PUBLISHED CLINICAL STUDIES WITH CLASS IV THERAPY LASERS

CONTENTS

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TREATMENTS FOR TRAUMATIC BRAIN INJURY WITH EMPHASIS ON TRANSCRANIAL NEAR-INFRARED LASER PHOTOTHERAPY

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BRAIN

ABSTRACT:

Traumatic brain injury (TBI) is a growing health concern affecting civilians and military personnel. In this review, treatments for the chronic TBI patient are discussed, including pharmaceuticals, nutraceuticals, cognitive therapy, and hyperbaric oxygen therapy. All available literature suggests a marginal benefit with prolonged treatment courses. An emerging modality of treatment is near-infrared (NIR) light, which has benefit in animal models of stroke, spinal cord injury, optic nerve injury, and TBI, and in human trials for stroke and TBI. The extant literature is confounded by variable degrees of efficacy and a bewildering array of treatment parameters. Some data indicate that diodes emitting low-level NIR energy often have failed to demonstrate therapeutic efficacy, perhaps due to failing to deliver sufficient radiant energy to the necessary depth. As part of this review, we present a retrospective case series using high-power NIR laser phototherapy with a Class IV laser to treat TBI. We demonstrate greater clinical efficacy with higher fluence, in contrast to the bimodal model of efficacy previously proposed. In ten patients with chronic TBI (average time since injury 9.3 years) given ten treatments over the course of 2 months using a high-power NIR laser (13.2 W/0.89 cm^2 at 810 nm or 9 W/0.89 cm^2 at 810 nm and 980 nm), symptoms of headache, sleep disturbance, cognition, mood dysregulation, anxiety, and irritability improved. Symptoms were monitored by depression scales and a novel patient diary system specifically designed for this study. NIR light in the power range of 10-15 W at 810 nm and 980 nm can safely and effectively treat chronic symptoms of TBI. The clinical benefit and effects of infrared phototherapy on mitochondrial function and secondary molecular events are discussed in the context of adequate radiant energy penetration.

KEYWORDS:

infrared, traumatic brain injury, TBI, transcranial infrared light therapy, transcranial laser therapy

INTRODUCTION

Traumatic brain injury (TBI) has recently moved into the limelight due to the recognition of its impact on professional athletes and military personnel. Yet, TBI is neither a new problem nor limited to those two populations. The Centers for Disease Control and Prevention estimated that 1.5 million Americans sustained TBI annually in 2000.[1] As of 2006, the estimates had risen to 1.7 million brain injuries annually.[2,3]

Undoubtedly, these point prevalence proportions will increase as military personnel return home,[4] and the problem of repeated mild TBI (mTBI) becomes more recognized in sports.[5] Current estimates of the prevalence of TBI among veterans range from 9.6%[6] to 20%,[7] with an estimated total of more than 300,000 cases of TBI among military personnel since 2000.[4] The current estimates of the combined number of sports-related concussions and brain injuries in the US are 1.6-3.8 million annually.[8-10]

TBI results in a wide spectrum of neurological, psychiatric, cognitive, and emotional consequences. In part, the variation is related to the severity of the injury (mild, moderate, severe TBI), which is stratified based on Glasgow Coma score, periods of unconsciousness, and degrees of amnesia. Furthermore, the diversity of sequalae can be related to the areas of the brain that are injured, the severity of the injury (highly variable within the classification of "mild" and "moderate"), and the evolution of the injury over time due to neuroinflammatory processes.[11,12] Additional mechanisms thought to underlie the damage of TBI include decreased

mitochondrial function, calcium and magnesium dysregulation, excitotoxicity, disruption of neural networks, free radical-induced damage, excessive nitric oxide, ischemia, and damage to the blood-brain barrier. Together, these can contribute to a progression of the damage over time.

Patients with TBI can experience headache, visual disturbances, dizziness, cognitive impairment, loss of executive skills, memory impairment, fatigue, impulsivity, impaired judgment, emotional outbursts, anxiety, and depression.[3,13-23]

The situation can be further clouded by secondary and/or comorbid posttraumatic stress disorder (PTSD), depression, and anxiety,[17-25] which can have symptoms that overlap with those described above and appear to be increasingly likely with repetitive concussive or subconcussive brain injury.[5,24,26]

TREATMENTS FOR TBI

Pharmacological treatments

Pharmacological treatment largely targets the neuropsychiatric sequalae of TBI, rather than providing any means of healing or repairing injury. In general, pharmacological treatment is focused on the modulation of major neurotransmitter systems – dopaminergic, serotonergic, noradrenergic, acetylcholinergic, and glutaminergic.[20] Disruption of the major neurotransmitter pathways may result from direct injury or excitotoxicity and other cytotoxic mechanisms.

The treatment of depression secondary to TBI is often approached with serotonin reuptake inhibitors. Several studies have examined the benefit of sertraline in post-TBI depression.[27-29] Other serotonin reuptake inhibitors also have been examined. Tricyclic antidepressants appear to have some use in the treatment of post-TBI depression, although cautious dose titration is required. Patients with TBI are at greater vulnerability to sedation and cholinergic side effects of confusion and memory impairment. With serotonergic agents other than sertraline, cognitive effects also have been reported.[30] Similarly, lithium may be a less desirable agent in this population due to sedation and cognitive impairment.

Patients with TBI may respond at lower doses and lower blood levels than expected.

