Phonophoresis versus ultrasound in the treatment of common musculoskeletal conditions

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ABSTRACT

KLAIMAN, M. D., J. A. SHRADER, J. V. DANOFF, J. E. HICKS, W. J. PESCE, and J. FERLAND. Phonophoresis versus ultrasound in the treatment of common musculoskeletal conditions. *Med. Sci. Sports Exerc.*, Vol. 30, No. 9, pp. 1349–1355, 1998. **Purpose:** The purpose of this study was to determine whether the pain response after phonophoresis (PH) differs from the pain response after ultrasound (US) alone. **Methods:** Forty-nine subjects with soft tissue injuries including epicondylitis, tendinitis, and tenosynovitis were randomly assigned (double blinded technique) to PH or US treatment groups. Both groups received 8 min of continuous US at 1.5 $w \cdot cm^{-2}$, three times per week for 3 wk. For the PH group a gel containing 0.05% fluocinonide was used as a coupling agent. An identical gel absent the steroid was used for the US group. Subjects indicated their pain level by marking on a visual analog scale (VAS) at the start of treatment and at the end of weeks 1, 2, and 3. Pressure algometry was used to note tolerance to direct pressure over the target tissue. ANOVA for repeated measures was used to analyze data. **Results:** At the end of 3 wk of treatment, both groups combined showed a significant decrease in pain level and an increase in pressure tolerance ($P < 0.05$), but there were no differences between groups from the onset of treatment to the end of week 3 (VAS: US 5.5–1.9, PH 5.0–2.0; algometry (involved limb): US 4.7 lb-7.1 lb, PH 5.1 lb-6.6 lb). **Conclusions:** We conclude that US results in decreased pain and increased pressure tolerance in these selected soft tissue injuries. The addition of PH with fluocinonide does not augment the benefits of US used alone. **Key Words:** MUSCULOSKELETAL INJURIES, TENDINITIS, PRESSURE ALGOMETRY, CORTICOSTEROIDS

Ultrasound (US) is a physical modality which has been used for over 40 yr in the treatment of soft-tissue injuries such as tendinitis, tenosynovitis, epicondylitis, bursitis, and osteoarthritis (14,16,22,29,36,40, 42). US transmission occurs when a high frequency potential field (1–3 MHz) is applied to a crystal in the US "sound head" or "transducer" which then vibrates to produce a high frequency acoustic wave. These acoustic waves travel readily through liquids and solids that are dense but less well through air. Thus a conductive medium such as cream or gel is required to fill the space between the transducer and the body's surface. The physical properties of US have been studied extensively (13,24,35). When these high frequency vibrations pass into the body, both thermal and nonthermal effects occur.

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Ultrasound is primarily used for its ability to deliver heat to deep musculoskeletal tissues such as tendon, muscle, and joint structures; the depth of penetration is roughly inversely related to the frequency (33,34). The therapeutic effects of heat likely involve increased regional blood flow, increased soft tissue extensibility, and decreased pain and muscle spasm (23). The nonthermal or mechanical properties of US are less well defined but are believed to alter cellular permeability and metabolism (17,45). The tissue response to these nonthermal effects may be important in the promotion of wound healing (18,50) .

Phonophoresis (PH) refers to a specific type of US application in which pharmacological agents such as corticosteroids, local anesthetics, and salicylates are introduced (2,5,6,8,9,12,14,15,25–28,31,32,37,38,41,43,46,51,53). PH has been used clinically since the early 1960s in attempts to drive these drugs transdermally into subcutaneous tissues. Conditions treated by PH have included epicondylitis, tendinitis, tenosynovitis, bursitis, and osteoarthritis. Both the thermal and nonthermal (mechanical) properties of US have been cited as possible mechanisms for the transdermal penetration of the pharmacological agents. Increases in cell

permeability and local vasodilation accompanied by the acoustic pressure wave may result in increased diffusion of the topical agent (5,6,15).

