

SOMATOSENSORY TRIGEMINAL EVOKED POTENTIAL AMPLITUDES FOLLOWING LOW LEVEL LASER AND SHAM IRRADIATION OVER TIME

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The effect on somatosensory trigeminal evoked potentials (STEP) and latencies by intraoral low level laser irradiation of the maxillary nerve was evaluated. After electrical input at the left infraorbital foramen on 24 experimentally blinded pain-free subjects, He-Ne laser irradiation (1.7mW, 632.5nm, 50Hz) was performed for two minutes on 12 of these subjects, and sham irradiation on the other 12, at the left maxillary third molar apical area. Far-field STEP latencies and amplitudes were recorded: at base-line, immediately after intervention, and ten and twenty minutes after intervention. In the irradiated group, an immediate (average) STEP amplitude decrease from base-line of 60 per cent occurred, with further reduction to 65 and 72 per cent, at the ten and twenty minute intervals ($p > .0001$). No significant change occurred in the sham irradiation group ($p > .05$), and no change in latencies occurred in either group ($p > .997$). Low level laser treatment is commonly used in musculoskeletal and neurologic conditions, with mixed results. This experiment demonstrates that intraoral laser application to the maxillary nerve, where covered only by mucous membrane, results in significantly reduced STEP amplitudes. This findings suggests that intraoral laser therapy may be an effective pain control treatment.

Keywords: Maxillary nerve; Laser Therapy, Trigeminal evoked potentials; Intraoral laser treatment.

Introduction

Low-level laser therapy is used in Asian and European countries for a variety of disorders, such as arthritis, soft tissue injuries, and pain [1]. However, in the United States, this therapy is still classified as an experimental treatment. Since an intraoral segment of the maxillary nerve has recently been identified with various painful conditions [2-4], we decided to objectively study the effects of low level laser irradiation (LLLi) on this area, by means of somatosensory trigeminal evoked potentials (STEP). This segment of the maxillary nerve in this area is covered only by mucous membrane, permitting relatively unhindered access to the nerve tissue within the mouth. The terminal branch of the maxillary nerve, the infraorbital nerve, can be accessed readily, at the infraorbital foramen as well.

Somatosensory evoked responses from the tongues of 20 normal adults and 20 with afferent trigeminal lesions resulted in latencies from 18 to 21 ms in the 20 normal individuals, and were entirely absent in 19 of the 20 with lesions [5]. These authors concluded that the STEP would provide a valid and reliable tool for monitoring trigeminal nerve components. The short duration, far field latencies of 18-24 ms are described [6,7] as the initial responses in the facial area of the somatosensory cortex. The N44 and

longer latencies are considered to be derived from the associative cortex, possibly involving attentional, perceptual, and cognitive processing [8].

Methods

Design and procedures

A placebo-controlled blinded time-series study of the effect of LLLi on the maxillary nerve was conducted, by evaluating STEP responses on 24 pain-free adults subjects, at base-line, immediately (within two minutes) after, and ten and twenty minutes later. Two STEP responses to stimulation of the infraorbital branch of the maxillary nerve were recorded, to determine the consistency of the base-line response. Identical procedures were performed on all 24 subjects, except that sham irradiation was used on 12 subjects, and LLLi on the other 12. All STEP recordings were made with the same train of stimuli at the same intensity for all participants. Including the base-line recordings, a total of four duplicated STEP recordings were made, for a total of eight tracings on each individual studied.

Laser Treatment

A low power (5mW, 632.5nm, 50 Hz) Helium-Neon laser (Gumem HN-205, Mayfair Medical Supplies, Ltd., Hong

Kong) was applied for 120 seconds at 1.7mW intensity, via the fiber-optic tip covered with a disposable plastic sheath, to a plexus formed by the posterior superior alveolar branch of the left maxillary nerve [9]. This is located approximately at the root apex of the maxillary third molar (Figure 1), even if the area is edentulous.



Fig 1: Intraoral Laser Irradiation Site. The plastic-covered laser tip is held with light contact against an area (arrow) located at the approximate apex of the maxillary third molar.

Subjects

After obtaining institutional review board approval and written informed consent, 24 participants were randomly selected from a population of healthy pain-free adults. The average age was 33.08 years for the LLLi group, and 31.25 years for the placebo group. Eight men and four women comprised the LLLi group, and the placebo group were made up of five men and seven women. There was no external evidence of the laser activation, which made blinding possible.

