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The effect of alternating and biphasic currents on humans' wound healing: a literature review

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Abstract

Although different types of currents, including bidirectional currents, have been used to promote healing, there is neither a summary about their effects nor consensus on best parameters to be used. The aim of this article is to provide an overview of current evidence on the effectiveness of bidirectional electrical stimulation on wound healing in accordance with the parameters used. Relevant articles were selected following a search of Medline, Cochrane, Embase, CINAHL, and PEDro for English, Spanish, Portuguese, Italian, or French articles published between 1980 and 2011. Ten trials and four case-series were found that deal with pressure ulcers, diabetic ulcers, venous ulcers, skin flaps, and amputation. Eight trials were of low-quality. Five of ten controlled trials found a statistically significant difference on wound healing, and another four trials found positive trends. Both of the two skin flap trials, one of two diabetic trials, and two of five pressure ulcer trials found a significant difference in bidirectional stimulated groups. Both TENS and NMES types of currents were used, but many parameters were not specified. In general, bidirectional currents appear to increase wound healing rates and reduce size of wounds, above all in skin flaps. However, there is a lack of well-designed studies on biphasic and alternating stimulation, and there is a need for improvement in description of parameters and in uniformity of nomenclature.

Introduction

Wound healing is a significant health problem, especially in the aging population and in persons with underlying comorbid conditions. Additional efforts are necessary to overcome those circumstances and maximize wound repair efficacy. Electrical stimulation (ES) is a treatment modality utilized in physical therapy that can help in this matter. It consists on the delivery of an electric current to transfer energy to the tissues, mainly for the excitation of nerve and muscle tissues.

There are three main types of electrotherapeutic currents: direct current (DC); alternating current (AC); and pulsed current (PC).[1] Unidirectional currents – DC and monophasic PCs – are characterized by a unidirectional flow of charged particles. Electrochemical effects resulting from a constant polarity and a certain duration can cause chemical burns. Bidirectional currents are those in which a reverse polarity occurs. This means alternating the charged particles that are attracted to the area under the electrode, which will avoid or diminish electrochemical effects. AC is an uninterrupted cyclic bidirectional flow of charged particles. Biphasic PC is defined as the interrupted bidirectional flow of charged particles. This means that a periodical brief cessation exists after the delivery of the pulse.

Studies of electrical stimulation effects on wound healing have used all these types of currents, most commonly unidirectional waves as low-intensity DC (LIDC) and high-voltage PC (HVPC). Bidirectional currents, such as transcutaneous electrical nerve stimulation (TENS), and some types of neuromuscular electrical stimulation (NMES) have been studied to a lesser extent. Bidirectional currents are promising as they have fewer adverse effects and are less invasive in their electrode placement (at the edge of the ulcer on healthy skin) than unidirectional currents. Nevertheless, currently there is insufficient evidence regarding its effectiveness and the best type and parameters to be used.[2] Studies using an animal model indicate that the pathway by which the repair mechanism is affected is dependent on the type of stimulation employed, so the unidirectional currents and bidirectional currents can enhance the healing process in different ways.[3] In the previous human studies, TENS and biphasic NMES currents have been shown to induce peripheral vasodilation and activate local blood flow,[4-10] which may promote wound healing. However, the results are not consistent,[11, 12] probably because of differences in stimulation parameters and population.[5, 6, 8, 10, 12-18]

To understand the relevant factors of the current that may have a role in healing, it is important to understand the parameters that characterize it.

TENS is a non-invasive and cheap treatment technique. It consists of a low-voltage stimulation current via skin surface electrodes using a low-frequency portable stimulator that delivers a rectangular biphasic PC at a frequency of 1–200 Hz and phase duration of 0.05–0.5 ms.[19] There are two principal types of TENS: conventional TENS, that acts mainly through peripheral mechanisms; and acupuncture-like TENS (AL-TENS), which primarily involves central mechanisms. Conventional TENS uses a high frequency (usually between 80 and 110 Hz), low amplitude or intensity (strong but comfortable sensation without muscular contraction), and a higher duration of application reaching in certain cases many hours a day. It is usually placed locally, covering the injured area. AL-TENS uses a low frequency (between 1 and 10 Hz), high amplitude (at a motor but non-painful level), and a shorter length of application (from 20 min to 1 h). The electrodes can be placed at muscles or at acupuncture points. Another kind of AL-TENS is burst TENS. The pulses are given at a high frequency, but they are interrupted systematically in order to get 1-5 bursts per second. Therefore, a few bursts of pulses delivered at 80–110 Hz are provided each second.

