Restoration of Sensation, Reduced Pain, and Improved Balance in Subjects With Diabetic Peripheral Neuropathy

A double-blind, randomized, placebo-controlled study with monochromatic near-infrared treatment

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OBJECTIVE — Diabetic peripheral neuropathy (DPN) has been thought to be progressive and irreversible. Recently, symptomatic reversal of DPN was reported after treatments with a near-infrared medical device, the Anodyne Therapy System (ATS). However, the study was not controlled nor was the investigator blinded. We initiated this study to determine whether treatments with the ATS would decrease pain and/or improve sensation diminished due to DPN under a sham-controlled, double-blind protocol.

RESEARCH DESIGN AND METHODS — Tests involved the use of the 5.07 and 6.65 Semmes Weinstein monofilament (SWM) and a modified Michigan Neuropathy Screening Instrument (MNSI). Twenty-seven patients, nine of whom were insensitive to the 6.65 SWM and 18 who were sensitive to this filament but insensitive to the 5.07 SWM, were studied. Each lower extremity was treated for 2 weeks with sham or active ATS, and then both received active treatments for an additional 2 weeks.

RESULTS — The group of 18 patients who could sense the 6.65 SWM but were insensitive to the 5.07 SWM at baseline obtained a significant decrease in the number of sites insensate after both 6 and 12 active treatments ($P < 0.02$ and 0.001). Sham treatments did not improve sensitivity to the SWM, but subsequent active treatments did ($P < 0.002$). The MNSI measures of neuropathic symptoms decreased significantly (from 4.7 to 3.1; $P < 0.001$). Pain reported on the 10-point visual analog scale decreased progressively from 4.2 at entry to 3.2 after 6 treatments and to 2.3 after 12 treatments (both $P < 0.03$). At entry, 90% of subjects reported substantial balance impairment; after treatment, this decreased to 17%. However, among the group of nine patients with greater sensory impairment measured by insensitivity to the 6.65 SWM at baseline, improvements in sensation, neuropathic symptoms, and pain reduction were not significant.

CONCLUSIONS — ATS treatments improve sensation in the feet of subjects with DPN, improve balance, and reduce pain.

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Diabetic peripheral neuropathy (DPN) is relatively common complication of long-term diabetes (1) and is thought to be progressive and irreversible (2). DPN may be characterized by perceived numbness and diminished sensation and/or pain (3). Diminished sensation associated with DPN presents a significant risk factor for subsequent diabetic ulcers and nontraumatic amputations (4,5) as well as for falls among the elderly (6). As such, DPN presents both a substantial economic cost to the health care system and potentially debilitating consequences for those affected.

Current medical treatment algorithms stress the importance of delaying the onset of DPN through excellent blood glucose control (7). After the onset of DPN resulting in diminished sensation, medical management focuses on the implementation of secondary measures for prevention of foot wounds and amputations such as intensive foot-care education and periodic professional foot evaluations (8). Extensive research into likely pharmacological agents designed to either delay the onset of DPN or reverse mild to moderate symptoms after onset is ongoing. Whereas there are encouraging reports (9), a satisfactory pharmacological treatment option has yet to present itself.

Recently, symptomatic reversal of DPN was reported (9) with the use of a noninvasive medical device, the Anodyne Therapy System (ATS). Although the reported results were quite significant, the study was not controlled nor was the investigator blinded. We initiated this study to determine whether treatments with the ATS would improve sensation diminished due to DPN under a sham-controlled, double-blind protocol.

RESEARCH DESIGN AND METHODS

— Twenty-seven subjects met entry requirements for this institutional review board–approved study and completed the treatment protocol. To be eligible, all subjects were required to exhibit a diagnosis of either type 1 or type 2 diabetes and a diagnosis of peripheral neuropathy based on patient history and physical examination. Additionally, all subjects had to be insensate to the 5.07

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Abbreviations: ATS, Anodyne Therapy System; DPN, diabetic peripheral neuropathy; LOPS, loss of protective sensation; MNSI, Michigan Neuropathy Screening Instrument; SWM, Semmes Weinstein monofilament; VAS, visual analog scale.
A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Semmes Weinstein monofilament (SWM) on at least two of five test sites on the plantar surface of both feet (great toe, fourth toe, and three sites on the metatarsal area), indicative of their having established DPN and loss of protective sensation (LOPS). All subjects were also subjected to additional testing with the 6.65 SWM to further quantify the extent of their sensory loss. Subjects were excluded if they exhibited uncontrolled hypertension, prior history of knee or back surgery, active malignancy, or were pregnant or likely to become pregnant.

