Improved Sensitivity in Patients with Peripheral Neuropathy

Effects of Monochromatic Infrared Photo Energy

Salvatore L. DeLellis, DPM*
Dale H. Carnegie, DPM†
Thomas J. Burke, PhD‡

The medical records of 1,047 patients (mean age, 73 years) with established peripheral neuropathy were examined to determine whether treatment with monochromatic infrared photo energy was associated with increased foot sensitivity to the 5.07 Semmes-Weinstein monofilament. The peripheral neuropathy in 790 of these patients (75%) was due to diabetes mellitus. Before treatment with monochromatic infrared photo energy, of the ten tested sites (five on each foot), a mean ± SD of 7.9 ± 2.4 sites were insensitive to the 5.07 Semmes-Weinstein monofilament, and 1,033 patients exhibited loss of protective sensation. After treatment, the mean ± SD number of insensate sites on both feet was 2.3 ± 2.4, an improvement of 71%. Only 453 of 1,033 patients (43.9%) continued to have loss of protective sensation after treatment. Therefore, monochromatic infrared photo energy treatment seems to be associated with significant clinical improvement in foot sensation in patients, primarily Medicare aged, with peripheral neuropathy. Because insensitivity to the 5.07 Semmes-Weinstein monofilament has been reported to be a major risk factor for diabetic foot wounds, the use of monochromatic infrared photo energy may be associated with a reduced incidence of diabetic foot wounds and amputations. (J Am Podiatr Med Assoc 95(2): 143-147, 2005)

Diabetes mellitus affects more than 15% of the US population older than 65 years.[1] The direct cost of this illness, which affects more than 17 million people, was recently estimated to be more than $91 billion annually, with more than half of this spent on those older than 65 years.[2] Lower-extremity foot wounds and amputations represent a significant portion of this cost.[3,4] Reductions in the incidence rates of these conditions to minimize the human and financial burden associated with diabetic foot wounds and amputations is one of the objectives of the US Surgeon General as stated in *Healthy People 2010*.[5]

Foot wounds are highly correlated with a loss of sensation in the lower extremities. Peripheral neuropathy is typically defined in a clinical setting as diminished sensation to the 5.07 Semmes-Weinstein monofilament in the foot. Recently, the Centers for Medicare and Medicaid Services determined that insensitivity to the 5.07 Semmes-Weinstein monofilament at two or more of five tested sites on either foot is considered to be loss of protective sensation and a localized illness of the foot.[6] Diabetic peripheral neuropathy is widely considered to be a very significant risk factor for diabetic foot wounds,[7] and lower-extremity ulcers occur much less frequently in diabetic patients who do not exhibit peripheral neuropathy.[8,9]

*Gulf Coast Foot, Ankle and Wound Center, Tarpon Springs, FL.

†Podiatric Service, Denver Health Medical Center, Denver, CO.

‡Research and Clinical Affairs, Anodyne Therapy LLC, Tampa, FL.

Corresponding author: Thomas J. Burke, PhD, Director of Research and Clinical Affairs, Anodyne Therapy LLC, 13570 Wright Cir, Tampa, FL 33626.

Until recently, no treatments have been effective in improving foot sensation after it has been compromised owing to peripheral neuropathy. As a result, physicians who treat these patients have only been able to determine those who are at high risk of lower-extremity ulcers and amputations and then to prescribe accommodative risk-reduction strategies, including patient education, frequent visits to their physicians, orthotic devices for off-loading, and diabetic shoes. Unfortunately, patient compliance has been less than exemplary, and these risk-reduction strategies have met with sporadic success.[10]

Even after using risk-reduction strategies, patients with diabetic peripheral neuropathy remain at higher risk of lower-extremity wounds than those without it. For example, Reiber et al,[10] in their evaluation of the effectiveness of diabetic shoes, reported that more than 93% of all foot wounds during the study occurred in patients with diabetic peripheral neuropathy. (The incidence of wounds in their study population was approximately 11%.)