NMES is a low-voltage current, commonly biphasic PC, or AC.[20] The frequency of the current, can be low (usually until 100 Hz) or medium (typically from 1000 to 2500 Hz). It is primarily designed to evoke muscular contraction and strengthening, so it uses a duty cycle with an "on" time (period of stimulation) and an "off" time (period of rest for the muscle recovery).

In summary, to describe a bidirectional current, it is necessary to know the parameters related to the following.

- Type of wave: symmetrical or asymmetrical, balanced or unbalanced, alternating or biphasic.
- Dosage: amplitude/cm^2 (current density), pulse duration, frequency, duty cycle (NMES) or number of bursts per second (AL-TENS), duration, and number of sessions. The objective is to know the amount of current delivered, mainly current dosage and whole time of treatment.
- Electrode characteristics and placement.

Objective

This article reviews studies on the effects of bidirectional currents on wound healing with regards to ulcers and skin flaps. There are, as well, assessments of clinical reports examining the effects on musculocutaneous flaps or amputation, only if at least one of the study outcomes is related to the healing of a skin wound.

Materials and methods

We conducted a review of the relationship between electrical stimulation and wound healing using the following keywords: "electric stimulation therapy"; "transcutaneous electric nerve stimulation"; "TENS", "NMES", "biphasic current*"; "alternating current*"; "ulcer*"; "wound healing"; "flap*". The following databases and periods were included: Medline; the Cochrane Central Register of Controlled Trials (Cochrane); Embase; Cumulative Index to Nursing and Allied Health Literature (CINAHL); and Physiotherapy Evidence Database (PEDro) from 1980 (when possible) to October 2011. Articles were also obtained by bibliography review. Articles in English, French, Portuguese, Italian, and Spanish were included. To be selected in the current review, studies had to state that they use a NMES, TENS, biphasic current, or AC, have 10 or more (human) subjects, and use a direct measure of wound healing. Studies combining electrical stimulation with another intervention treatment but standard care and trials that do not use surface electrodes were excluded. Selection was undertaken independently by two reviewers. Any disagreement was discussed and resolved, if necessary, by a third reviewer. Once the articles were accepted, a quality assessment was conducted for each controlled study using a modified Sackett scale (Table 1).[21]

Table 1. Levels of evidence (modified from Straus *et al.*[36])

Levels	Evidence
Level 1	RCTs with a PEDro score ≥6
Level 2	RCTs with a PEDro score <6, cohort and non-RCTs
Level 3	Case-control studies
Level 4	Case series

Results

Thirty-nine studies referred to wound healing and searched currents, but 25 did not meet the above criteria and were excluded.

Comparison with other studies requires uniformity in measurement. Percentage of healing per week is one of the most common measures reported and easy to calculate,[2] so this measure was used when there was enough information.

Controlled trials

Ten controlled trials were included, and their quality was assessed with the PEDro scale (Table 2). There were two randomized controlled trails (RCTs) not punctuated by PEDro evaluators.[22, 23] Stefanovska *et al.*[24] also was not included in PEDro evaluations as randomization was not mentioned, except for a crossover group. For the purpose of this review, it was included in the quality assessments. There were only two RCTs with a PEDro score ≥6.[23, 25] All of the clinical trials included control groups, six of them using a "sham" bidirectional ES, consisting of the same stimulation protocol except that the electrodes had no output. This system is not considered a true placebo, so no study scored on this item.

Table 2. PEDro scale score for clinical trials included

Study	Eligibility criteria	Random allocation	Concealed allocation	Similar baseline	Blind subject	Blind therapist	Blind assessor	Adequate follow-up	Intention-to-treat analysis	Between-group statistical comparisons	Point measures and variability data	Score
Asbjornsen *et al.*[22]	No	Yes	No	No	No	No	Yes	Yes	No	No	No	3
Atalay and Yilmaz[23]	No	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	7
Baker *et al.*[26]	No	Yes	No	Yes	No	No	Yes	No	No	Yes	Yes	5
Baker *et al.*[25]	No	Yes	No	Yes	No	No	Yes	Yes	No	Yes	Yes	6
Cukjati *et al.*[29]	Yes	Yes	No	No	No	No	No	Yes	No	Yes	Yes	4
Finsen *et al.*[30]	No	No	No	No	No	No	No	Yes	No	Yes	Yes	3
Jercinovich *et al.*[27]	Yes	Yes	No	No	No	No	No	No	No	Yes	Yes	3
Lundeberg *et al.*[28]	Yes	Yes	No	Yes	No	No	No	No	Yes	Yes	Yes	5
Lundeberg *et al.*[31]	No	Yes	No	No	No	No	No	Yes	No	Yes	Yes	4
Stefanovska *et al.*[24],a	No	No	No	No	No	No	No	Yes	No	Yes	Yes	3

[a] Non-randomized controlled trial.

