of a broad spectrum of conditions particularly in Europe (Moore, 1989; Baxter et al., 1991; Cambier and Vanderstraeten, 1997) and Japan (Ohshiro, 2001). A meta-analysis (Enwemeka et al., 2004) and systematic review of the literature (Bjordal et al., 2003) provide evidence of efficacy for LLLT in a range of painful conditions. Neck pain has been the subject of investigation in 21 randomized controlled trials identified through a systematic review of the literature; the earliest from 1981 to the most recent in 2004 (Chow and Barnsley, 2005). Seventeen studies reported the use of infrared wavelengths ($\lambda = 780$, 820–830, 904 nm) and 12 demonstrated positive outcomes. Interpretation of the generally positive findings was limited by small sample sizes, heterogeneous laser parameters and a diverse range of treatment protocols.

Moreover, the lack of a single, plausible mechanism for the pain-modulating effects of laser has led to skepticism about outcomes of trials, even when outcomes are positive. Exploration of neurally based mechanisms (Baxter et al., 1994; Kasai et al., 1996; Gabel, 1997; Navratil and Dylevsky, 1997; Chow and Armati, 2004) and anti-inflammatory activity (Lopes-Martins et al., 2005; Bjordal et al., 2006) are two parallel streams of current research, to further elucidate mechanisms of laser action.

Notwithstanding these limitations, there was a clear need for larger, methodologically sound studies to further clarify findings.

We aimed to determine the efficacy of LLLT for neck pain in an appropriately designed and powered study. The null hypothesis was that LLLT would not provide a clinically or statistically significant benefit over placebo for patients with chronic neck pain.

2. Subjects and methods

2.1. Ethical approval

The Sydney University Human Ethics Committee approved all aspects of the study. Informed consent was obtained from all participants prior to commencing the trial.

2.2. Patient recruitment and selection

The study was carried out between July 2002 and May 2003 at a large suburban medical centre of 17 general practitioners in Sydney, Australia.

2.3. Inclusion and exclusion criteria

Patients were included if they were 18 years of age or over; had unilateral or bilateral chronic neck pain (i.e. of more than 3 months duration (Merskey and Bogduk, 1994)); were able to attend a full course of 14 treatments given twice a week; were able to understand the nature of the trial and were naïve to treatment with LLLT (except laser acupuncture).

Patients were excluded if they had an injury in which litigation or compensation was still current; had abnormal neurological signs in the upper limbs relating to nerve entrapment or impingement from the cervical spine; were unable to discontinue temporarily any activity which exacerbated the pain; were pregnant; had previous surgery to the cervical spine; suffered from other systemic rheumatological disease such as rheumatoid arthritis; suffered from neck pain which was part of a widespread pain syndrome involving other areas; had known photosensitivity or had other illnesses unrelated to neck pain which precluded involvement for practical reasons e.g. impending surgery.

Recruitment to the trial was conducted by placing posters in the waiting room of the medical centre where the trial was to be conducted. A series of advertisements was also placed in the local newspaper. Patients expressing interest in participating were contacted by telephone or posted detailed information if telephone contact was not made at the first attempt. Suitability for the trial was initially assessed by a structured telephone interview based on the inclusion and exclusion criteria. Potential subjects were then offered a face-to-face appointment for formal assessment. The first 90 patients who fulfilled the inclusion criteria were to be recruited into the trial.

2.4. Randomization and blinding

Subjects were randomized to one of two identical lasers (labeled A or B) following allocation using 90 sequentially numbered, opaque, sealed envelopes which were prepared earlier by a third party, using a computerized table of random numbers and balanced to ensure equal numbers in each group. The contents stated which laser was to be used (i.e. "A" or "B") and each envelope was opened immediately before the first treatment.

The digital display of both machines and the sound emitted during operation were identical but only one emitted a laser beam. Before the machine was switched on, the subject and operator put on protective glasses specific for 830 nm. The glasses protected the eyes, as required for a Class 3B laser, Australian Standard:AS/NZS 2211.1.1997 (Standards Australia Limited, 1997) and "blinded" both the subject and the operator as to which laser (active or sham) was being used. At the completion of the first treatment, to determine the success of blinding, subjects were asked to record whether they had received active or sham treatment.