Two recent studies[11, 12] suggest that at least temporary increases in foot sensitivity to the 5.07 Semmes-Weinstein monofilament can be documented following the application of monochromatic infrared photo energy (MIRE; Anodyne Therapy LLC, Tampa, Florida) to diabetic patients who presented to their health-care professionals with an already significant loss of protective sensation associated with diabetic peripheral neuropathy. Another study[13] of patients with peripheral neuropathy showed that use of MIRE was associated with an increase in sensory nerve function based on testing conducted with the Neurometer CPT sNCT (Neurotron Inc, Baltimore, Maryland). Although one of these studies was randomized, double blind, and placebo controlled[12] and another used double-blind neurophysiologic testing,[13] the sample sizes were comparatively small. The present article details the improved foot sensation after treatment with MIRE in 1,047 patients (790 with diabetes mellitus) for whom sensory data had been collected in the course of medical treatment.

Research Design and Methods

The insurance claims of two durable medical equipment suppliers that offer the Anodyne Therapy System (Anodyne Therapy LLC), a piece of durable medical equipment that delivers MIRE, were reviewed to obtain a list of patients who had been treated with MIRE in physicians' offices and therapy clinics throughout the United States. The suppliers removed all patient identifiers in the data prior to submitting them to the investigators for purposes of this review and analysis. The Anodyne Therapy System delivers MIRE through therapy pads, each containing 60 superluminous diodes (890 nm of near-infrared wavelength), which are attached to a control unit that pulses the MIRE at 292 times per second.[14]

Before providing the Anodyne Therapy System to patients, these suppliers had received signed Certificates of Medical Necessity and chart notes (including, in most cases, the baseline 5.07 Semmes-Weinstein monofilament sensitivity value) from the attending physicians. These data supported both a diagnosis of peripheral neuropathy before and objective improvement after the patient had received a course of MIRE.

The suppliers maintained a searchable database containing a record of all claims filed, including *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) coding of the underlying conditions for which the Anodyne Therapy System had been ordered by referring physicians. The database, excluding any patient identifiers, was sorted to obtain a list of all patients who had a diagnosis of peripheral neuropathy based on ICD-9-CM code 357. The list was then stratified to obtain a list of those with type 1 or type 2 diabetes mellitus using ICD-9-CM codes 250.61 and 250.62, respectively. The period of inquiry was February 1, 2002, to January 23, 2004, and 2,070 patients treated with MIRE satisfied these criteria. Medical professionals who diagnosed peripheral neuropathy in their patients had been provided with pretreatment and post-treatment case report forms, which included a template of each foot on which were indicated five plantar sites to be assessed with the 5.07 Semmes-Weinstein monofilament before and after the application of MIRE. The five sites on the case report form were those recommended for evaluation of foot insensitivity by the National Institute of Diabetes and Digestive Diseases in "Feet Can Last a Lifetime,"[15] which had been incorporated into Centers for Medicare and Medicaid Services Decision Memorandum CAG-00059 issued on October 17, 2001,[6] and subsequently adopted in Centers for Medicare and Medicaid Services Program Memorandum AB-02-042 dated April 1, 2002. The suppliers had further advised the health-care professionals of the method of undertaking the Semmes-Weinstein monofilament evaluation consistent with "Feet Can Last a Lifetime," which included a "two-alternative, forced-choice method of evaluation" that has been validated as the most reliable method to test sensory input.[16] The medical records on file with the suppliers included 1,047 patient records containing completed case report forms, as previously described, of bilateral foot sensitivity data for the 5.07 Semmes-Weinstein monofilament before and after MIRE treatment.

Statistical Analysis

The results were analyzed using the paired two-tailed *t*-test with a null hypothesis that there would be no change in sensitivity (either an increase or a decrease) to the 5.07 Semmes-Weinstein monofilament following use of MIRE. Significance was defined as $P < .05$.

Results

The mean age of the study population (513 men and 534 women) was 73 years (range, 51–93 years) (Table 1). A total of 790 patients were diagnosed as having diabetic peripheral neuropathy, and 257 patients were diagnosed as having peripheral neuropathy associated with other etiologies. The mean number of sites insensitive to the 5.07 Semmes-Weinstein monofilament (bilaterally; a maximum of ten sites for both feet) was 7.9 before treatment and 2.3 after treatment ($P < .0001$). Of 1,047 patients, 452 (43%) exhibited insensitivity to the 5.07 Semmes-Weinstein monofilament at all ten sites before treatment with MIRE. At the conclusion of the initial MIRE treatments, these patients experienced a mean ± SD decrease of 6.9 ± 2.7 sites insensitive to the 5.07 Semmes-Weinstein monofilament, a 69% reduction in their sensory impairment ($P < .0001$) (Table 2). A total of 580 patients experienced a restoration of protective sensation after treatment with MIRE. Restoration of protective sensation was defined as having less than two sites on both feet insensitive to the 5.07 Semmes-Weinstein monofilament after MIRE treatment (Table 2).

