

A randomized controlled trial of electromagnetic therapy in the primary care management of venous leg ulceration

JE Kenkre, FDR Hobbs, YH Carter, RL Holder and EP Holmes

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Objective. The aim was to establish the potential efficacy, tolerability and side-effect profile of electromagnetic therapy as an adjunct to conventional dressings in the treatment of venous leg ulcers.

Method. A prospective, randomized, double blind controlled clinical trial was carried out in a dedicated leg ulcer clinic based in one urban general practice. Nineteen patients with leg ulcers of confirmed venous aetiology were assessed. The main outcome measures were rate and scale of venous leg ulcer healing, changes in patient-reported pain levels, quality of life, degree of mobility, side effect profile and acceptability to patients and staff.

Results. Sixty-eight per cent of patients attending this dedicated clinic achieved improvements in the size of their ulcer (4, 21%, healed fully) and in reduced pain levels ($P < 0.05$) during the trial, despite the chronicity of ulcer histories. Patients treated with electromagnetic therapy at 800 Hz were found at day 50 to have significantly greater healing ($P < 0.05$) and pain control ($P < 0.05$) than placebo therapy or treatment with 600 Hz. All patients reported improved mobility at the end of the study. The electromagnetic therapy was well tolerated by patients, with no differences between groups in reporting adverse events, and proved acceptable to staff.

Conclusions. Despite the small numbers in this pilot study, electromagnetic therapy provided significant gains in the healing of venous leg ulcers and reduction in pain.

Keywords. Electromagnetic therapy, RCT, leg ulcers, primary care.

Introduction

Leg ulceration affects approximately 0.15%¹ to 0.18%² of the UK population. At any one time around 100 000 people in the UK will have active ulceration.¹ These prevalence figures are likely to be underestimates due to under-reporting.³ Moreover, 1% of the population have experienced leg ulceration at some point in their life,⁴ with ulcers following lengthy cycles of ulceration, healing and re-ulceration, often spanning decades.⁵ Half of patients suffer their first ulcer before the age of 65 years,⁶ but there is a marked increase in incidence with age.^{1,3,7,8} Since the

population aged 60–74 years is predicted to rise by 43%, 75–84 years by 48% and over 85 years by 138% over the next 35 years,⁹ ulcer prevalence could rise dramatically.

Leg ulcers are associated with pain, immobility, social isolation and embarrassment.¹⁰ Pain is considered by patients to be the worst aspect of having an ulcer,¹⁰ but 55% of nurses were found routinely not assessing this.¹¹ Although patients may live in symbiosis with their ulcers for many years,¹² anxiety and depression have been shown to reduce following ulcer healing and pain reduction.¹²

Total costs of leg ulcer management in the National Health Service are unknown, but have been estimated at £100–600 million per year¹³ or £300 million.¹⁴ The annual cost per patient is calculated at £1000–5200.¹⁵ Over 60% of treatment costs are for

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Department of General Practice, Medical School, University of Birmingham, Edgbaston, Birmingham B15 2TT, UK. Correspondence to Professor Hobbs.

community nursing services,¹⁶ although this may be reduced by 60% by establishing dedicated clinics.¹² Community nurses may spend 44% of their time dressing and providing care for leg ulcers,¹⁷ yet treatment usually remains ineffective.¹⁸ Randomized trials have shown that compression therapy,¹⁹ by short stretch bandages or the four-layer bandage system,²⁰ improves ulcer healing rates, but these studies suffer from small sample size and are not placebo controlled. Therefore despite the high costs of many traditional treatment options, uncertainty remains regarding the most effective treatment for leg ulcers.

It is speculated that alternative therapies, such as electrical stimulation, may enhance ulcer healing,²¹ with significant improvements using a pulsed field device.²² Electrical stimulation is thought to have an anti-bacterial effect, enhancing wound healing by stimulating growth factors and therefore collagen synthesis.²³ Pulsed magnetic field treatment may increase collagen production by altering cyclic AMP metabolism.²⁴ Natural direct currents in the epidermis have a speculated involvement in normal regeneration of tissue.²⁵

This randomized controlled trial was therefore designed to pilot test whether electromagnetic therapy induced significant healing of confirmed, chronic venous leg ulcers in comparison to placebo therapy.

Methods

The study was conducted at a dedicated clinic within an urban general practice for 12 months commencing from June 1993. Patients were referred into the study by their general practitioners (GPs), practice/community nurses or consultants. To confirm eligibility, patients referred to the study underwent a specialist assessment in the vascular unit at the Queen Elizabeth Hospital, Birmingham. This assessment included a drawing, photograph, bacterial swab and pain assessment of the ulcer; ankle brachial pressure index (ABPI); blood pressure and mean arterial pressures; and a quality of life questionnaire.