Allocation concealment was maintained until statistical analysis was completed by the statistician (GH), blind to the coding.

2.5. Laser device and parameters

Subjects were treated with one of two Class 3B, Diolase devices (DioLase Corporation of Mountain View California, USA), marked A or B. The active machine emitted a laser beam with a fusiform shape, 15 mm in length and 3 mm at its widest with a wavelength of 830 nm and power of 300 mW in continuous wave mode at a Power Density (PD) of 0.67 W/cm^2. The laser parameters selected were based

pragmatically on those used in everyday practice by the principal author (RC) (Chow et al., 2003) and had been formally piloted in a previous trial designed to determine their feasibility for the present study (Chow et al., 2004).

2.6. Calibration of the laser

The output of the lasers was measured by a member of the Department of Laser Physics, Macquarie University, Sydney, at the start of the study, and on three occasions during the course of the trial.

2.7. Treatment protocol

The course of treatment consisted of twice-weekly treatments for 7 consecutive weeks with a maximum of half an hour allocated to each patient.

Subjects were seated comfortably with arms supported on a pillow and neck and shoulder muscles as relaxed as possible. Tender points in the neck were identified by systematic palpation using firm finger pressure, to one or both sides of the neck if pain was unilateral or bilateral. Palpation commenced at the mid-line at the external occipital protuberance, distally over each spinous process down to T8, the lowest insertion of the trapezius muscle aponeurosis, laterally along the nuchal line to the mastoid process on the affected side or sides. This was continued laterally over the articular pillars from C2 to C7 and paravertebral areas of T1 T8, extending laterally over muscle bellies to the tip of the shoulder including the acromioclavicular joint, the sternomastoid muscle bellies and insertion at the sternum and clavicle. The medial border of the scapulae and the insertion of muscles on the spines of the scapulae were also palpated to identify tenderness.

Tender points in the neck were treated for 30 s per point with up to 50 points being treated within the maximum half-hour allocated for treatment of each patient. The laser hand-piece was held perpendicularly to the skin using the contact-pressure technique (Ohshiro, 1990). The number of points treated was dependent on the severity of symptoms on the day of treatment. Both sides were treated if the pain was bilateral. Treatment was given to all patients immediately after palpation by a single operator (RC).

Subjects were requested not to have any other forms of physical treatment to the neck until all questionnaires had been completed, and were asked to maintain their usual pattern of medication intake, including pain medication, if any, until completion of the trial.

2.8. Baseline demographic data

Prospective data demographic data were collected for age, sex and duration of pain, to identify if any of these factors might be associated with response to laser therapy.

2.9. Outcome measures

The outcome measures adopted are in line with recommendations arising from the IMMPACT group (a multidisciplinary initiative which used consensus methods to develop a list of core outcome domains for use in chronic pain studies) (Turk et al., 2003).

The primary outcome measure was a horizontal 10 cm VAS for pain (graded from zero, representing no pain, to 10, the worst imaginable pain) (Scott and Huskisson, 1976; Price et al., 1994). Separate VAS scales were marked by the patient at baseline, immediately before each treatment, at the end of the course of treatment and 1 month after completion of the treatment (approximately 12 weeks from baseline). The scales were completed by the patients in a separate room from the operator and then placed into sealed envelopes and forwarded to a third party. Therefore, the operator applying the lasers remained blind to the patients' responses at all stages of the study. Also, patients were actively discouraged from discussing their progress or their response to treatment with the operator.

In addition to the VAS, the SF-36 (Brazier et al., 1992), the NPNQ (Leak et al., 1994), NPAD (Wheeler et al., 1999), the MPQ (Melzack, 1987), and a participant rating of global assessment (SAI) (Fischer et al., 1999) were used.

At the initial assessment, prior to any treatment, the set of questionnaires was explained in detail to the subjects and given to them for completion at home. At the end of the course of treatment and then one month later (12 weeks from baseline) the subjects were sent an identical set of questionnaires, with a reply-paid envelope, to be completed at home and returned by mail.

