The Effect of Monochromatic Infrared Energy on Transcutaneous Oxygen Measurements and Protective Sensation: Results of a Controlled, Double-Blind, Randomized Clinical Study

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Monochromatic infrared energy has been reported to restore protective sensation by increasing circulation. A controlled, double-blind, quasi-experimental, randomized clinical study was conducted to 1) examine the effects of monochromatic infrared energy treatments on tissue perfusion, 2) determine the effects of a published monochromatic infrared energy neuropathy protocol on sensation on the feet of patients with diabetes and a loss of protective sensation; 3) examine monochromatic infrared energy’s effect on pain; and 4) examine the relationship between transcutaneous oxygen levels and loss of protective sensation. The study was conducted at a wound and hyperbaric treatment center in Norwalk, Conn; 18 adults (12 men, six women; mean age 65 ±13 years, range 39 to 86 years) with diabetes and loss of protective sensation were recruited using convenience sampling methods. All patients served as their own control. Pre- and post treatment tests assessed sensation, pain, and transcutaneous oxygen measurements on two sites per foot. Participants underwent a series of 30-minute monochromatic infrared energy treatments (one foot active treatment, one foot sham). Monochromatic infrared energy was delivered at the manufacturer pre-set level of energy of 1.5 J/cm²/min at a wavelength of 890 nm; sham units delivered no energy. Scores were analyzed using paired t-tests and Pearson’s correlation coefficient. No significant differences were observed between active and sham treatments for transcutaneous oxygen values, pain, or sensation. Both active and sham monochromatic infrared energy-treated feet had significantly improved sensation when compared to pretest baseline scores (P <0.05). No statistical relationship was found between transcutaneous oxygen and sensation. This small study did not demonstrate any effects of monochromatic infrared energy treatment on transcutaneous oxygen measurements, pain, or sensation in adults with diabetes and loss of protective sensation.

KEYWORDS: monochromatic infrared energy, transcutaneous oxygen, loss of protective sensation


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Diabetic peripheral neuropathy often causes a loss of protective sensation (LOPS) that can lead to an increased risk for falls, foot wounds, or amputation. Loss of protective sensation is defined as insensitivity at two or more sites on the foot as measured by the 5.07 log, or 10-g, Semmes Weinstein monofilament (SWM). A relatively new modality using monochromatic infrared energy (MIRE) — a form of light therapy — has shown promise in improving sensation in people with diabetic neuropathy. It is delivered at an infrared wavelength of 890 nm, which is above the visible light spectrum, via the Anodyne Therapy System® (ATS; Anodyne Therapy LLC, Tampa, Fla) using therapy pads that contain 60 superluminous gallium aluminum arsenide diodes that pulse 292 times per second.

Monochromatic infrared energy has been in use since 1994 when it was cleared for marketing by the Food and Drug Administration (FDA) for increasing local circulation and for reducing pain. The proposed mechanism of action for MIRE is to increase the microcirculation of the tissues under the diodes as a result of hemoglobin absorbing the infrared wavelength and releasing small amounts of nitric oxide (NO) in the blood vessels. This is believed by some to increase endothelial cell formation of NO, a powerful vasodilator and angiogenesis mediator. Angiogenesis and vasodilation increase circulating oxygen levels in the treated tissues. Scanning laser Doppler has been used in case studies demonstrating improved tissue perfusion, or microcirculation, in the tissues receiving MIRE treatment.

Transcutaneous oxygen (TcPO₂) testing is a non-invasive way to measure local tissue oxygen perfusion. Clinically, TcPO₂ measurements are used to measure trends with hyperbaric oxygen (HBO) therapy, evaluate peripheral circulation in diabetes, assess wound hypoxia, and determine amputation level. Transcutaneous oxygen testing is performed by attaching an electrode to a quietly resting patient. The electrode warms the skin and measures the subsequent oxygen diffusion across the skin. Transcutaneous oxygen testing should be performed in a consistent manner from patient to patient using standardized test sites and appropriately calibrated machines and has been commonly used, with published suggestions and protocols for reproducible data, to qualify patients for HBO treatments. Despite its use in hyperbaric oxygen research, TcPO₂ testing has not been used clinically or in research to determine the effects of MIRE on local tissue oxygen perfusion.

