

PULSED ULTRASOUND DOES NOT IMPROVE HEALING OF VENOUS ULCERS

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ABSTRACT. A controlled study of the effects of pulsed ultrasound was carried out in conjunction with a standard treatment for healing chronic leg ulcers on 44 patients divided randomly into two groups. All patients received standard treatment (paste impregnated bandage and a self-adhesive elastic bandage) plus placebo-ultrasound or pulsed ultrasound (1:9, 0.5 watt/cm² at 1 MHz, for 10 min) 3 days a week for 4 weeks, thereafter twice weekly for 4 weeks and once weekly for the following 4 weeks. Percentage healed ulcer area and comparison of percentage healed ulcers were examined after 4, 8 and 12 weeks. There were no significant differences in the proportion of healed ulcers or ulcer area in the pulsed ultrasound group as compared with the placebo group.

Key words: venous ulcers, pulsed ultrasound.

Experimental work has suggested that ultrasound can improve tissue healing (9), and that healed insonated tissue has greater strength and elasticity than tissue that has not been treated with ultrasound (2). The beneficial results obtained with the right dosage is thought to be due to several cellular effects, including fibroblastic stimulation (5). However, the wrong dosage can lead to tissue damage (5). Previous studies have indicated that pulsed ultrasound (0.5 w/cm² two or three times weekly, can be of benefit in leg ulceration (6). In a recent study by Callam and collaborators it was shown that pulsed ultrasound 0.5 w/cm² given weekly in conjunction with a standard treatment for chronic leg ulcers improves the rate of healing (2). However, in that study the control group did not receive placebo ultrasound. In the present study we have compared the effects of standard treatment (paste impregnated bandage and a self-adhesive elastic bandage) and pulsed ultrasound with standard treatment and placebo ultrasound using the same inclusion criteria and dosage (0.5 w/cm²) as used by Callam and collaborators (2).

MATERIAL AND METHODS

Forty-four patients with venous leg ulcers were referred from departments of internal medicine, surgery and primary health care centers. The exclusion of patients from the study was for the following five reasons, skin allergy to the standard treatment, evidence of peripheral arterial disease, rheumatoid arthritis, diabetes and venous ulcer due to trauma. There was no significant difference between the two groups in age and sex or initial ulcer area (Table I). All patients gave their consent to participate.

The patients were randomly assigned to either a control group which received a standard therapeutic regimen and placebo ultrasound or a treatment group receiving the same standard regimen plus pulsed ultrasound. The distribution of the patients was based on the use of randomised permuted blocks. The regimen consisted of: cleansing with saline; application of a paste bandage followed by a support bandage plus advice on exercise given on a standard instruction sheet.

Demographic data and assessment of ulcer aetiology, based on clinical examination and a patient questionnaire were recorded for all patients. A baseline tracing of the ulcer area was drawn. The ulcers were classified as deep (>1 cm) or superficial (≤1 cm).

The patient then had the standard treatment regimen with pulsed ultrasound (1:9) or placebo ultrasound. The dosage was 0.5 watt/cm² of pulsed ultrasound at 1 MHz; using an Enraf-Nonius machine with aquasonic gel for contact. The ultrasound was applied to the ulcer surface area and surrounding tissue for 10 min, keeping the probe applied for 1 min per probe head area. The patients were treated three times weekly for 4 weeks, thereafter twice weekly for 4 weeks and once weekly for the following 4 weeks unless healing occurred earlier.

Patients refused to continue or withdrew from the study for any of the following reasons: allergy to treatment; excessive pain; intervening illness preventing treatment for more than 1 week.

At the end of the 12 week study all tracings were analysed using a computer graphics program to calculate the areas of each ulcer. The tracings were identified by code numbers to exclude observer bias. Wilcoxon ranks sum tests were used to compare the percentage change in ulcer area. The cumulative percentage of healed ulcers in the two groups were compared by the use of life-table methods. The number of patients chosen to be sufficient to detect a 30% increase of ulcer healing frequency with 80% power ($\alpha < 0.05$).

Table I. Comparison of placebo ultrasound and pulsed ultrasound groups

	Placebo ultrasound	Pulsed ultrasound
Number of patients	22	22
Sex ratio (male:female)	10:12	9:13
Mean age (SD)	63.8 ± 12.5	66.9 ± 14.2
Mean ulcer area in cm ² (SD)	18.3 ± 34.9	19.1 ± 26.3
Deep (> 1 cm):		
Superficial (≤ 1 cm) ulcer	2:20	3:19

NS between groups.

RESULTS

Twelve of the 44 patients (7 in the control group and 5 in the treatment group) were withdrawn from the study, Table II; the difference is not statistically significant. Ulcers healed within 12 weeks in 8 of the patients in the control group and in 10 in the treatment group. The two groups did not differ significantly in the cumulative percentage of cases healed in relation to time, Table III. The lack of difference was also maintained when taking withdrawals into consideration. If analyzed as intention to treat there were similar non-significant findings between the groups.

Comparison of decrease in ulcer area against time for all patients who completed the trial showed no significant difference between the control and treatment groups, Table IV. This lack of significant difference persisted for the duration of the study. Although there was no significant difference between groups there was a clear tendency that the actual ultrasound was more effective than the placebo.

DISCUSSION

Ultrasound has been shown to be beneficial in wound healing, both in the treatment of pressure ulcers and

Table II. Comparison of withdrawals

	Placebo ultrasound	Pulsed ultrasound
Allergy	3	2
Pain	1	1
Refusal/non-attendance	3	2
	7/22	5/22

NS between groups.

Table III. Comparison of cumulative percentage healed ulcers against time

During the first 4 weeks the patients received 3 treatments weekly. During the following 4 weeks they were treated twice weekly and during the last 4 weeks treatment was given once a week

Time (weeks)	Placebo ultrasound	Pulsed ultrasound
2	6 (n=1)	6 (n=1)
4	6 (n=1)	12 (n=2)
6	13 (n=2)	24 (n=4)
8	20 (n=3)	30 (n=5)
10	39 (n=6)	47 (n=8)
12	52 (n=8)	59 (n=10)

NS between groups.

in the preparation of trophic ulcers for skin grafting (6, 9). Experimental studies have shown that ultrasound can stimulate protein synthesis and that it influences the cellular activity of fibroblasts (5), enhancing healing at sites of injury. The clinical trial by Dyson and colleagues on ultrasound in chronic leg ulceration suggested that this could be of benefit, but there were only 9 patients in the treatment group (6).

Previous studies, on a variety of treatments for chronic leg ulcers, have shown "healing rates" of up to 65% in 3 months (3, 7), but these have been small uncontrolled studies. In a recent controlled trial it was shown that with the use of a standard weekly treatment 30% of ulcers healed in 3 months, and that this figure could be improved to 50% by the use of ultrasound (2). In the present study there was no significant difference between pulsed ultrasound and placebo ultrasound in the treatment effect of venous ulcers. However, the number of patients completing this study is not significant to detect a ≤ 30% difference in healing. It is possible that the effects obtained with

Table IV. Comparison of percentage ulcer area against time, mean ± SD, in patients completing the study

Baseline ulcer area of each patient defined as 100%. 0 = before start of treatment. After 4, 8 and 12 weeks of treatment

Treatment	Weeks			
	0	4	8	12
Placebo ultrasound	100	81 ± 9	53 ± 10	43 ± 6
Pulsed ultrasound	100	76 ± 12	47 ± 8	39 ± 5

NS between groups.

standard weekly treatment plus pulsed ultrasound by Callam and collaborators (2) reflects the effect of extra care and supervision given during the ultrasound treatment.

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