Percutaneous Electrical Nerve Stimulation: An Alternative to Antiviral Drugs for Acute Herpes Zoster

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Antiviral drugs decrease the pain and enhance the resolution of acute herpes zoster lesions in immunocompetent patients (1–6). However, the effect of antiviral therapy on postherpetic neuralgia (PHN) remains controversial. Whereas some studies reported a lower incidence of prolonged pain with antiviral therapy (4), others found no benefit with respect to prolonged pain (5). In an attempt to improve patient comfort and long-term outcome with respect to PHN, combinations of different drugs have also been evaluated (5–7).

Anecdotal reports have suggested that electroacupuncture may be helpful in the management of herpes-related pain (8,9). Clinical experience with a novel form of electroanalgesia known as percutaneous electrical nerve stimulation (PENS) in the treatment of patients with acute herpes zoster suggested that it is effective in decreasing herpes-related pain and is associated with rapid resolution of the cutaneous lesions (Craig WF, Taylor SM, Fort Worth Center for Pain Management, personal communication, 1997). Therefore, we designed this clinical study to compare PENS therapy with a standard antiviral regimen with respect to the severity of the associated pain, impact on the patient's physical activity and quality of sleep, resolution of the herpes lesions, and incidence and severity of PHN.

Methods

After obtaining institutional review board approval and written, informed consent, 50 adult patients (27 female and 23 male) with the recent acute onset (<72 h) of herpes zoster lesions were administered one of two different treatment modalities according to a randomized, single-blind study design. Exclusionary criteria included known hypersensitivity to the antiviral drugs, preexisting neurological impairment, women who were pregnant or nursing, any previous experience with acupuncture-like therapies, the presence of the zoster rash for >72 h, or secondary complications from the viral infection.

The patients were randomly assigned using a computer-based program to either the control group (which received famciclovir 500 mg three times a day for 1 wk) or the experimental group (which received PENS therapy for 30 min three times a week for 2 wk). The PENS therapy consisted of the placement of 32-gauge stainless steel acupuncture-like needle probes into the soft tissue to a depth of 1–2 cm at dermatomes one level above and below the cutaneous lesions (Figures 1 and 2). The needle probes were connected to a low-output (5 mAmp) electrical generator and stimulated at frequencies ranging from 4 to 100 Hz. Patients in both treatment groups were evaluated daily by a physician (HEA) not involved in either the famciclovir or PENS treatments. The patients were instructed not to use any topical medications or systemic treatments during the 2-wk study period.

Before receiving the study treatments, all patients were asked to assess their baseline degree of pain, level of physical activity, and quality of sleep using three separate 100-mm visual analog scales (VAS), with 0 = minimal (lowest) to 100 = maximal (highest). All patients were instructed to return to the medical center daily during the 2-wk study period to assess the appearance of their cutaneous lesions and to complete the pain, physical activity, and quality of sleep VASs. At the end of the study period, all patients were asked to complete a global assessment questionnaire to evaluate the change in pain, physical activity, and quality of sleep using the VASs.