Recent studies have indicated that MIRE helps restore LOPS in patients with peripheral neuropathy. Whether the improvement in LOPS in these studies was related to a concomitant change in oxygen perfusion remains unknown because randomized controlled trials investigating the effects of MIRE on tissue perfusion or the relationship between LOPS and tissue perfusion in people with diabetic peripheral neuropathy have not been conducted.

A quasi-experimental, randomized, double-blinded clinical study was conducted to: 1) examine the effects of published neuropathy protocol for MIRE treatments on tissue perfusion, measured as a change in TcPO₂ levels compared to self-controlled sham treatment; 2) determine the effects of the published MIRE neuropathy protocol on sensation on the feet of diabetic subjects with LOPS; 3) examine MIRE’s effects on pain; and 4) examine the relationship between TcPO₂ levels and LOPS.

**KEY POINTS**

- The potential benefits of an effective treatment to restore protective lower limb sensation (LOPS) among persons with diabetes mellitus are numerous and substantial.
- Because limited evidence suggests that monochromatic infrared energy treatments may improve circulation and restore LOPS, the authors conducted a double-blind randomized study to assess its effects on sensation, local tissue oxygen perfusion, and pain.
- The current study failed to show any difference between treatment and control group outcomes.
- Similar studies using larger sample sizes are needed to assess the effectiveness and efficacy of this treatment modality.
Literature Review

A number of studies have investigated the effects of MIRE on protective sensation. Kochman et al performed a prospective study of consecutive patients, ages 35 to 80 years, with established diabetic peripheral neuropathy but no lower extremity ulcers. Of the 49 participants, 25 had type 1 diabetes and 24 had type 2 diabetes. Sensory testing was performed and MIRE treatments applied. Semmes Weinstein monofilament testing was performed randomly at three test sites on the plantar aspect of the foot (great toe, plantar arch, fourth toe) using several monofilament sizes; each site was tested three times. Participants were asked to respond when they felt the SWM and to describe the location. Hot/cold testing was performed at the same test sites of the feet. Hot/cold discrimination was rated absent when no correct responses were given, intact with three correct responses, and impaired with one or two correct responses. The MIRE treatments used four diode pads per leg placed on the dorsal/ventral surfaces of the foot and the distal anterior/posterior surfaces of the tibia (two diode pads were placed on the plantar surface of the foot if the subject was uncomfortable with the posterior tibia region placement). At baseline, all 49 subjects had peripheral neuropathy, impaired or absent hot/cold discrimination, and abnormal results of gait analysis and 42 had LOPS. After 12 treatments, all subjects had improved sensory perception (SWM <5.07) compared to baseline (P <0.001), indicating return of protective sensation. Additionally, 13 subjects achieved intact hot/cold discrimination.

Leonard et al conducted a double-blind, randomized, placebo-controlled study (N = 27) to assess the effects of MIRE on sensation using the 5.07 SWM, the 6.65 SWM, and a modified Michigan Neuropathy Screening Instrument (MNSI). Inclusion requirements included diagnosis of type 1 or type 2 diabetes along with peripheral neuropathy based on patient history and physical examination. Loss of protective sensation was defined as insensitivity at two or more sites on the foot as measured by the 5.07 log, or 10-g, SWM. Pain was measured using a 10-point visual analog scale. The 27 subjects, 18 insensate to the 5.07 SWM (group 1) and nine insensate to the 6.65 SWM (group 2), received a 40-minute sham treatment on one leg and an active treatment on the other leg three times a week for 2 weeks. All 27 subjects subsequently received 40-minute active treatments three times a week for 2 weeks to both legs. All treatments used four diode pads per leg placed on the dorsal and plantar surface of the foot and on each side of the calf just above the ankle. The active units delivered 1.3 J/cm²/min and the sham units delivered warmth at 37°C. Data (ie, measurements of sensation, a pain questionnaire answers, and a physical exam) were collected at baseline (before starting MIRE/sham treatments), within 3 days after the sixth treatment, and within 3 days after the twelfth treatment. All subjects served as their own control for the first six treatments and no difference in baseline sensitivity between feet assigned to active or sham treatment were found for group 1. The authors did not report if a baseline difference for group 2 was found.

