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# A PLACEBO CONTROLLED TRIAL OF ULTRASOUND THERAPY IN CHRONIC LEG ULCERATION

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**ABSTRACT. A controlled study of the effects of ultrasound on healing chronic leg ulcers was carried out in conjunction with standard treatment on 38 patients divided randomly into two groups. All patients received standard treatment (paste impregnated bandage and a self-adhesive elastic bandage plus placebo ultrasound or ultrasound (1.0 watt/cm² at 1 MHz, for 10 min) twice weekly for 8 weeks. Percentage healed ulcer area and number of healed ulcers were compared after 2, 4, 6 and 8 weeks. There were no significant differences in the proportion of healed ulcers or ulcer area in the ultrasound group as compared with the placebo group.**

*Key words:* ultrasound therapy, chronic leg ulcer.

Ultrasound has been shown to be beneficial in wound healing, both in the treatment of pressure ulcers and in the preparation of trophic ulcers for skin grafting (6, 10). Experimental studies have shown that ultrasound can stimulate protein synthesis and that it influences the cellular activity of fibroblasts (4), enhancing healing at sites of injury (5, 7, 12). 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).

## MATERIAL AND METHODS

Thirty-eight patients with venous leg ulcers were referred from departments of internal medicine and surgery and from primary health care centers. 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 ulcer or venous ulcer due to trauma. There was no significant difference between the two groups in age, sex or initial ulcer area (Table I). All patients gave their consent of participation.

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 ultrasound. The regimen consisted of: cleaning with saline; application of a paste bandage followed by a support bandage plus advice on exercise given on a standard instruction sheet (1).

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 patients then received the standard treatment regimen with ultrasound or placebo ultrasound. The dosage was 1.0 watt/cm² of ultrasound at 1 MHz, using an Enraf-Nonius machine with aquasonic gel for contact. The diameter of the ultrasound head was 2.8 cm when treating the superficial ulcers and 1.2 cm when treating the deep ulcers. The reason for using a smaller ultrasound head when treating the deep ulcers was to enable treatment of the complete ulcer area. The placebo ultrasound was carried out using the same unit but there was no output into the ultrasound head. The treatment was applied to the ulcer surface area and surrounding tissue for 10 min. The patients were seen twice weekly for 8 weeks unless healing occurred earlier.

Patients refused to continue the study or withdrew 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 8 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

Table I. *Comparison of placebo ultrasound and ultrasound groups*

| | Placebo ultrasound | Ultrasound |
|---|---|---|
| Number of patients | 19 | 19 |
| Sex ratio (male : female) | 7 : 12 | 8 : 11 |
| Mean age (SD) | 59.2 ± 16.3 | 63.2 ± 13.4 |
| Deep (>1 cm) ulcer: Superficial (<1 cm) ulcer | 3 : 16 | 4 : 15 |
| Median ulcer area in cm² | | |
| Deep ulcers | 2 (2–6) | 2 (2–4) |
| Superficial ulcers | 10 (3–89) | 11 (4–97) |

NS between groups.

Table II. *Comparison of withdrawals*

| | Placebo ultrasound | Ultra-sound |
|---|---|---|
| Allergy | 2 | 3 |
| Pain | 1 | 2 |
| Refusal/non-attendance | 3 | 2 |
| | 6/19 | 7/19 |

NS between groups.

compare the percentage change in ulcer area. The cumulative percentage of healed ulcers in the two groups was compared by the use of life-table methods. The number of patients was chosen to be sufficient to detect a 40% increase of ulcer healing frequency with 80% power ($\alpha < 0.05$).

## RESULTS

Thirteen of the 38 patients (6 in the control group and 7 in the treatment group) were withdrawn from the study (Table II); the difference is not statistically significant. Ulcers healed within 8 weeks in 4 of the patients in the control group and in 6 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 analysed 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 differences persisted for the duration of the study. Although there was no significant difference between groups there was a tendency that the ultrasound was more effective than the placebo.

Table III. *Comparison of cumulative percentage healed ulcers against time*

| Time (weeks) | Placebo ultrasound | Ultra-sound |
|---|---|---|
| 2 | 0 | 8 |
| 4 | 8 | 17 |
| 6 | 15 | 25 |
| 8 | 30 | 41 |

NS between groups.

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

Baseline ulcer area of each patient defines as 100%. 0 = before start of treatment. After 2, 4, 6 and 8 weeks of treatment

| | Weeks | | | | |
|---|---|---|---|---|---|
| Treatment | 0 | 2 | 4 | 6 | 8 |
| Placebo ultrasound | 100 | 86±11 | 73±12 | 61±8 | 48±13 |
| Ultrasound | 100 | 79±9 | 65±14 | 54±9 | 42±9 |

## DISCUSSION

Experimental work has suggested that ultrasound can improve tissue healing (5, 7, 11, 12), and that healed ultrasound treated tissue has improved strength and elasticity (3, 7). The beneficial results obtained with ultrasound is thought to be due to several cellular effects, including fibroblastic stimulation (4). However, the wrong dosage can lead to tissue damage (4). Previous studies have indicated that ultrasound can be of benefit in leg ulceration (2, 6). In a recent study by Callam and collaborators it was shown that ultrasound given weekly in conjunction with a standard treatment for chronic leg ulcers improves the rate of healing (2). In the present study there was no significant difference between ultrasound and placebo ultrasound in the treatment effect of venous ulcers. These results are supported by a previous study using pulsed ultrasound (8). However, the number of patients completing this study was insufficient to detect a $<40\%$ difference in healing.

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