The SF-36 questionnaire consists of 11 questions concerning general health and can be divided into two aggregate summary measures, the Physical Component Summary (PCS) and Mental Component Summary (MCS) (Ware and Sherbourne, 1992; McHorney et al., 1993; Jenkinson et al., 1994). The NPNQ is a 9-item questionnaire, each with a possible score ranging from 0 to 4, developed to measure self-perceived disability from neck pain (Leak et al., 1994). The NPAD is a 20-item questionnaire measuring the intensity of pain, its interference with the vocational, recreational, social and functional aspects of living and the presence and extent of associated emotional factors, using a 5 cm VAS (Wheeler et al., 1999; Goolkasian et al., 2002). The MPQ is a multifaceted, pain questionnaire which provides an assessment of global pain and pain quality as well as sensory and affective components of pain as separate scores (Melzack, 1975; Melzack, 1987). A measurement of self-assessed global improvement or worsening (SAI) was included between baseline and 12 weeks (Fischer et al., 1999). This was expressed as percentage change and was completed at the end of treatment and 1 month later. A pain diagram was completed at baseline, prior to each treatment, to indicate the extent of pain on the day of treatment, at the end of the course of treatment and 1 month later.

To systematically capture any adverse effects of treatment, subjects were asked to record any new symptoms, from a list on a proforma, or use free text to describe any others.

2.10. Statistical methods

The analysis was conducted on the basis of intention-to-treat. The last observed data point was used for missing data at each of the three data collection points for five of the six subjects who had dropped out of the study.

The VAS provides data that are widely accepted as reliable and valid measures of pain intensity (Katz and Melzack, 1999).

How best to undertake statistical analysis of such data is the subject of much discussion. Some authors suggest that such data are ordinal and should not be analyzed using conventional parametric techniques (Svensson, 1998); others argue that it is interval in nature and use of parametric techniques is justified (Price et al., 1994; Myles et al., 1999). We analyzed change in raw VAS scores using both the Two-Sample *T*-test and ordinal regression for change in pain severity, grouped as ordinal data. For the latter analysis 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 based on range of VAS scores; 0 3 (none to mild); 3 6 (moderate); 6 8 (moderately severe); 8 10 (severe) (Jorgensen et al., 1995; Collins et al., 1997; Bodian et al., 2001). Improvements in pain scores were defined as <□5 (greatly improved), □5 to □3 (much improved), □3 to □1 (somewhat improved), □1 to 1 (about the same) and >1 (worse) (Dexter and Chestnut, 1995; Todd et al., 1996). Ordinal regression was used to test for a treatment effect after adjusting for possible confounding covariates (McCullagh, 1980). Differences in all other outcome measures were also compared across groups at baseline and between baseline and 12 weeks using either Two-Sample *T*-Test or Chi-square test as appropriate. The Mann Whitney test was used to compare the SAI across the groups, 1 month after completion of treatment. The program Statistical Package for the Social Sciences (SPSS), Version 11, was used for analysis.

2.11. Sample size and power calculations

Sample sizes for this study were calculated using the response rates and variances in principal outcome measures (percentage change in VAS) from a previous pilot study (Chow et al., 2004). The selected α value [probability of a false positive Type I error] was 0.05, β (probability of a false negative, i.e. type II error) was 0.2 (i.e. a power of 0.8) and d (detectable difference in VAS) of 2. We determined this to be a clinically relevant difference based on several studies. A total of 2724 of patients with chronic pain from 10 RCTs showed that a 2-point reduction on pain intensity scale where 0 = no pain and 10 = worst possible pain represented a clinically relevant reduction in pain of approximately 30% (Farrar et al., 2001). A minimum 2-point reduction in pain intensity on a 0 10 scale was also found to be clinically relevant in a study of 130 patients with breakthrough cancer pain (Farrar et al., 2000). In a study of acute pain, a minimum clinically relevant change in pain intensity of a 0 100 mm scale was found to be 13 mm (Todd et al., 1996).