For inclusion into the study, the patient's venous ulcer should have demonstrated unsatisfactory healing for at least the previous 4 weeks. Nineteen patients who conformed to the entry criteria were randomized to treatment by either an active or an indistinguishable placebo machine. All patients received a 30-minute treatment session on week days for a total of 30 days. This was followed by a 4-week observation period with dressing changes only and a final assessment on day 50. Patients' previous dressing regimens remained unchanged during the trial. However, if healing ulcers required fewer dressing changes, due to a decrease in exudate, a more suitable dressing was applied.

Patients were assessed on treatment days 1, 5, 20, 30 and the final observation on day 50. Parameters

measured included blood pressure, ABPI index, ulcer area, photograph of the leg, appearance of the ulcer and surrounding skin, pain intensity and clinical global assessment. The latter was a subjective opinion given by the investigator as to the overall appearance of the ulcer in relation to its appearance at the initial assessment. To measure the area of the ulcer, an outline was drawn onto sterile acetate sheets and the shapes cut out and weighed. The resulting weight in milligrammes was then assumed to be proportional to the ulcer area. The pain intensity was measured on an analogue scale.

The electromagnetic device (Elmedistraal) generates perpendicular electric and magnetic fields,²⁶ delivered through a pulse generator creating a frequency of 100, 600 or 800 Hz. The pulsed current is supplied to a pair of electromagnetic lenses and electrodes, generating a magnetic field of 25 μ Tesla. The electromagnetic lenses and the electrodes are positioned onto the patient's lower limb by means of an elasticated support, with fields orientated transversely to the axis of the limb. The degree of penetration through human tissue is approximately 30 cm in any direction from the lens/electrode system. Of the first nine patients, those randomized to active treatment received treatment of 600 Hz. Those randomized to active treatment amongst the following 10 patients received treatment of 600 Hz on days 1-5 then 800 Hz on days 6-30.

Data were analysed using Minitab and the Statistical Package for the Social Sciences (SPSS). Active versus placebo differences were analysed for statistical significance by using paired *t* tests, analysis for variance and chi-square tests of association.

Results

Of the 19 patients recruited, 9 were treated on the placebo machine (group A); 5 were actively treated with 600 Hz (group B1) and 5 with 800 Hz (group B2). No significant differences were found between these groups prior to treatment in all parameters measured, with the exception of age. The age of the patients participating in the study ranged from 42 to 87 years, with a mean age of 71 years. There was a significant difference ($P < 0.05$) in the mean age between group A (73 years), group B1 (59 years) and group B2 (78 years). The male to female ratio was 5:14, with both sexes represented in all three groups.

Fourteen (74%) patients were taking pain-relieving medication and eight (42%) were taking diuretics. Thirteen (68%) patients had been having their leg ulcers treated at home by community nurses, with 11 of these receiving three visits per week. For the remaining six (32%) patients having dressings changed at their own practices, one patient was seen on alternate days (including the weekend), one was making twice-weekly visits and four attended weekly.

TABLE 1 Duration of ulceration and size of ulcer in both active and placebo groups (n = 19)

	A (n = 9)	B1 (n = 5)	B2 (n = 5)
Mean duration of ulceration (weeks)	962.6	230.4	418
Range of duration of ulceration (weeks)	160-2548	36-728	36-1368
Mean length of present ulceration (weeks)	356.9 ^a	38.6	105.6
Mean length of ulcer (mm)	49.1	26.6	49
Range of length of ulcer (mm)	26-115	11-75	35-74
Mean ulcer area (mg)	119	63	81
Patients who have had repeated ulceration	8	4	3

^a The values for duration of ulceration are not homologous: two patients within group A had long histories of ulceration, producing two exceptionally large results.

Ulcer histories ranged from 7 months to 49 years. Mean ulcer length was 43.5 mm (range 11-115 mm). Four (21%) patients were suffering from ulcers for the first time, whereas 15 (79%) were in the cycle of ulceration, healing and re-ulceration (Table 1). Seven (37%) patients had a past history of varicose vein surgery. On examination, 11 (58%) had varicosities of the long and short saphenous veins, and six (32%) had perforating vein incompetence. Ankle oedema was present in eight (42%) of the patients. One or more of the signs associated with ulceration, such as hyperpigmentation, rubor, erythema, stasis dermatitis and lipodermatosclerosis, were seen in 18 (95%) of the patients. None of the ulcers was clinically infected, although 16 (84%) were colonized with bacteria.

No significant difference was found between the mean arterial pressures of the study groups at the initial assessment. Minor changes in mean pressures observed after treatment were not significantly different between the three groups. At the initial assessment there were no significant differences found in the systolic blood pressures taken in the supine, sitting and standing positions between groups A, B1 and B2. However, by day 30, the pressures had fallen in groups A and B1 but risen in two positions (sitting and standing) in group B2. This difference between groups A, B1 and B2 was found to be significant in the standing position ($P < 0.05$). No significant differences between the groups were detected in the changes in diastolic pressure from initial assessment.

