
Effects of Ice Massage on Neuropathic Pain in Persons With AIDS

Kristin Kane Ownby, PhD, RN, ACRN, AOCN, CHPN

Peripheral neuropathic pain is a unique form of chronic pain that afflicts up to 50% of persons with AIDS. The purpose of this pilot study was to examine the effects of ice massage to reduce neuropathic pain and improve sleep quality and to determine the feasibility of a larger study. A repeated measures design was used. The three treatments consisted of ice massage, dry-towel massage, and presence. Consecutive sampling was used to select 33 persons with AIDS who had neuropathic pain. Although the results of the study were negative, there was a decrease in pain intensity over time with both the ice massage and towel massage, suggesting that the intervention has some clinical benefit.

Key words: *peripheral neuropathy, pain, ice massage*

Peripheral neuropathy occurs in 35% to 88% of persons with AIDS (PWA) and is a painful condition commonly affecting the soles and dorsa of the feet (Simpson et al., 2000). Despite the introduction of antiretroviral agents and highly active antiretroviral therapy, the incidence of distal symmetrical peripheral neuropathy remains unchanged (Schifitto et al., 2002). Distal symmetrical peripheral neuropathy causes a burning or tingling type of pain and is associated with depression, decreased quality of life, anxiety, and sleep disturbances (Meyer-Rosberg et al., 2001). Dealing with peripheral neuropathy is challenging because there is no known effective treatment, and pain management strategies often fail to provide satisfactory relief.

Current treatments for neuropathic pain that afford partial relief include the use of tricyclic antidepres-

sants and anticonvulsants (Kiebert et al., 1998; Shlay et al., 1998; Simpson et al., 2000). Nonpharmacologic interventions such as the application of heat or cold, massage, or acupuncture/acupressure augment pharmacologic treatment with few side effects and are easy to apply. This pilot study examines the effects of the nonpharmacologic treatment of massage, specifically that of ice massage, for the reduction of neuropathic pain and the improvement of sleep quality.

Background and Significance

Pain in PWA causes considerable disability and discomfort, with peripheral neuropathy being one of the most frequently reported pain syndromes. Distal symmetrical peripheral neuropathy is a common neurological complication of HIV infection that becomes more prevalent as the disease progresses (Schifitto et al., 2002).

Treatment Modalities for Distal Symmetrical Peripheral Neuropathy

To date, no specific therapy reverses the course of HIV-related distal symmetrical peripheral neuropathy, and numerous symptomatic therapies report limited success (Simpson et al., 2000). Therapeutic trials

Kristin Kane Ownby, PhD, RN, ACRN, AOCN, CHPN, is an assistant professor in the Department of Acute and Continuing Care, University of Texas Health Science Center School of Nursing, Houston.

reporting partial relief include the use of amitriptyline (Kiebert et al., 1998), mexiletine (Kemper, Kent, Burton, & Deresinski, 1998; Kiebert et al., 1998), peptide T (Simpson, Dorfman, Olney, et al., 1996), acupuncture (Shlay et al., 1998), topical capsaicin (Paice et al., 2000), and lamotrigine (Simpson et al., 2000).

The use of opioids to manage neuropathic pain remains controversial. A metaanalysis of randomized controlled trials reported significant efficacy of opioids over placebos for conditions such as diabetic neuropathy and postherpetic neuralgia (Eisenberg, McNicol, & Carr, 2005). A result important for the HIV population is that acute and chronic opioid administration is known to have an inhibitory effect on humoral and cellular immunity (Vallejo, de Leon-Casasola, & Benyamin, 2004).

Because pain is a complex, multidimensional phenomenon, analgesic medications alone may not adequately reduce it. Limited research exists that explores nonpharmacologic methods for chronic pain management. Although ice massage is a well-described physical modality, few studies focus on its effectiveness to manage peripheral neuropathic pain.