The efficacy of PH has not been conclusively established. Some early studies have shown drug penetration as deep as 10 cm (14,25,27,28), but more recent studies have cast doubt on these findings (41). Other studies have examined the effects of PH with different corticosteroid concentrations and PH compared with US alone in the treatment of various musculoskeletal conditions (14,32). Unfortunately, these studies have a number of methodological shortcomings, including inadequate blinding, lack of randomization, and questionable assessment of pain relief. Recent papers have argued that many of the commonly used cream-based preparations are not allowing for adequate transmission of the acoustic wave (3,10,49). Gel-based preparations appear to be superior with respect to transmissivity of US. Consequently, gel-based corticosteroid compounds might be expected to be superior for PH applications.

Controlled clinical studies comparing the efficacy of PH treatment to US alone are still rare. Research questions that need to be answered relate to the actual depth of drug penetration, the appropriate concentration of drug, the type of vehicle preparation (cream, gel, or ointment), the US frequency, and the US mode (continuous or pulsed).

The purpose of this study was to examine the efficacy of US-driven Fluocinonide gel (Lidex (39)) compared with standard US therapy (1.5 $W \cdot cm^{-2}$, 1 MHz, continuous, 8 min treatment) in a selected number of superficial musculoskeletal conditions. Our null hypothesis was that there would be no difference in the perceived or measured pain response between subjects treated with Fluocinonide PH compared with subjects treated with US alone. Recovery was judged by responses to a Visual Analog Scale (VAS) and by tolerance to a pressure algometer. A Physician's Global Assessment (PGA) scale was also used for comparison with the VAS.

METHODS

Subjects. Forty-nine subjects 18 yr or older were recruited by posting flyers throughout the Clinical Center at the National Institutes of Health in Bethesda, Maryland and the Hospital for Special Care in New Britain, Connecticut. Acceptable subjects were diagnosed with one of the following conditions: lateral epicondylitis, bicipital tendinitis, supraspinatus tendinitis, DeQuervain's tenosynovitis, Achilles tendinitis, patellar tendinitis, plantar fasciitis. Specific criteria for these conditions are listed in Table 1.

Diagnosis by a physician was based on a consistent medical history and at least two positive provocative tests during physical examination. Provocative tests included resistance loading, stretch response, and range of motion tests. Routine radiographs were used to rule out fractures, dislocations, and malignancies. Range of motion, strength, and injury specific provocative testing were also assessed by a physical therapist upon entrance to the study and at the end of the study. A summary of subject conditions are presented in Table 2.

TABLE 1. Criteria required for identifying musculoskeletal conditions.

Condition	Observations
Lateral epicondylitis	Palpable tenderness over the lateral epicondyle Epicondylar pain with resisted wrist extension Epicondylar pain with passive elbow extension and wrist flexion
Bicipital tendinitis	Palpable tenderness over the bicipital groove Pain in the bicipital groove with resisted elbow supination and flexion Pain in the bicipital groove with resisted straight arm flexion
Supraspinatus tendinitis	Palpable tenderness over the supraspinatus insertion Pain with passive shoulder abduct. or flex. greater than 60° Negative drop arm test Positive empty can test
DeQuervain's tenosyovitis	Palpable tenderness over the abd. poll. brev. and ext. poll. long. (anatomical snuff box) Positive Finklestein's test Pain with resisted thumb extension
Achilles tendinitis	Palpable tenderness over the Achilles tendon Pain with passive ankle dorsiflexion Pain with resisted ankle plantarflexion
Patellar tendinitis	Palpable tenderness over the patellar tendon Pain with resisted knee extension Pain with passive knee flexion
Plantar fasciitis	Palpable tenderness over the plantar fascia Plantar pain exacerbated by ankle dorsiflexion Plantar pain exacerbated by first MTP hyperextension

TABLE 2. Subject characteristics.

	Phonophoresis	Ultrasound
Total Number	25	24
Sex and average age		
Male (N = 28, 47 yr)	16	12
Female (N = 21, 43.8 yr)	9	12
Condition		
Lateral epicondylitis	9	8
Supraspinatus tendinitis	9	8
DeQuervain's tenosynovitis	2	2
Bicipital tendinitis	1	2
Patellar tendinitis	1	0
Plantar fasciitis	2	0
Achilles tendinitis	1	4
Stage		
Acute (<6 weeks)	1	2
Subacute (6 weeks–3 months)	8	4
Chronic (>3 months)	16	18
Prior treatment (may include more than one)		
NSAID	13	13
Injection	6	3
Ultrasound	0	2
Physical therapy	5	4
Other	6	10

Exclusion criteria included infection at the US treatment site, bilateral extremity involvement, allergy to corticosteroid gel, reduced sensation for temperature and light touch, use of any topical medication at the US treatment site, local corticosteroid injection within the previous 3 months, the presence of peripheral vascular disease, cardiac pacemakers, malignancy, local hemorrhage, cemented prosthesis, and pregnancy.