No significant variation in heart rate was found between groups A, B1 and B2 in the mean heart rate on initial assessment in any of the positions measured. The change in heart rate prior to treatment compared with after treatment also did not differ significantly between

the groups initially but by day 30 the mean heart rate had lowered in groups A and B1, but had risen slightly in group B2 ($P < 0.05$)

Changes in ulcer area

The mean area of the ulcers (measured by weight of sterile acetate sheets just covering the sites) at the initial assessment did not differ significantly between the three groups. Thereafter, the overall trend was that the mean ulcer sizes decreased in groups A and B2 (Table 2). The increase in the mean ulcer size in group B1 was related to one female patient with a large ulcer with poorly defined boundaries.

By day 30, the end of the treatment phase, some ulcers had completely healed in groups A and B1 and nearly healed in group B2. This trend for healing was better in groups A and B2 than B1, compared to the initial assessment visit. By day 50, the reduction in the ulcer area from the initial assessment was significant in group B2 ($P < 0.05$) and significantly different between groups A, B1 and B2 ($P < 0.05$) with the largest reduction in ulcer size occurring in group B2. Percentage mean reduction was 63% in group B2 and 34% in group A and in all three groups some ulcers healed despite having long histories. The clinical global assessment ulcer scores achieved during the study can be seen in Table 3 (scale of +4 healed to -3 markedly worse).

TABLE 2 Mean weight of study ulcers (mg) and ranges within each group (mg equivalent to size)

	Mean size of ulcer	Ranges of ulcer size
Initial assessment		
A	119	35-526
B1	63	6-269
B2	81	46-197
Assessment day 5		
A	114	19-535
B1	98	6-426
B2	68	31-180
Assessment day 20		
A	102	4-506
B1	81	13-290
B2	61	21-192
Assessment day 30		
A	93	0-413
B1	111	5-458
B2	50	0-170
Assessment day 50 ^a		
A	78	0-373
B1	103	0-394
B2 ^b	30	0-100

^a Significant differences in the reduction from initial assessment ($P < 0.05$).

^b Significant reduction from initial assessment ($P < 0.05$).

TABLE 3 Progress or regression of the ulcers during the study

	Day 5	Day 20	Day 30	Day 50
Group A				
Patient 1	+1	0	+3	Healed
2	0	+3	+2	+3
3	0	0	0	-3
4	-2	0	-3	-2
				(Infected)
5	0	0	+1	+2
6	+1	+1	0	-2
				(Infected)
7	0	0	+1	0
8	+1	+3	Healed	Healed
9	0	-1	+1	+3
Group B1				
Patient 1	-1	-2	-2	-3
2	-1	0	+1	+1
3	0	0	+1	-2
4	+1	+3	+3	-2
5	0	+1	+3	Healed
Group B2				
Patient 1	+1	+2	+3	Healed
2	0	-2	+1	+2
3	0	+2	+3	+2
4	+1	+1	+2	-3 ^a
5	0	+2	+3	+3

^a Advanced ischaemic ulceration.

TABLE 4 Mean ulcer pain scores read from analogue scales in mm

	Mean pain (mm)	Range of mean values
Day 1 prior to treatment		
A	47	0-68
B1	60	37-76
B2	62	29-90
Day 30 ^a		
A	41	0-88
B1 ^b	17	0-44
B2 ^b	36	0-84

^a Significant differences in the reduction from initial assessment ($P < 0.05$).

^b Significant reduction from initial assessment ($P < 0.05$).

Pain and quality of life

There were significant reductions in pain scores from day 1 to day 30 (Table 4) with the largest decrease in pain being in group B1 ($P < 0.05$) with a mean reduction of 43 mm (72%), followed by group B2 ($P < 0.05$) with a mean reduction of 26 mm (42%) and a reduction of only 6 mm (not significant) in group A. There was also a significant difference in the reduction in pain scores between groups A, B1 and B2

TABLE 5 List of adverse events in groups A, B1 and B2

Symptom	Number of patients			Treatment day ADR occurred	Occurrence (days)
	A	B1	B2		
Headache	-	1	-	2	2-20
Headaches plus pins and needles in arm and leg	-	1	-	18	18-26
Rash on forearms	-	1	-	16	16-18
Rash on lower leg	-	-	1	5	5-8
Night cramp	-	-	1	7	7
Pain/rash	1	-	-	6	6-23
Pins and needles	1	-	-	3	3
Heat in foot	1	-	-	1	1-6
Heat in leg	1	-	-	5	5-7
Pins and needles and heat	-	1	-	1	1
Tickling sensation	-	-	1	2	2
Tingling sensation	-	-	1	2	2
Advanced ischaemia	-	-	1	-	-

($P < 0.05$). In group B1, the pain intensity in all the patients had diminished. Of the five patients in group B2, two patients with mild pain initially experienced no pain at the end of the treatment while the two patients who originally reported moderate pain improved to mild.