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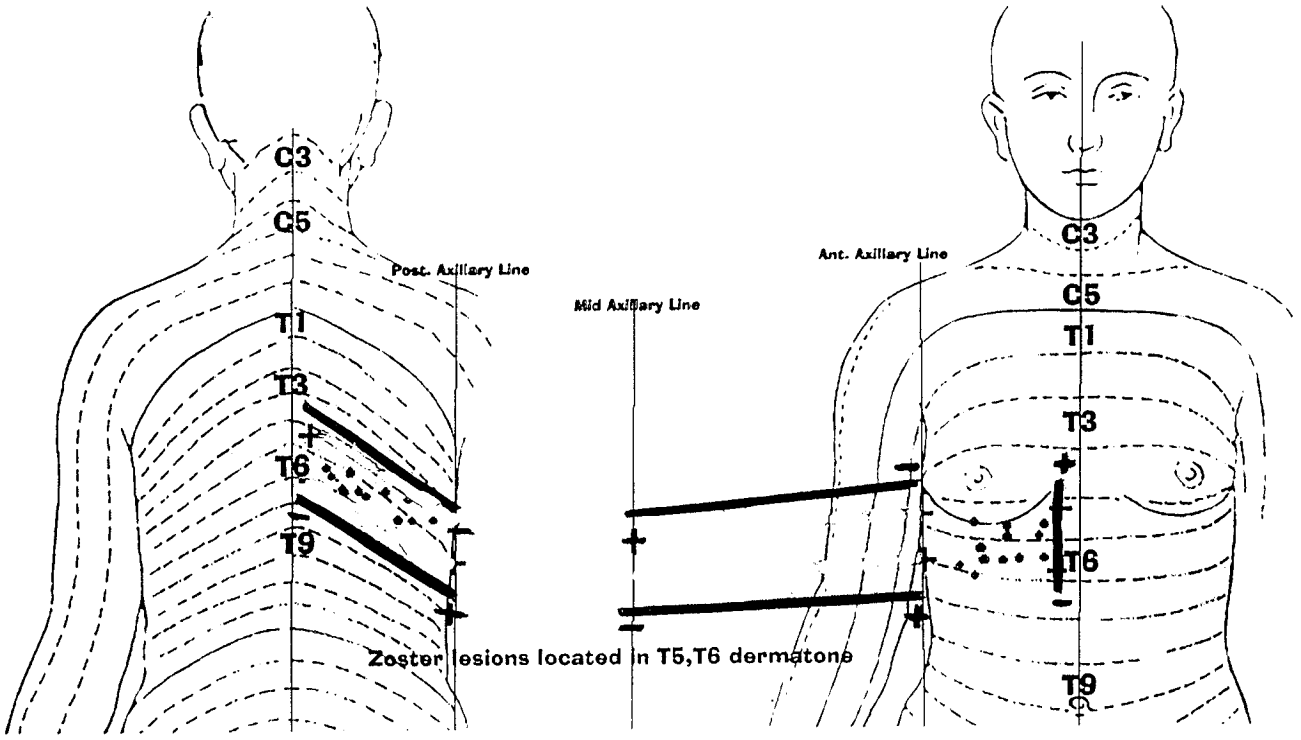

Figure 1. The "arc" montage was applied initially when the lesions were wet during the first week of therapy, consisting of bipolar leads connected to needle probes placed in the soft tissues at one dermatomal level above and below the acute lesions. Each lead was connected to a pair of needles, alternating the positive (+) and the negative (−) electrode positions as shown.

The assessment of the cutaneous lesions was performed by a blind observer and included: 1) location of the rash; 2) severity of the rash (i.e., number of the lesions in the involved dermatomes) using the following classification system: mild (<25), moderate (25–50), or severe (> 50); 3) the last day that new lesions appeared; 4) the first day without any new lesions; 5) the first day with full crusting of the lesions; and 6) the time to complete healing of the lesions. All patients were contacted at 3-, 6-, and 9-mo intervals to inquire about the presence of pain in a dermatomal pattern corresponding to the level of the acute lesions (i.e., PHN). The severity of the PHN pain was quantified using the 100-mm pain VAS.

Changes in the VAS scores were analyzed by using analysis of variance, with *t*-tests used to determine intergroup differences and Bonferroni's adjustment for multiple comparisons. Analysis of discrete data was performed using the χ^2 test, with P values <0.05 considered statistically significant.

Results

The two treatment groups were similar with respect to demographic characteristics, including the location and severity of the herpetic lesions (Table 1). The PENS group experienced more rapid resolution of the vesicles and complete healing of the lesions (Table 2). The VAS pain scores were consistently lower in the PENS group during the 2-wk observation period (Table 3). On the global assessment questionnaire, the percent decrease in the VAS pain score was 67% in the PENS group compared with 45% in the control group ($P < 0.05$). The percent improvement in the VAS physical activity and quality of sleep scores (78% vs 60% and 55% vs 37%, respectively) was also greater in the PENS- versus famciclovir-treated patients at the end of the second week. The older patients (≥50 yr) were more likely to develop PHN symptoms, and PENS therapy was associated with a decrease in the severity of pain at 3 and 6 mo in this subpopulation (Table 2). However, no differences in PHN symptoms were apparent at the 9-mo follow-up assessment period.