Modulation of the dopaminergic system may improve alertness, attention, and cognitive processing speed. The stimulants are most commonly used for this purpose. Methylphenidate facilitates the release of dopamine and slows its reuptake. Dextroamphetamine strongly inhibits reuptake of dopamine, slows down the breakdown of dopamine by monoamine oxidase, and somewhat increases the release of dopamine. These subtle differences are sometimes imperceptible to the patient, but at other times, a patient will do best on one or the other stimulant. Increasing dopamine in the reticular activating system leads to enhanced arousal. Increasing dopamine within the frontal cortex and the striatum leads to enhanced processing speed and attention. Some evidence suggests that the stimulants may enhance neuronal recovery after injury.[31-33] There are numerous potential side effects with stimulants, including abnormal heart rhythms, decreased seizure threshold, and death, but these severe side effects are extremely rare. The most common side effects with stimulants are decreased appetite, stomach upset, and headache. These are most severe at the beginning of treatment and improve over time for most patients. Insomnia is another common side effect, which may be more frequent in those with a TBI. Amantadine and bromocriptine may also increase dopamine. Studies of these agents have shown reduced abulia, anergia, and anhedonia in those with TBI.[34,35]

Amantadine may cause confusion, hallucinations, and hypotension. Small studies have suggested some benefits of bromocriptine in cognitive function.[36,37]

Arousal-enhancing agents also have found a use in the treatment of the neurocognitive sequalae of TBI. Modafinil is the oldest form of these medications, and armodafinil is an isomer of modafinil with longer activity and less side effects. These medications help to increase alertness and wakefulness. The precise mechanism of action of modafinil is unclear. It appears to increase histamine in parts of the brain involved in controlling the sleep-wake cycle; however, knock-out mice that lack histamine receptors still show increased wakefulness with modafinil.[38,39] The picture is also murky for modafinil's effect on orexins, which are wakefulness molecules in the hypothalamus.[40] Modafinil has been shown to weakly bind to the dopamine transporter – like the stimulants,[41] and dopamine transporter knock-out mice show no response to modafinil.[42] A number of research studies have examined the benefit of these agents in fatigue associated with multiple sclerosis, TBI, cancer, and other conditions.

Cognitive and memory impairments after TBI may reflect disruption of cholinergic function. The impact of anticholinergic agents on cognitive function of those with TBI supports this contention. Donepezil is the safest and most widely used of the cholinesterase

inhibitors. Several reasonably large studies have shown improved memory and cognitive function.[43-45] Donepezil has benefits in memory and cognition even several years after injury.[45,46]

Anticonvulsants are often prescribed initially after a TBI due to heightened risk for seizures. Post-TBI mania or mood lability may respond well to anticonvulsants, such as carbamazepine or sodium valproate. They are also often used to treat aggression after TBI. The anticonvulsant agent, topiramate, has been shown to adversely affect cognitive function in the TBI patients.[47]

While insomnia is a significant issue for patients with TBI, affecting between 15% and 84% (mean of 40%),[3,13,19,21,23,48,49] little has been published on the treatment of this aspect of TBI. Benzodiazepines may be effective but carry a risk of disinhibition. Kemp et al[48] found that commonly used sleep aid, melatonin, was not effective. Antidepressants, including serotonin reuptake inhibitors and tricyclic antidepressants, are not effective in resolving insomnia in this population.[49] No single agent has emerged as a good solution for this symptom.

Cognitive rehabilitation

Cognitive rehabilitation now takes many forms and is often individualized to the particular needs of the patients. Protocols have been devised to remediate cognitive difficulties often encountered in those with TBI, such as impaired concentration, executive dysfunction, inattention, visual disturbances, memory dysfunction, and impaired language function. They range from simple strategies (using a planner to aid memory and organization) to specific protocols targeting particular cognitive functions (eg, short-term memory) that can be monitored with sequential neuropsychological testing. These interventions have been extensively reviewed elsewhere.[50,51] Comprehensive programs which include psychotherapy and social skills components have been shown to have greater efficacy.[50,52,53]

Overall, reports of benefits have been mixed.[54,55]

Behavioral therapies

Behavioral remediation strategies to eliminate problematic behaviors following TBI have met with mixed success, most often in terms of the poor generalization of specific skills to the outside world. Behavioral deficits that create difficulties for those with TBI and their families include poor hygiene, decline in tidying/cleaning habits, social withdrawal, reduced social comprehension, impaired memory, and poor organization. Behavioral excesses that create difficulties for those with TBI and their families include aggression, sleep disruption, and perseverations. These have been reviewed elsewhere.[56]

Nutritional supplements

Nutritional supplements, herbs, and nootropics have been utilized for many years and are increasingly popular among the patient populations. There remains little clinical research on many of these agents, perhaps reflecting a lack of funding more than a lack of efficacy. Acetyl-l-carnitine is an ester of l-carnitine and is thought to protect brain cells after injury when glucose metabolic pathways are compromised. During this period, acetyl-l-carnitine supports alternative ketogenic pathways for metabolism.[57] It is also believed to enhance cholinergic function. While there are several clinical studies on patients with Alzheimer's disease and preclinical data on animal models of TBI, the clinical literature on TBI remains sparse. Ginkgo biloba is a natural product of the tree by the same name. It has been shown to improve membrane fluidity and increase resistance to free-radical damage. It provides some subtle benefits to cognitive function in clinical studies of stroke, dementia, aging, and hypoxia damage.[58] It has not been systematically studied in TBI but is used extensively in clinic, often in combination with meclofenoxate which is an avid scavenger of free radicals.[59] *S*-Adenosylmethionine (SAMe) is a nutritional supplement which improves cell membrane fluidity and promotes the production of glutathione, an antioxidant. The benefit of SAMe has been assessed in a single clinical study of TBI.[60] Patients receiving SAMe had a 77% improvement in clinical scores of post-concussive symptoms. Citicholine provides a source of choline which can cross the blood-brain barrier. It has been used extensively in Europe and Japan as a treatment for TBI, stroke, and dementia. However, two large US studies failed to demonstrate significant benefit.[61,62]

Piracetam and the related oxiracetam and phenyl-piracetam have shown some promise as nootropic agents. In one double-blind, placebo-controlled study, piracetam improved several symptoms of post-concussive syndrome, including headache and vertigo.[63] More recent clinical studies have shown marginal benefit.[64] Huperzine-A, an extract of Japanese club moss, is a natural acetylcholinesterase inhibitor. It may serve as a natural alternative to donepezil, rivastigmine, or galantamine. Galantamine warrants special mention as it appears to also modulate nicotinic receptors and appears to have more persistent benefit

in the treatment of Alzheimer's disease. It appears to modulate neuroimmune responses, in addition to its effects on acetylcholinesterase.[65] Cerebrolysin is a polypeptide that purportedly mimics the actions of neurotrophic factors.[66,67] Studies have shown that it can reduce beta amyloid and phosphorylated tau protein accumulation. It may promote neurogenesis, synapse formation, and functional recovery.[66] In animal models of acute TBI, cerebrolysin-treated rats had more surviving neurons in the area of impact and showed greater functional recovery.[67] In a clinical trial of acute TBI, patients were recruited within 24 hours of injury and treated for 3 months with daily intravenous infusion of cerebrolysin. At 3 months, those receiving cerebrolysin performed significantly better on the Cognitive Abilities Screening Instrument.[68] It remains unclear if cerebrolysin provides long-term nootropic benefit.

