reports

Case Report

High-Intensity, Low-Frequency Pulsed Electromagnetic Field as an Odd Treatment in a Patient with Mixed Foot Ulcer: A Case Report

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Abstract: Lower-extremity ulcers are associated with an increasing prevalence and significant economic and social costs. To date, there is no high-quality evidence related to an optimal treatment algorithm. A multimodal approach is needed particularly in patients with comorbidity and polytherapy. Herein, we report the case of a 94-year-old Caucasian female with comorbidity and polytherapy who was admitted to our observation for a history (1 year) of chronic painful malleolar mixed ulcer. After clinical evaluation, she was treated with a twice daily pain relief therapy and with a weekly diamagnetic therapy protocol plus a local treatment. During the clinical examination, we documented a statistically significant improvement in both pain (VAS score from 8 to 2 $p < 0.01$) and foot ulcer (surface reduction from 6 cm × 4 cm to 2 cm × 2 cm, $p < 0.01$) at the sixth week of combined treatment. The ulcer completely healed at the ninth week. This is the first study to document the effect of diamagnetic therapy as an add-on therapy in the management of wound healing. In conclusion, even if high-quality evidence is still lacking, diamagnetic therapy might represent an interesting option as an add-on treatment for ulcer.

Keywords: diamagnetic therapy; mixed ulcer; foot; treatment

1. Introduction

Lower-extremity ulcers, which are mainly represented by venous leg ulcers, diabetic foot ulcers, pressure ulcers, and arterial ulcers, affect up to 49 million people annually worldwide, with an expected further increase in prevalence [1].

Foot ulcers are associated with both economic (high cost of wound care and long time taken to heal) and social (morbidity, high risk of complications, and impact on patients' and relatives' quality of life) burdens [2]. Chronic wound management involves several

approaches related to the underlying disease (e.g., compression therapy and offloading of the affected area), [3] and in agreement with TIME (Tissue debridement, Infection control, Moisture imbalance, and Edge advancement) method [4], a multimodal approach is used [1]. Even if several compounds can be used in the management of foot ulcer [5–7], high-quality evidence is lacking [8]; therefore, new therapeutic strategies could be used to improve clinical assistance and to reduce the socioeconomic costs.

Notably, the use of magnetic fields (MFs) as a noninvasive and safe physical therapeutic option for pain relief and tissue repair has attracted particular interest.

MFs may affect cellular function and activities (e.g., tissue generation, cell migration, proliferation, and adhesion) and thus may be of benefit for wound healing [9–14].

With regard to intensity and direction, they can be classified as static MFs and dynamic MFs. Dynamic MFs include pulsed electromagnetic fields (PEMF), usually low-frequency fields with different intensities produced through pulsing current [9]. Low-Intensity, Low-Frequency Pulsed Magnetic Fields (LI-LF- PEMFs) are effective in treating musculoskeletal disorders and other pathologies. However, High-Intensity, Low-Frequency Pulsed Electromagnetic Fields (HI-LF-PEMF) also activate molecular-accelerator and water-repulsive (diamagnetic) biological effects, hence the neologism Diamagnetic Therapy or Diamagneto therapy [15,16].

We report the case of a 94-year-old Caucasian female in which diamagnetic therapy was used for the first time as an add-on treatment in wound healing.

2. Case Presentation

A 94-year-old Caucasian female patient (weight 75 kg, height 167 cm, BMI 26.9) came to us in a wheelchair for severe foot ulcer pain.

Clinical evaluation documented that she was spatiotemporally oriented and collaborative.

Her medical history revealed that, 10 years ago, she was affected by several systemic diseases requiring polytherapy (Table 1).

Table 1. Clinical characteristics of the patient.

