The Effect of Monochromatic Infrared Energy on Sensation in Patients With Diabetic Peripheral Neuropathy

A double-blind, placebo-controlled study

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OBJECTIVE — The purpose of this study was to determine the effect of monochromatic infrared energy (MIRE) on plantar sensation in subjects with diabetic peripheral neuropathy.

RESEARCH DESIGN AND METHODS — In this randomized, double-blind, placebo-controlled study, 39 subjects with diabetic peripheral neuropathy completed the 8-week study. Subjects received 30 min of active or placebo MIRE three times a week for 4 weeks. Plantar sensation was tested with monofilaments at the beginning of the study (M1), following 4 weeks of treatment (M2), and after an additional 4 weeks of nontreatment (M3). The number of sites that could sense the 5.07 monofilament was totaled at M1, M2, and M3. Data were analyzed using a special repeated-measures statistic followed by a post hoc Tukey-Kramer test.

RESULTS — The average number of sites that patients could sense the 5.07 monofilament increased for both the active and placebo groups. There were significant gains from M1 to M2 ($P < 0.002$), no significant gains from M2 to M3 ($P = 0.234$), and significant gains from M1 to M3 ($P < 0.002$) for both the active and placebo groups. There were no significant differences between active and placebo groups at any measurement.

CONCLUSIONS — Thirty minutes of active MIRE applied 3 days per week for 4 weeks was no more effective than placebo MIRE in increasing sensation in subjects with diabetic peripheral neuropathy. Clinicians should be aware that MIRE may not be an effective modality for improving sensory impairments in patients with diabetic neuropathy.

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Diabetes is an increasingly prevalent disease that can have serious complications resulting in escalating health care costs. Recent reports indicate that over 18 million Americans have diabetes (1–3) and almost 30% of adults with diabetes have peripheral neuropathy (4), which increases their risk for developing foot ulcers and contributes to the incidence of lower-extremity amputations (3,5–10). The total cost attributed to managing patients with diabetes in the U.S. was an estimated $132 billion in 2002 (3).

Screening for peripheral neuropathy in patients with diabetes is recommended to identify individuals at risk for foot ulcerations and lower-extremity amputations (11–16). After confirming peripheral neuropathy and the loss of protective sensation, treatment usually focuses on education in foot care and regular foot assessment (9,16). More recently, however, a variety of health care professionals have used devices that produce monochromatic infrared energy (MIRE) in an attempt to improve lower-extremity sensation in patients with peripheral neuropathy.

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Abbreviations: MIRE, monochromatic infrared energy.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

MIRE devices were approved by the Food and Drug Administration in 1994 to increase circulation and reduce pain (17,18). There are reports in the literature of the use of MIRE for treating patients with wounds (19) and soft-tissue trauma (20), but several recent studies (21–26) describe the use of MIRE in treating patients with lower-extremity sensory neuropathy. In two separate uncontrolled studies (21,22), MIRE was shown to produce significant improvements in sensation in patients with peripheral neuropathy after 12 treatments. In another uncontrolled study by Prendergast et al. (26), the authors reported significant improvements in sensation in 27 patients with peripheral neuropathy after 10 MIRE treatments. In a placebo-controlled study by Leonard et al. (23), 18 subjects with protective sensory loss demonstrated significant improvements in sensation after 6 and 12 active MIRE treatments. However, this study was placebo controlled for only 6 of the 12 treatments, had a small sample size, and the authors did not assess carryover effects. We, therefore, conducted this placebo-controlled study to assess the immediate and long-term effectiveness of MIRE in patients with lower-extremity peripheral neuropathy.

The purpose of this research study was to determine whether the application of MIRE to the lower extremities of patients with diabetic peripheral neuropathy would improve plantar sensation. The research hypothesis was that the mean number of sites on the plantar surface of the foot where patients could sense the 5.07 monofilament would be significantly greater in an active MIRE group when compared with a placebo MIRE group.

