The affect of MLS therapy on nerve conduction parameters in developing diabetic sensory peripheral neuropathy.

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ABSTRACT

The MLS laser is composed of an 808nm continuous emission laser and a 905nm pulsed emission laser that are synchronized. The purpose of this study was to determine the effect of the MLS laser on the injured tibial and peroneal nerves in diabetic sensory neuropathy. The sural nerve was chosen as an untreated control nerve.

A controlled prospective study was performed on ten patients with documented type 2 diabetes and peripheral sensory neuropathy. Nerve conduction parameters were determined prior to therapy and reevaluated post therapy. The course of therapy was three weeks. F-wave chronodispersion (Fc) measurements at the completion of the study showed significant improvement with this therapy. Peroneal Fc went from 8.99ms to 6.19ms (p=.015). Tibial Fc went from 10.30ms to 6.97ms (p=.001). The MLS laser therapy produced objective improvement in nerve function for persons with developing diabetic sensory neuropathy.

INTRODUCTION

As the prevalence of diabetes mellitus continues to rise throughout the world, so do the complications associated with this disease. Neuropathy is a common and serious complication associated with diabetes. The peripheral sensory type of diabetic neuropathy (DPN) is implicated as a causal factor in the development of foot ulcerations, infections and amputations. The loss of sensation in DPN has been shown to be a key component in the formation of foot ulcerations [1]. DPN is part of a triad of neuropathy, deformity and trauma that predispose the individual to pedal ulceration. Removal of one or more of the causal pathways is a goal in the prevention of foot ulcer development and healing of existing wounds [2]. In the United States, the cost associated with treating the sequelae of diabetic neuropathy is in the billions of dollars [3]. Often research and treatment are aimed at providing symptomatic pain relief. However, sensory restoration, not pain relief, is needed to interrupt the causal pathway leading to foot ulceration in DPN. Novel treatments have been tried that attempt to provide healing of the injured peripheral nerve. Subjective responses to these treatments have been published. Unfortunately, little objective evidence of reparation of the peripheral nerve in response to treatment has been demonstrated [4].

The MLS laser is a novel treatment for a variety of maladies causing pain and inflammation. The MLS laser is characterized by an 808 nm continuous emission laser and a 905 nm pulsed emission laser that are synchronized. In vitro and in vivo research has shown a beneficial effect of this technology on peripheral nerve injury [5]. Nerve conduction studies (NCS) are an objective measurement of peripheral nerve function. This controlled prospective pilot study was devised to look at the effect of the MLS laser on NCS parameters in developing DPN.

MATERIALS AND METHODS

Study subjects were taken from a cohort the author previously studied regarding the characteristics of developing diabetic sensory polyneuropathy [6]. 10 subjects were enrolled in this MLS laser pilot study.

Prior to inclusion in the study, subjects completed a subjective neuropathy screening questionnaire which was a modification of the Michigan neuropathy screening instrument. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki. Local IRB approval was obtained for the study design and informed consent was obtained from all subjects.

Exclusion criteria for the group included

any evidence of coronary artery disease or peripheral arterial disease including past surgical or medical intervention, claudication symptoms, rest pain or ischemia associated ulceration history. Exclusion criteria also included any disease diagnosis that may cause peripheral nerve dysfunction. The list of diseases were: thyroid disorders, vitamin B12 or folate deficiency, seronegative or seropositive spondyloarthropathy, hepatic or renal disease, lumbosacral pathology, toxin exposure including chemotherapeutic agents, familial polyneuropathy, any existing diagnosis of neuromuscular disorders, history of chronic alcohol abuse, previous medical or surgical intervention for peripheral nerve pathology or previous back or extremity surgery.

Inclusion criteria for the experimental group included a mandatory diagnosis of type 2 diabetes for less than 10 years prior to the test date. Subjects additionally had to be willing to discontinue their medications for symptomatic treatment of neuropathic pain for twenty-four hours prior to sensory testing. All included subjects provided pertinent medical histories and laboratory work along with their list of prescription and over-the-counter medications. All ten subjects were diagnosed with DPN according to the guidelines from the 1988 San Antonio Joint Consensus Statement requiring an elimination of confounding factors with a multiplicity of signs and symptoms. Additional factors monitored included age, height, weight, BMI and hemoglobin A1c.