All subjects signed a document verifying informed consent in compliance with the requirements of the National Institutes of Health and the Hospital for Special Care.

Study design. Subjects were matched in pairs according to condition, and then one of each pair was randomly

assigned to either the US group or the PH group. Double blinding was used to eliminate experimental bias. One investigator maintained the randomization codes but did not have contact with the subjects. Each group originally consisted of 25 subjects, but one subject was dropped from the study because of noncompliance, leaving a total of 49.

Subjects were instructed to maintain their current levels of activity through the duration of the study, and no additional therapies were provided, including physical therapy. Subjects were specifically asked to refrain from beginning new exercise programs or daily routines during the course of the study. If a subject had been taking a nonsteroidal anti-inflammatory medication upon entry to the study, he/she was maintained on that medication through the 3 wk. At the end of the study all subjects were informed of their treatment group and provided with a home exercise program that was specifically designed for their condition. A 2-month follow-up phone call was made by a physician to each subject inquiring about response to the exercise program and for a second administration of the PGA. If pain or dysfunction persisted, the subject was provided with a referral list of local practitioners.

VAS and pressure algometer measurements were administered at the initial evaluation and repeated at the end of each week of the study (total of four times—initial, week 1, week 2, week 3) by a physical therapist. A PGA was also administered at the end of the third week. For the PGA the subject's functional status was self-reported to a physician as either "complete recovery," "much improvement," "slight improvement," "no change," or "worse."

Visual analog scale. Pain was evaluated using a 10-cm horizontal visual analog scale. VAS scores were determined by direct measurement along the line to the subject's mark. No pain was equivalent to a VAS score of 0 (zero), and extreme pain was equivalent to a VAS score of 10. Our previous experience with tendinitis has shown that pain at rest is usually minimal. Therefore, patients were asked to mark the VAS to represent pain associated with a particular self-selected functional activity (e.g., shifting gears, shaking hands, turning door knobs, lifting a gallon of milk) which had consistently caused pain during the 3 wk before the study period. The VAS scores represent the pain level associated with this one self-selected activity for each subject. Subjects were asked to perform this one self-selected activity at least once before each evaluation period (weeks 1, 2, 3).

Pressure algometer. A pressure algometer was applied over the maximal point of tenderness (MPT) and again on the identical site of the contralateral limb (Fig. 1). The MPT on the tendon was located by palpation at the time of initial evaluation and marked with a permanent marker for the duration of the study. Algometry was performed by standard technique and has been supported as a reliable measurement (19–21,44,47). The algometer contact head was aligned perpendicularly to the affected tendon, the tendon was stabilized by the examiner's thumb, and algometer pressure was gradually increased until the subject reported pain. Pressure values recorded were the average of three consecutive measurements taken a minimum of 1 min apart at least 5 min after the completion of treatment. Lower algometer scores would indicate less pressure tolerance and hence greater pain. Higher algometer scores would indicate less pain.