Age, years	94
Sex	Female
Weight, Kg	75
Height, cm	167
BMI	26.9
Smoke	Ceased 20 years ago
Previous surgery	Right knee's arthroprotesis
Drug allergy	Diclofenac (referred)
Comorbidities and pharmacological daily treatments	
Asthmatic bronchitis	Salmeterol 50 mcg plus fluticasone 100 mcg bid Tiotropium 18 mcg qd Oxygenotherapy 3 lt qd
Cardiovascular and cerebrovascular disease	Acetylsalicylic acid 100 mg qd Clopidogrel 75 mg qd Losartan 50 mg plus hydrochlorothiazide 12.5 mg qd
Gastroesophageal reflux disease	Pantoprazole 20 mg qd
Hyperuricaemia	Allopurinol 300 mg qd
Rheumatoid arthritis (not documented)	Dexamethasone 4 mg qd

bid, twice daily; BMI, body mass index; qd, once daily.

About one year ago, she developed a foot malleolar ulcer not responsive to not specified local treatments with antibiotics and cicatrizing creams. The ulcer impaired her quality of life, reducing the possibilities of both going out and standing. She denied prior

history of similar wounds or known history of peripheral vascular disease or foot trauma. She also denied the use of alcohol but revealed a previous history of nicotine addiction, which ceased about 20 years ago.

During the clinical examination, we documented signs of poly-arthritis, with functional limitation of the upper limbs and a ulcer (6×4 cm) on the left lateral malleolus covered by slough, with slightly undermined and erythematous borders. The ulcer's surface was assessed with a ruler, reporting the greatest length and the perpendicular greatest width. Both edema and periwound hyperpigmentation were also detected (see Figure 1).

Figure 1. Ulcer at baseline.

The skin trophism was preserved an there were no varicose veins. The left leg was warmer than the right one, but clinical examination ruled out an infection at the ulcer level. The lower limb pulsations were weakly perceived; thus, the ankle brachial index (ABI) was 0.7, revealing a moderate peripheral artery disease.

Pain evaluation documented a severe pain (visual analog scale (VAS) score 8) with a nociceptive component and excluded the presence of allodynia or neuropathic pain. The impaired quality of life was assessed through the administration of the Italian validated version of the SF-36 questionnaire [17], which showed low scores mainly in bodily pain, general health, and the physical and social functioning domains.

Consultations with vascular surgeons confirmed the diagnosis of a mixed venous/arterial ulcer, but according to clinical assessment, there was no indication for arterial revascularization.

Wound treatment was prescribed according to the comorbidities and poly-therapy. Therefore, the patient started i) a bid oral treatment—oxycodone 5 mg plus paracetamol 325 mg, with gradual discontinuation of the steroid therapy; ii) weekly local treatment—debridement, advanced medications with idrocolloid, and bandaging with reduced compression levels (i.e., 23–30 mmHg). Before starting each weekly local treatment, the ulcer's surface was assessed and a photo was taken. To reduce the time of wound repair, diamagnetic therapy was also started.

Diamagnetic Therapy Protocol

The diamagnetic therapy session was performed one time/week. A protocol of at least 10 sessions was planned. The technical specifications of the intervention were established by combining the pre-specified protocols of the manufacturer with the clinical experience of the healthcare professionals. The number of sessions could be expanded/prolonged according to clinical response. Each treatment session lasted for 25 min (movement of

liquids: Intra L-Extra H for 10 min; endogenous biostimulation: cellular membrane for 15 min). During each intervention, the patient was in a sitting position with the lower leg and foot supported with a foot stand. Diamagnetic therapy was delivered (Diamagnetic Pump CTU MEGA 20®-Periso SA. Pazzallo-Switzerland) at the frequency of 5 Hz, with magnetic flux density of 86 mT at the site of treatment (measured on the solenoid axis).