NCS was performed on the tibial, peroneal and sural nerves of the left lower extremity. A single certified technician administered all of the testing. Testing was performed according to the manufacturer's instructions for the Neurometrix® NCS equipement. The tibial and peroneal nerves were treated with the MLS laser and the sural nerve

INDIVIDUAL PRE AND POST TREATMENT NCS RESULTS

#	1	2	3	4	5	6	7	8	9	10	Mean	p =	Ref. range
Ht	65	64	61	60	65	72	66	65	70	71	66		
Sex	F	F	F	F	F	M	F	F	M	M			
Age	58	82	64	39	64	63	74	39	64	49	59.6		
BMI	31.6	25.7	46.1	24.4	33.3	29.8	29.0	22.6	33.7	30.4	30.7		<25
A1c	7.8	6.3	11.3	11.0	7.1	7.7	6.8	7.0	6.9	6.1	7.8		4.0-5.7
pPFc	4.73	9.77	A	A	2.93	8.59	15.56	9.85	14.88	5.59	8.99		
3PFc	0.43	10.16	6.64	7.03	0	0.98	12.77	6.96	12.96	5.26	6.19	0.015	<18.05
pTFc	12.11	4.30	A	6.25	6.45	14.84	16.80	10.16	16.48	4.98	10.30		
3TFc	8.40	1.76	A	2.54	6.05	9.57	10.62	6.20	12.41	5.15	6.97	0.001	<14.49
pPA	1.42	2.79	0.25	1.84	1.41	3.67	0.44	2.26	0.96	1.60	1.67		
3PA	2.61	2.68	1.03	1.85	0.97	3.51	0.74	2.12	1.14	1.67	1.83	0.30	>1.15
pTA	4.53	2.54	A	3.04	2.63	3.04	2.88	2.41	2.90	4.74	3.19		
3TA	3.98	3.87	A	3.00	2.54	2.67	3.02	3.66	2.77	4.64	3.35	0.49	>1.41
pSV	42.73	A	A	A	50.50	46.29	A	43.66	38.70	57.84	46.62		
3SV	39.68	A	A	A	46.29	42.73	A	45.82	34.56	48.80	42.98	0.24	variable
pSA	6.09	A	A	A	4.92	9.27	A	2.22	6.04	1.76	5.05		
3SA	5.08	A	A	A	7.81	10.48	A	1.80	5.58	7.95	6.45	0.34	>3.39

Legend:
(subject number),
Ht (height inches),
BMI (body mass index),
A1c(hemoglobin A1c),
pPFc(pre treatment peroneal Fc),
3PFc(post treatment peroneal Fc),
pTFc (pre treat-ment tibial Fc),
3TFc (post treatment tibial Fc),
pPA (pre treatment peroneal CMAP),
3PA (post treatment peroneal CMAP),
pTA(pre treatment tibial CMAP),
3TA(post treatment tibial CMAP),
pSV(initial sural CV),
3SV(3rd week sural CV),
pSA(initial sural ampli-tude),
3SA(3rd week sural amplitude),
Ref. range(normal reference range),
A(absent).

was not treated. In this way, the sural nerve acted as an internal control.
Treatment was administered three times per week for 3 weeks. Each treatment session consisted of 1.50 J/cm2 (2.5 min) at the tarsal tunnel, 1.5 J/cm2 (2.5 min) at the fibular neck, and 4.00 J/cm2 at the dorsal foot. NCS parameters were taken prior to the first treatment and immediately following the final treatment. Statistical analysis was computed with mean, standard deviation, paired t-testing and p-value computation.