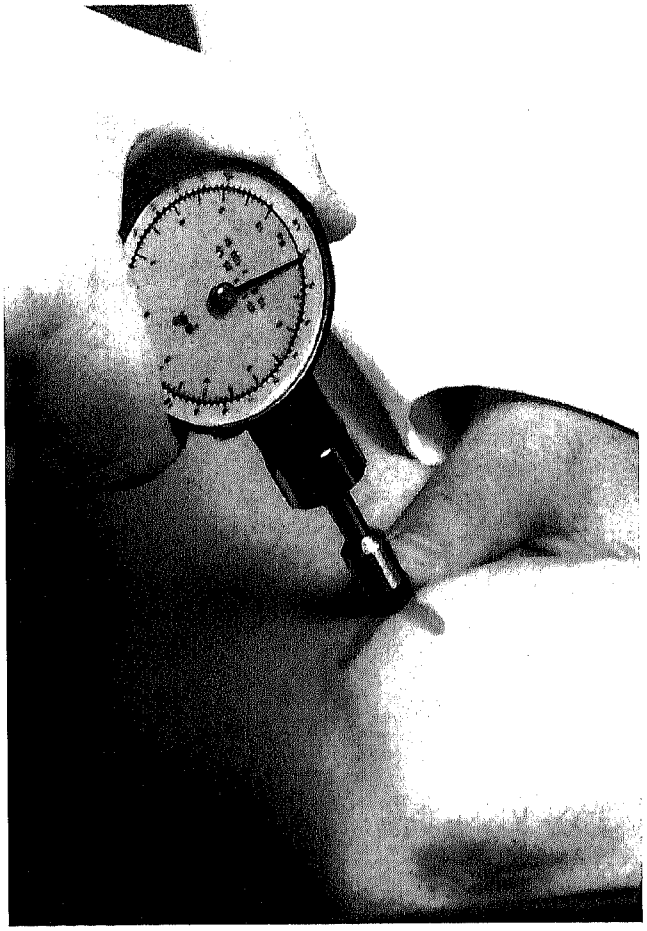

Figure 1—Application of pressure algometer over the lateral epicondyle.

Treatment. Ultrasound treatments were performed with the Sonicator 720 (Mettler Electronics, Anaheim, CA) 3 times per week for 3 wk. A continuous mode was used at a frequency of 1 MHz, and intensity of 1.5 $W \cdot cm^{-2}$. Each treatment lasted 8 min. A 3-cm soundhead was used, and the area covered was within a 4-cm radius of the MPT. Duration and frequency of treatment were chosen based on standard clinical practice with the use of ultrasound. For the PH group US treatment was administered using 0.05% Fluocinonide gel. The US group received US treatment using the identical gel absent the Fluocinonide. The transmissivity of US through the gel was tested in our laboratory according to a previously established technique (10).

Analysis. The VAS results were analyzed with a two-way ANOVA for repeated measures. The two factors were Group (2 levels: drug group vs US group) and Time (4 levels, repeated: initial score and at the end of 1 wk, 2 wk, and 3 wk).

The algometer measurements were analyzed with a three-way ANOVA for repeated measures. The three factors were

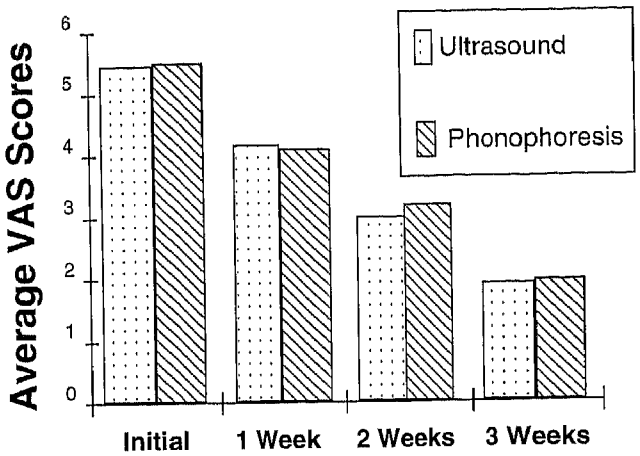

Figure 2—Average VAS scores for both treatment groups

TABLE 3. ANOVA summary for VAS scores.

Source	df	Mean Squares	F-statistic	Probability
Group	1	0.585	0.05	0.824
Subject	48	11.735		
Time	3	113.514	67.87	0.0001
Group × time	3	0.260	0.16	0.926
Time × subject	144	1.672		

Group (2 levels: drug group vs US group), Time (4 levels, repeated: initial score and at the end of 1 wk, 2 wk, and 3 wk), and Side (2 levels, repeated: involved vs uninvolved).