Evaluation measures

The primary endpoint in this study was observed change in sensitivity to the SWM 5.07 at the five tested sites. Secondary measures were changes in patient response to a modified Michigan Neuropathy Screening Instrument (MNSI) patient questionnaire and a physician foot examination (10).

The SWM tests were conducted by pressing the monofilaments at the five testing locations in random fashion avoiding heavily callused areas. With the subjects blindfolded, the monofilaments were pressed against the skin at each location until they bent and held in place for 1–2 s. The subjects were asked to respond "yes" if they felt the monofilament and further asked to describe the location on the foot where they sensed the monofilament. The same physician conducted all tests done with each subject to avoid interobserver bias.

The MNSI questionnaire provides a graded patient response of neuropathic symptoms. In general, a higher score represents more neuropathic symptoms. For purposes of this study, we omitted the questions "Have you ever been advised that you have neuropathy" and "Have you ever had an amputation," because the inclusion criteria included a diagnosis of neuropathy and ambulatory status. Thus, the maximum possible score was 11. To determine variation in subject response to active and sham treatment, the questionnaire was modified to elicit responses for both the left and right leg. Because those with diminished sensation associated with DPN often exhibit balance impairment (6), we added a question "Do you ever feel off balance or feel like you are going to fall?" Lastly, we asked the subjects to rate their pain level on a 10-point visual analog scale (VAS).

The MNSI physical examination is a graded clinical examination of the *1*) appearance of the foot as being normal or abnormal, *2*) presence or absence of foot ulceration, *3*) ankle reflexes as being either present, present with reinforcement, or absent, *4*) semiquantitative vibration perception of the great toe to a 128-Hz tuning fork as being either present, reduced, or absent, and *5*) light touch sensation of the great toe to the SWM 5.07 monofilament. The evaluation of the great toe with the SMW 5.07 was omitted from the clinical examination portion because a more thorough examination of five points on the plantar aspect of the foot was already documented in each subject.

Treatments were administered with the ATS Model 480, supplied for this study by its manufacturer (Anodyne Therapy, Tampa, FL). The ATS is a medical device consisting of a base power unit and therapy pads containing 60 near-infrared (890 nm) gallium aluminum arsinide diodes used to increase circulation by dilating arteries and veins. Inactivating the diodes so that no near-infrared photo energy was emitted and inserting heaters preset at 37°C created sham devices of identical appearance. Thus, neither the investigators nor the subjects could discriminate active from sham devices either visually or by temperature. Active versus inactive therapy pads were marked as A and B during the placebo phase of this study with only the manufacturer knowing active from sham. Active ATS units were preset to deliver 1.3 $J \cdot cm^{-2} \cdot min^{-1}$ of photo energy. Sham devices delivered only warmth at 37°C and no photo energy.

Treatment protocol

All subjects initially received treatment with both active and sham ATS therapy pads at our clinic three times per week for 40 min each visit for 2 weeks (six treatments) as described below. This was followed by six active treatments of the same duration administered to both limbs during the following 2 weeks. During each of the 12 40-min treatments, four ATS diode therapy pads were placed on each lower limb as follows: one on the top and one on the bottom of the foot and one on each side of the calf just above the ankle. Subjects were randomized so that irrespective of the degree of impairment in sensation noted at initial SWM evaluation, one lower limb received a sham treatment and the other an active treatment for the first six 40-min sessions. Sham-controlled treatments were administered only during the first 2 weeks of the protocol, because the results of a previously reported study (9) showed that a measurable change in sensitivity to the 5.07 SWM could be expected with this treatment protocol. Furthermore, we believed that extending the protocol to 1 month to deliver 12 sham treatments would have adversely affected recruitment and retention of subjects in this study. Fourteen of the subjects received initial active treatments on the left leg and the remainder on the right leg, and sham treatments were simultaneously given on the opposite leg. Neither the clinical staff nor the subjects knew which leg was receiving the active treatment. Patients returned to the clinic 3 days after the sixth treatment, were retested with the SWM, and then both limbs received the first of a series of six active treatments.

Thus, SWM testing, patient questionnaires, and physical examinations were conducted before entry into the study, just before initiation of the seventh treatment session (i.e., 3 days after completing the sixth treatment), and within 3 days after completing the twelfth treatment session, on each lower extremity.