3. Results

The combined treatment protocol induced a statistically significant improvement in both pain (VAS score from 8 to 2, $p < 0.01$) and foot ulcer (surface reduction from 6 cm × 4 cm to 2 cm × 2 cm, $p < 0.01$) after six weeks of treatment, followed by complete healing of the ulcer (see Figure 2). Local interventions, including the diamagnetic protocol, were interrupted at the ninth week of treatment (the ninth session was not performed since the ulcer already healed). The pharmacological treatment continued due to the benefits reported also in pain associated with poly-arthiritis. The patient stated an improvement in her quality of life, evaluated using the SF-36 questionnaire, revealing that she was able to walk without support. Indeed, higher scores were reported in the domains most affected at baseline (bodily pain, general health, and physical and social functioning). No adverse events related to both pharmacological and non-pharmacological treatment were reported.

Figure 2. Ulcer at the ninth week of treatment.

4. Discussion and Conclusions

In this case report, we documented the first add-on use of diamagnetic therapy in the treatment of foot mixed ulcer in an older woman. A mixed wound represents a challenge for clinicians, since there is still no optimal treatment algorithm [18]. Moreover, clinical management of older patients is further complicated by both comorbidity and polytherapy, which may reduce adherence to treatments and may increase the risk of drug interactions and adverse drug reactions [19,20]. Considering these factors, our patient was treated for 1 year with local treatments without a clinical improvement. After this period, she came to our observation, where medical doctors specializing in clinical pharmacology and vascular surgery suggested a combined treatment. Previous papers documented that patients with mixed ulcers should be managed with traditional methods or novel biologic dressings [5,18]. Compression therapy increases venous flow and lymphatic drainage and enhances fibrinolysis, improving the healing of ulcers and reducing ulcer recurrence rates [21]. However, it can only be performed in patients with ABI > 0.5 and an absolute ankle pressure >60 mmHg [22]. Other adjuvant therapy, such as hyperbaric oxygen therapy, showed benefits in short-term studies but reduced availability and costs limit its use [23].

In our patient, the vascular surgery excluded the possibility of surgery; therefore, a pharmacological treatment with the diamagnetic therapy was started with a rapid improvement in both pain and foot ulcer.

Magnetic fields, which are effective in pain relief, may have possible applications in chronic wounds, since they seem to affect all of the components in the healing process (e.g., fibrin, platelets, fibroblasts, and growth factors) [9,24]. Diamagnetism is a weak magnetic property of matter and its expression requires high MF values to exploit the diamagnetic properties of biological tissues, as with other forms of electromagnetic stimulation [25]. In this case report, the diamagnetic effect was exerted through HI-LF PEMF.

Several mechanisms have been proposed to explain why the PEMF may reduce the wound healing time. Preclinical data show that PEMF could stimulate vasodilatation, increasing the cutaneous capillaries' blood flow and organ perfusion, reducing soft tissue edema, and increasing the metabolic activity [26,27]. Improved blood perfusion in the magnetically stimulated tissue is a mechanism for stimulatory effects in regenerative process, resulting in both accelerated cell proliferation and inhibition of the inflammation [28]. Lee et al. [29] reported that electricity and magnetic fields can modulate both reparative cell migration and ion channel activity in the wound area, and ion channel activity is involved in wound healing. We considered treatment with magnetic fields useful to accelerate recover only in the absence of a physiological electric current or biological activity in the restoration process.

The electrical signals generated by PEMF may act on injured cell membranes generating a reduction in inflammation, increases in fibroblasts and macrophages in the ulcer, and an increased deposition of fibrin [30]. Markoll et al. evidenced a decrease in matrix metalloproteases (MMPs) and an increase in the tissue inhibitor of MMPs (TIMP) mediated by pulsed magnetic fields [31]. These components play roles in ulcer pathogenesis and remodeling [32]. PEMF may also elicit their action, reducing the production of reactive oxygen species (ROS) [33,34].

Several anecdotal data on the beneficial properties of electromagnetic therapy for skin wounds are available but are not conclusive. Pulsed magnetic fields accelerate wound healing in rats: Strauch et al. described an increase in wound tensile strength 21 days after wounding [35]. Electromagnetic fields showed a certain effect in the modulation of scapular wounds artificially made on animals: the application without frequency modulation was effective in diminishing inflammatory exudation [36].