Table 3 summarizes the results of the available studies. Four controlled trials focused on pressure ulcers,[22, 24, 26, 27] two on diabetic ulcers,[25, 28] and one on mixed cases.[29] One clinical trial was referred to amputation patients,[30] and two were flap studies.[23, 31] All the studies applied ES in addition to standard care.

Table 3. Summary of studies included

Reference	Problem, subjects and groups	Parameters used	Results
Controlled trials			
Asbjornsen *et al*.[22]	20 geriatric patients with sacral and heel pressure ulcers (no information about duration Gp 1: 10 AL-TENS Gp 2: 10 "sham" ES Four dropouts	Gp 1: square biphasic PC, amplitude until contraction without pain (usually 20–30 mA), 0.85 ms,a 100 Hz, 3 bursts, 30 min, 2 times/d, 5 d/week, 4–6 weeks One electrode in the web between the 1st and 2nd metacarpal bones; the other in the ulnar edge (unknown size) Treatment time: 20–30 h; current density: unknown	Negative Reduced ulcer size in 57% for Gp 1 vs. 100% for Gp 2 (22% completely healed) at 4 weeks. Similar results at 6 weeks Adverse events were not reported Healing rate/week: unknown Mean healing time (% healed): unknown (22%)
Baker *et al*.[26]	80 spinal cord-injured patients with 192 pressure ulcers (acute to chronic) Gp1: 20 asymmetrical NMES Gp 2: 21 symmetrical NMES Gp 3: 20 LIPDC Gp 4: 19 "sham" ES 27 (ulcers) dropouts, 63 changed of program and six were non-compliant	Gp 1: square, balanced, asymmetrical, biphasic PC, amplitude just below motor threshold; 0.1 ms phase duration, 50 Hz, 50% duty cycle (7 s on/7 s off), electrode that was negative during the leading phase proximal to the wound and the other distally Gp 2: square, symmetrical, biphasic PC, intensity just below motor threshold, 0.3 ms phase duration, 50 Hz, same duty cycle All Gp: 2.5 × 2.5 to 5 × 10 cm electrodes placed locally, 30 min, 3 times/d, 5–7 d/week, 4 weeks Crossover design: Gp 3 and Gp 4 until healing or for 4 weeks, then to group 1 or 2 (11 patients) Treatment time: up to 42 h; current density: unknown	Positive trend Adverse events were not reported Healing rate/week: 36.4 ± 6.2, 29.7 ± 5.1, 23.3 ± 4.8% and 32.7 ± 7.0% in groups 1–4, respectively, although failed to reach statistical significance For only the good response group a significant difference in healing rates was found in favor of Gp 1 (63.7 ± 7.2%) against Gp 3 (38.5 ± 5.6%) and Gp 4 (29.2 ± 8.1%). No significant differences were found between Gp 2 (50.6 ± 5.6%) and the control groups Crossover: greater healing rate (43.3 ± 12.5% change/week) than in control period (9.7 ± 3.4% change/week) Mean healing time (% healed): unknown
Jercinovich *et al*.[27]	73 spinal cord-injured patients with 109 chronic pressure ulcers Gp 1: 42 NMES (61 ulcers) Gp 2: 31 standard care only (48 ulcers) Baseline: ulcers in Gp 2 were more complex regarding their initial size; in Gp 1 regarding the appearance of tissue and their duration No information about dropouts	Gp 1: balanced, asymmetrical, biphasic PC, amplitude up to 35 mA (to achieve minimal muscular contraction), 0.25 ms pulse duration, 40 Hz, 4 50% duty cycle (4 s on/4 s off), 120 min/d, 5 d/week, 4 weeks 50–75 mm (in diameter) electrodes (20–44 cm^2) 3 cm from the edge of the ulcer Crossover design: patients from Gp 2 could change to Gp 1 when finishing 4 weeks (20 ulcers) Treatment time: 40 h; current density: up to 0.79–1.75 mA/cm^2	Positive trend Significant differences depended on the fitting method used for healing quantification. Linear method: mean healing rate per day of 2.2% in Gp 1 vs. 1.5% in Gp 2 ($P = 0.07$). Exponential method: 5.7% in Gp 1 vs. 2.7% in Gp 2 ($P = 0.006$) Stratified data: comparing sacral ulcers (similar initial complexity), both linear (2.6 ± 1.8% vs. 1.2 ± 1.5%) and exponential (6.2 ± 5.1% vs. 1.8 ± 2.8%) mean healing rates were significantly higher in Gp 1 ($P < 0.02$) Crossover: improvement with both fitting methods ($P = 0.001$) Healing rate/week (calculated): 15.4 and 39.9% in Gp 1; 10.5 and 18.9% in Gp 2 Mean healing time (% healed): unknown An increase in depth in 5 from control Gp and in 2 from NMES Gp
Stefanovska *et al*.[24]	82 spinal cord-injured patients with 170 pressure ulcers (acute to chronic) Gp 1: 82 (ulcers) NMES Gp 2: 18 (ulcers) LIDC Gp 3: 50 (ulcers) standard care only 20 (ulcer) dropouts	Gp 1: rectangular, balanced, asymmetrical, biphasic PC, 15–25 mA amplitude (contraction at minimum level), 0.25 ms pulse duration, 40 Hz, 4 s on/4 s off, 120 min/d A pair of self-adhesive electrodes at the edge of the wound, size of 30 ± 10 cm^2 on average Treatment time: unknown; current density: 0.5–0.83 mA/cm^2	Positive Normalized healing rate/day: 5.43 ± 4.40% in Gp 1, 3.11 ± 3.83% in Gp 2 and 2.21 ± 3.27% in Gp 3, which results in a significant difference between Gp 1 and Gp 2 ($P = 0.032$) and Gp 3 ($P < 0.001$) Stratified data (excluding very deep, superficial or long-term wounds): 5.40 ± 4.10% in Gp 1 (42 cases) vs. 2.87 ± 3.12% in Gp 3 (34 cases; $P = 0.003$); close to being statistically significant comparing with healing rate of 4.62 ± 3.29% in Gp 2 (12 cases) ES accelerated healing when unfavorable conditions were present Healing rate/week (calculated): 38% in Gp 1; 21.8% in Gp 2; 15.5% in Gp 3