The mechanisms by which thermal therapies reduce pain are not well explained in literature. A hypothesis is that applying cold slows peripheral nerve conduction velocity and decreases nociceptive information transmitted centrally through primary afferent fibers to the spinal cord. As activity in dorsal horn neurons is decreased, transmission of nociceptive information to higher brain centers is reduced, resulting in decreased pain perception (Sluka, Hoeger, & Skyba, 2002).

Because of the paucity of research on ice massage for pain management, studies on cutaneous stimulation, which includes transcutaneous electrical nerve stimulation (TENS), were reviewed. Ma and Sluka (2001) demonstrated that TENS reduces central sensitization by decreasing the responsiveness of wide dynamic range neurons in the dorsal horn to innocuous and noxious stimuli.

In using nonpharmacologic modalities for managing peripheral pain, TENS has been studied extensively. Of 94 patients treated with TENS for 6 months, 53% showed a favorable response (Meyler, deJonste, & Rolf, 1994). In another study, 31 subjects with diabetes-related chronic neuropathic pain

were randomly selected to receive either TENS or a sham treatment. The subjects receiving TENS reported a greater reduction in pain ($p \leq .05$) than the control group (Kumar & Marshall, 1997). A study of TENS administered over a course of 4 weeks nightly to subjects with diabetes-related neuropathy reported a significant decrease in pain intensity ($p \leq .005$) from baseline to week 4 (Armstrong, Lavery, Fleischli, & Gilham, 1997). In a study in which amitriptyline alone was administered, 88% of subjects with diabetes-related neuropathy experienced partial to no relief after 4 weeks. Those responding to partial or no relief were then randomly assigned to a sham treatment or to TENS. The subjects given TENS ($N = 14$) experienced a significant reduction in pain intensity (Kumar, Alvaro, Julka, & Marshall, 1998). Because these studies suggest that TENS may be an effective adjunctive modality for the management of neuropathic pain, and if ice massage can be considered comparable to TENS (Melzack, Jeans, Stratford, & Monks, 1980), then ice massage may also provide benefits in reducing neuropathic pain.

Melzack et al. (1980) compared results of ice massage with TENS and reported that both treatment modalities were comparable in decreasing low back pain for approximately the same length of time, an average of 9 hours. In a study comparing the effectiveness of TENS, electroacupuncture, and ice massage against that of a placebo, Yurtkuran and Kocagil (1999) reported that each treatment modality was significantly better than the placebo in reducing pain in subjects with osteoarthritis (Yurtkuran & Kocagil, 1999). In addition, ice massage produced a 75% pain intensity reduction compared with 60% for TENS and 55% for electroacupuncture.

Sleep Disturbance and Pain

Chronic pain is often closely related to sleep disturbance. Neuropathic pain can be worse particularly at night, affecting sleep quality. Studies using polysomnography in persons with chronic pain show decreased total sleep time, low sleep efficiency (Wilson, Watson, & Currie, 1998), and problems with sleep onset (Morin, Gibson, & Wade, 1998). Research shows that PWA suffer from sleep disturbances, which results in de-

creased sleep quality (Rubinstein & Selwyn, 1998). This suggests that insomnia may be widespread and underdiagnosed in the HIV-positive population. Research studies on effective interventions to reduce neuropathic pain and improve sleep quality would be beneficial.

Management of peripheral neuropathic pain in PWA remains a clinical challenge. Research needs to identify alternative methods of pain relief to augment the use of medications. TENS, one such alternative method, requires a physician's order and special equipment and can be expensive. Although several studies suggest that ice massage might be an alternative to TENS, further comparative research will determine if pain reduction with ice massage or TENS ultimately increases the quality of sleep.

Method

The study used a quasiexperimental design with repeated measures for assessing treatment effects in which the treatments were ice massage, dry-towel massage, and no massage. To reduce variability, a within-subjects design permitted subjects to serve as their own control. Each subject received all three treatment conditions one time only and on different days. The order of the administration of the treatment was randomized, and all treatments were administered between 7 p.m. and 9 p.m. over a 3-night period. Subjects used a visual analogue scale (VAS) to indicate their level of pain immediately before each treatment, 15 minutes after, and on the following morning upon waking. This gave a total of nine measurements per subject. Based on the result of Melzack et al. (1980) that pain relief with ice massage was sustained on the average of 9 hours, the time interval between the first pain measurement and the third pain measurement for each subject was 9 to 11 hours.

