APPLICATION OF THE LOW POWER LASER IN A SINGLE-BLIND RANDOMIZED TRIAL IN MIGRAINOUS HEADACHE PATIENTS

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ABSTRACT

Migrainous headache is extremely common in the United States, yet its pathophysiology is not well understood. In previous published non-blinded studies, we have shown the potential benefit of the low power laser in the treatment of migrainous headache. This randomized single-blinded pilot study consisted of 9 females, mean age 49.4 years, range from 41 to 60, with migrainous headache. The location of pain occurred in the frontal, temporal and/or occipital areas. Each patient was requested to grade their headache pain level from 0 (no pain) to 10 (severe disabling pain). After informed consent, each patient was then randomized either to low power laser therapy (830 nm, 100 mW) or sham for the first treatment, and then crossed over for the second treatment. After each treatment, the patients were asked to grade their pain level. Treatments lasted a maximum of ten minutes and were directed at anatomical sites around the head and neck where soft tissue lesions occurred based on the original method of Wong et. al. The overall pain level score significantly decreased from a mean baseline of 7.2 to 4.3 after laser treatment; whereas no change occurred from baseline after sham. No adverse effects were noted during or after laser therapy or sham. Thus this pilot study suggests that the low power laser may be a safe and effective modality in the relief of migrainous headaches. Further double-blind randomized studies are now in progress.

INTRODUCTION

Migrainous headache is extremely common in the United States (1), yet its pathophysiology is not well understood (2,3). Little progress has been made in the diagnosis of this malady, and current therapy has mostly been focused on the use of drugs. In a previous published non-blinded open-label study (4), we have observed that patients with headaches invariably have microscopic and macroscopic soft tissue lesions or injuries. These lesions are likely tears of Sharpey's fibers localized at the periosteal-osseous junctions. Chemicals released in these lesions cause and perpetuate muscle contraction/spasm and ischemia, producing pain and tenderness. In this randomized single-blind crossover pilot study, we determined the sites of the soft tissue lesions and explored whether or not the use of low power laser directed at these sites can relieve the common headache pain.

METHODS

Study patients. Nine female patients with migraine and migrainous headaches were studied; their mean age was 49.4 years and ranged from 41 to 60 years. These patients had common migraine or migrainous headaches, tension headaches, or mixed-type headaches. The location of pain occurred in the frontal, temporal and/or occipital areas. Each patient had to have a sufficient level of head pain at the time of the study.

Exclusion. Excluded from this protocol were patients who did not have at least moderate grade head pain as defined below, acute head trauma, known intracranial space-occupying lesions such as tumors, aneurysms, hematomas, abscesses, and elevations of intracranial pressure. Also

excluded were patients with infections, severe hypertension (i.e., >170/110), severe respiratory failure, congestive heart failure, severe liver and renal failure, and debilitated condition.

Low power laser. The low level laser used in this trial is a gallium-aluminum-arsenide (GaAlAs) diode laser. This laser emitted a continuous wave wavelength of 830 nanometers, and power output of 100 milliwatts. This unit was manufactured by DioLase Corporation, Berkeley, California.

Randomized single-blind trial. Patients who qualified were asked if they were willing to participate in this randomized protocol. The study objectives and procedures were explained to the patients, and the patients were given informed consent. In this single-blinded study the patients were given both laser or sham treatments in a crossover fashion; the patient did not know which treatment was being administered.

At baseline and after each treatment, patients were requested to rate their present headache pain symptom from a scale of 0 (no pain) to 10 (disabling pain). A pain level of at least grade 2 out of 10 was required for admission into the study. The investigators performed an examination by palpation of the major areas of muscle attachments in the head, neck and upper back.

Based on a randomized schedule, the first treatment with either the low power laser or sham treatment was performed. The duration of each treatment was limited to a maximum of ten minutes. After a ten minute resting interval, the second laser or sham treatment was then performed in a crossover manner. The patients were requested to quantitate their headache pain after each therapy. The investigators performed an examination by palpation on the areas treated.