RESULTS

All subjects completed the full course of therapy and returned for post study NCS evaluation. None of the study subjects reported any adverse reaction to the therapy.
The means are as follows: age 59.6 years (39-82), height 66 inches (60-72), weight 191 lbs (125-252), A1c level 7.8% (6.3-11.3). All ten subjects had a diagnosis of type 2 diabetes. Seven subjects were female and three were male. None of the enrolled subjects took medication for pain.
Individual results are reported in table I. F-wave chronodispersion (Fc) for the peroneal nerve pre treatment was 8.99ms. Post treatment the Fc was 6.19ms yielding a p- value of .015. Fc for the tibial nerve was 10.30ms pre treatment and 6.97ms post treatment. This yielded a p-value of .001. The amplitudes (CMAP) of the peroneal and tibial nerve pre and post treatment did not reach a $p<.05$. Similarly, the p values for the untreated sural nerve (CMAP and conduction velocity (CV) were followed) did not reach a $p<.05$. The sural nerve CMAP and CV was not obtainable 40% of the time leading to less reliable evaluation; however, the CVs were generally slower at the end of the study and the CMAPs were slightly increased.

DISCUSSION

NCS are objective, quantitative and reproducible evaluations of the function of peripheral nerves. Reproducibility of nerve conduction requires consistency of methods, including electrode locations, distances, and temperature [7]. These parameters are well controlled and permit reproducible results with the Neurometrix® testing equipment [8]. F-wave latencies are the most reproducible, with only a 2-3% variation. CMAPs have the lowest reproducibility (10-15% variation) and CV and distal latency are intermediate (4-7% variation) [9]. F-waves are the most sensitive measure of diabetic neuropathies [10].
Fc is a measure of the variability of conduction in different axons in the whole nerve. This makes Fc uniquely useful for detecting even mild abnormalities. For the relative diagnostic sensitivity of all F-wave parameters, Fc is the most often abnormal parameter. Fc is ideally suited for monitoring the treatment of DPN [11]. F-waves have been used as frequently as every two weeks to follow peripheral nerve healing in previously published studies. In this study, tibial ($p=.001$) and peroneal ($p=.015$) Fc improved significantly ($p<.05$) over 3 weeks. This improvement is much greater than the published 2-3% variation. This finding is indicative of nerve healing.
CMAP provides an indication of the number of functioning axons in a nerve and the amount of muscle that is still innervated. CMAPs and CVs are dependent upon the persistent myelinated fibers in the nerve conducting the applied stimulus [7]. An injured nerve will heal at approximately 1mm per day. Because of the relatively slow healing of the peripheral nerve, no change in the CMAP or CV over the course of a 3 week treatment is expected. The length of these nerves being tested would lead one to expect months not weeks of healing before the CMAP or CV would be profoundly affected. While CMAP did increase in both the tibial ($p=.49$) and peroneal ($p=.30$) nerves, it was within the reported 15% variability associated with this parameter.
The sural nerve served as the control in this study. Sural nerve CV did trend slower, but fell within the 7% published variation rate. In the same way, the sural CMAP results pre and post study fell within the published 15% variation rates. The control was statistically unchanged. Previous evaluation of sensory loss in DPN found the axonal pathology is not entirely length dependent and not purely of metabolic cause. An anatomic component for sensory loss was implied [6]. The anatomic regions chosen for application of MLS laser therapy were the tarsal tunnel, fibular neck region and dorsal foot. These regions represent anatomic sites predisposed to peripheral nerve entrapment and damage in DPN [12,13,14].
The small sample size, short period of treatment and immediate follow up are limitations of this pilot study. Future research should look at variable treatment parameters with the MLS laser and the effect of this promising therapy over a longer period of time. Evaluation of the NCS parameters over months instead of weeks should yield more dramatic improvements in the CMAP and CV of the treated nerves if regeneration and healing of the nerve fibers persists.

CONCLUSIONS

MLS laser therapy applied to the tibial and peroneal nerves in persons with documented DPN will lead to objective improvement in nerve function as demonstrated by NCS evaluation. A reasonable expectation is that this improvement in function will lead to improved sensibility in the feet. Improved sensibility interrupts the causal pathway leading to ulceration, infection and amputation. In this pilot study, MLS therapy appears to be uniquely capable of healing the injured nerve in DPN and shows great promise in the battle against the devastating sequelae of this disease.

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