

Laser Therapy

Infrared Photo Energy May Reduce Neuropathic Pain

Near infrared light therapy, together with physical therapy, may be able to reduce pain in neuropathy patients and possibly reduce medication dosage levels of those undergoing drug therapy.



Diabetic neuropathy is a common health problem today which often poses a variety of clinical challenges. In this article, Dr. Thomas J. Burke reports on the results of a study utilizing phototherapy (non-coherent light therapy) on patients with neuropathies. This is an exciting paper and demonstrates the potential value of light therapy in these clinical conditions. There is a rapidly increasing body of evidence that is demonstrating the clinical value of using non laser light therapy for a wide variety of painful conditions.

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In a recent issue of *Practical Pain Management*, two papers discussed treatment of pain patients using FDA cleared alternative modalities referred to generically as light therapy.^{1,2} This paper describes the effects of light therapy on the pain accompanying neuropathy. Pain

is a common complaint of patients with peripheral neuropathy (PN) due to either diabetes or other causes and it often interferes with quality of life, irrespective of pharmaceutical intervention.³ For example, painful PN may be a complication from 1) chemotherapy drugs, 2) metabolic diseases such as hypothyroidism, 3) abuse of alcohol, 4) environmental toxins or drugs, 5) certain viral infections, 7) scar tissue formation following surgery, or 6) it may be idiopathic.⁴ There are only a few FDA approved drugs for the pain of PN. These drugs do not modify blood flow and, therefore, they do not correct microcirculatory defects that can, in some cases, contribute to ischemic, neuropathic pain. Some of the approved drugs have significant side effects that compromise quality of life.⁵ Beyond pharmacology, there has been some success—in carefully selected patients—in effecting significant neuropathic pain relief with surgical intervention to decrease nerve compression.⁶

An alternative to drugs or surgery—monochromatic infrared energy (MIRE™) along with concurrent physical therapy—has been reported to provide significant pain relief to patients presenting with neuropathic pain due to either diabetes or other etiologies.⁷⁻¹⁰ This report documents the reduction in neuropathic pain achieved with use of MIRE in 493 consecutive, mostly elderly, patients treated in health care facilities from the beginning of May 2006 to the end of June 2006. These patients also detailed their use (or lack thereof) of various drugs for neuropathic pain relief prior to and during MIRE treatment.

Materials and Methods

The medical history and clinical notes related to pain were included as part of insurance claims made by a durable medical equipment (DME) supplier offering the Anodyne® Therapy System (ATS; Anodyne Therapy LLC, Tampa, FL) that delivers MIRE at 890 nanometers from gallium aluminum arsenide diodes. The ATS has FDA 510k clearance for temporarily increasing circulation and reducing pain, stiffness, and muscle spasm.¹¹

The medical records and clinic notes provided by the health-care professionals included:

- a physician diagnosis of peripheral neuropathy associated with diabetes (diabetic peripheral neuropathy; DPN) or other etiologies (peripheral neuropathy-other; PNO),
- the level of pre-treatment neuropathic pain measured on an 11 point numeric pain rating scale (NPRS; 10 equating to maximum pain and zero (0) equating to no pain), and
- pain levels measured after MIRE treatment.

456 separate physicians attested to the accuracy of the medical data that they supplied to justify these insurance claims. MIRE was administered as part of a comprehensive care plan that also included individualized physical therapy for various gait and balance problems that occur quite frequently in patients with PN.¹² Shurman and colleagues recommend physical therapy, exercise and integrated techniques in their powerful tool, the Share The Risk Model, for managing patients with pain.¹³ However, it is often difficult for patients to begin or complete a therapy program if they are in constant, unremitting pain.

Patients were told to anticipate being treated with MIRE approximately 12 times, 30 min. each time, 3 times per week, for their pain. After completing outpatient therapy, 493 out of 550 patients agreed to provide answers to a health questionnaire. This was done under HIPPA protection assurances by the DME.