The elevation of free radicals in TBI suggests that antioxidants should be beneficial. Clinical trials of pharmacological antioxidants over the past 30 years have not yielded a useful agent in acute TBI.[69] Agents, such as tirilazad[70] and polyethylene glycol-conjugated superoxide dismutase, have failed to show benefit in acute TBI. Omega-3 fatty acids may enhance brain repair and recovery, based on animal and clinical studies.[71] Similarly, vitamin D may offer neuroprotective and restorative benefits[72] in the acute TBI setting. In chronic TBI, vitamin D and omega-3 fatty acids may work synergistically, as they both may reduce neuroinflammation, apoptosis, and oxidative stress.[73] Other nutritional supplements have been recommended, but prolonged therapy is necessary to possibly see benefits in TBI. A 6-month trial of ginkgo, vinpocetine, acetyl-l-carnitine, huperzine, alpha-lipoic acid, *n*-acetyl-cysteine, multivitamins, and over 5 g of omega-3 fatty acids daily yielded improved performance in cognitive testing and increased perfusion (function) in single-photon emission computed tomography (SPECT) scan.[74] Long-term use of dietary flavanols may improve cognition in mTBI.[75]

Transcranial magnetic stimulation

Transcranial magnetic stimulation (TMS) has shown some promise in animal models of TBI.[76] However, a Cochrane review of the clinical application of TMS for depression noted no difference between repetitive TMS (rTMS) and sham rTMS using the Beck Depression Inventory (BDI) or the Hamilton Depression Rating Scale, except during the initial 2-week period.[77] The application of TMS in the post-TBI patients is limited by the risk of seizure induction.[78]

Hyperbaric oxygen

Hyperbaric oxygen treatment has been explored as a treatment for TBI.[79-91] Hyperbaric oxygen therapy is neither a benign treatment, given the concerns of oxygen toxicity,[79] nor a clear treatment in that the placebo condition of moderate hyperbaric room air also effectively improves cognitive function.[80,81] The most carefully performed study compared a group in a cross-over design with an interval of both null treatment and hyperbaric oxygen at 100% oxygen and 1.5 atm.[82] The study described improvement in many of the symptoms associated with persistent TBI including headache, tinnitus, vision disturbance, memory dysfunction, and impaired cognitive function. Cognitive testing also showed improvement in attention, information processing speed, and a battery of cognitive tests. In an uncontrolled case series of 16 subjects, Harch et al[83] demonstrated that an abbreviated series of hyperbaric treatments using 100% oxygen at 1.5 atm could mitigate subjective symptoms of TBI (eg, headache, sleep disruption, irritability), improve cognitive testing scores, and improve cortical function based on SPECT imaging.[83] A study of a higher dose (2.4 atm) did not reveal any significant benefit of hyperbaric oxygen therapy compared to a sham-control group treated with 1.3 atm,[84] and this result has been extended and confirmed by a related group.[85] However, this may reflect an inverse dose-response curve, rather than an absence of benefit, in that the low-dose sham group demonstrated significant changes in cognitive testing and symptom frequency.[86] Hyperbaric oxygen remains a controversial area in both acute TBI[86-89] and chronic TBI.[82,83,85,86,90,91]

Physical exercise

High-energy activities and exercise programs completed through a health club facility or comprehensive rehabilitation program should focus on the same parameters of an age-adjusted and diagnosis-specific program for aerobic conditioning – flexibility, stabilization, and strength. Though it appears safe and is an accepted intervention for TBI, there is a need for further well-designed studies.[92] Exercise was a part of a 6-month study of lifestyle changes described above which yielded improved function based on cognitive testing and perfusion SPECT scans.[74]

A NEW TREATMENT FOR TBI

Unfortunately, little has been found to reverse the damage of TBI or repetitive concussion which is the root cause of residual cognitive and psychological impairment following TBI.[20,93] One potential avenue

of treatment for TBI is infrared light, which has shown promising data in a number of applications. Near-infrared (NIR) light has been investigated for its ability to modulate intracellular mechanisms related to healing. The application of NIR light by low-power laser or by light-emitting diode (LED) is also known as laser phototherapy[94] or near-infrared photobiomodulation.[92] NIR irradiation can facilitate wound healing,[95,96] promote muscle repair,[95] and stimulate angiogenesis.[95,96] NIR phototherapy has been studied and applied clinically in a wide array of ailments, including skin ulcers,[97] osteoarthritis,[98] peripheral nerve injury,[95,96] low back pain,[99] myocardial infarction,[100] and stem cell induction.[101]

The finding that NIR light passes relatively efficiently through bone has spurred interest in its application to treating disorders of the brain. Over the past decade, transcranial near-infrared light therapy (NILT)[102] has been studied in animal models to understand its ability to repair damaged or dysfunctional brain tissue resulting from stroke and TBI. The first published study of NILT for TBI in humans described two cases of chronic mTBI with significant disability.[103] Each patient was treated with an LED device delivering low-level low-level light therapy (LLLT) in the red and NIR range for 6-10 minutes per area daily for several months. Both patients had marked neuropsychological improvement after a minimum of 7-9 months of LLLT treatment.

The precise mechanisms underlying photobio–modulation and its therapeutic benefits are not fully understood.