The PGA results were evaluated by calculating the percentage change of VAS scores and comparing these with PGA judgments after completion of treatment. The percentage change of VAS scores were defined as follows:

$$\%\Delta VAS = (VAS\ initially - VAS\ at\ 3\ weeks)/VAS\ initially$$

RESULTS

VAS scores broken down by group and time are shown in Figure 2. The results of the ANOVA are summarized in Table 3. When both groups are combined, a significant decrease in VAS scores over time is found (equivalent to a decrease in pain).

Algometer forces tolerated can be seen in Figure 3. The ANOVA summary for these results is in Table 4. Tolerance to algometer force for both groups combined showed a significant improvement (i.e., higher algometer scores, which are equivalent to a decrease in tenderness) over the 3 wk of treatment. In addition the uninvolved limb tolerated algometer pressures significantly higher than the involved limb. The interaction between time and side showed a significant improvement for the involved limb but no change for the uninvolved limb over time.

No other comparisons resulted in significant differences. In particular, there were no differences found between the PH group and the US group for either measure.

PGA scores compared with average percentage change of VAS for each score category are shown in Table 5. The number or frequency of subjects rated in each category are listed next to their average changes in VAS scores.

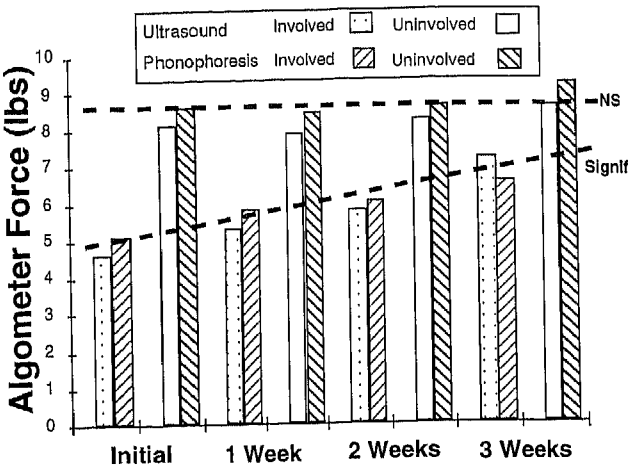

Figure 3—Pressure algometer force values for both treatment groups and for both limbs.

TABLE 4. ANOVA summary for algometer pressures.

Source	df	Mean Squares	F-Statistic	Probability
Group	1	12.421	0.27	0.603
Subject	48	45.212		
Time	3	28.933	11.45	0.0001
Group × time	3	1.331	0.53	0.665
Time × subject	144	2.527		
Side	1	689.531	44.32	0.0001
Group × side	1	3.473	0.22	0.639
Side × subject	48	15.558		
Time × side	3	9.430	4.59	0.004
Group × side × time	3	1.494	0.73	0.538
Side × time × subject	144	2.055		

TABLE 5. Physician Global Assessment compared to average changes in VAS.

PGA Assessment	N	% Change VAS
Complete recovery	4	100
Much improvement	33	72.4
Slight improvement	9	49.8
No Change	2	−17
Worse	1	−11

DISCUSSION

Transcutaneous drug delivery through the use of topically applied agents has been used for the treatment of systemic conditions such as motion sickness, hypertension, and angina, and for the local treatment of musculoskeletal injuries. The use of physical modalities like US has been studied as a way to enhance the delivery of these compounds. Phonophoresis has been used typically with local anesthetics, anti-inflammatories, and counterirritants to treat both pain and inflammation. The potential advantages for this application are that it is noninvasive, minimizes the risk of hepatic and renal injury from drug elimination, is essentially reversible by removing the drug from the skin, and is well tolerated by patients. A number of questions remain, however, regarding the extent of transdermal penetration, the bioavailability of medications delivered by this method, the most effective doses of US, the concentration of medications to be used, the type of coupling agents, and the most appropriate clinical indications.

The outermost layer of the epidermis, or the stratum corneum, is recognized as the primary barrier to the transdermal penetration of medications and physical agents like US. Factors that alter the integrity of this layer can dramatically affect diffusion across it. Skin that is thick, dry, and hypovascularized, for example, can significantly limit diffusion. Alternatively, when the stratum corneum is denuded because of abrasion or burn, movement can be greatly facilitated. Preheating the skin has also been shown to enhance transdermal drug delivery. Heating alters cell permeability and may dilate hair follicles and sweat glands, both potential sites of entry for drug molecules (11).