Treatment sites. Each patient received sham or laser treatment in a randomly determined order. The probe (laser light or sham) was directed at anatomical target sites over the head and neck where soft tissue lesions occurred based on the studies of Wong et. al. (4-7) Briefly, in patients with frontal, parietal or occipital headaches, the probe was directed at the occipital protuberance and nuchal line. In patients with temporal headaches, the probe was directed on the same side at the styloid process and posterior auricularis muscle behind the ear. In the neck, if the cervical spinous processes were tender to palpation, the tips of the spinous processes were treated. In the upper back and shoulders, if the medial angle and spine of the scapula were tender to palpation, these sites were treated. Treatment lasted one to two minutes per site; the duration of therapy and sites treated were similar for the first and second treatments. At the end of the treatments, the patient was asked whether they had more muscle relaxation, reduced tenderness upon palpation of the nuchal line, spinous processes, and styloid processes, and whether any adverse effects occurred.

Statistical analysis. The patients' self assessment pain level score were measured before and after low power laser therapy and the differences were evaluated. The differences were analyzed using a paired t test. Statistical significance was considered when $p < 0.05$ (two-sided).

RESULTS

The nine patients with headache (at baseline) were randomized in the study. Five patients received sham treatment first and then had laser treatment; four had laser treatment first and then had sham treatment. Overall the pain level score significantly decreased from a mean baseline of 7.2 to 4.3 after laser treatment in the nine patients ($p < 0.01$).

Post-first treatment (table 1). For patients administered sham first, the mean grading scale for pain did not change from baseline of 7.2. For patients who initially received low power laser therapy, the pain level decreased from baseline of 7.25 to 4.5 after the laser treatment.

Post-second treatment (table 2). When laser was the initial treatment followed by sham as the second treatment, the pain scale was unchanged from the initial treatment. Subsequent sham or placebo did not affect the beneficial effect of the improved condition. However, when sham was followed by laser, the pain scale dropped from 7.2 (sham) to 4.2 (laser).

Patient preferences. When patients were asked which therapies offered the most muscle relaxation and reduced tenderness upon palpation of tender sites, the patients preferred the laser treatment (table 2).

Adverse effects. No adverse effects were observed during or after low power laser therapy or sham in this single-blind randomized trial.

DISCUSSION

These data from this randomized single-blind trial demonstrate that the low power laser does have a beneficial effect in relieving the common headache. The pain level is dramatically reduced after use of the low power laser. In patients who received the laser as the initial therapy, the benefits appeared to be sustained throughout the second sham treatment. This protocol placed a time limit of ten minutes for each treatment; it is not known whether a longer period of treatment might have improved the pain scores even more.

Soft Tissue Lesions

The great majority of persons with head pain have soft tissue lesions resulting from injuries remembered or forgotten. These lesions are capable of perpetuating themselves for decades and are the basis for histories of head pains (aches) spanning many years. Muscles, tendons, ligaments, fascia and periosteum are all capable of being injured following falls, sports injuries, auto accidents, birth traumas, etc. However, when one examines each of these tissues histologically, one finds that muscles are capable of being torn, but usually heal readily due in part to their increased vascularity. Tendons and ligaments are made of long collagen fibers whose individual fibers are weak, but collectively they are very strong capable of withstanding hundreds of pounds of stress per square inch. The periosteum, on the other hand, is also composed of collagen fibers; many of which are near attachments of tendons and ligaments and

interwind with collagen fibers surrounding these attachments. Many of the collagen fibers of the tendons and ligaments penetrate the periosteum and bury themselves into the cortical plate of the bone. Together with the Sharpey fibers of the periosteum and those that are continuous of the tendons and ligaments, the periosteum of the tendons and ligaments is quite strong to normal functional stress. However, if these fibers at the periosteous-osseous junction is subjected to sudden tears from any acceleration deceleration injury, the detachment of the Sharpey fibers may result.

Pain From Chemical Stimuli

Physiologists have long known that the purpose of pain is to alert the body the fact that tissue is being injured, and there are only three known stimuli capable of directly causing pain; they are thermal, mechanical, and chemical (8). Injured tissue has been known to release such noxious chemicals as kinins, bradykinins, prostaglandins, histamines, substance P, proteolytic enzymes, potassium, acids, etc. within the interstitial tissue and stimulating the free pain nerve endings to cause pain. Thus, if thermal and mechanical causes are eliminated, then the chemical stimulus is the only factor capable of causing pain when there is soft tissue injury. Psychogenic factors such as depression, anxiety, worry, and anger may lower the threshold of pain but are not capable of causing pain directly.

