The Effect of Noncontact, Low-Intensity, Low-Frequency Therapeutic Ultrasound on Lower-Extremity Chronic Wound Pain: A Retrospective Chart Review

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Pain associated with chronic wounds and related wound care modalities presents a persistent clinical challenge in patient care, yet evidence supporting the effects of interventions on wound pain remains sparse. In response to initial clinical observations that several patients with painful chronic lower-extremity wounds reported a reduction in wound pain shortly after ultrasound therapy was initiated, a retrospective chart review and analysis of reported pain scores was conducted. The records of 15 consecutive patients (eight women, seven men, age range 28 to 88 years) with painful, nonhealing, lower-extremity wounds treated for 2 to 4 weeks with noncontact, low-intensity, low-frequency therapeutic ultrasound were reviewed and recorded pain scores abstracted. Mean pain scores decreased from 8.07 (± 1.91) pre-treatment to 1.67 (± 1.76) post-treatment (P = 0.0003). No patients reported worsening pain after treatment commenced. This preliminary evidence suggests that prospective, controlled clinical studies to evaluate the effect of this treatment on wound-related pain are warranted.

KEYWORDS: ultrasound, pain, wound modalities, lower-extremity wounds, debridement


Chronic lower-extremity wounds affect patient quality of life, morbidity, mortality, and healthcare costs. Recalcitrant wounds require prolonged therapy, which may include various topical treatments such as dressings, compression, antimicrobial agents, or physical wound care modalities (pulsatile lavage, whirlpool, and thermal ultrasound). A review of the literature suggests that some treatments are associated with pain during and after they are provided. An evidence-based model for consistently and adequately relieving wound-related pain is lacking.

Noncontact, low-intensity, low-frequency ultrasound therapy (MIST Therapy® System; Celleration; Eden Prairie, Minnesota) is an ultrasound modality designed to enhance wound healing without thermal effects or direct tissue contact. Ultrasound is defined as a mechanical vibration transmitted at a
frequency above the upper limit of human hearing (>20 kilohertz [kHz]). Therapeutic ultrasound, using devices that operate in the 1 to 3 megahertz (MHz) range, has been used for years in the treatment of a variety of musculoskeletal disorders. Diagnostic ultrasound relies on high-frequency (20 to 40 MHz) ultrasound devices.

The therapy system discussed herein operates at a frequency of 40 kHz with a maximum intensity of 1.7 Watts/cm² and a therapeutic range of 0.1 to 0.8 Watts/cm². The device was cleared for marketing by the US Food and Drug Administration (FDA) in 2005 to promote wound healing through wound cleansing and maintenance debridement by removal of yellow slough, fibrin, tissue exudate, and bacteria.

The wound-healing effects of low-intensity, low-frequency ultrasound energy are thought to be primarily attributed to the mechanisms of cavitation and microstreaming. Cavitation involves the creation and oscillation of microscopic bubbles (or vapor-filled voids) that concentrate acoustic energy into shearing and microstreaming fields. The movement and compression of these bubbles can cause changes in cellular activities. Microstreaming is the physical forces of sound waves that are capable of displacing ions and small molecules. The mechanical pressure applied by the microstreaming wave produces a unidirectional movement of fluid along and around cell membranes. Based on both in vivo and in vitro laboratory studies, the combination of cavitation and microstreaming, both of which occur more frequently with kilohertz than megahertz ultrasound, appear to provide a mechanical energy capable of altering cell membrane activity and, therefore, cellular activity.

The ultrasound-generated mechanical energy also stimulates signal-transduction pathways, which results in a broad range of cellular effects. Laboratory studies have demonstrated the following ultrasound-induced cellular effects that may affect wound healing: leukocyte adhesion in bovine tissue cultures; growth factor production in a co-culture of human osteoblastic and endothelial cells; collagen production and increased angiogenesis in human fibroblasts, osteoblasts, monocytes and excised flank tissue from adult rats; enhanced macrophage responsiveness; increased fibrinolysis in human plasma cells; and increased nitric oxide production in human osteoblasts.

In a randomized, controlled, double-blind trial of 55 patients with recalcitrant diabetic foot ulcers receiving standard wound-care therapy, a larger proportion of ulcers treated with the ultrasound therapy (40.7%) healed in 12 weeks compared with those treated with a sham procedure (14.3%; P = 0.0366). Additionally, compared to historical controls, use of this therapy was reported to reduce time to healing in chronic lower extremity wounds of various etiologies (N = 23) from 10 to 7 weeks (P = 0.0005). In a case series of 51 patients using ultrasound therapy, average time to healing was 5.5 weeks.

Anecdotal reports suggest this type of therapy may reduce pain and shorten healing time compared with standard therapies in patients with painful chronic wounds. The current retrospective study was conducted in response to the initial observation that several patients with painful, chronic, nonhealing lower-extremity wounds at the authors’ center reported reduction in wound pain shortly after beginning this ultrasound therapy.

**Methods**

**Patient population.** Data from 15 consecutively treated patients with ongoing painful, chronic, nonhealing lower-extremity wounds of various causes (eight patients with vascular ischemia, four patients with sickle cell anemia, and three patients with venous stasis-associated ulcerations) were included.

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**KEY POINTS**

- After treatment with noncontact, low-intensity, low-frequency ultrasound therapy was initiated, the authors of this article noticed that many chronic wound patients reported a reduction in pain.
- A retrospective review of patient charts confirmed these clinical observations.
- Studies to evaluate the effects of this and other commonly used physical treatment modalities on healing and patient pain are needed.
in this retrospective analysis of patient medical records at the authors’ institution. Outpatient clinic records include a self-reported visual analog scale (VAS) pain measurement at each visit as a routine patient evaluation variable. All patients were treated with the ultrasound therapy to facilitate healing of their chronic wounds, not to address wound pain. Wounds had been present an average of 17 months (range 5 weeks to 96 months) before the start of ultrasound treatment.