The purported effects of NIR are illustrated in Figure 1. Light in the wavelength range of 600-1,200 nm has significant photobiomodulation capability.[104] Current data most strongly support that absorption of NIR photons by cytochrome c oxidase in the mitochondrial respiratory chain is the key initiating event in photobiomodulation.[95,96,104,105] This induces an increase in cytochrome c oxidase activity which in turn increases adenosine triphosphate (ATP) production. Such an increase in ATP in wounded or underperfused cells may be sufficient to activate cells in areas of injury or metabolic derangement.[106] Data from numerous tissue culture and animal studies point to the importance of several secondary molecular and cellular events. For example, NIR photonic energy can modulate reactive oxygen species,[95,96,102] activate mitochondrial DNA replication,[95,96] increase early-response genes,[95] increase growth factor expression, induce cell proliferation, and alter nitric oxide levels.[95,96,102] These mechanisms are more fully described in the companion paper.[105]

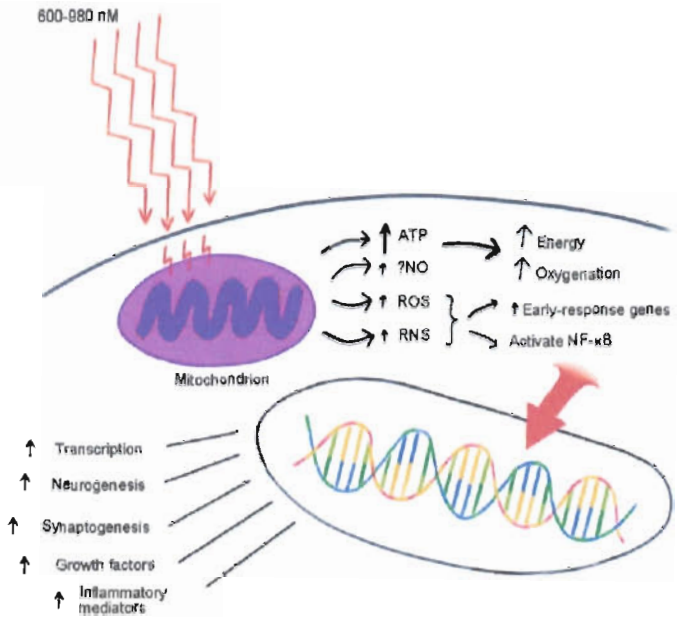

Figure 1 Hypothesized mechanism of action of NiR light therapy.

Notes: NiR light (600-980 nm) penetrates tissue to variable depths depending on wavelength, the tissue involved, coherence, and time. A fraction of the photonic energy reaches the mitochondria and is absorbed by cytochrome c oxidase. This activates increased ATP production, increases production of ROS and RNS, and possibly increases NO. Downstream events include increased early-response genes (*c-fos* and *c-jun*) and activation of NF-κB, which in turn induces increased transcription of gene products leading to synaptogenesis, neurogenesis, and increased production of inflammatory mediators and growth factors.

Abbreviations: NiR, near-infrared; ATP, adenosine triphosphate; ROS, reactive oxygen species; RNS, reactive nitrogen species; NO, nitric oxide; NF-κB, nuclear factor kappa B.

When examined in the specific model of neural tissue injury, NIR phototherapy can lead to demonstrable neural repair and recovery. For example, LLLT of a power density of 0.9-36 J/cm^2 applied at 24 hours poststroke in a rodent model yielded a 32% reduction in neurological deficits, as well as histochemical evidence of neuron proliferation and migration.[106-108] LLLT had similar benefits in a rodent model of TBI.[96,109-111] Interestingly, these cellular changes evolved over a period of days after light exposure and persisted for considerably longer than the interval of actual NIR exposure. These findings are consistent with a progressive regeneration cascade set in motion by the NIR light exposure.

NILT in stroke

NILT, predominately in the form of LLLT, has been investigated in laboratory models of stroke. LLLT applied in a single dose to an ischemic stroke model appeared to induce expression of the growth factor transforming growth factor – beta 1 and suppress the production of peroxynitrite.[112] In a rat model of middle cerebral artery occlusion, LLLT at a dose of 0.5-7.5 mW/cm^2 using continuous wavelength light at

808 nm was administered at 24 hours after the acute stroke.[108,113] This single application was estimated to deliver 1.8 J/cm^2 in total to the cortex surface and resulted in demonstrable neurological improvement. Functional changes were not manifested until approximately 2 weeks after the single treatment. While there was no significant change in the size of the stroke lesion, histochemical evidence of neurogenesis and migrating neurons[108] indicate that a cascade of secondary processes was initiated by NILT. A rabbit model of stroke utilizing injection of a blood clot embolus also demonstrated benefit from LLLT.[102,114,115] Herein, 808 nm light was applied with an LED delivering 7.5 mW/cm^2 and an estimated 0.9-2.6 J/cm^2 to the cortical surface. Cortical ATP levels were increased, indicative of increased mitochondrial activity.[114]

Significant behavioral recovery was also noted; however, neither ATP increased nor neurological function changed at doses less than 0.3-0.7 J/cm^2.[114,115] At higher doses of 0.9-15 J/cm^2, neurological improvement was seen.[114,115]

The clinical trials of NILT in acute stroke, the NeuroThera Effectiveness and Safety Trials 1, 2, and 3 (NEST-1,-2, -3), were conducted between 2006 and 2009. The Phase II clinical trial (NEST-1) involved 120 patients in a double-blind, placebo-controlled study of the effects of NILT within 24 hours of ischemic stroke.[116,117] Approximately 60% of the patients experienced clinical benefit, and the safety profile was very good. Thus, NEST-2, a Phase III clinical trial, was undertaken in 2007. A total of 660 patients were enrolled.[118]

Somewhat surprisingly, the study did not demonstrate statistical clinical improvement using a different outcome measure.[119] Post hoc analysis revealed that a portion of the patients who were moderately affected and/or had strokes limited to the cerebral cortex did realize clinically and statistically significant improvement.[102] The NEST-3 trial was halted midpoint when it failed to demonstrate statistical benefit on futility analysis.[120]

A key factor in the interpretation of the results of NEST-3 is that, different from NEST-1, all types of stroke were included as opposed to just cortical strokes. Continuous laser light has a limited depth of penetration (#1 cm into brain tissue) which likely prevents an effect on deeper brain matter. Therefore, the lack of significant benefits from NIR phototherapy in NEST-3 could be related to the fact that ischemic penumbra was not reached by the light (Luis DeTaboada, personal communication, January 2015). While pulsed NIR was not used in the NEST-3 study, it is estimated that pulsed NIR could penetrate up to 3 cm in depth from the cortical surface, therefore possibly extending the therapeutic target to deeper strokes (Luis DeTaboada, personal communication, January 2015).