Compared to baseline, sensation improved for group 1 after both six (P <0.02) and 12 (P <0.001) active MIRE treatments. No significant change in the number of sites able to sense the 5.07 SWM after six sham treatments in either group 1 or group 2 was observed. Monochromatic infrared energy significantly decreased the number of sites insensitive to the 5.07 SWM in group 1 but improvements in sensation, pain reduction, or neuropathic symptoms among participants with more profound sensory loss (group 2) were not statistically significant. The authors reported no significant improvements in ankle reflexes or vibratory sensitivity to a 128-Hz tuning fork during the study.

According to information listed on the Anodyne Therapy, LLC website (www.anodynetherapy.com), TcPO₂ levels improved on a single patient (accessed December 12, 2003) and several scanning laser Doppler (Moor Instruments, Devon, UK) images show increased circulation. Burke reported that in 30 minutes, MIRE can increase local microcirculation by as much as 3,200%. He further reports, based on an online NO overview for which references are not provided, that in neuropathic feet, MIRE treatment increased microcirculation 10 times more than warmth alone. Finally, Burke reported on wound centers in Wisconsin that have noted increases in TcPO₂ with MIRE, which he
contributes to increased oxygen availability from the vasodilation induced by NO.

Wimberley et al. report use of TcPO₂ measurements as a major trend parameter and valuable indicator of tissue PO₂ in adults. A repeated measures study compared laser Doppler flowmetry, skin perfusion pressure, and TcPO₂ (44°C) on 21 consecutive patients with severe lower extremity arterial disease and found the same magnitude of variation with short-term measurements for all three methods. When the authors excluded TcPO₂ measurements below 10 mm Hg, the mean coefficients of variations were 0.08 short-term and 0.31 day-to-day.

Methods

This study expands on the methods used by Leonard et al. All study participants served as their own control and the same inclusion criteria (diabetic neuropathy), MIRE pad placement, sensation testing protocol, and sites using the 5.07 (10-g) SWM were used. This study was approved by both the Norwalk Hospital and Nova Southeastern University IRBs.

Design. This was a quasi-experimental, randomized, double-blinded, pretest-posttest controlled study. All participants served as their own control by having each leg randomly assigned to either the sham or active treatment group. The first participant was randomized, by the toss of a coin, to which leg received the active/sham treatment with MIRE units labeled A or B. Subsequent participants were sequentially assigned A or B units for each leg to ensure equal groups. This assignment was consistent for all the treatments, with each leg receiving the same-labeled MIRE units as the first treatment.

The manufacturer, who disabled the sham units internally so no energy was emitted even though the machine power indicator light was on, provided all treatment units. Furthermore, because MIRE therapy pads do not emit visible light on either the active or the sham units, it was impossible for the investigators to distinguish the active from sham units. Thus, the authors, additional investigators, and participants were blinded to the active or sham status of the MIRE units. The principle author performed all pre- and posttest measurements. Investigators were notified of the sham/active status of the MIRE units by the manufacturer on return receipt of the units at the end of the study before data analysis.

Participants. Using convenience sampling methods, adults with diabetes were recruited via word of mouth, diabetic support group lectures, flyers displayed throughout the hospital, press releases, and a newspaper advertisement. Eighteen adults with diabetes participated in this study conducted at the Norwalk Hospital Wound Care and Hyperbaric Medicine Center in Norwalk, Conn. The inclusion criteria included self-reported diabetes with LOPS on each foot and the ability to complete the study protocol for all active/sham MIRE treatments and all pre- and posttest visits. Loss of protective sensation was determined at the pretest visit using the 5.07 SWM according to National Institute of Diabetes and Digestive and Kidney Disease guidelines. Persons were excluded if they had a history of lower extremity amputations, cancer, or MIRE treatments. Persons with active malignancy, who were pregnant or breastfeeding, undergoing dialysis, and unable to comfortably lay supine for TcPO₂ testing or provide informed consent also were not eligible to participate. Because one purpose of this study was to determine the effect of MIRE on LOPS, persons also were excluded if the pretest sensation assessment did not reveal LOPS on each foot and if the initial TcPO₂ was less than 10 mm Hg — the latter stipulation to ensure TcPO₂ results would be within the literature-supported variation.