Discussion

Until recently, peripheral neuropathy, particularly that associated with diabetes mellitus, was thought to be progressive and irreversible. Recent studies,[11-13] conducted in relatively small populations, have shown that symptomatic peripheral neuropathy is reversible with MIRE treatment. The present study shows that improvement can occur in a larger study population (1,047 community-dwelling patients with peripheral neuropathy) treated in routine clinical practice.

Notably, more than half of the patients who were initially diagnosed as having loss of protective sensation (56.1%) obtained at least a temporary return of protective sensation. Those with the most severe peripheral neuropathy (all ten sites insensitive to the 5.07 Semmes-Weinstein monofilament) had a striking restoration of sensation.

Figure 1 shows the number of insensate sites before and after treatment in this group of patients. Before treatment with MIRE, most of the patients exhibited a loss of sensation at nine or ten sites, and 75% of all patients had documented loss of sensation at six or more sites. After treatment, 50% of patients were insensate at none or only one or two sites and 75% were insensate at less than four sites. The change in distribution of insensitivity graphically demonstrates the MIRE treatment effect in this patient population.

The results of this analysis demonstrate that sensory loss associated with peripheral neuropathy, even when it has advanced to and beyond loss of protective sensation, is not necessarily irreversible. Moreover, most of these patients experienced a significant

Table 1. Demographic Characteristics of 1,047 Patients with Established Peripheral Neuropathy

	Value
Sex (No. [%])	
M	513 (49)
F	534 (51)
Diabetic peripheral neuropathy (No. [%])	790 (75)
Nondiabetic peripheral neuropathy (peripheral neuropathy associated with other etiologies) (No. [%])	257 (25)
Age (mean ± SD) (years)	73 ± 8.3
Insensate sites (mean ± SD) (No.)	7.9 ± 2.4

Table 2. Foot Sensitivity to the 5.07 Semmes-Weinstein Monofilament Before and After Treatment

	Value
All patients (No.)	1,047
Pretreatment insensate sites (mean ± SD) (No.)	7.9 ± 2.4
Post-treatment insensate sites (mean ± SD) (No.)	2.3 ± 2.4[a]
Decrease in insensate sites (mean ± SD) (No.)	5.6 ± 2.7[a]
Pretreatment patients with LOPS (No. [%])	1,033 (98.7)
Post-treatment patients who regained protective sensation (No. [%])	580 (56.1)
Post-treatment patients with LOPS (No. [%])	453 (43.9)
Pretreatment patients with all 10 sites insensate (No. [%])	452 (43)
Post-treatment insensate sites (mean ± SD) (No.)	3.1 ± 2.7[a]
Decrease in insensate sites (mean ± SD) (No.)	6.9 ± 2.7[a]

Abbreviation: LOPS, loss of protective sensation.
[a]$P < .0001$.

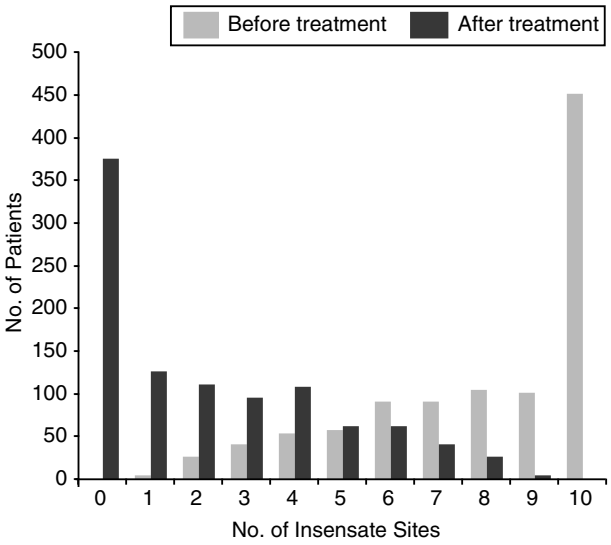

Figure 1. Number of patients with sites (on both feet) insensate to the 5.07 Semmes-Weinstein monofilament before and after treatment.

