PULSED ELECTROMAGNETIC FIELD (PEMF) : EFFECTIVE ADJUVANT THERAPY IN VENOUS AND VASCULITIC LEG ULCERS

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ABSTRACT

**Background**: Chronic leg ulcers occur in 1% of the adult population with considerable associated morbidity and tend to follow a chronic course of recurrent healing and breakdown. Venous insufficiency is the commonest cause of chronic leg ulcers in the community, but vasculitic ulcers are known to be more resistant to treatment and also more painful than ulcers of other aetiologies. A proportion of leg ulcers will heal on conservative treatment, those which do not respond cause considerable distress. Many modalities have been used for conservative treatment of leg ulcers and pulsed electromagnetic field (PEMF) was used for wound healing as it has a number of well-documented physiological effects on cells and tissues.

**Patients and methods**: A total of 48 patients with 53 resistant venous and vasculitic leg ulcers unresponsive to medical treatment were enrolled in this study. The patients were randomly divided into control group who received standard wound care and active (study) group who received standard wound care plus active (PEMF) therapy 3 days per week for 12 weeks for a total of 36 sessions. Ulcer size, appearance of the ulcer and surrounding skin, and pain inten-
including rheumatoid arthritis (RA) (5), scleroderma, lupus erythematosus (6).

Patients with RA are predisposed to developing chronic leg ulcers. Approximately 9-10% of patients with rheumatoid arthritis will experience leg ulceration (7,8,9), and as many as 10% of leg ulcers of any cause (10) and 12% of patients with a chronic venous ulcer can be seen in association with RA or have positive tests for RF (11). Whereas the exact incidence of leg ulcers in patients with systemic sclerosis (scleroderma) is currently not defined (12), however, some may consider it as the most common collagen disease causing leg ulceration (13). They may develop leg ulcers of varied aetiologies, including venous disease, infection and inflammation (vasculitis or pyoderma gangrenosum). The leg ulcers in these patients may involve several of these aetiological factors and are often difficult to heal (8,14). Leg ulceration is one of the cutaneous manifestations in Behcet’s disease and sometimes is very difficult to treat (15) while, incidence of leg ulcerations was found to be 5% of SLE patients (16) and can occur in SLE patients with antiphospholipid antibodies and/or vasculitis (17). Until now, the treatment of leg ulcers in patients with collagen-vascular disease remained rather ill-defined (18).

There is a wide variety of treatments of leg ulcers available which focused on alleviating the local hemodynamic changes include hemodynamic preventive measures, ulcer dressings, topical treatments and surgical or endovascular repair of the microvasculature (19). But it is generally agreed that elevation of the legs and compression bandaging is of central importance especially for venous ulcers. Pulsed electromagnetic fields (PEMF) have been used in the last years mainly in connection with healing of bone fractures, burns, wounds, and in treatment of various acute soft tissue injuries (20) and it is becoming more and more widely accepted as an alternative method for treatment. In such conditions, not only magnetic field therapy aids in recovery, but also, it allows these conditions to heal better, more quickly, and with less scar tissue. Magnetic treatment has been shown to decrease healing time.
groups; group A (study group) received active treatment and further subdivided into; group A1 which included twenty patients with chronic venous leg ulcer (diagnosed according to Standards recommended by the Society for Vascular Surgery/ North American Chapter and the International Society for Cardiovascular Surgery as criteria to define chronic venous leg ulcer (26)) and group A2 which included fifteen patients with collagen vascular disorders with a total of 18 ulcers (6 patients with RA, 5 patients with scleroderma, 2 patients with SLE, and 2 patients with Behcet's disease) who fulfilled the American College of Rheumatology criteria for each disease (27,28,29,30) and group B (control group) included thirteen patients with a total fifteen ulcers (8 patients with venous ulcer, 2 RA patients, 2 scleroderma patients, and 1 patient with Behcet's disease).