Based on a Two-Sample *T*-test, 36 patients were required in each arm of the trial. To allow for drop-outs, contamination or other adverse contingencies 45 patients were recruited into each arm.

3. Results

Three hundred and fifty-five patients contacted the medical centre in response to the advertisement. The first 90 patients who met the eligibility criteria were included in the study (Fig. 1).

3.1. Characteristics of the study group

Fifty-nine women and thirty-one men were enrolled. The baseline characteristics of the groups after randomization are reported in Table 1. The mean age was 56.1 years (SD ± 12.7) and duration of pain was 15.1 (SD ± 12.6). The mean VAS score in the laser group was 5.9 and 4.0 in the placebo group.

3.2. Dropouts

Six subjects withdrew from the study during the course of treatment (two from the active and four from the control group). In only one case was the reason related to the neck pain or treatment complications (Fig. 1).

3.3. Primary and secondary outcome measures

3.3.1. VAS

The mean improvement in raw VAS was significantly greater in the treatment than the placebo group (□2.7 compared with +0.3, $p < 0.001$) (Table 2).

Using categorical groups based on change in pain severity 37/45 of the laser group and 13/45 of the placebo group demonstrated an overall improvement in pain scores from baseline to 1 month after treatment with 1 patient in the treatment group and 12 in the placebo group reporting worsening of pain (Table 3).

Change in pain severity based on categories of VAS scores, from baseline to 1 month after the end of treatment, displayed a shift of 45% of patients moving from more severe to mild pain categories. In contrast, there was a small shift of patients towards improvement in placebo groups and a 7% increase in patients in the most severe pain group (Table 4).

Using ordinal regression, with change in pain level to 1 month after end of treatment as the response, it was found that laser treatment was significantly associated with a fall in VAS ($p < 0.001$). Baseline pain levels were the only significant covariate ($p < 0.0038$). Results of the ordinal regression are given in Table 5.

The effect of being in the treatment group compared with the placebo group is an increase of eight times in the odds of an improvement in pain level. The effect of baseline pain level is (approximately) the worse the baseline pain level, the greater the odds of an improvement. For example, the effect of moderate baseline pain level compared with none to mild is an increase of 2.77 times in the odds of improvement in pain level. This is increased to 9.48, the greatest increase, in the "moderately severe" group and 6.47 in the "severe" group. Thus the data suggest that the more severely affected patients achieve the best outcome while those with mild pain do not experience high levels of improvement.