response to MIRE treatment. Improvement in sensation seems to occur even in patients with totally insensate feet (inability to sense the 5.07 Semmes-Weinstein monofilament at all tested sites). Because diabetic peripheral neuropathy is commonly associated with lower-extremity wounds and amputations as well as falls among people with diabetes mellitus, the sensory improvement reported in this study may also be associated with a decrease in these peripheral neuropathy–associated comorbidities. In fact, a reduced incidence of wounds has been reported in patients who have received nerve decompression surgery that resulted in improved sensory nerve function.[17] If additional studies support a relationship between improvement in sensory nerve function and a decreased incidence of wounds or falls (ie, peripheral neuropathy–attributable comorbidities), then interventions designed to improve this condition might offer significant benefit to these patients as well as a cost savings to the US health-care system.[3,4]

These observations and the conclusions derived must be analyzed in the context of certain limitations of the study design. For example, there was no control group against which the results of this study were measured. However, when a disease such as diabetic peripheral neuropathy is known to be progressive and irreversible, the use of historical controls from the published literature may be appropriate.[18] In the case of diabetic peripheral neuropathy, there have been no reports of either spontaneous reversal of this condition or efficacy of any nonsurgical intervention. Furthermore, these data were obtained from the records of patients who exhibited some improvement in their neuropathic symptoms. The data do not suggest that patients, before MIRE treatment, were early in their course of peripheral neuropathy or that they had a mild form of this condition. Rather, a significant proportion of patients, more than 75%, had well-defined peripheral neuropathy, a condition that would be the least likely to spontaneously reverse or to respond to pharmacologic treatment. However, we acknowledge that we cannot generalize these results to all patients with peripheral neuropathy. Clearly, there may be some patients who would not respond to MIRE treatment. Thus we conclude only that these 1,047 patients obtained objective improvement in foot sensitivity to the 5.07 Semmes-Weinstein monofilament after treatment with MIRE.

We also cannot totally discount physician or therapist bias, because the 5.07 Semmes-Weinstein monofilament, although objective, is only a patient-blinded test. These studies were initiated in February 2002, approximately 4 months after Medicare Decision Memorandum CAG-00059[6] was issued and all healthcare providers had been made aware of its implications for their patients by the suppliers and relevant professional associations. In addition, all of the patients knew that they were receiving active treatment. However, it is unlikely that the more than 300 evaluators systematically misinterpreted the sensitivity to the 5.07 Semmes-Weinstein monofilament before and after MIRE treatment.

The 5.07 Semmes-Weinstein monofilament is the most widely used testing method to clinically measure the existence of loss of protective sensation resulting from diabetes mellitus and to implement strategies to prevent foot ulceration and amputation. Mayfield and Sugarman[19] reported sensitivity of 85% to 100% and specificity of 34% to 100% depending on the number of sites tested and the testing method. In addition, Semmes-Weinstein monofilament testing has been reported to correlate with abnormal nerve conduction velocity testing, particularly as the extent of nerve impairment progresses.[20] However, the accuracy of this test depends on the method of testing and the achievement of maximal response from an alert and cooperative patient.[19] To maximize the validity of the test results, those performing Semmes-Weinstein monofilament testing were given case report forms adapted from "Feet Can Last a Lifetime,"[15] which recommends measuring five sites on the plantar aspect of the foot. In addition, these individuals were reminded to use the testing protocol contained in that publication, which is a two-alternative, forced-choice testing method that has been reported to minimize

patient bias.[16] Furthermore, this technique includes random testing sites on the feet and the avoidance of heavily callused and active wound sites.

Bias on the part of the evaluators should have been further minimized because none of the results were obtained with the goal of publishing the outcomes, which on analysis are consistent with recent published reports, one of which included randomization and double blinding.[11-13] Last, no multivariate analysis of these data was possible because this was a postmarket analysis of the efficacy of MIRE treatment. Because there are no known treatments for diabetic peripheral neuropathy in particular or for peripheral neuropathy in general, we cannot envision other variables that might have affected these outcomes.