Thirty-five patients were randomized to the active treatment group and 13 patients to the control group. The control group were randomly allocated to receive standard wound-care treatment only, while The active group patients received standard wound-care and were treated by a course of PEMF therapy which was provided using commercially available apparatus, Magnetic Bio stimulation Device mbs-system: (G-pulse 210µp) applied by coil. PEMF therapy applied with intensity equal to 3mt and frequency of magnetic field impulses equal to 4 Hz. All patients in the active treatment group received a 30-minute treatment session 3 days per week for 12 weeks for a total of 36 sessions. This was followed by a 4-week observation period with dressing changes only. 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 allowed to continue systemic treatments for rheumatoid arthritis, scleroderma, Behcet's and lupus.

Assessment of the outcome of treatment was based on the parameters measured on the day of admission, at six weeks, and at the end of the treatment included ulcer size (calculated from the maximal length and breadth measured by cm), photo-
group A2 (fig.2) and only 2 (13.3%) ulcers in group B had completely healed, whereas, 10 (50%) ulcers in group A1, 7 (38.9%) in group A2 and only 2 (13.3%) in group B had shown a reduction of 50% in the ulcer area. The reduction in the ulcer area from the initial assessment was significant in groups A1 and A2 (P<0.001, P=0.004 respectively). Percentage mean reduction was 56.4% in group A1, and 48.6% in group A2 compared to only 17.2% in group B and significantly different between groups A1, A2 and B (P<0.01, =0.007 respectively) (table 2, fig.3). In both active subgroups, there were significant negative correlations between the initial size of the ulcer, ulcer duration and the percentage change in the ulcer area (P< 0.02, =0.007) for the venous ulcers and (P< 0.05, 0.02) for the vasculitic ulcers.

Pain at the ulcer site:

There were significant reductions in pain scores from start day to end day with the larger decrease in pain being in groups A1 and A2 (P< 0.001) with a mean reduction of 2.05 (61.17%), and 2.11 (54.28%) respectively and a reduction of only 0.47 (14.46%) (not significant) in group B (table 3, fig.4).

Adverse effects:

There were no reports of any adverse attributable to the use of PEMF therapy apart from increased feeling of desire to sleep after the session.
Figure 1. *Venous ulcer (A) at the enrollment of the study. (B) at the end of the treatment*.

Figure 2. *Vasculitic ulcer (A) at the enrollment of the study. (B) at the end of the treatment after 12 weeks*.
DISCUSSION

Vasculitic necrosis and ulceration of the skin are frequent complications of connective tissue diseases and are very difficult to heal \(^{(31)}\), as it may rapidly extend widely and deeply. Many vasculitic ulcers fail to respond to conservative treatment, and patients have to be admitted for long periods of bed rest, cleansing, ulcer excision and repeated skin grafting which often fail to take. Procedures that increase blood flow such as adjuvant prostacyclin infusion or lumbar sympathectomy may help \(^{(32)}\). A common vasculitic ulcer occur in RA, the causation of leg ulcers in patients with RA was found to be multifactorial—predominantly a mixed vasculitic and venous aetiology\(^{(33)}\). A proportion of rheumatoid ulcers will heal on conservative treatment, those which do not respond cause considerable distress and may end by the demand for amputation \(^{(34)}\). In short, vasculitis leg ulcers are an interdisciplinary therapeutic challenge. On the other hand, there is a paucity in alternative non-surgical therapies for ulcers that do not respond to conventional treatment that increases the need for new modalities in treatment, mean-while, PEMF has been used to promote wound healing with a growing increase of data demonstrating its biological effects \(^{(35)}\). So, this was a motive to design this study to assess whether low-frequency PEMF has a beneficial effective role as an adjuvant to non-surgical management of resistant leg ulcers.

RA patients with persistent leg ulcers tend to have long-standing, seropositive, erosive disease with a mean duration of open ulceration of 5-15 months \(^{(36,37)}\). This compares with a median duration of 6 months in patients with venous ulceration \(^{(11)}\). Although treatment regimes were not strictly comparable, these figures support the notion that ulcers in patients with RA are more resistant to treatment \(^{(8)}\). This was confirmed by our results.