Statistics

Data were analyzed by paired and unpaired Student's *t* test where appropriate and by repeated measures with a null hypothesis that treatments would have no effect on either *1*) increasing the number of sites sensitive to the 5.07 SWM, *2*) the numerical score on the MNSI questionnaire, *3*) physician foot examination, or *4*) self-reported pain. Significance was accepted when $P < 0.05$. The statistical package StatView from Abacus Concepts (Berkley, CA) was used. Values are expressed as mean ± 1 SD.

RESULTS — The 27 subjects who were insensitive to the SWM 5.07 were stratified into two groups (group 1 and group 2) based on their ability to sense the SWM 6.65. Group 1, consisting of 18 subjects, was able to sense the SWM 6.65 at all tested sites. Group 2, consisting of nine subjects, was unable to sense the SWM 6.65, which requires 30 times the bending force of the SWM 5.07, at no less than one tested site. Thus, group 2 subjects presented with a more profound level of sensory impairment than those in

Table 1—*Subject characteristics at initial evaluation (pretreatment)*

Subject no.	Age (years)	Sex	Weight (lbs)	Type	Duration (years)
Group 1*	61 ± 12		212 ± 35		
1	62	F	207	2	10
2	58	F	151	1	33
3	57	M	234	2	30
4	78	M	219	2	9
5	52	F	251	2	22
6	70	M	220	2	4
7	62	M	225	2	7
8	41	M	297	2	5
9	61	M	260	2	2
10	69	M	180	2	12
11	48	M	235	2	9
12	48	F	190	1	38
13	70	F	198	2	5
14	35	M	200	2	3
15	61	F	190	2	2
16	67	M	215	2	3
17	82	M	173	2	4
18	72	M	200	2	2
Group 2*	64 ± 9		218 ± 38		
1	75	M	275	2	5
2	76	F	176	2	15
3	53	M	250	2	30
4	68	F	162	2	7
5	67	M	215	2	5
6	48	M	211	2	1
7	67	M	193	2	30
8	66	M	225	2	6
9	60	M	260	2	2

*Data are means ± SD.

group 1. Other than for the level of sensory impairment, the subjects in these two groups were substantially homogenous in terms of age, sex, and weight.

Subject demographics (Table 1)

Average age of the subjects was 61 ± 12 years in group 1 and 64 ± 9 years in group 2 (NS). All but 2 of the 27 subjects had type 2 diabetes.

SWM (Table 2)

Group 1 subjects. At initial evaluation, there was no difference in sensitivity to the 5.07 SWM between the feet that initially received active treatments and the feet that received sham treatment for the first six sessions (NS). Six active treatments with the ATS reduced the number of sites insensitive to the SWM 5.07 ($P < 0.02$ vs. baseline), but the foot treated with the sham diodes did not demonstrate a significant decrease (NS). Six additional active treatments (12 active treatments total) resulted in a further improvement in sensation as the ability to detect the 5.07 SWM increased significantly ($P < 0.001$ vs. baseline). Six active treatments administered after initial sham treatments resulted in improved SWM 5.07 sensitivity ($P < 0.002$ vs. baseline).

Group 2 subjects. At initial evaluation, group 2 subjects exhibited profound diminished sensation, as evidenced by both the inability to sense the SWM 6.65 at one or more sites and by the average number of sites insensitive to the SWM 5.07 compared with group 1 subjects (Table 2). Neither 6 nor 12 active treatments significantly decreased the number of sites insensate to the SWM 5.07. After the initial 6 active treatments and after 12 treatments, no sites became sensitive to the 5.07 SWM (NS versus baseline). Likewise, among group 2 patients, sham treatment did not significantly affect sensitivity to the SWM 5.07 (Table 2).

MNSI patient questionnaire (Table 3)

Group 1 subjects. At initial evaluation, there was no difference to the modified MNSI patient questionnaire score (maximum 11) for the foot that initially received active treatments (4.7 ± 1.8) as compared with sham treatments (4.7 ± 1.9) (NS). Six active treatments resulted in a reduction of the MNSI score ($P = 0.0001$ vs. baseline). Six additional treatments with active diodes resulted in a further reduction in the MNSI score ($P < 0.05$ vs. baseline). There was also a statis-

Table 2—*Number of sites on the plantar surface of the foot that were insensate to SWM 5.07 (10 g) before (baseline) and after 6 and 12 ATS treatments (active diodes versus placebo)*