Using the Richards-Campbell Sleep Questionnaire (RCSQ), subjects indicated their level of sleep quality before the first treatment and on the morning after each intervention. This resulted in four measurements per subject. The morning measurements were taken between 7 a.m. and 9 a.m. for uniformity.

Sample and Setting

The location settings were an 8-bed inpatient hospice dedicated to the care of PWA and an apartment complex for PWA recovering from substance abuse within a large metroplex in the southwestern United States. All PWA with distal symmetrical peripheral neuropathies in these two settings were invited to participate in the study. The inclusion criteria required that the subjects meet the following: (a) have a capillary refill less than or equal to 2 seconds to diminish the risk of frostbite, (b) be 18 years or older, (c) speak and read English, and (d) be diagnosed with distal symmetrical peripheral neuropathy by a physician. Subjects with comorbidities associated with peripheral pain (e.g., diabetes mellitus, rheumatoid arthritis, cryoglobulins, or vitamin B₁₂ deficiency) or that interfere with cognitive capacity (e.g., AIDS dementia) were excluded from the study. Also excluded were PWA whose neuropathy manifested as numbness only (without pain) or who took medications known to cause distal symmetrical peripheral neuropathy, when such medications included certain chemotherapeutic agents (e.g., vinblastine or vincristine), antituberculosis medications (e.g., isoniazid or ethambutol) or antiretroviral therapy (e.g., dideoxyinosine or dideoxycytosine). Throughout the study, subjects continued taking their prescribed pain medications.

Instruments

Demographic data determined included age, gender, race, education, current medications, history of opportunistic infections or neoplasms, current CD4 count, and if used to alleviate pain, the dose of amitriptyline taken. For measuring pain intensity, subjects responded to a VAS constructed with a range of 0 to 100 on a 100-mm horizontal line, on which the verbal anchors were "no pain" and "the worst pain imaginable." Each subject completed the VAS twice with a 2-hour interval between each administration, and the resulting test-retest stability score was high ($r = .85$).

Sleep quality was measured with the RCSQ (Campbell, 1986; Richards, 1985). The 5-item instrument uses a visual analog scaling technique to mea-

sure the ease with which the subject fell asleep at bedtime, the duration of sleep, the ease of falling back to sleep after awakening, feelings of restfulness in the morning, and overall sleep quality. On a scale of 1 to 100, the anchors indicated extremes of sleep, with 0 indicating poor sleep quality. Adding the five-item scores and dividing by 5 yielded the total sleep score, with a maximum score possible of 100.

According to the authors, reliability and validity of the RCSQ have been established, with internal consistency reliability ranging from .82 to .92 (Campbell, 1986). Criterion-related validity was established with electroencephalogram recordings during sleep with correlation coefficients ranging from .51 to .70 (Richards, 1985). The test-retest results for this study showed high internal consistency (Cronbach's $\alpha = .85$).

Description of Intervention

An ice massage produces intense sensory input and anesthetizes the area. The theorized mechanism underlying ice massage is that it is a counterirritant. Ice massage may activate nerve fibers responsible for carrying the sensation of cold to the spinal cord. The central nervous system is plastic, and a barrage of nociceptive input conceivably changes the response properties of the dorsal horn neurons. Although neuropathic pain may be exacerbated by cold, allodynia related to postherpetic neuralgia may be decreased with regular applications of cold packs (Chin, 2001).

Procedure

Nurses at the settings housing the PWA identified potential subjects, and the nurse researcher visited with each subject to obtain informed consent to participate. Participants completed baseline measures of pain intensity and sleep quality. Each subject received, in random order and on different days, one session of ice massage, one of dry-towel massage (without ice) and one session of no intervention.