Table 1. Patient Demographics

Total Patients with PN	493	
Male	214	43%
Female	279	57%
Diabetic (DPN)	248	50%
Non-Diabetic	245	50%
Age (years) ^a	72 ± 8.4	Range (44-94)
Pre-Treatment Pain (10 max) ^a	6.9 ± 2.2	
a = mean ± SD PN = peripheral neuropathy DPN = diabetic peripheral neuropathy PNO = peripheral neuropathy from other causes		

Table 2. Changes in pain in response to MIRE treatment in DPN and PNO Patients

	All Patients	DPN	PNO
Number of Patients	493	248	245
Pre-Treatment Pain (10 max) ^a	6.9 ± 2.2	6.9 ± 2.2	6.9 ± 2.1
Post-Treatment Pain	2.5 ± 2.1 ^b	2.5 ± 2.4 ^b	2.5 ± 2.0 ^b
Mean Decrease in Pain	4.4 ± 2.3 ^b	4.4 ± 2.4 ^b	4.4 ± 2.1 ^b
a = mean ± SD b = p<0.0001 DPN = diabetic peripheral neuropathy PNO = peripheral neuropathy from other causes			

Furthermore, patients had signed HIPAA and informed consent documents in both the physician and therapist's office. Patient identifiers were removed prior to the analysis of the data. Patients answered the following questions: 1) the duration of the neuropathic pain, 2) which medications (if any) they were using prior to initiating MIRE, and 3) whether they had increased, decreased or changed medications or dosage during MIRE treatment.

The answers to the questionnaire were gathered over a 7-week period during the late spring of 2006. Neuropathic pain intensity—before and after MIRE—was determined separately for patients collected into four groups, as follows:

Group 1: Patients not utilizing medications for pain prior to and during MIRE treatments (n=129)

Group 2: Patients utilizing drug therapy prior to MIRE and were able to reduce their dosage by the completion of MIRE treatments (n=187)

Group 3: Patients utilizing drug therapy prior to MIRE and did not alter this

use during MIRE treatments (n=151)

Group 4: Patients utilizing one or more drugs prior to MIRE and either changed dosage or switched to a new medication, or both, prior to the conclusion of MIRE therapy (n=26).

Statistics

The pain outcome among the four treatment groups was analyzed by one-way ANOVA to test the null hypothesis that decreases in neuropathic pain would depend on pharmacologic interventions during the course of MIRE treatments. All values are reported as mean ± one standard deviation (SD). Significance was accepted if P<0.05.

Results

Mean age of the respondents (214 male, 279 female) was 72 years (see Table 1). 248 patients were diagnosed with DPN and 245 patients were diagnosed with PN associated with other etiologies (PNO). Mean pre-treatment neuropathic pain reported on an 11-point NPRS was 6.9 ±

2.2 with no difference between the DPN and PNO groups (see Table 2). Post-treatment pain averaged 2.5 ± 2.3, a 64% reduction; there was no significant difference in the decreased pain between the DPN and PNO groups (see Table 2). The average number of PT visits during which MIRE was also given was 15±8. At the initiation of MIRE therapy, 129 patients (26%) were not taking medications for their neuropathic pain, whereas 364 patients (74%) were taking one or more medications. As one would expect, based on the medical literature for neuropathic pain, drugs included anticonvulsants, antidepressants, and opiates. In 263 out of 364 patients (72%), more than one drug was being consumed. The most frequently used medication was the anticonvulsant gabapentin, with 197 patients (54%) using this pharmacologic agent.

Of the 364 patients who were taking medications for their neuropathic pain at initiation of MIRE therapy, 187 (51%) reported that they had reduced the use of medications during MIRE therapy, 151 (41%) reported that their use of medications was unchanged throughout therapy, and 26 (7%) reported either a change in medication, an increase in the dosage of one or more of the initial medications, or both, during MIRE therapy.