For the current study, this would indicate a 12.4 mm Hg, day-to-day variation for a baseline of 40 mm Hg.

Procedures. During the pretest, participants provided informed consent and their recent caffeine, nicotine, and medication use was reported. Years since onset of diabetes mellitus was recorded and participants were asked to rate their pain from 0 to 10 (0 = no pain and 10 = the worst possible pain) for each foot separately. Sensation testing was performed by one investigator using a 5.07 (10-g) SWM randomly at five locations on the plantar aspect of each foot: the first and fourth toes and the first, third, and fifth metatarsal head areas. Sensation testing was performed in a quiet room with no distractions. Participants saw and touched the SWM before testing and then were asked to close their eyes and say “yes” or “now” when they
felt a touch and describe the location on which foot the sensation occurred.

Participants found to have LOPS on each foot then rested for approximately 15 minutes, lying supine on a stretcher while their skin was prepared for TcPO₂ pre-testing. Pre-testing was performed on two standard test sites per bare foot: the dorsal first-second distal metatarsal area and the proximal dorsal lateral midfoot. Per manufacturer protocol, each subject’s skin was shaved with a safety razor if needed, cleansed well with alcohol wipes, then pressed several times with silk tape to remove excess dry epidermal cells to improve electrode adhesiveness. Electrode fixation rings were applied to the skin at the test sites and drops of contact fluid were applied per manufacturer guidelines. The electrodes were attached after the Radiometer (Copenhagen, Denmark) TCM400 machine was calibrated for use with each patient. The TCM400 machine is a computerized model that automatically calibrates to barometric pressure and 44°C. (The manufacturer donated the TCM400 machine with four electrodes, membranes, and fixation rings for the duration of this study.) A clinic temperature of 68° to 72° F was maintained for all pre- and posttest visits.

After the electrodes were connected, a photograph was taken to ensure same electrode placement at the posttest. Each subject used one pillow that could be folded in half for comfort and was covered with a lap blanket during testing. Participants were asked to remain still and quiet and were checked intermittently. Readings were recorded at 20 minutes.

Next, participants were scheduled to receive 12, 30-minute MIRE and sham treatments to their bare feet and legs two to four times per week for 3 to 5 weeks, the number of treatments determined according to manufacturer suggested protocol and subject availability. Due to inclement weather and seasonal conflicts, the protocol was modified to allow for 11 or 12 treatment sessions. This modification is consistent with other published studies providing a range of treatments. The manufacturer (Anodyne Therapy, LLC) donated four MIRE Model 120 home units for use in this study. Two units delivered active MIRE at the standard manufacturer pre-set energy level of 70% full power of the professional system (1.5 J/cm²/min) and two units were sham, delivering no energy or warmth.

Per manufacturer guidelines for infection control, the skin of each participant was protected by a clear plastic barrier at the pad placement locations. Two diode pads were placed on the dorsal and plantar surfaces of each foot and two diode pads on the medial and lateral sides of each lower leg. This pad placement has been used by other investigators and directly treats the tissues being tested. Elastic Velcro straps, supplied by the manufacturer, were used to hold the pads in place. The units were turned on and a timer was set for 30 minutes. Participants were checked every 10 minutes during the first treatment to minimize the potential for superficial burns and to ascertain the treatment was comfortable. Subsequent treatments occurred with each leg receiving the same-labeled unit as the first visit.

Within 3 days of the last treatment, the posttest questionnaire was completed for medication changes and the pain level for each leg was reassessed. Participants again rated their pain on a scale from 0 to 10 without prompting to their initial pain reports. After rating their pain levels, they were informed of their pretest pain levels as a point of interest. Participants could add statements but the pain rating provided without prompting was not changed. Then sensation and TcPO₂ tests were performed in the same manner as the pretest; investigators referred to the pretest photographs to best duplicate electrode placement.

