

Confirmation: LASER Application to the Cervical Spine in the Absence of Pathology Has no Effect on Sympathetic Nervous System Outflow

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Summary

To verify response mechanisms and the feasibility of clinical models of pain research, the effect of laser phototherapy on neurophysiological pain mechanisms needs to be determined first in the absence of pathology. A randomized, placebo-controlled, double-blind, repeated measures study was undertaken to investigate the possible involvement of the sympathetic nervous system (SNS) following laser irradiation. Nineteen healthy subjects participated in a study that consisted of 5 treatments to the right posterior neck region at a dose of 4.0 J/cm², using 820 nm laser. Each subject received active laser, placebo laser and a control condition over a three-day period, with a minimum of one day between sessions. Heart rate, blood pressure, bilateral skin temperature and skin conductance were measured distally. Results indicated that there was no alteration in sympathetic outflow, with no change in any of the outcome variables. It was concluded that in the laser phototherapy strategy used in this study, no effect on SNS outflow occurs in normal subjects. The model described raises the prospect for continuing research in clinical models of pain to determine if the SNS is involved in pain mediation subsequent to laser irradiation.

Introduction

Low powered lasers have become a common tool in the management of pain and other conditions¹. Many therapists and patients testify to the hypoalgesic properties of laser irradiation yet others have observed negligible responses.

Karu² was the first to suggest that a phototherapeutic response from laser occurs only in a setting where cell activity is not optimal. Amongst other factors, this observation may account for some of the wide variation in clinical responses recorded in the literature.

Despite numerous studies to quantify the hypoalgesic effects, the specific neurophysiological mechanisms of laser phototherapy have not been demonstrated conclusively. Walker³ initially proposed that central descending inhibitory pathways (and thus perhaps endogenous opioids) could be responsible for the analgesia related to laser phototherapy. In Walker's study, pain-free subjects demonstrated no 5-HIAA excretion on exposure to laser phototherapy, whereas subjects with chronic pain demonstrated possible effects on serotonin alteration when exposed to repeated treatments with helium-neon (HeNe) laser phototherapy. Laakso et al⁴ followed on from this hypothesis, investigating the plasma adrenocorticotrophic hormone (ACTH) and specifically b-endorphin levels in response to laser phototherapy to myofascial trigger points. Laakso et al⁴ found significantly increased levels of these factors at different time points using different treatment dosing strategies and it was concluded that the analgesic response to phototherapy may be mediated through hormonal / opioid mechanisms.

In investigating the neurophysiological mechanism of action, animal studies have demonstrated interesting results. Ponnudurai et al⁵ found the rat tail-flick was significantly reduced following 4 Hz HeNe laser applied to the low resistance point located at the base of the tail, indicating immediate hypoalgesia in rats. Ponnudurai et al⁵ noted that laser hypoalgesia was not naloxone reversible (or only partially so) and concluded that the hypoalgesia associated with laser phototherapy (detected using a hot-plate test) was non-opioid based yet supra-spinal in origin when applied to the rat nervous system.

Snyder-Mackler et al⁶ conducted a randomized, double-blind, placebo controlled study in humans to ascertain the effect of a HeNe laser on the resistance of areas of skin overlying musculoskeletal trigger points. They demonstrated a statistically significant increase in skin resistance (perhaps implying a sympathoinhibition or opioid-based analgesia). Seitz and Kleinkort⁷ studied auricular point laser stimulation and demonstrated a significant temperature decrease that they believed was produced by reflexogenic or autonomic nervous system responses. These examples of the inconsistent findings of the laser-induced effect on the opioid / stress / immune / sympathetic nervous systems warrant further attention in attempting to elucidate the effect mechanism for laser hypoalgesia.