NILT in TBi

Oron et al[109] conducted the first animal studies of NILT for TBI. They found that a single application of NIR light at 808 nm from a 200 mW emitter at 4 hours post-injury resulted in a significant reduction in lesion size by 5 days.[109] To date, several groups have studied NILT in animal models, and this material has previously been reviewed.[95,121-123] Single applications of 800-810 nm NIR light within 4 hours of injury have been shown to improve neurological function significantly.[110,124-126] The same dose of NIR light at 6 hours was less effective[125] and at 8 hours had no appreciable benefit.[125] NIR photonic energy at other wavelengths was less effective. Wu et al[110] examined red light (670 nm) at 4 hours and found a similar improvement in neurological function; however, 730 nm and 980 nm had no neurological benefit. Similar data for lesion volume have been reported. A single dose of 800-810 nm NIR light (fluence of 36 J/cm^2) yielded an approximate 50% reduction in the volume of the lesion at 3-4 weeks[110,111,124-126] and a possible reduction in the initial spread of neurological injury, based on the marked reduction in lesion volume found at 5 days post-injury.[109]

Repeated NIR phototherapy treatments appear to have some benefit, but the frequency and number of treatments are critical factors. While a single NIR light application had benefit, daily applications for 3 days yielded much greater neurological benefit[126,127] with smaller lesion size,[126] fewer degenerating neurons,[126] more proliferating cells,[126] and greater levels of brain-derived neurotrophic factor (BDNF)[127] compared to a single treatment in a mouse model. In contrast, daily treatment for 7 days[128] or 14 days[126] showed no difference from controls. NIR energy densities in the range of 0.9-36 J/cm^2 resulted in significant biochemical and behavioral changes.[109-111,124-127]

Pulsing of NIR light appears to yield a greater neurological response but only within certain parameters. Pulsing at 10 Hz yielded greater neurological improvement and a significant reduction in lesion size compared to either continuous-wave or pulsed NIR at 100 Hz.[111] In the mouse model of moderate TBI, NILT (800-810 nm) improved learning and memory (Morris water maze performance),[128]

of patients. Further work in the use of high-wattage NILT in the treatment of TBI, depression, and other neurological disorders is encouraged.

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DISCLOSURE

Dr. Larry D Morries is the CEO of Neuro-Laser Foundation, a nonprofit foundation. He has a private practice in Lakewood, CO. Theodore A Henderson is the president of The Synaptic Space, a medical consulting firm. He is the president of Dr. Theodore Henderson, Inc., a clinical service firm. He is the co-owner of Neuro-Luminance, a clinical service organization. He is the president of the International Society of Applied Neuroimaging. He is the CFO of the Neuro-Laser Foundation, a nonprofit foundation. Dr. Paolo Cassano received funding from the Brain and Behavior Research Foundation; Photothera Inc and from the Dupont Warren Fellowship (Harvard Medical School) to conduct research on NIR light for the treatment of major depressive disorder.

ABOUT THE AUTHORS:

Larry D. Morries, DC brings a distinguished 30-year career studying and treating the brain and body through his private practice based in Lakewood, Colorado. As Neuro-Laser Foundation's co-founder, his chiropractic expertise is complemented with extensive study of near infrared-light therapy applications, clinical radiology, clinical neurology and sports injury and rehabilitation.

In practice since 1973, Dr. Morries has contributed extensively to both chiropractic and medical professions throughout his career. He is a recognized expert often called upon for review services, treatment utilizations, and documentation presentations. In recent years, he has guided the Colorado State of Colorado Workers Compensation Board with a review of treatment guidelines for Chronic Pain, and Complex Regional Pain Syndrome, Shoulder Pain, Low Back Pain, Traumatic Brain Injury, and was asked to present in 2016 on Thoracic Outlet Syndrome. Other professional involvement include:

- Colorado Chiropractic Association, Board member, President in 1982, Chairman in 1984
- Colorado Chiropractic Society, Vice President and Secretary in 1995-2004
- Colorado Chiropractic Journal Club, Chairman, since 2008

Dr. Morries has continued his study of the human body and brain with postgraduate work in Neurodiagnostic testing at the American Academy of Neurology, and Harvard Medical School-Massachusetts General Hospital. He is also educated on Spinal Mechanics at Chicago Rehabilitation Institute. He earned his Doctorate in Chiropractic from Logan Chiropractic College, with recognition as Student Clinical Director, Teaching Assistant in Radiology.

Dr. Morries is most proud of his research papers and awards, in America Academy of Pain Medicine, Sciatic and Suprascapular Nerve Blocks with Dr. Steve Gulevich, MD. He was asked to share two Poster presentations at the North American Laser Foundation in 2011on Low Back Pain, plus Polyneuropathy treatment with Laser (NIR) therapy. His Podium Presentation and publication on Hip dysplasia, in American Board of Chiropractic Sports Physicians®. Additionally, he has given presentations abroad at State of Chiropractic Research, Foundation of Chiropractic Education and Research, in Bournemouth England and Vancouver, BC, Canada.

Dr. Theodore Henderson has extensive training and experience to the practice of Psychiatry. He trained in Psychiatry at the prestigious Barnes/Jewish Hospitals at Washington University in St. Louis. Dr. Henderson completed a fellowship in Child & Adolescent Psychiatry at the University of Colorado. He also has training in Radiology, Nuclear Medicine, and the genetics of psychiatry. He established his private practice in Centennial Colorado in July of 2000. Dr. Henderson brings a unique blend of expertise in psychopharmacology, neurobiology, and an understanding of human nature to the practice of psychiatry.