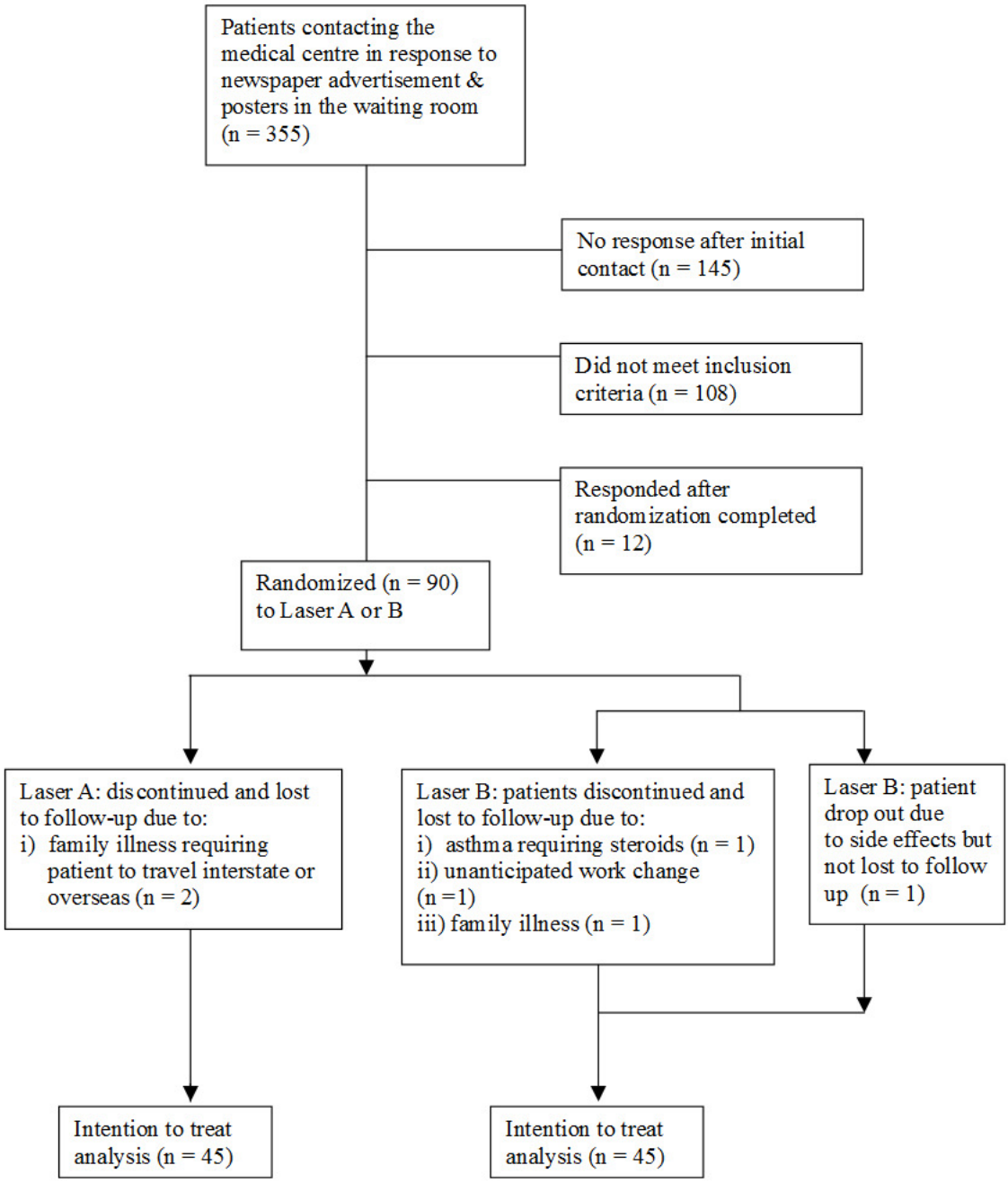

Fig. 1. Flow chart of patient recruitment.

Table 1
Baseline characteristics

	Laser A (active) mean	Laser B (placebo) mean
N	45	45
Age	56.8 (SD ± 12.8)	55.4 (SD ± 12.8)
Sex		
F	29	30
M	16	15
Duration of pain (years)	16.90 (SD ± 12.5)	13.37 (SD ± 12.7)
VAS	5.9 (95% CI – 5.2–6.7)	4.0 (95% CI – 3.4–4.7)

VAS – Visual Analogue Scale.

3.4. Other outcome measures

Over the 3 months of the study, there was a mean improvement in the SF-36 PCS, NPNQ, NPAD, MPQ-VAS and SAI over the entire study population (Table 2). There was no change in the mean MPQ (sensory and affective components) or the SF-36 MCS. The degree of improvement was significantly greater in the laser group than the control group for the SF-36 PCS, NPNQ and NPAD. Patients in the laser group reported a self-assessed global improvement (SAI) of 43.3% compared with 2.1% in the placebo group.

Table 2
Within and between group differences in primary and secondary outcome measures from baseline to 12 weeks