RESEARCH DESIGN AND METHODS

— Study sample size was targeted to detect a moderate effect size of $f = 0.20$, with 80% power given a two-tailed α of 0.05. The power analysis revealed that for an average correlation of subject outcomes over time of $r = 0.40$, a minimum of 25 subjects was needed in

each treatment level to meet the power objective. Subjects were recruited from the middle Tennessee area and included adult men and women of any race or ethnic background with a confirmed diagnosis of peripheral neuropathy (defined as the inability to detect the 5.07 monofilament at any of the four test sites on the plantar surface of the foot). Excluded from participation in this study were individuals who were pregnant or who had open wounds or active malignancies in the treatment area. Forty-three (43) individuals with self-reported diabetes met the inclusion criteria and volunteered to participate in this study. From these 43 subjects, 77 lower extremities with peripheral neuropathy were used in the study. After explaining the procedures and obtaining informed consent from eligible participants, subjects were randomly assigned to an active MIRE group or a placebo MIRE group.

Semmes-Weinstein monofilaments were used to assess sensation on the plantar surface of the foot of each subject. A new test kit containing 20 monofilaments ranging in size from 1.65 to 6.65 was used in this study (Touch-Test Sensory Evaluators; North Coast Medical, Morgan Hill, CA). The number assigned to each monofilament represents 10 × the log of the force exerted at the tip of the monofilament with applied pressure (9,27). The higher the number of the monofilament, the more force required to bend it when pressed on the plantar surface of the foot. The most sensitive monofilament (1.65) requires 0.008 g of force and the least sensitive monofilament (6.65) requires 300 g of force for bending (28). According to the package insert, the monofilaments were calibrated at the factory to deliver the specified force within a 5% SD. In two separate studies, Diamond et al. (29) and Mueller et al. (30) assessed the reliability of monofilaments using the κ statistic. Diamond et al. (29) reported that interrater and intrarater reliability values ranged from 0.72 to 0.83, while Mueller et al. (30) reported an interrater reliability of 0.78 and an intrarater reliability of 0.81. Both researchers concluded that monofilament testing has acceptable reliability.

The four MIRE units used in this study were Anodyne Model 120–4 Infrared Therapy Systems (Medassist, Tampa, FL). Each device has a main power unit with four flexible therapy pads; each pad measures 3.0 × 7.5 cm and contains 60 superluminous gallium-aluminum-arsenide diodes that emit light energy in the near-infrared spectrum (890-nm wavelength). Two active treatment units were preset by the manufacturer to deliver 1.95 joules · cm^{-2} · min^{-1} when activated, and two sham units were inactivated (delivered no energy) even though the indicator lights illuminated when the power switch was turned to the on position. Each unit was labeled with a number, but neither the therapist who administered the treatment nor the therapist who conducted the measurements were aware of the operating status of the MIRE units during the treatment and data collection phases of the study.

Measurement procedures

At the initial session, the 5.07 monofilament was applied to the dorsum of each subject's hand to demonstrate the testing procedure. The test was then administered to four test sites on the plantar foot with the subject's eyes closed. The test sites were located at the great toe, first metatarsal head, third metatarsal head, and fifth metatarsal head (31–33). If callus or scar was present at any of the test sites, the monofilament was applied to the perimeter of the test area. The sites were tested in a random order with a 2- to 3-s pause between test sites. The 5.07 monofilament was held perpendicular to the skin and applied for 1–2 s in a three-step sequence: touch the monofilament to the skin, bend the monofilament, and then lift the monofilament from the skin (31). If the subject responded "yes" at the testing site, the next smaller monofilament was used until the patient did not respond. If the subject did not respond when testing with the 5.07 monofilament, the test was repeated with the next larger monofilament. The value of the most sensitive monofilament detected at each test site was recorded for each subject. Measurements were performed at the beginning of the study (M1), after 4 weeks of active or placebo MIRE treatment (M2), and after an additional 4 weeks of nontreatment (M3). The number of sites that could sense the 5.07 or smaller diameter monofilament was totaled at M1, M2, and M3. All measurements were performed by one physical therapist who was blind to group assignment and was not involved in treatment.