Topically applied drugs can induce both local and systemic effects distinguished typically by local tissue drug concentrations and blood or urine levels. Research has suggested that these effects occur by separate mechanisms, supporting the notion of a unique local delivery system (38).

The mechanisms by which US acts as an enhancer of drug delivery are poorly understood. Both the thermal and nonthermal properties of US have been considered. Temperature elevations of approximately 5°C can cause detectable changes in cell membrane permeability and this level of heating is attainable with 1.5 $W \cdot cm^{-2}$ or higher (5). The nonthermal, or mechanical, properties of US are less well defined. These are believed to influence drug delivery by increasing cell permeability, causing particle oscillations within the tissue and drug milieu, and perhaps inducing drug molecule motion through radiation pressure forces. The most likely mechanical explanation is thought to be intercellular diffusion from high-speed vibration of drug molecules along with vibration of the cell membrane and its components (8).

The present study was designed to evaluate the efficacy of PH using a corticosteroid gel with proven US transmissivity. In addition, the use of pressure algometry as an outcome tool has not been reported in prior studies using this modality. The results suggest that US appeared to be effective in reducing the symptoms of this group of subjects. They reported a decrease in pain (VAS), and they tolerated higher algometer pressures after 3 wk of treatment. These changes were especially noteworthy because many of these subjects had been chronically involved with symptoms for longer than 3 months (34 of the 49 subjects).

The addition of Fluocinonide with US did not improve clinical outcomes. Incorporation of a control group receiving sham US would have improved the study design and allowed us to conclude that the US alone caused the reduction in symptoms. We did not introduce a "nontreatment" group into this study. While US has been frequently used as a treatment for soft-tissue inflammation, it cannot be considered a gold standard because the available research remains inconclusive regarding its clinical efficacy (1,4,16,22,29,36,40,42). However, given the chronicity of symptoms in the majority of these subjects, their precondition constituted a baseline form of control. Specifically, there was no change in their symptoms for many months, but after 3 wk of US treatment there was a significant improvement.

VAS proved to be an effective technique for monitoring our subject pain levels and the VAS has been shown to be a valid technique for pain evaluation (7,30,48,52). These scores were quick and easy to use and clearly demonstrated the pain status of subjects as it related to a self selected functional activity. The VAS also agreed well with the more subjective PGA. Clinicians should be able to apply the PGA when keeping records of patient conditions over extended time periods.

The pressure algometer also seems to be an effective and sensitive tool in assessing these conditions and evaluating treatment outcome. Algometry has previously been validated in assessing myofascial tender points (19–21,44,47). However, we are unaware of any published reports applying algometry directly to tendons. Pressure tolerance increased over the 3 wk of treatment for the involved limb and also clearly indicated differences between the involved and uninvolved limbs. Use of a standard technique is critical for successful measurements and a period of training is highly recommended for those considering this tool. Given the obvious variability in tissue sensitivity, exact localization of tender points is also required.

A breakdown of results by individual conditions was not possible because of an insufficient number of subjects in several of the symptom categories (Table 2). Because the ultrastructural characteristics, vascularity, and biomechanical demands of the involved tissues are quite different, a uniform response to treatment should not be assumed. Future studies might investigate the effects of US on specific conditions.

Transdermal identification of corticosteroid in the clinical setting has proven difficult and was not addressed in this study. Additional work is required to address not only the controversy over the potential depth of drug penetration with this technique, but to tie this together with clinical outcomes. A number of other variables that were held constant in this study also require investigation to gain a better understanding of this technique. These include the effects of different frequencies and intensities of US, the mode of therapy (continuous vs pulsed), duration of treatment, and the transmission of US through different agents and with varying concentrations of drugs.

CONCLUSIONS

Ultrasound can be used to reduce pain and pressure sensitivity in selected musculotendinous conditions. The addition of a corticosteroid (Fluocinonide) to the US gel does not change the efficacy of treatment.

Both the VAS and pressure algometer can be used to monitor changes in pain level and pressure sensitivity. The PGA can also be used effectively to describe patient progress. Levels of change in the PGA can be related to VAS scores.

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