Discussion

This comparative study suggests that PENS, a novel, nonpharmacologic analgesia technique, may be a viable alternative to antiviral drugs for the treatment of acute herpes zoster lesions. The use of PENS therapy provided pain relief, increased physical activity, and an improved quality of sleep that compared favorably

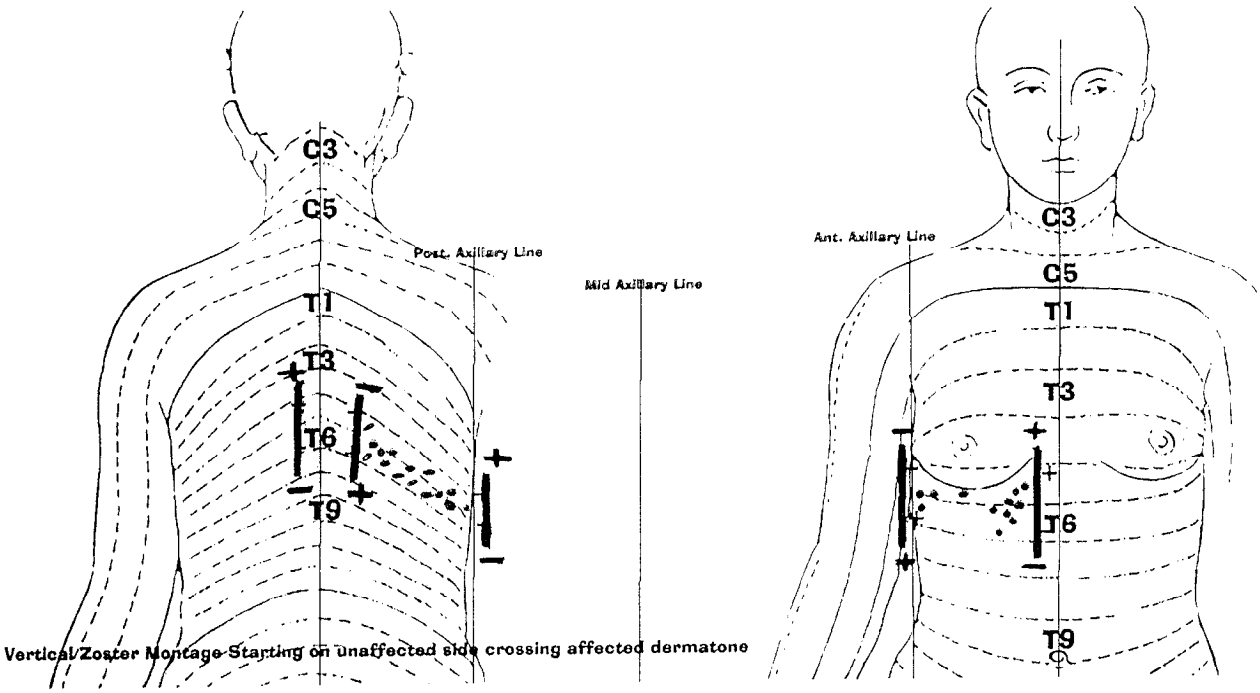

Figure 2. The "vertical" montage was applied after the lesions became crusted during the second week of therapy, consisting of bipolar leads stimulating across the dermatomal region from C4 to C7. Each lead was connected to a pair of needles, alternating the positive (+) and the negative (−) positions as shown.

Table 1. Demographic Characteristics of Patients with Acute Herpes Zoster Receiving Antiviral Drug (Control) or PENS Therapy

	Control	PENS
Patients (*n*)	25	25
Male/female (%)	44/56	48/52
Age (yr), mean ± SD	53 ± 15	56 ± 15
≤50 yr (%)	32	28
≥50 yr (%)	68	72
Location of rash (%)		
Thoracic	56	60
Cervical	16	12
Lumbar	16	16
Cranial	0	4
Sacral	12	8
Severity of rash (%)		
Mild (<25 lesions)	32	20
Moderate (25–50 lesions)	40	48
Severe (>50 lesions)	28	32

PENS = percutaneous electrical nerve stimulation.