The results of this study showed that PEMF stimulation had decreased the ulcer area by 61.2% of venous ulcers, and 54.3% for the vasculitic ulcers after 12 weeks of treatment in patients who received active treatment. These were consistent with the study of Jaran et al \(^{(38)}\) who found

MANSOURA MEDICAL JOURNAL
(39) found that the control group in their study exhibited a 48% increase in wound area, they explained that by the stringent protocol inclusion-exclusion criteria they followed and because their study sites were tertiary referral centers making the ulcers in their study particularly recalcitrant.

An important factor in the pathogenesis of venous ulcer, is increased production of oxygen free radicals and lipid peroxides by both the trapped white cells due to reduced perfusion resulted from increased venous pressure (43), and by the cutaneous iron overload from the extravasated RBCs. Those in turn will produce endothelial damage and tissue destruction (44). Recent study has reported that PEMF had reduced lipid peroxidation, increased antioxidants production to stimulate endogenous defense against free radicals and protected cells against O2 toxicity and cellular lysis (45).

Inflammatory process is the main contributing factor in vasculitic ulcer. Earlier studies have shown that PEMF has significant antiinflammatory effect. Though the exact mechanism by which PEMF exhibits such effect is not clearly understood, the cell membrane is most often considered as the main target for PEMF signals (46). Oxidative stress and defective antioxidant defense system could cause lipid peroxidation of cellular membranes, resulting in inhibition in the activities of Ca2+-ATPase which, in turn, could increase intracellular concentration of Ca2+ which could activate phospholipase A2, which, in turn resulted in release of arachidonic acid and production of PGE2 (47), which plays a major role in inflammation. Recently, it has been found that PEMF could stabilize the membranes subsequently restoring the membrane protein activity (Ca2+-ATPase) thereby maintaining intracellular Ca2+ level at extremely low level. This, in turn, decreases the inflammatory PGE2 levels and consequently suppressed the inflammation (45). PEMF has also a number of well-documented physiological effects on the immune system as it amplifies the phagocytic activity of polymorph nuclear leukocytes, increases the number of circulatory neutrophils and enhances the formation of antibodies (48).

MANSOURA MEDICAL JOURNAL
inflammation and edema and reduction of PGE2 as mentioned above. Another possible mechanism is that PEMF stimulates opioid receptors and increases the release of endorphins and encephalins at the reticular formation. Also, electromagnetic currents in the treatment area block the painful stimuli either in the receptor level or at cortical or subcortical areas (55).

However, in an earlier study of Todd et al. (20) although they stated that both active and control groups in their study showed an overall reduction in ulcer size over the study period and there was a trend in favour of improved healing in the ulcers treated with the active coils, but they failed to show a statistically significant improvement in the ulcers treated with the active coils. There was no effect on the percentage change of pain between the active and inactive groups. They attributed that to the discrepancy in ulcer duration between the two groups, low inadequate selectivity of the patients with regard to the aetiology of ulceration, or other circumstances, such as the degree of patients mobility and the adequacy of the ulcer therapy on the days not seen in the outpatient department.

We found that one important predictor of ulcer healing was ulcer size—there was a more successful outcome for smaller ulcers. Another predictor of ulcer healing was ulcer duration. This indicates the earlier the management of the ulcer, the better the outcome.

Regarding the safety of PEMF therapy, no adverse effects were complained by the patients during the study period apart from feeling sleepy after the session which rather considered as a benefit by some patients. This could be attributed to the calming and sleep-inducing effect of PEMF due to stimulation of melatonin hormone, which anti-stressful (56). These findings coincided with those of Stiller et al. (39), they found no reports of patient complaints or adverse events attributable to the use of PEMF in their study, and also with those of Canedo-Dorantes et al. (41) who reported that negative secondary effects were absent in their study during treatment and follow-up periods.