Dr. Henderson attended medical school at Saint Louis University School of Medicine. While in medical school, he began studying heart pathology under Dr. Vernon Fischer. He earned an American Heart Association Medical Student Research Fellowship. With this fellowship, he spent one year at the University of Washington studying the pathology of atherosclerosis.

In 1991, Dr. Henderson founded the Child Abuse Prevention Task Force at Saint Louis University.

This program taught children, parents, and teachers about child sexual abuse and how to prevent it. Each year, this program reached over 8,000 children throughout the metro St. Louis area, primarily in the poor inner-city schools. The program was awarded numerous awards, including a Saint Louis University Community Service Award, Commendations from the school districts, and an award from the American Medical Student Association. Dr. Henderson was nominated for a Student Life Leadership Award and earned a Departmental Award from the Department of Community and Family Medicine. He also received a Weis Humanitarian Award recognizing outstanding humanitarian care as a medical student. Dr. Henderson wrote a training manual on this program that was implemented at other medical schools and he co-wrote a book chapter in the book, *A Parent's & Teacher's Handbook on Identifying and Preventing Child Abuse* (1998).

During graduate school and medical school, Dr. Henderson published numerous research studies. He published 9 articles and 27 abstracts about his research in brain development. He also published a book chapter on brain development in collaboration with his research professor, Dr. Mark Jacquin. His research focused on the role of neural growth factors and impulse activity on the development of brain organization. He collaborated with leading researchers, including Drs. Thomas Woolsey, Eugene Johnson, and Thomas Rhoades. While a medical student, Dr. Henderson wrote two research grants (as part of program project grants). Both were funded. He continued conducting research at Saint Louis University and Washington University throughout his residencies.

Dr. Henderson trained for one year in Radiology, focusing on neuroimaging and pediatrics. With this strong base, he then undertook a residency in Psychiatry at Washington University's program at Barnes/Jewish Hospitals in St. Louis. His residency included extended training in general pediatrics at St. Louis Children's Hospital. In 1997, He was awarded the National Institute of Mental Health Outstanding Resident Award for his ongoing work in child abuse prevention and his neurobiological research while a resident.

Dr. Henderson completed a residency in Adult (or General) Psychiatry and then undertook a fellowship in Child Psychiatry at the University of Colorado. This included additional specialization in Autism and Autism Spectrum Disorders. He completed the Child Psychiatry fellowship in 2000 and has a breath of experience in mental health centers, refugee health centers, and programs specifically for children and adults with autism, mental retardation, and other developmental disabilities. Currently, he participates in psychopharmacology web forums, the Society of Nuclear Medicine Brain Imaging Council, and is a guest editor for journals of psychiatry.

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J Altern Complement Med. 2013 May;19(5):445-52. doi: 10.1089/acm.2011.0398. Epub 2012 Nov 23

EFFECTS OF CLASS IV LASER THERAPY ON FIBROMYALGIA IMPACT AND FUNCTION IN WOMEN WITH FIBROMYALGIA

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BACK, NECK, & SHOULDERS

ABSTRACT

OBJECTIVES:

This study evaluated the effects of Class IV laser therapy on pain, Fibromyalgia (FM) impact, and physical function in women diagnosed with FM.

DESIGN:

The study was a double-blind, randomized control trial.

SETTING:

Testing was completed at the university and Rheumatologist office and treatment was completed at a chiropractic clinic.

PARTICIPANTS:

Thirty-eight (38) women (52±11 years; mean± standard deviation) with FM were randomly assigned to one of two treatment groups, laser heat therapy (LHT; n=20) or sham heat therapy (SHT; n=18).

INTERVENTION:

Both groups received treatment twice a week for 4 weeks. Treatment consisted of application of LHT or SHT over seven tender points located across the neck, shoulders, and back. Treatment was blinded to women and was administered by a chiropractic physician for 7 minutes.

OUTCOME MEASURES:

Participants were evaluated before and after treatment for number and sensitivity of tender points, completed the FM Impact Questionnaire (FIQ) and the pain question of the FIQ, and were measured for function using the continuous scale physical functional performance (CS-PFP) test. Data were evaluated using repeated-measures analysis of variance with significance accepted at $p \leq 0.05$.

RESULTS:

There were significant interactions for pain measured by the FIQ (LHT: 7.1±2.3 to 6.2±2.1 units; SHT: 5.8±1.3 to 6.1±1.4 units) and for upper body flexibility measured by the CS-PFP (LHT: 71±17 to 78±12 units; SHT: 77±12 to 77±11 units) with the LHT improving significantly compared to SHT. There was a time effect for the measure of FM impact measured by the FIQ, indicating that FM impact significantly improved from pre- to post-treatment in LHT (63±20 to 57±18 units), while no change was observed in the SHT (57±11 to 55±12 units).

CONCLUSIONS:

This study provides evidence that LHT may be a beneficial modality for women with FM in order to improve pain and upper body range of motion, ultimately reducing the impact of FM.

Source of Study: AspenLasers.com

PMID: 23176373
DOI: 10.1089/acm.2011.0398

CLASS IV LASER THERAPY; EFFECTIVE FOR BACK AND NECK/SHOULDER PAIN (RETROSPECTIVE, PRACTICE BASED CLINICAL PRELIMINARY INVESTIGATION)

Author: L.D. Morries, DC, CCSP®

Presented: ACBSP: 2010

BACK AND NECK/SHOULDER PAIN

BACKGROUND:

Class IV laser therapy is a recent modality that is used to treat pain and promote healing of muscular tissue. The procedure is minimally invasive and easily performed. Laser therapy was added to conventional chiropractic treatment of spinal manipulation and an exercise program for treating patients with back pain. The objective of this investigation was to assess efficacy and safety of the combination and generate preliminary results for a randomized controlled trial.