Data analysis. All variables collected were entered into Microsoft Excel 2000. Descriptive statistics were calculated for the following variables: age, gender, years with diabetes, and smoking status. Medication use was reported at each pre- and posttest session and changes were noted. Paired t-tests were calculated for the pretest scores of the active and sham feet to determine likeness for each of the three endpoints. Paired t-tests were used to compare baseline to posttest for the average of two TcPO₂ measurements, pain and sensation, for each foot and to compare the change scores between the active and sham groups. Pearson’s correlation coefficient was calculated to examine the relationship between TcPO₂ results and LOPS and the relationship between the number of days from pre- and
Results

The study group consisted of 18 participants (12 men and 6 women) with a mean age of 65 ± 13 years (range 39 to 86 years). Three were current smokers and the mean self-reported length of time since the onset/diagnosis of diabetes was 14.6 ± 11 years (see Table 1). As per the study design, each treatment group (active and sham) consisted of nine right and nine left feet. The mean number of 30-minute treatments received during the 3 to 4 week study was 11.7.

Paired t-tests showed no statistically significant difference in the pain or sensation pretest scores between the active or sham treatment groups. However, a statistically significant difference (P = 0.04) was noted in the TcPO2 pretest values between the sham and active group (see Table 2). The average mean values varied 3.6 mm Hg (clinically insignificant) from 48.9 mm Hg (sham group) to 45.3 mm Hg (active group). No statistically significant difference was found in the amount of change in TcPO2 scores between the active and sham treatment groups (P = 0.07). The mean change (± SD) in TcPO2 scores was 1.5 ± 9.6 mm Hg for the active feet and -1.3 ± 7.7 mm Hg for the sham feet. No statistically significant differences were noted between the active and sham groups for changes in sensation (P = 0.4) or pain (P = 0.4) (see Table 3).

No significant correlation was found between changes in TcPO2 and sensation (r = 0.1, P > 0.05) or between actual TcPO2 and sensation scores (r = 0.3, P > 0.05). Additionally, no significant differences were noted when pre- and posttest data for TcPO2 or pain were compared. However, a statistically significant change in sensation was noted for both the active (P = 0.002) and sham (P = 0.01) treatment groups between pre- and posttest.

During the seventh treatment session, one participant reported discomfort on one foot, now known to have been receiving active treatment. The research assistant immediately inspected the foot and noted a linear scabbed wound located at the distal lateral edge of the diode pad placed on the dorsum of the foot. The wound was not consistent with a burn. It was not possible to determine if the wound was an incidental scratch or caused by the edge of the diode pad. The wound was covered with a transparent film dressing and closed within 7 days. The participant did not wish to withdraw from the study and completed the protocol with no other adverse events.

None of the four participants who consumed caffeine or nicotine before a testing session had a significant change in TcPO2 scores that would skew results.

During the course of the study, four participants had medication changes. One decreased the dose of furosemide and started linezolid; one started taking insulin, gabapentin, and lisinopril during the course of the study; one started taking a beta-blocker; and one started azithromycin and had a cortisone shot in the left knee earlier in the posttest evaluation day.

### Table 1

<table>
<thead>
<tr>
<th>Number of years with diabetes mellitus</th>
<th>Number of participants</th>
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<tr>
<td>&lt;5 years</td>
<td>4</td>
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<tr>
<td>5–10 years</td>
<td>4</td>
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<tr>
<td>11–15 years</td>
<td>2</td>
</tr>
<tr>
<td>16–20 years</td>
<td>4</td>
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<tr>
<td>21–25 years</td>
<td>0</td>
</tr>
<tr>
<td>26–30 years</td>
<td>2</td>
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<tr>
<td>&gt;31 years</td>
<td>2</td>
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</table>

### Table 2

<table>
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<tbody>
<tr>
<td><strong>Sham</strong></td>
</tr>
<tr>
<td>Mean (standard deviation)</td>
</tr>
<tr>
<td>Median</td>
</tr>
<tr>
<td>Mode</td>
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<tr>
<td>Highest (1)</td>
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<tr>
<td>Lowest (1)</td>
</tr>
<tr>
<td>&lt;40 mm Hg (n)</td>
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* TcPO2 = transcutaneous oxygen measurements in mm Hg. Values represent average of two dorsal feet TcPO2 pretest scores; 40 mm Hg is considered the threshold for healing.

| Statistically significant difference, P = 0.04.