Preparation

Following appropriate scalp preparation, to decrease the impedance to less than 1200 Ohms, gold cup EEG electrodes were fixed to the area 2 cm posterior to C6, on the right side of the head. The common reference electrode was secured to Fpz in the same manner. Similarly, the ground electrode was fixed to the zygomatic process on the left side of the face at the same level of impedance. The international 10 to 20 system of EEG electrode placement was used as a guide for the proper placement of the recording electrode [10]. The subjects were instructed to clench their teeth, while the electrode placement area was palpated, to identify temporal muscle contraction near the recording electrode. To avoid EMG signal contamination, an amuscular area was selected. As an added precaution, participants were instructed to allow the lower jaw to drop slightly during stimulation. Additionally, the stimulus intensity was below that necessary to evoke a motor response in

the muscle.

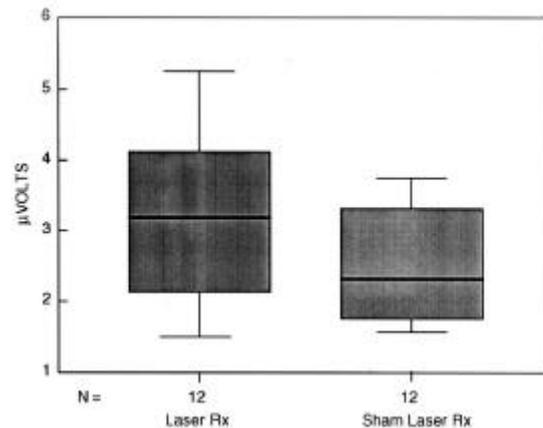


Fig 2: STEP Amplitudes Prior to Laser and Sham Laser Application. A pre-treatment analysis of variance, demonstrating no significant difference between laser and sham irradiation groups ($p > .202$)

Recording equipment

A Quantum 84 (Cadwell Laboratories, Kennewick, WA) electrophysiological instrument was used for all testing. The equipment settings were: (1) a field of 50 ms, to view the short latency potentials of P1 and N1, occurring in the region of 18 to 24 ms, respectively, (2) the gain at 10 microvolts, (3) the frequency band width at 0-3,000 Hz, (4) the number of stimulus sweeps averaged 250, and (5) the intensity employed was three times the intensity for threshold sensory perception of the stimulus to the left infraorbital foramen. No muscular twitch was observed at this low intensity level. The trace was repeated, superimposing each to determine adequacy of replication and reliability of the STEP recording.

Data analysis

The STEP amplitudes were subjected to a one-way analysis of variance (ANOVA) with repeated measures. The STEP latencies were also subjected to a one-way ANOVA with repeated measures.

Results

Base-line mean amplitudes

The mean amplitudes of the experimental and placebo groups prior to LLLi were 3.20 ± 1.33 and 2.59 ± 0.86 microvolts, respectively (Fig. 2). When subjected to an analysis of variance, no significant difference was observed between the two groups at base-line ($p = 0.202$; Table 1). The STEP amplitudes of N1-P1 in the study by Stohr et al.,[8] revealed a mean of 2.6 ± 1.1 microvolts, which compared to the overall mean amplitude of 2.89 ± 1.1 in this current study ($N=24$).

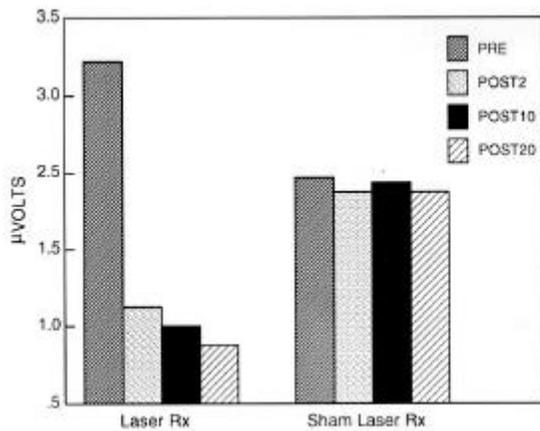


Figure 3: STEP Amplitudes Prior to Laser or Sham Irradiation and at three intervals following irradiation. Three STEP amplitude recordings demonstrate a significant amplitude decrease at two ($p < .001$), ten ($p < .0001$) and 20 ($p < .0001$) minutes in the LLLi group, but no significant change in the sham group.