It is known that there are pain receptors or free nerve endings in the skin, scalp, periosteum, fascia, muscles, cranial sinuses and arterial wall (3,8). There are only two known types of free pain nerve fibers capable of propagating pain impulses to the central nervous system, the A delta and C fibers. The A delta fibers are myelinated, fast-acting fibers producing sharp, stabbing pains. The site of injury can be readily and precisely localized. These fibers are particularly sensitive to mechanical and thermal stimuli. The C fibers, on the other hand, are unmyelinated, thin fibers which can propagate pain impulses at a much slower rate than the A fibers. Activation of the C fibers produces dull, aching, burning pain which is difficult to locate the precise site of injury. C fiber pains tend to arborize in various set patterns from the site of injury and tend to accompany all lymphatic and blood vessels, somatic and autonomic nerve fibers. Of all soft tissues, the periosteum has been found to be the most sensitive to pain.

Basic Mechanisms of Common Head Pains

In the diagnosis of common head pains (aches), virtually all patients with migraine and migrainous-type headache have muscle-tendon and ligament insertion injuries (4-7). The initial soft tissue lesions are usually located at vulnerable attachment sites, namely the periosteal-osseous junctions where Sharpey's fibers insert in the head and neck. In other instances, injuries to the myotendinous junctions may occur (9). Where there is soft tissue injury of ligaments, tendons, muscles, and fascia, pain from chemical stimuli is produced. The noxious chemicals cause pain directly or sensitizes the pain receptors (e.g., prostaglandins). Further, they also irritate muscles, increasing muscle tension, spasm, and ischemia; the latter can further intensify pain and expand the location of pain. Pain impulses are also transmitted to the dorsal horn of the spinal cord and via interneuronal connections to anterior horn cells which activate motor efferents to muscles remote from the soft tissue lesion, causing further muscle activity and ischemia; the latter can also become the primary nociceptor stimulus.

The initial soft tissue injury event when mildly traumatic with little chemical released may be forgotten by the patient and may be recalled only by eliciting a careful history. The initial lesions if not fully healed are perpetuated and exascerbated by more further injuries due to accidents, falls, and even abnormal postures while working, standing, sitting, and sleeping. Chemicals released from these areas of soft tissue lesions cause local pain, edema, muscle spasm and ischemia. Sites of soft tissue lesion or injury locations are determined by palpation, usually at periosteal-osseous sites at insertions or origins of muscles. Previously we have been treating and relieving pain in patients with common headache problems by injecting a few drops of an anesthetic agent such as Xylocaine or Bupivacaine at these sites. To provide evidence for this concept, Feinstein injected 1 ml of 6% saline solution (i.e., chemical stimulus) into the various interspinal spaces of 140 normal individuals (mostly medical student volunteers) (10). Stimulation of the area at C-1 interspinal area evoked pain in the occipital as well as the temporal and frontal areas, and injection at the C-7 area caused pain in the muscles of the brachial plexus. The pain patterns were reproducible, at times eliciting autonomic responses, and may last several days. None of the pain patterns involved the peripheral nervous system or followed vascular pathways. These studies were further substantiated by the classic work of Inman and Saunders (11).

Low Level Laser and its Medical Uses

Laser is the acronym for light amplification by stimulated emission of radiation; its unique light is coherent, monochromatic and collimated, and has been used in industry and in medicine. Medically, high power laser has conventionally been applied as a surgical tool to cut and coagulate tissue. The low power laser, on the other hand, uses a power level that is 100 mW or less and cannot cut or coagulate tissue. With the emergence of low power diode laser, it is small, light in weight, portable, easy to use, and safe. Low power laser has been used for more than two decades in anesthesia, wound healing and relief of pain. Zhou had used low level laser as acupuncture anesthesia in more than 7000 patients for tooth extractions and minor maxillofacial surgery (12,13). Mester had treated more than 1300 patients with open wounds and ulcers which would not heal with conventional methods and plastic surgery (14,15). A number of investigators had successfully applied the low level laser for relief of pain in a variety of conditions including rheumatoid arthritis, post-herpetic neuralgia, etc. (16-20) Despite the many studies demonstrating the efficacy of the low power laser, the studies have been criticized for inadequate design and methodolgy due to the use of different lasers, wavelengths and dosing schedules. Thus there is a strong need for controlled randomized studies such as the present trial to take into account the placebo effect.