Conclusion

Treatment with MIRE was associated with improved foot sensation to the 5.07 Semmes-Weinstein monofilament in a cohort of 1,047 patients initially diagnosed as having peripheral neuropathy. The extent of this improvement was substantial, even in patients with advanced loss of protective sensation. Because loss of protective sensation has been reported to be a major risk factor for diabetic foot wounds, an improvement in foot sensitivity obtained through the use of MIRE may also be associated with a reduced incidence of diabetic foot wounds and its sequelae, such as amputations.

Acknowledgment. More than 300 physicians and therapists who first documented peripheral neuropathy in their patients and then noted the improved sensation after treatment with MIRE. The detailed medical records supported their findings. Also, the staff of the two suppliers who worked with us to access their de-identified database and removed applicable patient identifiers from the records prior to our data review and analysis, and Amy Spirides, MBA, for assistance with the statistics and chart.

References

1. Harrington C, Zagari MJ, Corea J, et al: A cost analysis of diabetic lower-extremity ulcers. Diabetes Care **23:** 1333, 2000.
2. Hogan P, Dall T, Nikolov P: Economic costs of diabetes in the US in 2002. Diabetes Care **26:** 917, 2003.
3. Gordois A, Scuffham P, Shearer A, et al: The health care costs of peripheral neuropathy for people with diabetes in the U.S. Diabetes Care **26:** 1790, 2003.
4. Shearer A, Gordois A, Scuffham P, et al: Predicted costs and outcomes from reduced vibration detection in people with diabetes in the U.S. Diabetes Care **26:** 2305, 2003.
5. US Department of Health and Human Services: *Healthy People 2010*, 2nd Ed, US Government Printing Office, Washington, DC, November 2000.
6. Centers for Medicare and Medicaid Services: *Decision Memorandum for Diabetic Peripheral Neuropathy with Loss of Protective Sensation (LOPS) (CAG-00059)*, Centers for Medicare and Medicaid Services, Baltimore, October 2001.
7. Bild DE, Selby JV, Sinnock JA: Lower extremity amputation in people with diabetes: epidemiology and prevention. Diabetes Care **12:** 24, 1989.
8. Gibbons GW, Marcaccio EJ, Habershaw GM: "Management of the Diabetic Foot," in *Vascular Surgery: Theory and Practice*, ed by AD Callow, CBN Ernst, p 167, Appleton & Lange, Stamford, CT, 1995.
9. Pham T, Rich J, Veves A: Wound healing in diabetic foot ulceration: a review and commentary. Wounds **12:** 79, 2002.
10. Reiber GE, Smith DG, Wallace C, et al: Effect of therapeutic footwear on foot reulceration in patients with diabetes: a randomized controlled trial. JAMA **287:** 2552, 2002.
11. Kochman AB, Carnegie DH, Burke TJ: Symptomatic reversal of peripheral neuropathy in patients with diabetes. JAPMA **92:** 125, 2002.
12. Leonard DR, Farooqi MH, Myers S: Restoration of sensation, reduced pain, and improved balance in subjects with diabetic peripheral neuropathy. Diabetes Care **27:** 168, 2004.
13. Prendergast JJ, Miranda G, Sanchez M: Reduced sensory impairment in patients with peripheral neuropathy. Endocr Pract **10:** 24, 2004.
14. Burke TJ: Questions—and answers—about MIRE treatment. Adv Skin Wound Care **16:** 369, 2003.
15. Feet Can Last a Lifetime. Available at: http://www.ndep.nih.gov/diabetes/pubs/Feet_HCGuide.pdf. Accessed April 8, 2004.
16. Sekuler R, Nash D, Armstrong R: Sensitive, objective procedure for evaluating response to light touch. Neurology **23:** 1282, 1973.
17. Dellon AL: Preventing foot ulceration and amputation by decompressing peripheral nerves in patients with diabetic neuropathy. Ostomy Wound Manage **48:** 36, 2002.
18. Sima AA, Laudio C: Design of controlled clinical trials for diabetic peripheral polyneuropathy. Semin Neurol **16:** 187, 1996.
19. Mayfield JA, Sugarman JR: The use of the Semmes-Weinstein monofilament and other threshold tests for preventing foot ulceration and amputation in persons with diabetes. J Fam Pract **49:** S17, 2000.
20. Perkins BA, Olaleye D, Zinman B, et al: Simple screening tests for peripheral neuropathy in the diabetes clinic. Diabetes Care **24:** 250, 2001.