METHODS:

Between 9/2009 and 2/2010, a total of 55 patients with non-surgical lower back pain (sciatica) presented to my office and gave consent for treatment. Twenty-four patients with back pain received spinal Class IV laser therapy in addition to manipulation for back pain. Twenty-one patients (historical controls) received spinal manipulation without Class IV laser therapy. All patients completed VAS scales before treatment (VAS0), at one week (VAS1), and at four weeks (VAS4). Regardless of treatment group, all patients received a personalized regimen of spinal manipulation, manual therapy, and exercise, under the direction of the principal investigator (LDM). Percent difference between VAS0 and VAS4 was compared between groups.

RESULTS:

Demographics were similar for both groups (Table 1). Patients in the manipulation + laser group reported pain relief after 2-3 sessions of laser therapy (clinical observation). No adverse events were noted following laser therapy

A positive-valued percent differences of VAS between pretreatment and 4wk points; indicate that a quantitative reduction in pain by both treatment groups. Statistical comparison of the groups using an unpaired t-test indicated that the manipulation + laser offers greater pain reduction when compared to manipulation only ($p=0.007$). Interval estimates indicate a 21.18 larger reduction in VAS (95% Confidence Interval: 6.00, 36.35) in the manipulation + laser group.

CONCLUSIONS:

These results indicate that both treatments successfully reduced the VAS by the fourth week of treatment, and that a higher reduction in VAS occurred in the group treated by manipulation + laser at week four.

SUMMARY

Class IV laser therapy is a safe and effective modality for treating low back pain when added to conventional treatment of manipulation and exercise. Further study is indicated to support these initial findings.

Source of Study: AspenLasers.com

Table 1 – Patient demographics and dependent variables

	N	Age	VAS 0	VAS 4	% Difference
Laser + Manipulation	24	54.2 ± 11.1	6.5 ±1.9	1.75 ± 1.6	71.7 ± 22.0
Manipulation Only	21	51.0 ± 12.7	5.5 ± 1.4	3.5 ± 2.1	50.5 ± 28.4

Lasers Surg Med. 2013 Jul;45(5):311-7. doi: 10.1002/lsm.22140. Epub 2013 Jun 3.

THE EFFECTIVENESS OF THERAPEUTIC CLASS IV (10 W) LASER TREATMENT FOR EPICONDYLITIS

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ELBOW

ABSTRACT

BACKGROUND AND OBJECTIVE:

Photobiomodulation has been shown to modulate cellular protein production and stimulate tendon healing in a dose-dependent manner. Previous studies have used class IIIb lasers with power outputs of less than 0.5 W. Here we evaluate a dual wavelength (980/810 nm) class IV laser with a power output of 10 W for the purpose of determining the efficacy of class IV laser therapy in alleviating the pain and dysfunction associated with chronic epicondylitis.

METHODS:

Sixteen subjects volunteered for laser therapy, or an identically appearing sham instrument in a randomized, placebo-controlled, double-blinded clinical trial. Subjects underwent clinical examination (pain, function, strength, and ultrasonic imaging) to confirm chronic tendinopathy of the extensor carpi radialis brevis tendon, followed by eight treatments of 6.6 ± 1.3 J/cm^2 (laser), or sham over 18 days. Safety precautions to protect against retinal exposure to the laser were followed. The exam protocol was repeated at 0, 3, 6 and 12 months post-treatment.

RESULTS:

No initial differences were seen between the two groups. In the laser treated group handgrip strength improved by 17±3%, 52±7%, and 66±6% at 3, 6, and 12 months respectively; function improved by 44±1%, 71±3%, and 82±2%, and pain with resistance to extension of the middle finger was reduced by 50±6%, 93±4%, and 100±1% at 3, 6 and 12 months, respectively. In contrast, no changes were seen until 12 months following sham treatment (12 months: strength improved by 13±2%, function improved by 52±3%, pain with resistance to extension of the middle finger reduced by 76±2%). No adverse effects were reported at any time.

CONCLUSIONS:

These findings suggest that laser therapy using the 10W class IV instrument is efficacious for the long-term relief of the symptoms associated with chronic epicondylitis. The potential for a rapidly administered, safe and effective treatment warrants further investigation.

Source of Study: AspenLasers.com

PMID: 23733499 DOI: 10.1002/lsm.22140

Lasers Med Sci. 2014 Jul;29(4):1371-6. doi: 10.1007/s10103-014-1529-0. Epub 2014 Feb 1.

HIGH-INTENSITY VERSUS LOW-LEVEL LASER THERAPY IN THE TREATMENT OF PATIENTS WITH KNEE OSTEOARTHRITIS: A RANDOMIZED CONTROLLED TRIAL

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KNEE

ABSTRACT

The aim of this randomized controlled study was to compare the effects of low-level laser therapy (LLLT) and high-intensity laser therapy (HILT) on pain relief and functional improvement in patients with knee osteoarthritis (KOA). A total of 53 male patients participated in this study, with a mean (SD) age of 54.6 (8.49) years. Patients were randomly assigned into three groups and treated with HILT and exercise (HILT+EX), LLLT and exercise (LLLT+EX), and placebo laser plus exercise (PL+EX) in groups 1, 2, and 3, respectively. The outcomes measured were pain level measured by visual analog scale (VAS) and knee function measured by Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Statistical analyses were performed to compare the differences between baseline and posttreatment measurements. The level of statistical significance was set as $P<0.05$. The result showed that HILT and LLLT combined with exercise were effective treatment modalities in decreasing the VAS and WOMAC scores after 6 weeks of treatment. HILT combined with exercises was more effective than LLLT combined with exercises, and both treatment modalities were better than exercises alone in the treatment of patients with KOA.

Source of Study:
AspenLasers.com

PMID: 24487957
DOI: 10.1007/s10103-014-1529-0

Lasers Med Sci. 2015 Jan;30(1):325-32. doi: 10.1007/s10103-014-1671-8. Epub 2014 Oct 2.