For the ice massage, a moistened towel was wrapped around crushed ice (100 cc) and lightly rubbed over the dorsal and plantar aspect of each foot for 7 minutes. The towel was dampened because

moisture increases the intensity of the cooling sensation more than dry wrappings (McCaffery & Pasero, 1999). In the dry-towel massage, each foot was lightly rubbed for the same length of time. Light rubbing was used in both massage conditions to avoid triggering the large-diameter nerve fibers. In the control condition, the researcher talked with the subject for 15 minutes but did not massage the patient's feet.

The treatments were administered between 7 p.m. and 9 p.m. on 3 consecutive days. Pain intensity was measured immediately before (Time 1) and 15 minutes after (Time 2) each treatment and in the morning upon waking (Time 3). Sleep quality was measured before the first treatment and the following morning between 7 a.m. and 9 a.m. after each intervention.

The rationale for the two types of massage was determination of the efficacy of cold or tactile stimulation to decrease pain. The control condition was included to determine whether just the presence of the researcher decreased pain. All treatments were administered by the researcher to ensure intrarater reliability.

Data Analysis

A repeated measures design with three treatment levels was used to test the administration of ice massage on pain and sleep quality. Data were examined for spurious results such as outliers; however, none were observed. Demographic data were analyzed using descriptive statistics and are presented in Table 1. Means for the pain intensity scores are presented in Table 2. Data were numerically coded and analyzed using the SPSS (Statistical Package for Social Science) program (SPSS Inc., Chicago) (Norusis, 1990).

Results

The sample was a convenience sample of 34 PWA. One participant experienced cold allodynia and was unable to tolerate the ice massage intervention. Subjects ranged in age from 21 to 51 years with a mean of 36.4 years ($SD = 1.14$) and were primarily men (64%) and African American (73%). The sam-

Table 1. Demographic Characteristics of the Sample ($N = 33$)

Characteristic	Value
Ethnicity	
White	8 (24%)
African American	24 (73%)
Hispanic	1 (3%)
Gender	
Men	21 (64%)
Women	12 (36%)
Education	Range 7 to 12 years, $M = 11.9$ years
Age	Range 21 to 51 years, $M = 36.4$ years
CD ₄ count	Range 18 to 500, $M = 312$

Table 2. Descriptive Statistics for Visual Analogue Scale Scores for Persons With AIDS Who Suffer Peripheral Neuropathic Pain ($N = 33$)

Treatment	Mean	SD
Baseline visual analogue scale score ^a		
Ice massage	48.727	23.681
Towel treatment	54.484	26.606
Control condition	36.424	27.305
9-11 hours after an intervention		
Ice massage	33.030	26.168
Towel treatment	37.000	25.081
Control condition	37.606	25.044

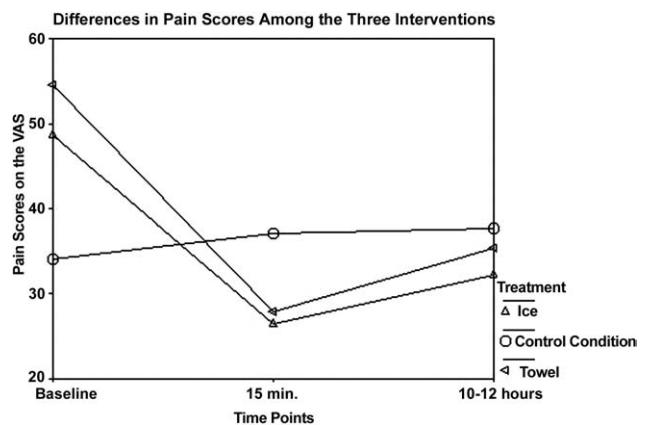
a. Range for the visual analogue scale is 0-100.

ple is consistent with the changing demographics of those with HIV infection (Centers for Disease Control and Prevention, 2003). The CD4 counts ($n = 26$) ranged from 18 to 500 with a mean of 312. A total of 8 of the subjects (24%) used amitriptyline to manage neuropathic pain. Although data among pain scores, sleep quality scores, and the amitriptyline dose were analyzed to determine if amitriptyline should be a covariate, the correlations were not statistically significant.