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| Statistically significant difference, P = 0.04.
Discussion

No statistically significant differences in pain, sensation, or TcPO₂ measurements were found between feet treated with active MIRE and feet treated with sham MIRE in participating persons with diabetes who served as their own controls. Definitive conclusions cannot be drawn about MIRE's effect on TcPO₂ measurements because randomization led to an unequal baseline distribution. Sites randomized to the active treatment group had significantly lower TcPO₂ values than those receiving sham treatment. While statistically significant, the observed mean difference (3.6 mm Hg) is not clinically significant. Additionally, post-hoc analysis showed that when outcomes for both feet of the participant with the lowest scoring foot are removed from the analysis, the pretest scores are no longer significantly different. It could be argued that the lower pretest scores in the active treatment group provided a competitive advantage by increasing the potential for improved circulation given the wide range of normal TcPO₂ values (45 to 96 mm Hg).²⁴,²⁵ Similarly, although the circulation of the feet in the active group may not have been capable of a response sufficient to be significant, such an occurrence is unlikely because the lowest scoring foot at pretest had a change score of +20 mm Hg for the average of the two dorsal TcPO₂ test sites — the highest change experienced by any foot in the study. Additionally, five feet in the active group compared to two feet in the sham group had a >15% increase in TcPO₂ scores — above literature reports for percentage variation associated with TcPO₂ testing.²²,²⁶,²⁷

Despite these responses, neither the change experienced in each group nor the difference in posttest TcPO₂ scores for the active and sham groups were statistically significant and the overall change was within the literature-reported variability for TcPO₂ testing.²²,²⁷ While no significant differences for pain were observed, statistically significant improvements in sensation, similar to the results reported by other authors,¹,²,⁶ were found. However, the change was significant for both the active- and sham MIRE-treated feet. These results are consistent with the findings of the only other double-blinded study¹⁸ comparing the effects of 12 active MIRE treatments to 12 sham MIRE treatments on sensation. Several factors can explain these results. First, these results may be attributed to the Hawthorne effect, as others have suggested.¹⁸ Second, local heating effects of the MIRE may result in a consensual reflex type response affecting the contralateral limb. There may be other yet unidentified relationships related to the physiology of neuropathy and MIRE that result in a more general response capable of producing such effects. The fact that both active and sham groups had significantly improved sensation in this and another study¹⁸ warrants further research. Although an interesting objective, no correlation could be drawn between LOPS and TcPO₂. Likewise, no other studies have reported any such relationship.

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Pre-sham: Mean/SD</th>
<th>Post-sham: Mean/SD (P value)</th>
<th>Pre-active: Mean/SD</th>
<th>Post-active: Mean/SD (P value)</th>
<th>Sham change: Mean/SD</th>
<th>Active change: Mean/SD (P value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TcPO₂ (mm Hg)</td>
<td>48.9 ± 8.7</td>
<td>47.6 ± 8.6 (0.5)</td>
<td>45.3 ± 11.5</td>
<td>46.8 ± 10.9 (0.3)</td>
<td>-1.25 ± 7.7</td>
<td>1.53 ± 9.6 (0.07)</td>
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<tr>
<td>Sensation</td>
<td>1.2 ± 1.3</td>
<td>2.1 ± 2.1 (0.01)</td>
<td>1.1 ± 1.2</td>
<td>2.1 ± 1.9 (0.002)</td>
<td>0.89 ± 1.3</td>
<td>1 ± 1.2 (0.4)</td>
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<tr>
<td>(range 0–5 sites)</td>
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<td></td>
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<tr>
<td>Pain (0–10 scale)</td>
<td>2.8 ± 2.7</td>
<td>3.1 ± 2.7 (0.7)</td>
<td>2.8 ± 2.7</td>
<td>2.9 ± 2.5 (0.5)</td>
<td>0.22 ± 2.6</td>
<td>0.06 ± 2.1 (0.4)</td>
</tr>
</tbody>
</table>

* Paired t-test

TcPO₂ values represent average of two dorsal sites per foot
Sensation outcome values are average number of sites sensing the 5.07 SWM per foot (range 0 to 5). Pain values are 0–10 pain analog scale ratings for each foot.
Overall, this study controlled many variables lacking in previous studies. First, it was prospective, randomized, and double-blinded, using each participant as his or her own control. Second, every participant received the same treatment parameters with no confounding additional interventions. Third, one researcher performed all pre- and posttests in a consistent manner and in a clinically controlled environment using established guidelines. Fourth, changes in medications were documented and examined for potential effects. Finally, data analysis was performed to compare the effects of the active and sham intervention as well as to ascertain the within-group difference between pre- and posttest results.