Outcome measures	Mean within group difference in outcome measures from baseline to 12 weeks		Between group difference in means [95% CI]	p value
	Laser (A) mean [95% CI]	Placebo (B) mean [95% CI]		
VAS (raw)	□2.7 [□3.3 to □2.1]	0.3 [□0.4 to 0.9]	□3.0 [□3.8 to □2.1]	$p < 0.001$*
SF-36				
PCS	3.2 [0.6 to □5.7]	□1.3 [□3.9 to □1.4]	4.5 [0.7 to 8.2]	$p < 0.022$*
MCS	2.4 [□0.3 to □5.1]	5.4 [2.1 to □8.6]	□2.9 [□7.2 to 1.3]	$p - 0.065$
NPNPQ	□3.5 [□5.1 to □1.9]	□0.6 [□1.8 to 0.6]	□3.0 [□5.0 to □0.9]	$p < 0.005$
NPAD	□15.2 [□20.4 to □ 9.9]	□3.1 [□7.6 to 1.4]	□12.1 [□19.3 to □4.8]	$p < 0.001$*
MPQ				
Sensory	□3.4 [□5.4 to □1.4]	□1.9 [□4.07 to □0.35]	□1.5 [□4.5 to 1.5]	$p - 0.32$
Affective	□1.3 [□2.3 to □0.4]	□0.7 [□2.1 to 0.6]	□0.6 [□2.3 to 1.1]	$p - 0.497$
VAS	□2.1 [□ 3.0 to □1.1]	0.1 [□0.9 to 0.7]	□2.2 [□3.5 to □0.9]	$p < 0.001$*
% SAI	43.8% [33.9 to 53.7]	2.1% [□7.4 to 11.6]	41.7% [27.7 to 55.8]	$p < 0.001$*

VAS – Visual Analogue Scale; SF-36 – Short Form 36, Quality of Life Questionnaire; PCS – Physical component score; MCS – Mental component score; NPNPQ – Northwick Park Neck Pain Questionnaire; NPAD – Neck Pain and Disability Scale; MPQ – McGill Pain Questionnaire; SAI – Self-assessed improvement.
* Statistical significance $p < 0.05$.

3.5. Dropouts

Six subjects withdrew from the study during the course of treatment (two from the active and four from the control group). In only one case was the reason related to the neck pain or treatment complications (Fig. 1).

3.6. Assessment of blinding

Thirty-two of 45 subjects in the placebo group and 30 of 45 subjects in the actively treated group stated they did not know which treatment they had received. Twelve subjects in each group thought they had active laser treatment and two subjects in the active and one patient in the control group thought they had placebo treatment. There was no significant difference between the two groups in their ability to identify which was the active laser ($p = 0.82$) after the first treatment. This indicates that the patients were effectively blinded to the treatment.

3.7. Adverse effects

A large number of adverse effects were reported with the same frequency in both groups during the period of data collection. However, nausea was reported significantly more frequently in the placebo group ($p < 0.02$) and stiffness in the laser group ($p < 0.02$) (Table 6).

3.8. Calibration of the laser

The laser output was measured as 300 mW prior to commencing the first treatment in the trial. At a mid point in the trial, the laser was measured as having an output of 285 mW and 4 months later, the laser output had declined to 210 mW.

4. Discussion

This prospective, randomized placebo-controlled study provides evidence for the use of 300 mW, 830 nm laser in the treatment of chronic neck pain over a 12-week period, with the laser treated group demon-

Table 3
Overall change in pain categories in laser and placebo groups

Change in pain level: baseline to 1 month after end of treatment	Laser	Placebo
Greatly improved	5 (11%)	0 (0%)
Much improved	13 (29%)	3 (7%)
Somewhat improved	19 (42%)	10 (22%)
About the same	7 (16%)	20 (44%)
Worse	1 (2%)	12 (27%)
Total	45	45

Table 4
Characterization of patients with VAS scores

	Baseline		One month after end of treatment	
Pain level:	Laser	Placebo	Laser	Placebo
None to mild	5 (11%)	17 (38%)	25 (56%)	18 (40%)
Moderate	16 (36%)	19 (42%)	14 (31%)	17 (38%)
Moderately severe	15 (33%)	8 (18%)	4 (9%)	6 (13%)
Severe	9 (20%)	1 (2%)	2 (4%)	4 (9%)
Total	45	45	45	45

Table 5
Results of ordinal regression for the response, change in pain level from baseline to 1 month after end of treatment

Effect	Odds ratio	95% CI	p
Laser			<0.0001
Placebo (referent)	1.00	–	
Active	8.00	(3.09–20.69)	
Baseline pain level			<0.0038
None to mild (referent)	1.00	–	
Moderate	2.77	(0.97–7.91)	
Moderately severe	9.48	(2.77–32.46)	
Severe	6.47	(1.38–30.31)	

strating a statistically significant and clinically relevant improvement in the primary outcome measure, VAS. Although severity of baseline VAS was a predictor of response, when baseline differences were adjusted for, change in the laser group was significantly greater than the placebo group. Indeed, patients with more severe pain had a greater probability of improvement.