After treatment, patients in group A and B2 improved in their ability to walk up a flight of stairs. All three groups improved when walking a distance consistent with a block of houses, which may be due to increased mobility whilst attending the daily clinic. At the initial assessment, 11 (58%) patients stated that, since their ulceration, they went out for entertainment less often, seven (37%) were less sociable to friends and neighbours and 12 (63%) went out visiting less frequently. By day 30 these numbers changed to eight (42%), three (16%) and eight (37%) respectively.

Adverse events

Thirteen patients (68%) experienced adverse events during the study (Table 5): two uncharacteristically suffered moderate to severe headaches during treatment periods (both on active treatment) and six experienced sensations of heat, tingling, and pins and needles in the lower half of the limb during treatment (three active and three placebo). No patients withdrew from the study because of these adverse events.

Discussion

Recruiting patients with suitable ulcers into the study proved difficult, despite the expected prevalence of 1500-1800 ulcer sufferers in Birmingham, of whom

54–75% would be of venous origin. The frequency of ulcer dressings prior to the study was comparable with that in other studies.⁵ Six different types of dressings were being used and notes revealed a plethora of previous dressings, ointments, powders and solutions. Compression bandaging has been shown to be effective in the healing of venous ulcers,^{19,20} yet only two patients were receiving adequate compression therapy. Colonizing bacteria were found in the ulcers of 16 patients at the initial assessment. Healing may not be impaired by the presence of bacteria,^{27,28} rather infection in wounds may accelerate healing by evoking an inflammatory response.^{29,30}

The study ulcer area in the group treated with 800 Hz was found, at the final assessment, to have a significantly greater healing area than the 600 Hz and placebo groups. However, the group treated with 600 Hz was found to have achieved less healing than the placebo group. The degree of pain experienced by patients was not related to the extent of ulceration. None of the patients in group A experienced a reduction in pain despite healing of ulcers. However, perceived pain showed a marked reduction in both the active treatment groups, especially in the patients treated with 600 Hz. The severity of pain experienced was found to be significantly improved in the 800 Hz treatment group. In a study by Stiller *et al.*²² in which leg ulcer patients were treated with pulsed electromagnetic fields, a significant improvement in the healing of leg ulcers and a marked reduction in pain intensity was recorded in the active group against a placebo group.

Although 84% of the patients had concurrent disabilities which could affect their walking ability, the majority felt that most restriction in this area was due to their leg ulceration. Patients were acutely aware of the smell produced by their ulcer (although in most cases it was undetectable) and embarrassed by the unsightliness of their dressings when the ulcer leaked. In this study a combination of these factors reduced the patients' desire to leave the house and some became restricted to their homes. As a consequence of restricted mobility, 48% of the patients were unable to carry out light household tasks and 74% could not do heavy housework. During the course of the study, the mobility of all patients improved, they felt more sociable, and were more willing to go out visiting and for entertainment.

The findings that patients within all groups improved, despite them representing a resistant group, was encouraging for both the dedicated nature of the clinic and the electromagnetic therapy. This study provides further impetus to establish leg ulcer clinics within the community. Moffat *et al.*¹² found that the healing rates improved as the clinics developed. Advantages were found in bringing together several patients with a common problem, many of whom have a limited contact with the world outside their own home. In many cases,

the patients had initially been very reluctant to give up an hour or two of the day to visit the clinic, despite few other calls on their time. Community based clinics have been shown to give the patient a sense of belonging and also a chance of an 'outing' without long delays in outpatients.^{12,31} They have also been shown to be cost effective.³¹

Ieran *et al.*³² found significant wound healing in patients being treated with pulsed electromagnetic therapy at 75 Hz after a 90-day treatment period: healing was within 71 days on average. In this study, ulcer healing improved in patients receiving electromagnetic therapy which continued after the cessation of treatment; this was consistent with Ieran's findings. Treatment with 800 Hz exhibited significantly more rapid healing, with reduced pain levels, over and above the improvement provided by the dedicated ulcer clinic care. All of the patients in this study tolerated their treatment sessions well.

In this pilot study, most patients with long-standing venous leg ulcers resistant to routine therapy improved in terms of ulcer healing and pain suffered, through the provision of consistent care in dedicated practice based clinics. Despite the small numbers, the addition of electromagnetic therapy provided significant additional gains in the rate and degree of ulcer healing and reduction in pain. There is need for further work to determine the optimal treatment dose, timing and duration of electromagnetic therapy.

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