Low Power Laser - Potential Mechanism for Pain Relief

To explain the action of the low power laser, soft tissue lesions produce a sterile inflammation and local accumulation of tissue chemicals released from these injury sites and irritate the muscles and stimulate a withdrawal reflex. Sympathetic nerves in the immediate vicinity of an injury causes the contraction of smooth muscles of blood and lymphatic vessels. Lymphatic vessels being made up of a single layer of endothelial cells whose smooth muscle contraction restricts the lymphatic pumping action and results in edema. Chemicals build up in the intersitial spaces and pain results. In order to eliminate the pain, one can evacuate the

noxious chemicals that excite the C fibers, by releasing the muscle spasm of the smooth muscles of the lymphatic vessles and prevent further injury. Some investigators have found higher levels of endorphin released in patients after low power laser therapy. Thus the pain of neurogenic and neuromuscular origin can be eliminated. This is in essence what the low level laser does in relieving head pains.

Patients who have pressure and/or pulsating pain in the frontal area of the head, especially around the eyes and/or nasal ridge may have soft tissue lesions at the tendinous periosteal junctions of the occipital protuberance, nuchal line around the trapezius and/or occipitalis muscles. The occipitalis-frontalis muscles above and below the nuchal line can go into spasm and lead to muscle ischemia. This process can stimulate a chain reaction with spasm and ischemia of the orbicularis oculi, procerus and corrigator supercilli muscles, causing pain around the eyes and nasal ridge. The low power laser directed near the periosteal-osseous junctions in the occipital protuberance and along the nuchal line most likely stimulate removal of the noxious chemicals via lymphatics (21,22). Such therapy appears to stop the above chain reaction by removing the pain stimuli. Thus muscle tension is diminished and pain can be lessened or abolished within minutes without apparent adverse effects. Furthermore, tenderness and edema are reduced at lesion sites. This method of treatment is a viable alternative to drug therapy, the latter can interfere with pain stimuli but can also have major adverse effects.

Similarly, patients with temporal head pains (aches) frequently have soft tissue lesions or injuries of the styloid process, a slender spike-like bony process that is attached to the base of the skull (6,7). The styloid process and its attachments are common sites of soft tissue injuries which produce a constellation of symptoms including neurogenic, neuromuscular and autonomic pain. Treatment with the low power laser at the styloid process and stylomandibular ligament attachment at the inner angle of the mandible has been an effective, safe, non-invasive modality for this clinical entity.

In conclusion, based on this randomized single-blind crossover study, the low power laser is efficacious in relieving migrainous headaches. Moreover the laser is safe and devoid of adverse effects. This modality may be an alternative and is perhaps especially applicable to elderly patients or patients who do not tolerate or have adverse reactions to potent analgesic medications. However, it is important to emphasize that this modality may not be effective without an good understanding of functional anatomy and pathophysiology of head pain. Further double-blind randomized studies are now in progress.

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TABLE 1: Pain level scores in nine patients.

PAIN LEVEL SCORES

Pt.	Sex	Age	Base	1st 2nd Sham to LPL	1st 2nd LPL to Sham
LJ	F	49	5	5 to 0	
EC	F	60	10	10 to 8	
LM	F	46	5	5 to 3	
EBr	F	56	10		10 to 10
IJ	F	43	7		0 to 0
ER	F	51	6	6 to 3	
EBa	F	41	10		8 to 8
RC	F	53	2		0 to 0
MY	F	46	10	10 to 7	
		Mean score	7.2	7.2 to 4.2	4.5 to 4.5

Base = baseline, LPL = low power laser therapy

TABLE 2: Reported improvements after low power laser therapy

REPORTED IMPROVEMENTS AFTER LOW POWER LASER THERAPY

Pt.	Sex	Age	Mus Rel	Red Ten	Adv Eff
LJ	F	49	yes	yes	no
EC	F	60	yes	yes	no
LM	F	46	yes	yes	no
EBr	F	56	yes	yes	no
IJ	F	43	yes	yes	no
ER	F	51	yes	yes	no
EBa	F	41	yes	yes	no
RC	F	53	yes	yes	no
MY	F	46	yes	yes	no

Mus Rel = muscle relaxation, Red Ten = reduced tenderness, Adv eff = adverse effects.