There were no significant differences in the pre-treatment pain levels, the post-treatment pain levels, or the extent of pain relief among these four groups, nor were there differences in the number of MIRE treatments given (Table 3). Questionnaire responses indicated that patients had experienced neuropathic pain, on average, for at least 3.5 – 4.5 years (Table 3). The actual duration of neuropathic pain may have been much longer because the maximum duration of pain entered as data for any one patient was input as 99 months even if it was longer. Those patients with 99 (or more months of neuropathic pain) made up the following percentages of each group:

- Group 1:** 20 of 129 patients (16%)
- Group 2:** 40 of 187 patients (21%)
- Group 3:** 44 of 151 patients (29%)
- Group 4:** 9 of 26 patients (35%)

Discussion

These data demonstrate that using MIRE in an outpatient setting is associated with a significant and strikingly similar decrease in neuropathic pain intensity in both diabetic and non-diabetic patients.

Table 3. Pain Response to MIRE is independent of medication usage.

	No Meds during MIRE	Decreased Meds	No Change in Meds	Changed Meds
	Group 1	Group 2	Group 3	Group 4
Patients (n)	129	187	151	26
Male	66	72	63	13
Female	63	115	88	13
Age (Range)	74(53-94)	72(44-90)	73(46-93)	69(54-94)
Duration of Neuropathic Pain (Months) ^a	41.5 ± 31.4	49.9 ± 32.9	54.3 ± 35.3	54.7 ± 38.8
Initial Pain ^a	6.7 ± 2.4	7.2 ± 1.9	6.7 ± 2.3	7.3 ± 1.9
Post Pain ^a	2.4 ± 2.2 ^b	2.5 ± 2.2 ^b	2.6 ± 2.0 ^b	2.6 ± 1.9 ^b
Mean Pain Decrease ^a	4.3 ± 2.5 ^b	4.7 ± 2.1 ^b	4.2 ± 2.3 ^b	4.7 ± 2.4 ^b
Number of Treatments ^a	15 ± 9.2	15 ± 8.2	16 ± 9.1	19 ± 8.9

a = mean ± SD. b = P<0.0001 vs. initial pain. Meds = medications. (n) = number of patients. Changed meds indicates either a different dose or a different medication, or both.

These outcomes are consistent with a growing body of clinical evidence showing MIRE is able to significantly decrease pain in diabetic and non-diabetic neuropathy patients.⁷⁻¹⁰

Perhaps more important, the decrease in pain intensity in response to MIRE combined with therapy was independent of concomitant use of medications that are typically used for neuropathic pain. Patients who were not taking drugs for their pain responded exactly like those patients who were taking medications at the initiation of the therapy. For those who were already taking drugs, the reduction in symptomatic pain was not related to either a continuation of current drug usage, to a reduction in drug use or to changes in either the dosage or class of medications consumed throughout the period of treatment. Indeed, 51% of patients achieved significant neuropathic pain reduction and were concomitantly able to decrease the dosage of medication(s) they had been taking at the initiation of MIRE therapy. The similar degree of pain mitigation was not due a difference in the number of treatments, age or gender, or the length of time the patients had been aware of neuropathic pain severe enough to cause them to seek medical attention.

Clearly, pharmacologic agents have been found to be effective in reducing pain in both diabetic and non-diabetic patients.¹⁴⁻¹⁷ However, as is the case with virtually all drugs, side effects may limit the patient tolerance. Side effects also become more evident with the use of higher drug doses that are often necessary when low doses are no longer effective or when patients report a waning effect. High drug doses often relieve pain but the quality of life may be adversely affected. The answers to the questionnaire revealed that a few patients were using some of the newer medications that had been approved recently by the FDA for the reduction of neuropathic pain. However the vast majority of patients were continuing to take gabapentin and/or antidepressants, which have been clinical mainstays for many years for the treatment of neuropathic pain. Therefore, the results of this post-marketing survey may not apply to patients who have begun to use newer drugs. MIRE has not been reported to

be associated with any systemic side effects. There have been a few reports of superficial burns when treatment guidelines were not followed.