Baseline	After 6 treatments	After 12 treatments
Group 1 (sensate to 6.65 SWM)		
3.5 ± 1.0	2.4 ± 1.5 (with active diodes) $P < 0.02$	1.9 ± 1.7 (active diodes) $P < 0.001$
3.6 ± 1.1	3.0 ± 1.5 (sham diodes) (NS) $P < 0.09$	2.3 ± 1.8 (active diodes) $P < 0.002$
Group 2 (insensate to 6.65 SWM)		
4.7 ± 0.5	4.0 ± 1.7 (with active diodes) (NS) $P = 0.21$	3.7 ± 1.7 (active diodes) (NS) $P = 0.10$
4.4 ± 0.7	4.0 ± 1.7 (sham diodes) (NS) $P = 0.27$	3.9 ± 1.7 (active diodes) (NS) $P = 0.28$

Data are means ± SD. Five sites were tested on each foot. *P* values are compared with baseline in that limb. All subjects completed 12 treatment sessions with either active or sham diode arrays. In group 1 ($n = 18$), these 18 subjects were insensate to the 10-g, 5.07 SWM but were sensate to the 6.65 SWM. In group 2 ($n = 9$), these nine subjects were insensate to the 5.07 and were also insensate to the 6.65 SWM at one or more sites on the foot.

Table 3—*MNSI scores before and after 6 and 12 treatments with the ATS*

	Baseline	After 6 treatments	After 12 treatments
MNSI questionnaire scores (maximum 11)			
Group 1 (n = 18)			
Active diodes	4.7 ± 1.8	3.5 ± 1.7 ($P < 0.0001$)	3.2 ± 1.5 ($P < 0.001$)
Sham diodes	4.7 ± 1.9	3.8 ± 1.5 ($P < 0.01$)	3.7* ± 1.9 ($P < 0.05$)
Group 2 (n = 9)			
Active diodes	3.7 ± 1.4	3.0 ± 1.6 (NS)	3.0 ± 1.3 (NS)
Sham diodes	3.6 ± 1.6	3.3 ± 1.5 (NS)	3.1* ± 1.4 (NS)
MNSI foot examination scores (maximum 4)			
Group 1 (n = 18)			
Active diodes	1.5 ± 0.5	1.4 ± 0.7 (NS)	1.3 ± 0.6 (NS)
Sham diodes	1.6 ± 0.5	1.3 ± 0.7 (NS)	1.3* ± 0.6 (NS)
Group 2 (n = 9)			
Active diodes	2.1 ± 0.7	1.9 ± 0.6 (NS)	1.8 ± 0.6 (NS)
Sham diodes	2.1 ± 0.7	1.9 ± 0.6 (NS)	1.8* ± 0.6 (NS)

Data are means ± SD. Sham treatments (sham diodes) for the first 6 sessions were followed by treatment with active diodes for sessions 7 through 12. *These feet received active ATS treatments for sessions 7 through 12.

tically significant decrease in the MNSI after six sham treatments ($P < 0.01$ vs. baseline). The "sham" foot, treated for the final six sessions with active diodes demonstrated a reduction in the MNSI score ($P < 0.05$ vs. baseline).

Group 2 subjects. Treatment with active diodes for six sessions did not result in a statistically significant decrease in the MNSI (NS versus baseline) nor did six additional treatments with active diodes (NS versus baseline). There was no statistically significant decrease in the MNSI score after six sham treatments (both values are NS versus baseline).

Foot examination (Table 3)

Group 1 subjects. At baseline examination, only 2 of the 18 group 1 subjects had feet with an abnormal appearance (dry skin or Charcot), and only one had an ulcer. Thus, reported abnormalities, if any, in the foot examination would be due mainly to changes in either ankle reflexes or semiquantitative vibratory sensation. Foot examination score did not significantly change with either 6 or 12 active treatments. Likewise, the foot examination did not change significantly with either six sham treatments or the subsequent administration of six active treatments (both values are NS versus baseline).

Group 2 subjects. Foot examination score at initial evaluation for the group 2 subjects indicated more significant impairment compared with the group 1 subjects (Table 3). As in the group 1 subjects, there was no significant change in foot examination scores after either active or sham treatments.

Pain

Group 1 subjects. Overall self-reported pain (VAS) in the group 1 subjects, which was not reported by extremity, decreased from 4.2 ± 2.3 at baseline to 3.2 ± 1.9 after the first 6 treatments (i.e., active diodes on one leg and sham on the opposite leg; $P < 0.03$) and to 2.3 ± 1.7 after 12 treatments ($P < 0.0001$ vs. baseline).

