Treatment of Joint Inflammation & Pain using a Sonotron®

by

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INTRODUCTION

The Sonotron® (Sonotron Medical Systems, Inc., ADM Tronics Unlimited, Inc., Northvale, New Jersey) is a non-invasive device which employs modulated radio frequency energy in the form of a visible and audible discharge beam emanating from a discharge electrode and has been used therapeutically in animals and is currently being evaluated for safety and efficacy in humans for relief of joint pain and improvement in the overall functional capacity of the joint (Dr. Stephen L. Brenner, data on file, ADM Tronics Unlimited, Inc., 3/19/96).

Results in animal models have demonstrated beneficial effects following treatment with the Sonotron. Rats with adjuvant-induced arthritis had less soft tissue swelling and joint destruction after treatment with this device compared with controls (Dr. James J. Sciubba, data on file, 7/10/86). In a study of horses, the group treated with the Sonotron had greater recovery from injury when compared to an untreated group (Crawford et al., 1991). In a multicenter, placebo-controlled comparative clinical study involving patients with osteoarthritis

of the knee, those patients receiving treatment with the Sonotron reported greater reduction of pain, improvement in function, and no adverse effects (Dr. James C. Houge, data on file, ADM Tronics Unlimited, Inc., 7/18/88).

The study described herein was conducted to determine the safety and effectiveness of Sonotron treatment on various painful inflamed joints, with study outcomes of change in degree of pain and mobility.

PROCEDURE

This single-center study was conducted at an AA Northvale Medical Associates Clinic located in the Lido Spa Pain Center and operated under the aegis of SonoTech, Inc in Miami, Florida.

Patient Selection

Selection of patients was based upon the following criteria: patients had to be over age 21 and ambulatory, and had to have a clinical diagnosis of a painful joint condition accompanied by roentgenographic confirmation thereof. When X-rays from a primary care physician were not available, verification of inflammation was established with X-rays taken at the clinic. All narcotic analgesics were to be

discontinued at least 48 hours prior to study entry, but non-narcotic analgesics and nonsteroidal anti-inflammatory drugs taken daily could be continued.

On screening, patients were excluded if they had a systemic disorder which might interfere with or impair evaluation, circulatory impairment of the lower extremity, previous major arterial vascular surgery, impaired sensory function in the lower extremity, infection or tumor or significant skin rash in or overlying the joint or surrounding soft tissue, metallic prosthetic joint replacement, a cardiac pacemaker, or a history of gout or calcium pyrophosphate arthritis. Potential patients were also screened out if they had been administered intra-articular corticosteroids in the previous three months, parenteral corticosteroids in the preceding month, treatment with oral or injectable gold, or any other remission-inducing or immunosuppressive drug within the previous six months. Pregnant women were excluded from the study, as were all patients who were unable or unwilling to comply with all study requirements.

Once selected, patients had to sign an informed consent form to indicate their willingness to participate in the study. An attending physician had to sign a form certifying that he explained the treatment with the Sonotron device, that the

Sonotron is new and investigational and as yet unapproved by the FDA, and that no assurance could be given regarding adverse side effects or reaction to treatment.

Patient Evaluation

Patients were evaluated at the time of selection for participation in the study. Evaluations included a complete medical history and physical examination, joint/site evaluation (described below), and fulfillment of the entry criteria.

Treatment

Sonotron treatment was administered by a technician to the anterior and posterior surface of the joint in three consecutive 15-second treatment units (TUs). A 15-second TU required a circular movement of the Sonotron device at the site of treatment in order to ensure uniform distribution of energy to the treated area. All TUs were uniform with respect to energy level, distance from the skin and duration of treatment.

After one week, treatment was repeated; at the end of the second week, treatment was repeated again. Thus, each treatment site was exposed to three

treatment sessions, each session involving three 15-second TUs, for a total of nine TUs over the 2-week period.

Treatment Sites

The sites of pain treated were as follows: back, shoulder, knee, hip, wrist, ankle, neck, elbow, finger, toe, and heel.

Scoring of Results

At the time of selection for entry into the study as well as at the end of the completed series of three treatments, each patient's perception of pain at the inflamed joint was scored using a horizontal number scale ranging from 0 (none) to 10 (most severe). The patient's evaluation of ability to use the joint or site was scored in a similar fashion, using a horizontal number scale ranging from 0 (no use) to 10 (normal).

Statistical Methods

Since both pain and ability to use joint or site scales are intrinsically ordinal (ranked) scales, summary statistics are presented as medians and ranges.

The properties of the data required that the differences in rank orderings be tested for significance using the Wilcoxon Sign Rank test rather than parametric tests. The difference in pain before and after treatment and the difference in ability to use the joint/back/muscle group before and after treatment were tested for significance for sites with evaluations by 8 or more patients. Since no power analysis was performed, the decision to test the significance of differences for sites with 8 or more patients was somewhat arbitrary and reduced the number of outcomes tested. Each test of significance was two-tailed and performed using an alpha level of 0.05.

RESULTS

Seventy three (73) ambulatory patients, 30 males and 43 females, age range 32 to 87 years, median age 59.5, with clinical diagnosis and roentgenographic evidence of joint or site inflammation completed the study. Their first treatments occurred between October 11, 1994 and October 1, 1995. One patient had been enrolled on two separate occasions during this time period. Data from his first set of treatments are used in this analysis to avoid lack of independence among

observations. The numbers and percentages of total patients affected in selected sites are listed in Table 1. Thirteen patients were treated in two areas.