STEP Amplitudes Over Time

The pre to post laser versus sham laser effects are indicated in the STEP analysis of variance (Table 1). The LLLi group had a significant fall in amplitude, from a pre irradiation mean of 3.2 microvolts, to post irradiation of 1.22 microvolts. At 10 min the mean amplitude fell from 1.22 to 1.08 microvolts, and at 20 min, it fell from 1.08 to 0.88 microvolts ($p > .001$). There was no significant change in the mean value of the sham laser group, which was 2.59 ± 0.86 microvolts prior to irradiation, and 2.52 ± 0.74 microvolts at the end of 20 min (Fig. 3). The STEP amplitudes for the twelve participants receiving LLLi revealed more than a 60% decrease in the amplitude of P18-N24 waves immediately after maxillary nerve irradiation. After 10 and 20 min, the STEP amplitude decreased to 65 and 72 %, respectively ($p > .001$). No significant change in amplitude was recorded in the sham laser group ($p < .121$).

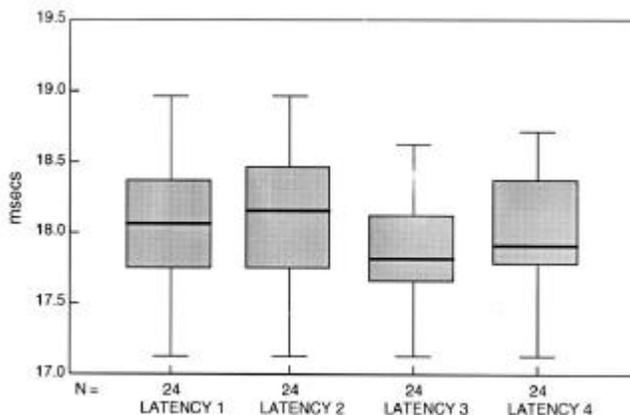


Figure 4: STEP Latencies prior to irradiation and at three time intervals following irradiation. Four recordings of the mean STEP latencies and standard deviations, with two recordings at each time interval, revealing no significant differences for LLLi or sham LLLi groups ($p > .997$). $N = 24$.

Table 1.

Comparison of STEP Amplitudes in Laser vs Sham Treatment using ANOVA

		Sum of Squares	df	Mean Square	F	P
PRE	Between groups	2.190	1	2.190	1.729	.202
	Within groups	27.861	22	1.286		
	Total	30.052	23			
POST2	Between groups	9.985	1	9.985	13.428	.001
	Within groups	16.358	22	.744		
	Total	26.343	23			
POST10	Between groups	13.380	1	13.380	17.191	.000
	Within groups	17.123	22	.778		
	Total	30.504	23			
POST20	Between groups	16.072	1	16.072	33.326	.000
	Within groups	10.610	22	.482		
	Total	26.682	23			

Table 2. STEP Latencies in Laser and Sham Laser Groups

		Sum of Squares	df	Mean Square	F	P
LATENCY 1	Between groups	4.167E-06	1	4.167E-06	.000	.997
	Within groups	6.117	22	.278		
	Total	6.117	23			
LATENCY 2	Between groups	1.667E-03	1	1.667E-03	.006	.939
	Within groups	6.071	22	.276		
	Total	6.073	23			
LATENCY 3	Between groups	.000	1	.000	.000	1.000
	Within groups	3.460	22	.157		
	Total	3.460	23			
LATENCY 4	Between groups	1.667E-05	1	1.667E-05	.000	.993
	Within groups	4.215	22	.192		
	Total	4.215	23			

Latencies Over Time

ANOVA with repeated measures of the latencies revealed no significant differences between or within either laser or sham irradiation group, at all four of the time intervals measured ($p > .997$; Table 2). The latency and amplitude values obtained were within the range of values obtained by Stohr et al., [8]. They found a mean of 18.5 ± 1.51 ms for the P1 latency. In the current study, the P1 latency averages for the four separate testings were: (1) 18.05 ± 0.51 , (2) 18.09 ± 0.51 , (3) 17.87 ± 0.39 , and (4) $18.00 \pm$

0.42 ms for the 24 participants, tested twice at each of the four testing times (Fig. 4). The total was eight trials on each subject over a twenty minute period. A grand total of 192 tracings derived from the 24 participants were studied. The longer latencies of P33 and N44 were observed, but were not included for study, as these latencies are thought to involve perceptual processing, considered beyond the scope of this investigation.