Group 2 subjects. VAS in the group 2 subjects was much more variable than in group 1. Whereas self-reported pain decreased over the month-long trial, this was not statistically significant due to the wide variation in VAS and the small number of subjects. Pain averaged 4.2 ± 3.9 at baseline, 2.6 ± 2.3 after 6 treatments, and 2.00 ± 2.3 after 12 treatments (NS versus baseline for both 6 and 12 treatments).

Balance improvement

Group 1 subjects. The questionnaire required a yes or no response to the following question: "Do you feel off balance or feel like you are going to fall?" At initial evaluation, 16 of the 18 group 1 subjects (89%) answered this question affirmatively. After six treatments, only seven subjects answered affirmatively (39%), and after 12 treatments, only three subjects answered affirmatively (16.7%). After 12 treatments, balance impairment was no longer reported by 81% of the subjects.

Group 2 subjects. Most subjects (seven of nine; 78%) in group 2 also answered the balance impairment question affirmatively before the start of treatment. After six treatments, only four of nine subjects (44%) answered this question affirmatively. However, no further improvements were noted after 12 treatments as four of nine subjects continued report balance impairment. Thus, after both 6 and 12 treatments, self-reported balance impairment was no longer reported by 43% of the group 2 subjects.

CONCLUSIONS — The results of the present study demonstrate that treatments with near-infrared photo energy delivered in the manner specified in the study protocol resulted in a significant decrease in the average number of sites insensitive to the 5.07 SWM in diabetic subjects with LOPS who had not progressed to profound sensory loss, defined as their inability to detect a much larger monofilament (Table 2). After 12 such treatments, the average number of sites insensitive to the SWM 5.07 among subjects in group 1 decreased to less than two sites, representing almost a 50% improvement in sensation. Comparatively, six sham treatments did not significantly decrease the number of foot sites insensitive to the SWM 5.07, but statistically significant sensory improvement was noted when these feet later received six active treatments.

We did not observe a significant improvement in sites sensitive to the SWM 5.07 in those subjects (group 2) with LOPS who also presented with profound sensory loss, as characterized by their inability to detect a SWM 6.65 (300 g) at one or more tested sites after either active or sham treatment. There may have been some improvement in sensory perception of monofilaments, sized between 5.07 and 6.65, but we did not perform tests using intermediate-sized monofilaments in the context of this study.

DPN, as documented by the failure to sense a 5.07 SWM at two sites on either foot, is considered as LOPS and recognized as a "localized illness of the foot" (11). The present results suggest that ATS treatments in those subjects who had not progressed to

profound sensory loss, namely group 1, may result in at least a temporary restoration of protective sensation.

Subject response to the MNSI questionnaire showed that neuropathic symptoms decreased among those with LOPS (group 1) after 6 to 12 active treatments with the ATS. This was not the case in the group 2 subjects who exhibited profound sensory loss in addition to LOPS, even though they had lower self-reported neuropathic symptoms at entry. Based upon physician examinations, neither ankle reflexes nor vibratory sensitivity to a 128-Hz tuning fork significantly improved during the course of 12 active treatments with the ATS in either group 1 or group 2 subjects. Based on these data, we would tentatively conclude that administration of 12 ATS treatments only improves light touch sensation as measured by the SWM 5.07.

Self-reported pain (VAS) decreased significantly in group 1 subjects after both 6 and 12 treatments, but there was no significant reduction in the group 2 subjects after either 6 or 12 treatment sessions. Thus, 6 to 12 active treatments with ATS may be able to reduce pain but only in those whose DPN has not evolved to profound sensory loss. However, several of the subjects with profound sensory loss did self-report diminished pain during the course of the treatment protocol. Due to the limited number of subjects ($n = 9$), the pain response attenuation for the entire group did not reach statistical significance. Pain reduction might be significant among those with profound sensory loss if the sample was larger.

The only lifestyle change that we addressed was in subject-reported balance impairment. Both group 1 and group 2 subjects exhibited substantial improvement in self-reported balance after the initial six treatments (56.3 and 42.9%, respectively). No further improvement was reported among the group 2 subjects after 12 treatments, but group 1 subjects reported additional improvement (81% of subjects reporting improvement overall). The association between DPN and increased incidence of falls in diabetic subjects has been well documented (6). Although there are certainly factors other than DPN that contribute to falls, the improvement in balance may offer an opportunity for fall-related risk reduction in this population despite the severity of their sensory impairment before treatment.