Patients charts were retrospectively analyzed. All patients described ongoing pain that was not related to clinical signs of infection; pain was of >1 month duration and >5 intensity on a scale of 0 to 10 (0 = no pain and 10 = worst pain imaginable). Two patients who met the criteria for inclusion in the data analysis and were treated for chronic painful wounds were excluded from this analysis—one failed to complete more than two treatments due to compliance issues and one had non-wound related, ischemic, limb pain.

**Treatment procedure.** The therapy device (see Figure 1) includes an ultrasonic power supply unit and a transducer with disposable applicator that is moved over the wound in close proximity to the wound bed without contacting the tissues. Ultrasound energy is delivered to the wound bed in conjunction with an atomized solution of sterile saline to promote cell stimulation and bacterial reduction. Treatments were administered by a physical therapist three times per week for 3 to 5 minutes based on wound size for the duration of this observation period, regardless of extent/lack of slough. Concomitant therapies and dressings included moist wound healing and compression, enzymatic debridement, and topical antimicrobial therapy as appropriate to the wound type and condition (see Table 1). None of the topical therapies was altered during the treatment period.

**Pain assessment.** At the start of each visit and before removing the existing dressing, patients were asked to rate their “worst wound-related pain” since the last visit using a VAS that ranges from 0 (absence of pain) to 10 (intense pain). This widely used, easy-to-apply pain rating system is understood by most patients and has been validated in multiple studies.

**Data management and statistical analysis.** Charts were reviewed by the CWOCN. Variables included patient data, wound size, medicines, pain score, and treatment modalities. Data were collected for 2 to 4 weeks from start of treatment based on pain scores reported. Because patients received more than one treatment per week, mean pain scores were calculated. Formal power calculations for determining sample size were not performed because this was a retrospective chart review of consecutively treated patients with wound pain. The sample was all patients treated with the ultrasound therapy over the study period. The study was conducted because of anecdotal evidence that warranted exploration.

The difference between pre- and post-therapy pain scores was calculated using the Wilcoxon
signed-rank test (both one-tailed and two-tailed) with 95% confidence intervals.

**Results**

Patients (eight women, seven men) ranged in age from 28 to 88 years. Treatment was provided for 2 to 4 weeks, with patients each receiving from four to 12 treatments based on the wound’s need for ongoing debridement and the manufacturer’s instructions for use (see Table 1). The group included 10 patients with diabetes mellitus (all eight patients with ischemic ulcers had diabetes mellitus). Whirlpool therapy previously provided to six patients was discontinued when the ultrasound therapy commenced. All patients treated for ulcerations associated with sickle cell anemia had histories of recurrent admissions for sickle cell crisis events.

All patients reported a substantial reduction in pain after initiating the ultrasound treatment. Mean pain scores decreased by approximately 80% from pre-treatment (8.07, SD 1.91) to post-treatment (1.67, SD 1.76), a statistically significant difference using both one-tailed test ($P = 0.0003$) and two-tailed test ($P = 0.0007$; 95% confidence interval 5 to 7.56 [pre minus post means]). The reduced pain scores over multiple consecutive visits continued for the duration of therapy and were consistent for each patient; no increase in pain was noted. Inclusion of the patient with limb pain not localized to the wound (pain unchanged during treatment) would have yielded a mean pain reduction of 75%. Of the 15 evaluated patients, five were anecdotally observed and lack of prescribed narcotic documented; the patients reported discontinuing or reducing their use of narcotic analgesics within 2 weeks of starting ultrasound therapy.

**Discussion**

This is the first report of a noncontact, low-intensity, low-frequency ultrasound therapy alleviating pain in chronic, painful wounds. Data from
this retrospective analysis showed that treatment with ultrasound therapy resulted in a statistically significant reduction in pain scores. The rapid pain reduction occurring in 4 weeks or less in these non-healing wounds makes it unlikely that the initial decrease in pain is related to healing alone but wound status was not analyzed as part of this study because of short treatment duration in wounds with an average chronicity of 17 months.

As a small, single-center study with an uncontrolled, retrospective design, these findings should be considered an initial step in evaluating the potential palliative benefits of noncontact, low-intensity, low-frequency ultrasound therapy in chronic wound care. It should be noted that the evidence supporting use of the palliative benefit of current thermal ultrasound therapies for treatment of venous leg ulcers is also limited. While the observed pain relief after 2 to 4 weeks of care may be related to wound healing, the chronicity of the wounds (17 months) suggests otherwise. Based on the reported preliminary findings, it appears that this ultrasound therapy may offer a reasonable alternative to commonly used physical wound debridement therapies (pulsatile lavage, whirlpool, and thermal ultrasound), which have not been associated with any palliative benefit. Larger, prospective studies would offer an opportunity to carefully evaluate changes in pain scores in the period immediately after initiating therapy (ie, weeks 1 and 2) while controlling for treatment type, healing rate, and changes in non-wound related pain.

**Conclusion**

The results of this small study confirmed the author’s clinical observations that noncontact, low-intensity, low-frequency therapeutic ultrasound administered for healing of chronic lower-extremity wounds may reduce wound pain. Further study of this modality for wound management and associated pain relief is needed to fully characterize the effects of this ultrasound therapy.

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