Treatment procedures

Each subject sat in a standard chair with socks and shoes removed. The four therapy pads were placed over the following sites in accordance with procedures used by Kochman (21) and recommendations of the manufacturer: *1*) distal posterior leg, *2*) distal anterior leg, *3*) plantar foot over metatarsal heads, and *4*) plantar arch of foot. The placement of pads 3 and 4 formed a "T" on the plantar surface of the foot. Commercial plastic wrap was placed between the skin and the MIRE pads for hygienic purposes, and the pads were held in position with neoprene straps supplied by the manufacturer. Before activating the MIRE units, all subjects were told that they may or may not feel anything from the treatment and were instructed to notify the therapist if they felt any discomfort during the treatment session. Subjects received the treatment protocol for peripheral neuropathy as recommended by the manufacturer: 30-min treatments three times a week for 4 weeks for a total of 12 treatments. A second therapist, who was not involved in the measurements, performed all treatment procedures.

Statistics

All descriptive and inferential statistics in this article were calculated using version 9.1.3 of the SAS System for Windows. Examination of observation variation and covariation revealed considerable heterogeneity. To model the heterogeneity, three separate mixed-effect covariance pattern models were fitted using SAS Proc Mixed (35). Those patterns, in order of increasing complexity, consisted of *1*) a compound symmetry pattern (i.e., common variance and common covariance), *2*) a homogenous unstructured pattern (i.e., a common unstructured covariance pattern across treatment levels), and *3*) a heterogeneous unstructured covariance pattern (different unstructured covariance patterns by treatment level). Results from likelihood ratio χ^2 tests supported the heterogeneous unstructured covariance pattern model as the most appropriate model for estimating treatment, measurement point, and the treatment by measurement point interaction effects. Hence, data analysis was parallel to the traditional one between one within-subjects ANOVA but additionally incorporated an improved representation of random effects (i.e., variances and covariances).

RESULTS — Thirty-nine (39) of the 43 subjects completed the study; three subjects were hospitalized and one moved out of the area during the course of the study. From the remaining 39 subjects, 35 lower extremities received active MIRE

Table 1—*Baseline characteristics*

Variable	Active MIRE	Placebo MIRE
Limbs (*n*)	35	35
Age (years)*	63.9 ± 9.6 (45–89)	63.6 ± 10.2 (37–89)
Sites sensitive to 5.07 monofilament*	0.57 ± 0.95 (0–3)	0.86 ± 1.24 (0–3)
Sex (male/female)	21/14	25/10
Race/ethnic group		
Caucasian/African American	34/1	34/1

Data are means ± SD (range), unless otherwise indicated. *NS differences between groups (independent *t* test, $P > 0.05$).

treatment and 35 lower extremities received the placebo MIRE protocol. The majority of subjects were Caucasian (34 of 35) and male (21 of 35 in the active group and 25 of 35 in the placebo group). There were no significant differences between groups in age and number of sites sensitive to the 5.07 or smaller diameter monofilament at baseline (see Table 1). Two patients in the active MIRE group received superficial burns: one burn occurred under the posterior leg pad and one under the anterior leg pad. The affected areas were covered with a thin hydrocolloid dressing by the attending physical therapist, and both healed within 1 week. Since both subjects wished to remain in the study, the leg pads were repositioned to a more lateral location and both subjects completed the study without missing any sessions or experiencing any other adverse effects.

The analysis detected a significant main effect for measurement ($P = 0.001$) but could detect neither a significant main effect for treatment ($P = 0.186$) nor for the treatment by measurement point interaction ($P = 0.622$). The estimated difference between mean active and placebo measurements was negative but nonsignificant, specifically −0.38 (95% CI −0.95 to 0.19). The Tukey-Kramer procedure was used for follow-up of the significant repeated measure. Estimates, adjusted probabilities, and CIs assessing average change over time were as follows: *1*) a significant average gain from baseline (M1) to 4 weeks (M2) of 0.47 ($P < 0.002$; 95% CI 0.16–0.79), *2*) a nonsignificant average gain from 4 weeks (M2) to 8 weeks (M3) of 0.17 ($P = 0.234$; −0.08 to 0.42) resulting in *3*) a significant overall average gain from baseline (M1) to 8 weeks (M3) of 0.64 ($P < 0.002$; 0.22–1.06) (Fig. 1).