Secondary outcome measures also improved significantly. We used two neck pain-specific measures (NNPQ and NPAD) to assess the degree of functional improvement, as visual analogue scores of pain are not directly correlated with improved physical functioning (Dawson et al., 2002). Each measure showed significant improvement, increasing the internal validity of the trial.

We also used a generic measure of quality of life, SF-36, to assess the multiple domains of function measured with this instrument. Somewhat surprisingly, we found that patients' physical functioning (PCS) was significantly improved, consistent with the functional improvement in neck pain-related functions, with no change in emotional domain scores (MCS). When baseline scores of MCS were examined it was apparent that subjects functioned at a relatively low degree of emotional distress in spite of an average pain duration of 15+ years. This suggests that a "floor" effect may have precluded the demonstration of any improvement. These data also suggest that patients in general practice manage pain more effectively and, although being physically limited, are not highly disabled, compared with those who attend Multidisciplinary Pain Clinics (Crook et al., 1986, 1989; Weir et al., 1992).

Patients also reported significantly greater self-assessed global improvement in the laser therapy group, reporting a mean improvement of 43.8% compared with 2.1% in the placebo group, again consistent with the improvement in VAS scores.

In contrast, the MPQ did not show any statistical improvement in either the sensory or affective dimension of the scores. Limitations are recognized for all instruments which measure pain and although widely used, the MPQ has been criticized for inadequately assessing each dimension of pain due to their high inter-correlation, which may be reflected in our findings (Turk et al., 1985).

It may be argued that self-selection of patients by their response to advertisements about the trial may have skewed the cohort to those with more severe pain or those experiencing an exacerbation of pain. However, it is plausible that the number of patients responding to advertisements for this trial, and the severity of their baseline pain scores, unmasks the large population of patients in the general community who have significant pain levels and who no longer seek treatment for their chronic pain due to the inadequacy of current therapies (Croft et al., 1998).

Adverse effects occurred in both groups with more nausea being reported in the placebo group. It is not clear why this should be so but it may be that a subgroup of patients responded to the discomfort of palpation with an increase in autonomic phenomena. Stiffness following treatment was significantly more common in the laser group (Table 6), but again the reason for this is not clear. Overall, the low frequency and mild nature of the reported adverse events are reassuring. There is no a priori reason to believe that there are infrequent serious adverse effects associated with LLLT which would have been missed in this study.

The clinical relevance and generalizability of the present findings is augmented by the undifferentiated nature of the neck pain treated and the treatment of non-specific tender points. Tender points are common to many types of neck pain and we did not seek to identify any particular structure as specific anatomical diagnoses of neck pain may not always be possible (Barnsley, 2003). The intra- and inter-rater reliability of identification of tender points by examination has been confirmed (Wolfe et al., 1992).

Table 6
Adverse effects experienced in both laser and placebo groups

Number of patients reporting symptoms	Laser	Placebo	p values
Mildly increased pain	35	29	0.16
Moderately increased pain	27	23	0.40
Severely increased pain	14	12	0.64
Increased pain elsewhere	35	28	0.11
Mild headache	27	24	0.5
Moderately increased headache	18	13	0.27
Severe headache	10	10	1.0
Nausea	9	19	0.02*
Light-headed/dizzy	16	20	0.39
Tingling in extremity	8	6	0.56
"Spaced-out" feeling	14	10	0.34
Sleepiness	18	19	0.83
Tiredness	24	21	0.53
Skin sensitivity	6	4	0.50
Jaw pain	3	2	0.65
Intercurrent infection	11	8	0.44
Stiffness	9	2	0.02*
Depression	2	3	0.65

* Statistical significance $p < 0.05$.