EFFECT OF HIGH-INTENSITY LASER THERAPY IN THE MANAGEMENT OF MYOFASCIAL PAIN SYNDROME OF THE TRAPEZIUS: A DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

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NECK

ABSTRACT

Myofascial pain syndrome (MPS) of the trapezius muscle is one of the main causes of neck pain. In this randomized, double-blind study, we evaluated the effects of high-intensity laser therapy (HILT) in female patients with chronic MPS of the trapezius muscle. The patients were assigned to two groups. The HILT group was treated with HILT and exercise, and the sham therapy group was treated with placebo HILT and exercise. The patients were assessed for pain, cervical active range of motion, disability, and quality of life. Evaluations were performed before treatment (week 0) and after treatment (weeks 4 and 12). Both groups showed significant improvement in all parameters at weeks 4 and 12. However, in a comparison of the percentage changes in the parameters at weeks 4 and 12 relative to pretreatment values, the HILT group showed greater improvement in pain scores, the neck disability index, and several subparts of the short-form 36 health survey (SF-36) (physical functioning, role limitations due to physical functioning, bodily pain, general health perceptions, social functioning, and role limitations due to emotional problems) than did the sham therapy group. We conclude that HILT is an effective therapeutic method in the treatment of patients with chronic MPS of the trapezius muscle.

Source of Study:
AspenLasers.com

A PILOT STUDY TO DETERMINE THE EFFICACY OF THERAPEUTIC CLASS IV LASER TREATMENT ON LOCAL MUSCLE SPASM ASSOCIATED WITH MYOFASCIAL PAIN SYNDROME IN PATIENTS WITH NECK PAIN

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NECK

INTRODUCTION:

The pathophysiology of myofascial trigger points is incompletely understood[1]. Low levels of visible or near infrared light for reducing pain and inflammation[3,4], has been known for many years. Despite positive findings in vitro animal models and randomized controlled clinical trials, low level laser therapy (LLLT) remains controversial[5]. The mechanism of LLLT at the cellular level suggests mitochondria and cytochrome c-oxidase contribute to cellular response and reduce prostaglandin synthesis[2,6].

METHODS:

A class IV laser (LT-1000) was used on 10 patients with at least one month of myofascial neck pain. Patients underwent an initial evaluation, two-week laser treatment, and follow up at 15 and 30 days post treatment. A Visual Analogue Scale (VAS), patient reported global impression of change, and muscle pain detection device (MPDD)(7), were used for measurements. Institutional IRB approval was obtained.

RESULTS:

Baseline mean scores of VAS were 52.9 SD of 32.4, post treatment(Day 15), mean scores reduced to 30.0 SD of 19.9. 77.8% of participants improved after treatment; 22% very much improved, 33% moderate improvement, 22% no change. Objective detection of painful muscles with MPDD showed 71% of patients with positive points pretreatment had no positive trigger points post treatment.

CONCLUSION:

Class IV laser therapy showed a majority of patients who underwent treatment reported improvement, as assessed by VAS, Global impression, and MPDD trigger points detection. This encouraging pilot study justifies further studies with larger populations and addition of control groups for laser therapy as a potential non-pharmacological and non-interventional adjunct treatment, for patients with chronic myofascial pain.

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Source of Study: AspenLasers.com

The Lancet, Volume 374, Issue 9705, Pages 1897-1908, 5 December 2009

EFFICACY OF LOW-LEVEL LASER THERAPY IN THE MANAGEMENT OF NECK PAIN: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMISED PLACEBO OR ACTIVE-TREATMENT CONTROLLED TRIALS

Authors: Dr. Roberta T Chow MBBS, Prof. Mark I Johnson PhD, Prof. Rodrigo AB Lopes- Martins PhD, Prof. Jan M Bjordal PT

NECK

SUMMARY

BACKGROUND

Neck pain is a common and costly condition for which pharmacological management has limited evidence of efficacy and side-effects. Low-level laser therapy (LLLT) is a relatively uncommon, non-invasive treatment for neck pain, in which non-thermal laser irradiation is applied to sites of pain. We did a systematic review and meta-analysis of randomised controlled trials to assess the efficacy of LLLT in neck pain.

METHODS

We searched computerized databases comparing efficacy of LLLT using any wavelength with placebo or with active control in acute or chronic neck pain. Effect size for the primary outcome, pain intensity, was defined as a pooled estimate of mean difference in change in mm on 100 mm visual analogue scale.

FINDINGS

We identified 16 randomized controlled trials including a total of 820 patients. In acute neck pain, results of two trials showed a relative risk (RR) of 1·69 (95% CI 1·22-2·33) for pain improvement of LLLT versus placebo. Five trials of chronic neck pain reporting categorical data showed an RR for pain improvement of 4·05 (2·74-5·98) of LLLT. Patients in 11 trials reporting changes in visual analogue scale had pain intensity reduced by 19·86 mm (10·04-29·68). Seven trials provided follow-up data for 1-22 weeks after completion of treatment, with short-term pain relief persisting in the medium term with a reduction of 22·07 mm (17·42-26·72). Side-effects from LLLT were mild and not different from those of placebo.

INTERPRETATION

We show that LLLT reduces pain immediately after treatment in acute neck pain and up to 22 weeks after completion of treatment in patients with chronic neck pain.

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EFFECTIVENESS OF HIGH-INTENSITY LASER THERAPY IN SUBACROMIAL IMPINGEMENT SYNDROME

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SHOULDER

ABSTRACT

OBJECTIVE:

The short-term effectiveness of high-intensity laser therapy (HILT) was investigated as a retrospective case series for the treatment of the pain and disability associated with subacromial impingement syndrome (SAIS).

MATERIALS AND METHODS:

A total of 42 patients, who were diagnosed with subacromial impingement syndrome, underwent a total of nine sessions (three sessions per week) of high-intensity laser therapy. The patients were evaluated before therapy and 8 weeks after therapy using the pain and disability subscales and the total scores of the Shoulder Pain and Disability Index (SPADI), as well as scores for the University of California at Los Angeles (UCLA) shoulder rating scale.

RESULTS:

Significant differences were observed between SPADI pain, disability, and total scores and UCLA scores of the patients.

CONCLUSIONS:

HILT was found to be effective in the short term in the treatment of pain and disability in patients with SAIS.

Source of Study:
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