This study did not include an examination of the biological mechanism through which the improvements in sensation demonstrated after treatment with ATS were obtained. Because both the active and placebo diode pads emit a comparable thermal effect, it is apparent that the results were not simply due to warmth.

The data obtained in this study are limited in some important respects. The 5.07 SWM, although validated and very widely used as a diagnostic tool, determines a gross measure of sensory loss in those with DPN. More discreet quantitative sensory tests would be helpful in determining the exact degree of sensory improvement experienced after the administration of ATS treatments (12). Furthermore, changes in pain and balance were only secondary endpoints in this study, and the study design did not permit us to measure pain reduction or balance improvement in active compared with sham treatment of individual limbs. An alternative study design that would evaluate subjects receiving either active or sham treatment on both limbs, rather than by extremity as in this study, would address this question. Additionally, objective measures of balance, such as the Tinetti Assessment Tool (13), would provide more objective data on actual improvements in gait and balance. Interestingly, a preliminary report showing improved Tinetti Assessment scores and a reduced risk of falling in elderly subjects treated with ATS was recently published (14). Lastly, the present study only evaluated treatment effect after 6 and 12 treatments and did not include analysis of the durability of ongoing treatment. However, the results of this study are so encouraging that we have obtained institutional review board approval to extend this study to include additional quantitative sensory tests and measures of durability.

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References

1. Carrington AL, Abbott CA, Griffiths J, Jackson N, Johnson SR, Kulkarni J, Van Ross ER, Boulton AJ: Peripheral vascular and nerve function associated with lower limb amputation in people with and without diabetes. *Clin Sci (Lond)* 101:261–266, 2001
2. Sima AA, Laudadio C: Design of controlled clinical trials for diabetic polyneuropathy. *Semin Neurol* 16:187–191, 1996
3. Valk GD, Grootenhuis PA, Bouter LM, Bertelsmann FW: Complaints of neuropathy related to the clinical and neurophysiological assessment of nerve function in patients with diabetes mellitus. *Diabetes Res Clin Pract* 26:29–34, 1994
4. Frykberg RG, Lavery LA, Pham H, Harvey L, Veves A: Role of neuropathy and high foot pressures in diabetic foot ulceration. *Diabetes Care* 21:1714–1719, 1998
5. Olmos PR, Cataland S, O'Dorisio TM, Casey CA, Smead WL, Simon SR: The Semmes-Weinstein monofilament as a potential predictor of foot ulceration in patients with noninsulin-dependent diabetes. *Am J Med Sci* 309:76–82, 1995
6. Conner-Kerr T, Templeton MS: Chronic fall risk among aged individuals with type 2 diabetes. *Ostomy Wound Manage* 48:28–35, 2002
7. Boulton AJ: Treatment of symptomatic diabetic neuropathy. *Diabetes Metab Res Rev* 19 (Suppl. 1):S16–S21, 2003
8. Perkins BA, Bril V: Diagnosis and management of diabetic neuropathy. *Curr Diab Rep* 2:495–500, 2002
9. Kochman AB, Carnegie DH, Burke TJ: Symptomatic reversal of peripheral neuropathy in patients with diabetes. *J Am Podiatr Med Assoc* 92:125–130, 2002
10. Michigan Neuropathy Screening Instrument, produced by the Michigan Diabetes Research and Training Center. Available from http://www.med.umich.edu/mdrtc/survey/index.html#mnsi. Accessed 1 March 2002
11. CMS Decision Memorandum: Medicare announces it's intention to expand foot care coverage for some beneficiaries with diabetes [article online], 2001. Available at http://cms.hhs.gov/media/press/release.asp?Counter=314. Accessed 29 January 2002
12. Freeman R, Chase KP, Risk MR: Quantitative sensory testing cannot differentiate simulated sensory loss from sensory neuropathy. *Neurology* 60:465–470, 2003
13. Tinetti ME: Clinical practice: preventing falls in elderly persons. *N Engl J Med* 348:42–49, 2003
14. Kochman AB: Risk of falls in elderly patients is markedly reduced through improvement in sensation, balance, and gait with monochromatic infrared photo energy and other physical therapy (Abstract). *J Geriatric Phys Therapy* 25:29, 2002