An analysis with repeated measures showed a significant interaction between treatment and time ($F = 6.28$; $df = 4, 128$; $p = .0001$) (Table 3). Pain scores on the VAS decreased over time when the subject received both the ice massage and the dry-towel massage intervention (Table 2). Paired t -tests were used to compare the interventions at different time points. Pain scores significantly differed between Time 1 and Time 3 for the ice massage treat-

Table 3. Repeated Measures Analysis of Variance ($N = 33$)

Effect	F value	p value
Treatment	.36	.697
Time	10.44	.0001
Treatment \times Time	6.28	.0001

**Figure 1.** Differences in pain scores among the three interventions.

ment ($t = 3.016$; $df = 32$; $p = .005$), and for the dry-towel massage ($t = 3.440$; $df = 32$; $p = .002$) but not for the control group ($t = -.345$; $df = 32$; $p = .732$). The results suggest that both massage interventions decrease pain intensity as compared with the control condition (Figure 1). However, analysis showed no significant differences between the treatments.

The effect size for ice massage (.56) and dry-towel massage (.60) are comparable to the effect size (.50) that Simmonds, Wessel, and Scudds (1992) reported in their study comparing the use of TENS with a sham treatment. These treatment modalities appear to have a moderate effect size.

A second variable studied related to sleep quality. A multivariate approach for repeated measures was used to determine whether the interventions improved sleep quality. The results did not support a significant difference ($F = 1.95$; $df = 1, 32$; $p = .159$), suggesting that pain reduction using ice or

dry-towel massage does not necessarily improve the quality of sleep.

Discussion

Although the results from this pilot study do not show that ice massage is superior to dry-towel massage in reducing peripheral pain, they suggest that tactile stimulation, in which nerve fibers are activated, may result in partial pain reduction. Previous research showed that using TENS significantly reduces neuropathic-related pain. If the mechanism of action for TENS is similar to that for ice massage, this supports further studying the efficacy of ice massage. In light of the study conducted by [Melzack et al. \(1980\)](#) and evidence of the clinical benefit resulting from the current study, using ice massage may indeed be helpful. Because the use of ice massage is relatively simple and inexpensive, a trial of this treatment for a patient with peripheral neuropathy may be indicated.

A possible reason why greater effects were not reported with ice therapy versus dry massage is that wrapping the ice in a towel caused a time delay for the sensation of coldness to penetrate, thus delaying the anesthetic effect. As the target temperature for cooling skin for pain relief is 10° C to 15° C, the researcher cannot ensure that this temperature was reached. Applying a frozen confection to the area may permit subjects to feel the full impact of the coldness and should be tried in subsequent studies.

An interesting result was the change in mean VAS pain scores from baseline to the third time point (9-11 hours later). Subjects receiving one of the two massage interventions reported higher baseline pain intensity scores than those receiving no massage. As the study was a within-subjects design and the order in which the subjects received the treatments was randomized, the difference cannot be attributed to a carryover effect. In an earlier study conducted by [Melzack et al. \(1980\)](#), the researchers reported that ice massage alleviated low back pain for an average of 9 hours. Based on the results by [Melzack et al. \(1980\)](#), it is hypothesized by the researcher that the differences in mean pain scores between the two massage interventions and no massage cannot be attributed to a carryover effect. One hypothesis to

explain this situation is the subject's expectation. The subjects expecting pain relief may have rated their initial pain high. In the control condition, the subjects may not have expected their pain to change and consequently, rated their pain lower.

The results of the study failed to show that the interventions significantly impacted sleep quality of subjects with chronic peripheral pain. That a number of the subjects took possibly sedating medications in the evening (e.g., phenytoin or traxodone) may have been a confounding variable.

A limitation of the study is that each intervention was applied once. A one-time application of ice or dry-towel massage may not have provided enough tactile stimulation to modulate sensory input to the dorsal horn neurons. Another cautionary note when interpreting the results is that because there are few treatments for neuropathic pain, the subjects' optimism that the new interventions would reduce their pain may have affected results.