It is known that *'the sympathetic nervous system is involved in pain'* and that *'certain pain syndromes are characterized by changes in sympathetic outflow to the affected region, and interruption of the sympathetic supply to the affected region produces relief of pain'*^{8(p1)}. Wright⁹ discussed two distinct analgesic pathways both closely related to the SNS, one of sympathoexcitation or non opioid-based analgesia, and sympathoinhibition or opioid-based analgesia. A method exists for testing the effect of laser phototherapy on sympathetic outflow. A number of studies have refined the measurement of human SNS activity and used it to elucidate effect mechanisms for physiotherapeutic

interventions^{10,11}. Using a validated and reliable system of data collection, a series of studies was planned in order to further examine laser-induced analgesia. The first of the studies described here, set out to test whether laser phototherapy affects SNS outflow in asymptomatic subjects.

Materials and Methods

Subjects

Nineteen healthy subjects (8 male, 11 female) ranging from 17 to 55 years (mean=21.2 years \pm 8.3 years) were recruited from The University of Queensland student population. Subjects were excluded if they reported pregnancy, malignancy, venous thrombosis, phlebitis, arterial disease, ingestion of photosensitizing agents, or involvement in compensation / litigation for an injury. Two subjects withdrew from the study without reason after only one session. To limit confounding variables, subjects were instructed not to consume photosensitizing agents such as alcohol, aspirin, insulin or antibiotics / anti-malarial agents for 24 hr prior to the study. In addition, subjects were only included if they were not heavily tanned or tattooed on the posterior neck. Participation in this study was on a voluntary basis, and all subjects read and signed a consent form informing them of the procedure and possible side effects of the study. The study had ethical clearance from the Human Research Ethics Committee at The University of Queensland, Australia and all participants provided written informed consent

Apparatus

The study used an infrared 820 nm continuous output Unilaser. The laser treatment probe consisted of a single output diode (1mm² aperture, maximum power output 50mW). An energy density of 4.0 J/cm² was utilized. The power output of the laser was evaluated prior to the study using a Spectra-Met SDH-2 Detector Head and MU-1 power meter (Laserdyne Technologies Pty Ltd).

Subject's blood pressure and heart rate were measured at the left arm using a Digital Electronic Blood Pressure Monitor DS-115. Two skin conductance (SC) monitors (Autogenic Systems AT64) were used to analyze the SC from the right and left second and third distal digital palmar surfaces. Skin temperature was recorded using four skin temperature (ST) monitors (Autogenic Systems AT42) positioned on the subject's right and left thumb tip and lateral epicondyles of the humeri, based on the model used successfully by Peterson et al¹². Output signals were sampled and recorded at a rate of 20Hz by a computerized data acquisition system (National Instruments Corporation software), situated in an adjoining room along with the blinded investigator who recorded the data. To aid analysis, a footswitch was connected to the software to record voltage signals at the start and end of each treatment stage.

Experimental Procedure

To standardize the study, a randomized repeated measures template was

utilized. Each participant received all three experimental conditions, and acted as their own control. All research was undertaken in a copper-shielded, sound-proofed, environmentally controlled room with constant room temperature and humidity.

To maintain participant blinding, the instrument panels recording SC and ST were disabled such that the output of the recording units was not visible to the participants or treating therapist. Prior to recording data, the measurement devices were calibrated to ensure that there were no discrepancies between the SC and ST units. The digital BP / HR monitor was standardized against a mercury sphygmomanometer.

At the first session, subjects chose from plain envelopes containing codes for laser treatment, placebo or control conditions known only to the therapist applying the laser, thus preserving the double-blind status of the study. The code for each subject was not broken until the completion of testing. Testing was undertaken on the first day of the study, and continued on two separate days, with a minimum of one day separating each session.

Subjects were positioned in prone on a plinth with a pillow supporting the ankles. Subjects were requested to refrain from moving, coughing or talking, except to notify the therapist of discomfort. Monitors were attached to the subject as described above. Subjects were left alone in the room for two minutes to allow for stabilization of readings representing SNS outflow. After this time, the investigator returned to the room, and measured the subject's HR and BP. The investigator exited the room once more and instructed the subject that the therapist would enter the room to apply the appropriate treatment condition. The therapist would then enter the room, activate the footswitch and administer one of the three possible treatments (laser treatment, placebo treatment or control). Following this, the therapist exited the room, instructing the participant that the investigator would immediately re-enter the room to record the BP and HR once more. A 5 minute rest period followed and a final BP / HR reading was taken.