Treating undifferentiated tender points alone risked "lumping" together patients with a variety of pathophysiological diagnoses but nevertheless, a positive outcome was achieved. This begs the question as to whether even better results may be achieved in more selected groups, such as those with altered central pain processing, reflected as hyperalgesia, rather than those with a specific peripheral pain generator such as a painful cervical zygapophysial joint.

This study differs from previously reported trials of laser in several ways (Chow and Barnsley, 2005). We used a power output measured from 200 to 300 mW in contrast to the output range of 5–100 mW in the other trials. Furthermore, our treatment regime was 14 treatments compared with a maximum of 10 in other studies. This was designed to overcome under-dosing, suggested as a potential reason for negative outcomes in previous studies (Bjordal et al., 2001, 2003).

It has been suggested that laser therapy may act by stimulating ligament repair (Enwemeka and Reddy, 2000), by anti-inflammatory effects (Sattayut et al., 1999; Sakurai et al., 2000; Bjordal et al., 2006), increasing production of endogenous opioids (Laakso et al., 1994) and/or by reducing interstitial swelling by stimulating the motoricity of lymphatics (Lievens, 1991; Carati et al., 2003). However, in this study we treated tender points, begging an alternative explanation. At the wavelength used in this study ($\lambda = 830$ nm) laser has been shown to disrupt fast axonal transport by causing perturbation of microtubule arrays of small diameter neurons in rat dorsal root ganglia in culture and by reducing ATP synthesis in axonal mitochondria (Chow and Armati, 2004). There is also in vivo and in vitro evidence that 830 nm laser inhibits A-d and C fibre transmission (Tsuchiya et al., 1993, 1994). It is possible that laser-induced neural blockade may then lead to long-term altered nociception (Wall, 1998), analogous to the prolonged analgesia seen in some patients with local anesthetics (Arner et al., 1990). The repeated application of laser may reduce tonic peripheral nociceptive afferent input to the dorsal horn and facilitate reorganisation of synaptic connections in the CNS producing pain modulation (Coderre et al., 1993; Mense, 1993).

4.1. Limitations of the study

VAS scores at baseline were significantly higher in the laser group than the placebo group. VAS scores are limited by the fact that there are qualitative differences between pain at the mild and severe ends of the scale so that the same absolute change in a high VAS may not be clinically equivalent to the same change in pain in patients with mild pain (Price and Harkins, 1992). Moreover, simple biological variation and the concept of regression to the mean would result in patients with higher baseline scores being more likely to show a fall. In the present study, this would mean that the laser group might be more likely to show improvement irrespective of the efficacy of the intervention, leading to bias in favor of laser. Two observations refute this concern. First, in the ordinal regression analysis which controlled for the effect of initial VAS, LLLT vs placebo remained a significant predictor of pain relief. Second, concurrent measures of pain other than the VAS also improved significantly.

While the duration of follow-up of 1 month after the completion of treatment may be criticized, this study provides evidence for proof-of-principle for LLLT as an efficacious monotherapy. Modification of this protocol, its use in combination with other therapies and long-term outcomes remain to be explored in further trials.

Output power of the active laser fell from 300 to 210 mW over 12 months of the study. Aging diodes with falling output power are a common problem with laser devices (Nussbaum et al., 1999), as this study in which more than 1200 treatments were administered demonstrates. Nevertheless the output power, even at 200 mW is more than three times greater than the highest output used in previous studies (Chow and Barnsley, 2005).

The nonspecific effects of any therapy for pain are important to consider in any trial of therapy for pain. Blinding of treatment allocation is therefore particularly important. In this study, neither group of patients was able to determine laser or placebo-group allocation at the first visit, confirming the lack of any significant sensation from the device, such as heating, and the effectiveness of blinding.

5. Conclusion

Laser therapy with a wavelength of 830 nm and an output power of 300 mW provides clinically relevant benefit in the management of chronic neck pain as a monotherapy. The treatment is virtually painless, appears to have a low incidence of adverse effects and is relatively easy to administer. Further studies could explore variations to the presented protocol, such as shorter courses of therapy, decreased duration of laser exposure, reduced palpation pressure, prospective identification of patients with different physical findings and the use of LLLT as an adjunct to other therapies such as exercise or medications.

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