Implications for Further Research and Clinical Practice

Further research using a two-group randomized trial to compare ice massage and no treatment would illuminate any benefits of ice therapy. Longitudinal, prospective studies are needed to determine long-term effects. A question to answer is whether subjects develop a tolerance to the therapy over time or whether using ice creates a nuisance effect. Because the results showed that tactile stimulation decreased pain on a one-time application basis, additional research over an extended trial period to parse out possible differences is indicated. Additionally, a pilot study exploring the use of rhythmic rubbing with a dry towel may be an appropriate avenue to test effectiveness for reducing pain.

Because [McCaffery and Pasero \(1999\)](#) note that cold application drops the muscle temperature in slender people after 10 minutes and in obese people after about 30 minutes, future studies should take the subject's body mass index into account in determining the length of time for the application of cold.

Neuropathic pain remains a syndrome that is challenging to manage. Although nursing literature reports physical modalities for the management of

pain, very little research has been conducted on the efficacy of applying cold or heat. Further research is needed to explore the role of various forms of massage to manage this unique type of pain. Opportunities exist for nurse researchers to explore nonpharmacological techniques such as ice massage to assist in the management of pain.

Acknowledgement

The author thanks Jeanette McNeill, DrPH, RN, AOCN, and Nina Selz, PhD, at the University of Texas Health Science Center School of Nursing at Houston for their helpful critique of the manuscript. The research was supported through a grant from Texas Woman's University School of Nursing in Houston.