Laser treatment condition

The therapist palpated the right C1/2 zygapophyseal joint (Level 1). The laser probe was applied to the structures overlying the zygapophyseal joint, namely the exiting nerve roots, paraspinal muscles, skin and associated subcutaneous structures for 133 seconds perpendicular to the skin surface, at 100% output. The therapist then palpated the right C2/3 zygapophyseal joint (Level 2) and the laser was again applied. This procedure was repeated for the right zygapophyseal joints of C3/4, C4/5 & C5/6 (Levels 3 to 5), giving a total of 5 treatments of 133 s.

Placebo condition

During the placebo condition, the second investigator applying the laser would cover the probe with a plastic shield when the subject was in prone with vision obscured. When the placebo condition was being administered, the machine emitted audible signals identical to the active treatment. For the

placebo condition, the therapist palpated and applied sham laser to each cervical zygapophyseal level as described above.

Control condition

During the control condition, the subject remained in prone throughout the session. The therapist stood in the same position as during a laser treatment but did not touch the subject. The footswitch was activated at the predetermined intervals replicating the treatment and placebo application time periods, so data analysis was standardized for any time effects and facilitated the double-blind status of the study.

The recorded voltages from the six monitors were collated using *Labview 6i* (National Instruments, Australia). A base line period of two minutes, the five treatment stages at each cervical level, and a period five minutes after each experimental condition was recorded. The area under the curve (AUC), minimum (MIN) and maximum (MAX) values, and time of each treatment period were all calculated by the program. Data was entered into a Microsoft Excel® spreadsheet. AUC values were standardized to produce an average AUC per second. *Statistical Package for Social Sciences (SPSS) version 10.1* was used to perform a 1-way within-subjects ANOVA, using 0.05 level of significance.

Results

The change in SNS outflow, demonstrated by the average SC for all subjects during the seven treatment stages (i.e., baseline prior to treatment, each of the five vertebral levels, and five minutes following treatment) were plotted against the area under the curve (AUC). Similar plots were mapped for changes in mean elbow temperature over the seven treatment stages, and for the mean hand temperature for all experimental conditions and for each of the seven treatment stages. No significant changes were detected between sides for any of the SC AUC variables (treatment AUC, placebo AUC or control AUC), calculated using repeated measures ($p = 0.230$). No significant differences were noted between SC experimental conditions (treatment / placebo / control: $p = 0.638$).

Repeated measures analysis was undertaken on the grouped elbow and hand ST data. Hand temperature yielded similar results to SC, with no significant differences in sides for ST treatment AUC, placebo AUC or control AUC ($p = 0.273$). No significant differences were noted between separate ST conditions ($p = 0.440$). BP and HR were analyzed using repeated measures. No significant differences were found between the conditions ($p = 0.206$) or at different times ($p = 0.114$). Only one subject reported any side effects during treatment and these were considered unrelated to the laser phototherapy.

Conclusions

This study found no significant changes in SNS outflow (either

sympathoexcitatory or sympathoinhibitory) in normal pain-free subjects resulting from the application of 830 nm laser at 4.0 J/cm² to the posterior neck. The most likely reason for the lack of effect is that asymptomatic subjects are not disposed to laser phototherapy, and hence cannot demonstrate a placebo or hypoalgesic response². Previous studies have suggested that the SNS may be involved in the physiological pathway of hypoalgesia^{3,4}. Future studies of laser phototherapy should focus on symptomatic subjects, with monitoring of associated responses in the SNS outflow. This study provides a model for research into the possible neurophysiological mechanisms underpinning laser phototherapy for investigation of different doses, wavelengths and treatment areas, examining both the SNS response and pain for perceived hypoalgesia.

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