Limitations

Limitations of this study include the small sample size and small effect size. A Type II error (failure to identify an existing difference) may have occurred because the assumptions on which this study was designed were not realized — a large effect size and a sample size of 20. The effect size was small, demonstrated by the low change scores, and only 18 patients met the study inclusion criteria. This study could not demonstrate a significant impact of MIRE on circulation using TcPO₂ measurements, partly because of a lack of power related to the sample size and the unequal baseline distribution for this variable as a result of randomization. However, this finding was surprising, given claims of circulation increases up to 3,200% based on laser Doppler images.⁹¹ The effect size was small, demonstrated by the low change scores, and only 18 patients met the study inclusion criteria.

This study could not demonstrate a significant impact of MIRE on circulation using TcPO₂ measurements, partly because of a lack of power related to the sample size and the unequal baseline distribution for this variable as a result of randomization. However, this finding was surprising, given claims of circulation increases up to 3,200% based on laser Doppler images.⁹¹ No participants improved to the literature-supported²⁹ threshold of 25 mm Hg difference for intra-week variation.

Additionally, 31 feet had TcPO₂ measurements (average of two dorsal sites) from pre- to posttest within ±11 mm Hg, with only eight feet varying more than 11 mm Hg between pre- and posttest measurements. Three of the eight feet had TcPO₂ change scores of 11.5 mm Hg; thus, only five feet varied more than 11.5 mm Hg. These findings are consistent with TcPO₂ reliability studies⁹⁶,²⁶ reporting repeated measurements in shorter time frames and indicate the observed change was a normal variation of TcPO₂ testing (±11 mm Hg) instead of a treatment effect. These scores may further support the use of TcPO₂ testing as a measure of perfusion over time.

Implications

This study demonstrated no statistically significant treatment effect for MIRE compared to sham on a small group of persons with diabetes who served as their own controls. This study calls into question results of previous studies that demonstrate significantly improved sensation with MIRE treatments. In this study, significant improvements in sensation were observed in both the sham and active treatment group but no differences were found between the two treatment groups on any of the outcome measures studied. This is not to say that MIRE is completely ineffective; as described in the literature review, previous research has demonstrated restored protective sensation.¹²,₂₁,₂₈,₂₉

Because no other modality or intervention has been reported in the literature to restore protective sensation in the same manner, this remains an interesting and valuable avenue for future research. For now, clinicians using MIRE should be aware that the evidence supporting restored sensation may not be as strong as previously reported.

Recommendations

To answer some of the remaining questions surrounding the effectiveness of MIRE, this study should be repeated using a larger sample size and with patients who do not serve as their own control. Including more objective measurements of nerve response, such as current perception threshold, also would be valuable.

Observed improvements in both the active and sham groups warrants further research because it may have a physiological basis or represent a Hawthorne or placebo effect. Studies that continue to use patients as their own control could help determine if a more general physiological effect to the contralateral limb occurs. Additionally, it would be interesting to assess if any other modality — eg, transcutaneous electrical nerve stimulation (TENS) — has the ability to alter sensation in persons with diabetes and LOPS.
Conclusion
A randomized, double-blind, quasi-experimental random controlled trial design attempted to address many variables lacking in previous studies in order to examine the treatment effects of MIRE on TcPO₂, sensation, and pain compared to sham treatment on the feet of adults with diabetes and LOPS. This small, 18-person study was unable to demonstrate a treatment effect for MIRE on these outcomes. More research using larger sample sizes is needed to determine the treatment effects of MIRE on circulation, sensation, and pain in adults with diabetes and LOPS.

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