Table 2. Effect of Antiviral Drug (Control) or PENS Therapy on Resolution of Acute Herpes Zoster Lesions and the Incidence and Severity of Postherpetic Neuralgia

	Control	PENS
Vesicles (days)	5.6 ± 0.7	4.6 ± 0.5*
Ulcers (days)	7.3 ± 0.7	6.4 ± 0.5
Crusting (days)	7.8 ± 0.5	7.4 ± 0.8
Healing (days)	18.8 ± 1.4	16.9 ± 0.9*
Postherpetic neuralgia		
At 3 mo (n)	9	6
Age (yr)	66 ± 8	65 ± 5
Pain severity (mm)	44 ± 8	32 ± 4*
At 6 mo (n)	6	3
Age (yr)	64 ± 6	66 ± 5
Pain severity (mm)	46 ± 8	30 ± 2*
At 9 mo (n)	3	2
Age (yr)	65 ± 6	65 ± 4
Pain severity (min)	55 ± 13	49 ± 11

Values are means ± SD or *n*.
Pain severity was measured on a scale from 0 = minimal to 100 = maximal.
PENS = percutaneous electrical nerve stimulation.
* Significantly different from control group ($P < 0.05$).

with a standard antiviral therapy. In this preliminary study, PENS therapy was also more effective than famciclovir in preventing PHN-related pain symptoms 3 and 6 mo after resolution of the cutaneous lesions.

Although this study can be criticized because it did not include a placebo (or sham) group, the benefits of antiviral therapy have been firmly established during the acute phase of the illness, and other investigators (4) have suggested that it would be unethical to include a placebo treatment group. The outcome assessments were blinded because the physician making the assessment was unaware of the treatment that the patients were receiving. Furthermore, the small cutaneous needle puncture sites (0.2 mm) produced by the PENS probes were not apparent to the individual

Table 3. Effect of Antiviral Drug (Control) or PENS Therapy on Pain Scores, Physical Activity, and Quality of Sleep in Patients with Acute Herpes Zoster

	Control	PENS
Pain score (mm)		
Baseline	58 ± 15	61 ± 11
1 wk	46 ± 13	39 ± 8*
2 wk	32 ± 8*	20 ± 9*†
Activity score (mm)		
Baseline	47 ± 13	46 ± 13
1 wk	62 ± 13	67 ± 10
2 wk	75 ± 11*	83 ± 8*
Sleep score (mm)		
Baseline	55 ± 15	53 ± 15
1 wk	65 ± 12	70 ± 12
2 wk	76 ± 9*	83 ± 10*

Values are mean ± SD of visual analog scale scores, 0 = minimal (lowest) to 100 = maximal (highest).
PENS = percutaneous electrical nerve stimulation.
* Significantly different from the baseline value ($P < 0.05$).
† Significantly different from the control group ($P < 0.05$).

performing the clinical assessments. Nevertheless, future studies should include a sham PENS group that receives the antiviral therapy in combination with the needle probes but without electrical stimulation. Unfortunately, the inclusion of a sham PENS group would not blind the patients because it does not mimic the sensation provided by the electrical stimulation associated with PENS therapy.

The improved physical activity and quality of sleep during the second week of treatment in the PENS group may be secondary to the decrease in the intensity of pain. Although the mechanism of PENS-induced analgesia is not known, it may be related to both neural modulation produced by the electrical stimulus (10) and an increase in endogenous morphine-like substances (e.g., dynorphins, endorphins, enkephalins) within the central nervous system (11). Using a rat model for studying electroacupuncture, Chen et al. (12) reported that an alternating 2-Hz and 15-Hz pattern of electrical stimulation was more effective than a fixed frequency of stimulation at either 2 Hz or 100 Hz in producing experimental analgesia. In a clinical study, Han et al. (11) reported that low- and high-frequency electrical stimulation resulted in increased cerebrospinal fluid levels of met-enkephalin and dynorphin, respectively. Further studies are clearly needed to determine the precise central nervous system mechanism(s) of PENS-induced analgesia.

Because herpes zoster is caused by a reactivation of the varicella virus residing in the sensory ganglia and spinal cord after the primary viral infection, the beneficial effects of PENS therapy may also be related to electrical stimulation of the involved peripheral sensory nerves. The electrical current can produce localized vasodilation and may stimulate the release of antiinflammatory mediators at the site of injury. Further studies evaluating the efficacy of PENS therapy in immunosuppressed patients would be helpful in understanding the basis for its apparent analgesic and antiinflammatory activity. However, PENS therapy should be evaluated as a supplement to antiviral therapy in this high-risk patient population.

In conclusion, PENS therapy is a unique nonpharmacologic approach to treating immunocompetent patients with acute herpes zoster that compared favorably with standard antiviral drug therapy in this preliminary study.

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