CONCLUSIONS — In this study, we found no significant differences between active and placebo MIRE in improving plantar sensation in patients with diabetic peripheral neuropathy. Although there are case reports (17) and several uncontrolled studies (21,22,26) that support the use of MIRE for reversing peripheral neuropathy, we did not find any evidence that active MIRE improved sensation any more than placebo MIRE.

Our results are also partially contradictory to the results of the only other identified placebo-controlled study by Leonard et al. (23). Both studies were similar in design, but several procedures differed. We treated all subjects for 12 treatments with foot pads placed in a "T" on the plantar surface; subjects in the Leonard et al. (23) study received 12 treatments, but the study was placebo controlled for only the first 6 treatments

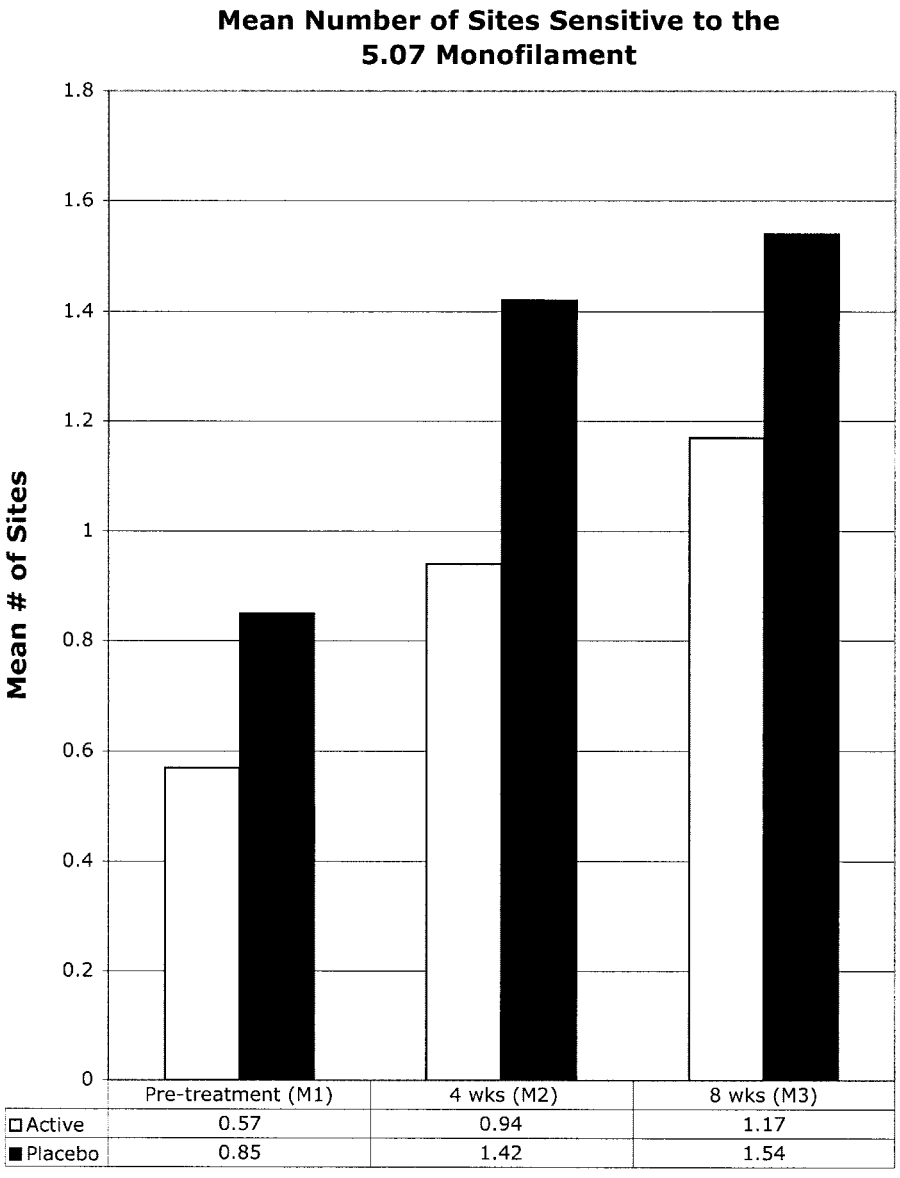

Figure 1—*Significant mean gain from M1 to M2 of 0.47 (P < 0.002), nonsignificant mean gain from M2 to M3 of 0.17 (P = 0.234), and significant gain from M1 to M3 of 0.64 (P < 0.002) for both groups. No significant differences between groups at M1, M2, and M3.*

and their foot pads were placed on the dorsal and plantar surfaces. In both studies, subjects were treated three times per week, but the treatment time used by Leonard et al. (23) was 40 min and we used 30-min treatment times. Another notable difference was the operating status of the inactive MIRE units: Leonard et al. (23) used a sham MIRE unit that delivered a mild heat (37°C) but no MIRE, and our placebo units delivered no energy. Similar trends were observed in both studies: subjects in both the active and placebo groups demonstrated improvements in sensation at each measurement period. However, during the placebo-controlled phase of the Leonard et al. (23) study, the authors reported a significant difference in the active treatment group and no significant difference in the sham group as compared with baseline, but they did not report if they had analyzed their data to determine whether there was a significant difference between the groups after six treatments. After 12 treatments (M2), we found a significant difference in the active group, as well as the placebo group, when compared with baseline (M1), but there was no significant difference between the active and placebo groups. When we retested the subjects after an additional 4 weeks without treatment (M3) to assess any carry-over effects, both the active and placebo groups continued to exhibit slight, but nonsignificant, improvements in sensation compared with M2 measurements. For all subjects in our study, the average values climbed significantly from baseline to 4 weeks (treatment phase) but not from 4 to 8 weeks (nontreatment, follow-up period).