References

- Armstrong, D., Lavery, L., Fleischli, J., & Gilham, K. (1997). Is electrical stimulation effective in reducing neuropathic pain in patients with diabetes? *Journal of Foot and Ankle Surgery*, 36, 260-263.
- Campbell C. (1986). *A comparison of patient's and nurses' perception of patient sleep in the intensive care unit*. Unpublished master's thesis, Northwestern State University, Natchitoches, LA.
- Centers for Disease Control and Prevention. (2003). *HIV-AIDS surveillance report*. Atlanta, GA: Author.
- Chin, K. F. (2001). Clinical management of neuropathic pain. *The Hong Kong Practitioner*, 23, 439-448.
- Eisenberg, E., McNicol, E., & Carr, D. B. (2005). Efficacy and safety of opioid agonists in the treatment of neuropathic pain of nonmalignant origin: Systematic review and meta-analysis of randomized controlled trials. *The Journal of the American Medical Association*, 293, 3043-3052.
- Kemper, C., Kent, G., Burton, S., & Deresinski, S. (1998). Mexiletine for HIV-infected patients with painful peripheral neuropathy: A double-blind, placebo-controlled, crossover treatment trial. *Journal of Acquired Immune Deficiency Syndrome and Human Retrovirology*, 19, 367-372.
- Kiebertz, K., Simpson, D., Yiannoutsos, C., Max, M. B., Hall, C. D., Ellis, R. J., et al. (1998). A randomized trial of amitriptyline and mexiletine for painful neuropathy in HIV infection. AIDS clinical trial group 242 protocol team. *Neurology*, 51, 1682-1688.
- Kumar, D., Alvaro, M. S., Julka, I. S., & Marshall, H. J. (1998). Diabetic peripheral neuropathy. Effectiveness of electrotherapy and amitriptyline for symptomatic relief. *Diabetes Care*, 21, 1322-1325.
- Kumar, D., & Marshall, H. J. (1997). Diabetic peripheral neuropathy: Amelioration of pain with transcutaneous electrostimulation. *Diabetes Care*, 20, 1702-1705.
- Ma, Y. T., & Sluka, K. A. (2001). Reduction in inflammation-induced sensitization of dorsal horn neurons by transcutaneous electrical nerve stimulation in anesthetized rats. *Experimental Brain Research*, 137, 94-102.
- McCaffery, M., & Pasero, C. (1999). *Pain, Clinical Manual* (2nd ed.). St. Louis, MO: Mosby.
- Melzack, R., Jeans, M., Stratford, J. G., & Monks, R. C. (1980). Ice massage and transcutaneous electrical stimulation: Comparison of treatment for low back pain. *Pain*, 9, 209-217.
- Meyer-Rosberg, K., Burckhardt, C. S., Huizar, K., Kvarnstrom, A., Nordfors, L. O., & Kristofferson, A. (2001). A comparison of the SF-36 and Nottingham health profile in patients' chronic neuropathic pain. *European Journal of Pain*, 5, 391-403.
- Meyler, W., deJonste, M., & Rolf, C. (1994). Clinical evaluation of pain treatment with electrostimulation: A study on TENS in patients with different pain syndromes. *The Clinical Journal of Pain*, 10, 22-27.
- Morin, C., Gibson, D., & Wade, J. (1998). Self-reported sleep and mood disturbances in chronic pain patients. *The Clinical Journal of Pain*, 14, 311-314.
- Norusis M. (1990). *SPSS base system user's guide*. Chicago: SPSS Inc.
- Paice, J. A., Ferrans, C. E., Lashley, F. R., Shott, S., Vizgirda, V., & Pitak, D. (2000). Topical capsaicin in the management of HIV-associated peripheral neuropathy. *Journal of Pain and Symptom Management*, 19(1), 45-52.
- Richards K. (1985). *A description of sleep patterns in the intensive care unit*. Unpublished master's thesis, University of Arizona, Tucson.
- Rubinstein, M., & Selwyn, P. (1998). High prevalence of insomnia in an outpatient population with HIV infection. *Journal of Acquired Immune Deficiency Syndrome and Human Retrovirology*, 19, 260-265.
- Schiffitto, G., McDermott, M. P., McArthur, J. C., Marder, K., Sacktor, N., Epstein, L., et al., & the Dana Consortium on the Therapy of HIV Dementia and Related Cognitive Disorders. (2002). Incidence of and risk factors for HIV-associated distal sensory polyneuropathy. *Neurology*, 58, 1764-1768.
- Shlay, J., Chaloner, K., Max, M., Flaws, B., Reichelderfer, P., Wentworth, D., et al. (1998). Acupuncture and amitriptyline for pain due to HIV-related peripheral neuropathy: A randomized controlled trial. Terry Bein Community Programs for Clinical Research on AIDS. *The Journal of the American Medical Association*, 280, 1590-1595.
- Simmonds, M., Wessel, J., & Scudds, R. (1992). The effect of pain quality on the efficacy of conventional TENS. *Physiotherapy Canada*, 44, 35-40.
- Simpson, D., Dorfman, D., Olney, R., McKinley, G., Dobkin J., So, Y., et al. (1996). Peptide T in the treatment of painful distal neuropathy associated with AIDS: Results of a placebo-controlled trial. The Peptide T Study Group. *Neurology*, 47(5), 1254-1259.

- Simpson, D. M., Olney, R., McArthur, J. C., Khan, A., Godbold J., & Ebel-Frommer, K. (2000). A placebo-controlled trial of lamotrigine for painful HIV-associated neuropathy. *Neurology*, 54, 2115-2119.
- Sluka, K. A., Hoeger, M. K., & Skyba, D. A. (2002). Basic science mechanisms of nonpharmacological treatments of pain. In Giamberardino (Ed.), M. A. *Pain—an updated review: Refresher course syllabus*. Seattle: IASP Press.
- de Leon-Casasola, O. Vallejo, R., & Benyamin, R. (2004). Opioid therapy and immunosuppression: A review. *American Journal of Therapeutics*, 11, 354-365.
- Wilson, K., Watson, S., & Currie, S. (1998). Daily diary and ambulatory activity monitoring of sleep in patients with insomnia associated with musculoskeletal pain. *Pain*, 75, 75-84.
- Yurtkuran, M. & Kocagil, T. (1999). TENS, electroacupuncture, and ice massage: Comparison of treatment for osteoarthritis of the knee. *American Journal of Acupuncture*, 27, 133-140.