Discussion

The power density at the plastic covered fiber-optic tip of the laser was 1.73 W/cm². Multiplying the power density by the exposure time of 120 s equals 207.56 J/cm². When divided by the irradiated area of 1.5mm of a divergent unfocused beam, it equals 138.4 J/cm². In a compilation of 34 low-level laser experiments for pain relief, many of the outputs and exposures ranged from 5 to 60mW, applied from five to 30 min, respectively [1]. Compared to our 1.7mW intensity and 120 s exposure, this is classified as a mild dose of photostimulation. This intensity and exposure was selected because of our successful pain relief experiments, using these parameters [11]. The depth of penetration is wavelength-dependent; 632.5nm penetration in the skin is approximately 1-2mm [1], which is assumed to be greater in an area with only a minimal mucous membrane covering.

The mechanism of photostimulation on peripheral nerve tissue is poorly understood, but it has been demonstrated that laser cortically evoked potentials revealed selective stimulation of small diameter fibers in diabetics with axonopathies [12]. Both low-level and Nd:YAG laser irradiation of myelinated and non-myelinated fibers in rat peroneal nerve revealed nerve conduction changes confined to the nonmyelinated fibers, producing reversible changes in the organelles [13]. If the larger maxillary nerve fibers are preserved, it might explain the lack of latency changes and the amplitude reduction in the current study. As the 632.5nm wavelength of the laser used in this investigation has moderate depth of penetration, this would expose most of the axons within the maxillary alveolar branches to the laser irradiation, because of its minimal covering of mucous membrane at this site.

LLL irradiation of the median nerve was also shown to produce a reduction in amplitude with no loss of conduction velocity, similar to the current study.¹² They reported that 20 min He-Ne exposure (1mW, 632.5nm, 3.1Hz) to the median nerve at the wrist resulted in a 20 to 90 % decrease in amplitude, monitored at Erb's point, with no significant difference in latencies. This is similar to the response

obtained in the current study, except that our duration of laser irradiation was much shorter. However, the maxillary nerve is not covered by skin, subcutaneous fat and deep fascia, at the point of irradiation, as was the case with the median nerve.

A recent study [14] revealed that LLLi of human gingival tissue inhibited prostaglandin E₂ production, thereby acting as an anti-inflammatory agent. Therefore, LLLi to the maxillary nerve may act as an antiinflammatory agent in the area associated with facial pain [2] and where there is local edema, increased temperature, and headache [4].

Low-level laser is mainly used for pain reduction [15-19]. Instruments with minimal power, as commonly used for research in the United States, do not permit tissue effects to any significant depth, particularly when the treated area is covered by skin. Criticism has centered on the ineffectiveness of these low power lasers [20,21], although such lasers have been used to treat acupuncture and trigger points, with reported success in relieving pain [22]. The limited clinical results has prevented regulatory approval in the United States.

Analgesics have been evaluated using somatosensory evoked potentials [22-25]. The STEP provides a more objective method of pain assessment than the commonly used verbal ratings or visual analogue scales [26]. The observed decrease in STEP amplitude after LLLi is convincing evidence that laser irradiation depresses the amplitude, and could prove to be an effective alternative treatment to drugs, for painful trigeminal system disorders [4]. A randomized placebo-controlled double-blind crossover study of analgesic drug potency, evaluated by laser somatosensory evoked (LSE) potentials [26], revealed significant depression of the LSE potentials when the drug was peripherally active. It was also noted [26] that habituation can depress the STEP response, and that this should be accounted for by using a sham group receiving the same trains of electrical stimulation as the experimental group.

In summary, the STEP provided an objective assessment of change in amplitude following He-Ne LLL irradiation to the maxillary nerve, in this blinded placebo-controlled investigation, performed on healthy adults. The amplitude reduction is considered to be the result of transient loss of conduction in the thin fibers that are involved with pain and autonomic function. Further research is required to identify the effect of LLLi on the STEP when it is conducted on those with painful disorders of the trigeminal nerve.

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