In attempting to explain why all subjects in our study demonstrated improvements in sensation regardless of the operating status of the MIRE unit, we present two possible hypotheses: *1*) improvements in sensation may be partly due to a Hawthorne effect (36), because significant sensory improvements occurred during the treatment phase of our study but not during the follow-up, nontreatment phase; and *2*) all subjects in this study had access to two free pamphlets on diabetes and foot care, and we speculate that improved skin condition from subjects' use of lotions and creams may also have attributed to improvements in plantar sensation.

In this study, we used Semmes-Weinstein monofilament testing to assess plantar sensation because it is one of the simplest and most practical screening methods to detect loss of protective sensation (6–14). The 5.07 monofilament is commonly used by clinicians to identify patients with loss of protective sensation and is sensitive in identifying patients at risk for foot ulceration (7,8,15). Other methods are available for testing plantar sensation, but most researchers (21–25) who examined the effectiveness of MIRE used monofilament testing. Only Prendergast (26) used an alternate testing procedure: current perception threshold. Because there is no consensus in the literature regarding the appropriate number of sites for assessing plantar sensation in patients with diabetes, we chose to test sensation at the four sites recommenced by Smieja et al. (32) and Sosenko et al. (33). These same four sites were also recommended by the Lower Extremity Amputation Prevention program (31) when this study was conducted.

Based on the results of our study, we believe that MIRE may not be any more effective than placebo in improving plantar sensation in patients with diabetic neuropathy. If our study had been done without a placebo control, the active MIRE treatment would have appeared to be therapeutically effective. Clinicians should be aware that MIRE may not be an effective modality for treating sensory impairments in patients with diabetic peripheral neuropathy. We recommend that future studies should be only double-blind and placebo-controlled with adequate sample sizes to determine whether active MIRE is any more effective than placebo MIRE. Other researchers may also want to examine the effects of longer treatment times, different pad placements, or the use of different assessment techniques (e.g., current perception threshold or vibration threshold testing) in assessing the effectiveness of MIRE in treating patients with peripheral neuropathy.

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