In a previous double-blind study, Ieran et al. [37] evaluated in 20 patients the effect of an electromagnetic field on the healing of venous ulcers, documenting that, with respect to the placebo, an electromagnetic field is able to improve the clinical symptoms, lowering the rate of ulcer recurrence ($p < 0.02$).

In agreement with this, in a prospective, randomized, double-blind, placebo-controlled study, Stiller et al. [38] evaluated the effect of pulsed electromagnetic limb ulcer therapy (PELUT) in the healing of recalcitrant, venous leg ulcers and showed that PELUT induced significant decreases in wound depth ($p < 0.04$) and pain intensity ($p < 0.04$) with respect to a placebo-treated group. Kenkre et al. recruited nineteen patients and used different frequency (600 Hz and 800 Hz) irradiations compared with a placebo. Patients treated with PEMF showed improvement in pain control and ulcer size, 800 Hz therapy seemed to be more effective than 600 Hz or placebo, and 68% of patients experienced adverse events: headache (treatment group only), sensation of heat, pins, and tingling (placebo and treatment groups) [39].

A lack of standardization of PEMF devices in terms of type, duration, frequency, and intensity and length of exposure is a relevant issue [30]. Gordon described an increase in time (dB/dt) as a critical determinant of efficacy in this kind of treatment, performing a major effect in the activation of restoration genes [33]. Magnetic field therapy should be provided in doses similar to a drug [9]; therefore, physicians should develop the ability to tailor the right protocol for patients' pathology and characteristics. Despite the presence of vascular effects supporting their use [9,26,27,29], there were no data on patients suffering

from arterial ulcers treated with PEMF. In a mixed etiology leg ulcer, a combined 9-week treatment including hyperbaric oxygen, an extremely low-frequency variable magnetic field, and low-energy light radiation resulted in complete healing and subsequent pain relief [40]. Magnetic fields seem to have promising application prospects also in diabetic wound healing, notwithstanding the lack of general agreement on the mechanisms underlying its biological and therapeutic effects [41].

Although the literature documents a lack of high-quality evidence regarding PEMF in ulcer management [30], we observed the complete healing of a mixed ulcer from which a patient suffered for a year at the ninth week of a combined protocol without the development of adverse events. However, the impact of the global care process should be considered, since the interventions carried out during the entire treatment period cannot be separately assessed.

Indeed, being a single case, we cannot exclude that other factors could have a role in the management of venous ulcer, e.g., the quality of debridement and compression and the discontinuation of steroid therapy.

In the future, advanced visualization of magnetic fields and the presence of physicists in the medical team may be useful in deeply understanding the interaction of waves with the organism and in achieving a more specific administration [42]. Indeed, it would be of interest evaluate the possibility of using magnetophoresis (i.e., the enhancement of drug permeation across the biological barriers through a magnetic field) to deliver topical drugs in addition to magnetic fields in wound treatment. This process may exert an enforcing action in the treatment of ulcer. Magnetophoresis has been shown to increase the dermal bioavailability of certain drugs, potentially enhancing delivery and pharmacological effects [43,44]. However, to our knowledge, there are no known add-on drugs used in diamagnetic therapy in the management of ulcers. Furthermore, whether magnetic fields may exert other effects on drugs pharmacokinetics and pharmacodynamics should be considered.

In conclusion, our case report suggests that diamagnetic therapy might represent an interesting noninvasive option as an add-on treatment for patients with venous ulcers. Preclinical data describe several mechanisms through which it might accelerate healing processes and promote drainage, whereas clinical data are limited to anecdotal reports and small clinical studies. Larger randomized control trials and standardized diagnostical and therapeutical procedures are needed to compare the results and to obtain high-quality evidence. Furthermore, the interactions between magnetic fields and add-on drugs need further analysis.

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