Safety

No patient experienced any adverse effects.

Pain

When pain from all sites was taken into account, 71 (97.3%) patients reported some alleviation of pain and two (2.7%) reported no change.

The median amount of pain indicated by patients using a number scale ranging from 0 (none) and 10 (most severe) was 7 (range, 2 to 10) before treatment and 4 (range, 0 to 7) after treatment. The median difference in pain before and after treatment was -3 (range, -8 to 0), *i.e.*, a reduction of 3 units which was a statistically significant difference ($p<0.001$). No patient experienced an increase in pain.

The results analyzed by site are summarized in Table 2.

Joint/Site Use

When joint use for all sites was taken into account, 56 (76.7%) patients reported an increase in the use of the problem joint or site, 12 (16.4%) reported no difference in use after treatment, four (5.5%) reported less use after treatment, and one (1.4%) patient's evaluation was not available.

Before treatment, the median value for ability to use the joint/back/muscle group was 5 (range, 1 to 9), and after treatment this value rose to 7 (range, 3 to 10). The median difference in joint/back/muscle use before and after treatment was 2 (range, -2 to 6) ($p<0.001$).

The results analyzed by site are summarized in Table 3.

DISCUSSION

Following treatment with the Sonotron, nearly all patients (97.3%) in the population studied had some reduction in pain, and more than three-quarters (76.7%) experienced an increased ability to use the joint. Furthermore, despite small sample sizes, analysis by treatment site revealed large differences in pain and joint use before and after treatment. Treatment of the inflamed site with the Sonotron alleviated pain to a significant degree at the following sites: back, shoulder, knee, hip, and wrist,. Significant improvement in the ability of the patient to move the affected joint was observed in the back, shoulder, knee, and wrist. Some improvement in ability to use the hip was observed, but the difference before and after treatment was not statistically significant.

It has been hypothesized that the mechanism by which the Sonotron works is via low frequency sound waves with high tissue penetrance. Sound waves can have dramatic effects on both soft and hard tissue, from the destruction of stones and viruses to the more gentle and pain-relieving effects of localized therapeutic ultrasound. It is possible that the mechanism of action of the Sonotron is similar to that of ultrasound, even though each use different ranges of the sound spectrum. Absorption of ultrasonic radiation which produces localized heat

occurs in those areas with the greatest differences in acoustic impedance. The largest temperature increases occur in muscle tissue. Localized heat has been thought to increase local metabolism, cause hyperemia, inhibit sensory nerves, and cause muscle relaxation. Stimulation of fibroblasts with sound waves has been associated with increased protein synthesis in these cells. Changes in connective tissue extensibility and increases in membrane permeability have been observed. Many of these effects have been attributed to the generation of localized heat, but the use of pulsed ultrasound has largely eliminated any temperature increase within the tissue, indicating that non-thermal effects may also be present (James Sciubba, and Howard Kerpen, data on file, 3/10/86).

Additional consideration as to the mechanism of action of Sonotron should be given to the reduction in protein levels in synovial fluid of Sonotron treated joints (Crawford et al, 1991).

Possible limitations of this study include small sample sizes for some sites and lack of an independent concurrent control. Larger controlled trials are recommended to evaluate alternative treatment schedules and dosages and other factors associated with optimal response.

In summary, this study provides evidence that the Sonotron relieves pain and increases range of motion in patients with painful joint conditions following the treatment regimen defined in the study protocol. In addition, certain joints respond with varying degrees of improvement, e.g., from significant reduction of pain and increased range of motion for the knee, hip, and shoulder to moderate pain reduction and improvement of the range of motion in the back.

Overall, the beneficial effects observed following treatment with the Sonotron are in agreement with those of other studies in animals and humans.

REFERENCE

Crawford WH, Houge JC, Neirby DT, Di Mino A, Di Mino AA: Pulsed radio frequency therapy of experimentally induced arthritis in ponies. *Can J Vet Res* 1991;55:76-85.

Table 1. Patients affected at a selected site

SITE	N	% (N/73)
Back	21	28.8
Shoulder	14	19.2
Knee	11	15.1
Hip	8	11.0
Wrist	8	11.0
Ankle	7	9.6
Neck	6	8.2
Elbow	4	5.5
Finger	4	5.5
Toe	2	2.7
Heel	1	1.4

Table 2. Difference in pain before and after treatment.

SITE	N	MEDIAN DIFFERENCE	RANGE	P-VALUE
Back	21	-4.0	-7,0	<0.001
Shoulder	14	-4.5	-8,-1	<0.001
Knee	11	-3.0	-5,-1	0.001
Hip	8	-2.5	-5,0	0.016
Wrist	8	-3.5	-6,-2	0.008

Table 3. Difference in ability to use joint/back/muscle group before and after treatment.

SITE	N	MEDIAN DIFFERENCE	RANGE	P-VALUE
Back	21	2	0,5	<0.001
Shoulder	14	4	-2,6	0.004
Knee	11	1	-1,4	0.031
Hip	8	2	-1,5	0.063 (NS)
Wrist	8	3	2,5	0.016