Mechanism of Action

While the mechanism of action underlying neuropathic pain relief associated with MIRE is not well understood, it may be due, in part, to a combination of topical heat and an increased local release of nitric oxide that has been reported using this wavelength (890nm) of near infrared photo energy.^{18,19} The source of released nitric oxide may be endothelial cells or red blood cells, or both.^{20,21} Nitric oxide production is compromised in both type 1 and type 2 diabetic patients.²²⁻²⁴ If near infrared light is able to favorably alter local nitric oxide availability in the diabetic patient, this may improve microcirculation via an alteration of cGMP-mediated vasodilation at the site of treatment.²⁵ Better blood flow may, in part, explain the symptomatic decrease in pain these patients.

Nitric oxide also appears to be able to mitigate pain via a mechanism similar to morphine,²⁶ namely via nitric oxide mediated production of cGMP and phosphorylation of ATP-dependent potassium channel activity.²⁷ There may be a significant analgesic effect of MIRE if local concentrations of nitric oxide are increased. Nitric oxide was not measured in any patient during MIRE treatments.

Study Limitations

There are, of course, limitations to our conclusions. First, information about the use and types of medications is based solely upon patient response to a health questionnaire administered just after the conclusion of outpatient MIRE therapy. However, since patients self-administer medications for neuropathic pain based on perceived pain levels or physician prescription, we believe they were competent to accurately comment on the use of medications during the fairly brief period of MIRE therapy (6-7 weeks). Additionally, the health questionnaire was very specif-

ic. Patients were required to name the actual medications they were taking for neuropathic pain; this increased the likelihood of an accurate response.

Second, we cannot ascertain with absolute certainty whether the decrease in pain intensity in this group of patients was not due to a "placebo effect" since there was no control group using either placebo MIRE or no treatment at all. However, these patients experienced a mean reduction of 64% in their pain intensity during MIRE treatments, which is much greater than either any placebo effect in response to infrared therapy (less than a 20% decrease in pain) for neuropathic pain²⁸ or the pain reductions documented with placebo treatment during clinical trials of duloxetine hydrochloride (Cymbalta®) and pregabalin (Lyrica®), which have been approved by the FDA for the management of neuropathic pain.^{29,30} Furthermore, the magnitude of pain reduction among the present group of patients is consistent with other published reports on the effectiveness of MIRE for neuropathic pain.⁷⁻¹⁰

While our analysis permits us to conclude that the decrease in pain was not dependent on the concomitant use of medications (i.e., Group 1), we cannot exclude other possible variables that might have affected these outcomes. All patients received MIRE adjunctively as part of a plan of care that also included skilled therapies, if necessary, to improve balance and gait that are often complications of neuropathic pain.³¹ However, we can find no published information indicating that balance and gait related physical therapy interventions, in and of themselves, are effective for the reduction of neuropathic pain. Moreover, in each of the medical records, the 456 attending physicians certified that, in their medical judgment, the reductions in neuropathic pain were in direct response to the MIRE treatments. Finally, many patients—either those using no medications for their pain or those who were taking one or more pain relieving drugs—responded equally well to MIRE despite, in some cases, having experienced neuropathic pain for over 99 months. This suggests that the duration of neuropathy may not be a complicating factor in the effect of MIRE plus physical therapy to diminish neuropathic pain.

Conclusion

Based on these data, MIRE—adminis-

tered as part of a care plan prescribed by physicians—is associated with a substantial reduction in neuropathic pain. Use of MIRE may be an alternative for physicians to consider for patients with neuropathy, especially those who have obtained an unsatisfactory level of neuropathic pain relief while using various oral medications. MIRE might also be an alternative first line treatment in some patients with significant neuropathic pain who have not yet begun drug therapy. ■

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