Table 3. Summary of studies included

Reference	Problem, subjects and groups	Parameters used	Results
			Mean healing time (% healed): unknown Adverse events were not reported
Cukjati *et al*.[29]	214 patients with 300 chronic ulcers of mixed etiology (mainly pressure ulcers) Gp 1: 181 (ulcers) NMES Gp 2: 42 LIDC Gp 3: 23 “Sham” ES Gp 4: 54 standard care only Gp 1 is larger because, later, used only NMES 126 cases not followed until wound closure 24 (ulcer) dropouts for estimating healing time	Gp 1: balanced, asymmetrical, biphasic PC, amplitude for contraction at a minimum level (15–25 mA), 0.25 ms pulse duration, 40 Hz, 50% duty cycle (4 s on/4 s off), a pair of electrodes at the edges of the wound ES for Gp1 and 2: 30 min, 60 min or 120 min/d for 7 d/week until complete wound closure, but in 126 cases was not possible 120 min daily ES was the only condition with a sham group Treatment time and current density: unknown	Positive (small effect) Healing rate/week: wounds at Gp 1 healed faster than Gp 3 ($P = 0.008$) or Gp 4 ($P = 0.031$), without significant differences with Gp 2 ($P = 0.365$) Stratified data considering 120 min daily ES: Gp 1 healed faster, at 0.166 mm/d (0.097–0.328), than Gp 3, at 0.162 mm/d (–0.046 to 0.205; $P = 0.018$) and at the same rate as Gp 2 (0.217 mm/d (0.098–0.450; $P = 0.170$). Gp 2 wounds healed faster, but not significantly ($P = 0.085$), than Gp 3 wounds. Gp 3 and 4 wounds healed at the same rate Mean healing time (% healed): 60 weeks (90% in Gp 1 and 2; 70–72% in Gp 4 and 3). No significant difference ($P = 0.631$) in time to complete wound closure between groups when non-healing wounds were not considered Adverse events were not reported
Baker *et al*.[25]	80 patients with 114 diabetic ulcers (acute to chronic) Gp1: 21 asymmetrical NMES, (33 ulcers) Gp 2: 20 symmetrical NMES, (28 ulcers) Gp 3: 19 LIPDC (28 ulcers) Gp 4: 20 “sham” ES (25 ulcers) 28 (ulcers) dropouts, 24 changed of program and 17 were non-compliant	Same protocols as Baker *et al*.[26] but unknown size of the electrodes and weeks of treatment (47, 67, 72 and 32 h of treatment in Gp 1, 2, 3 and 4, respectively) Crossover design: Gp 3 and Gp 4 until healing or for 4 weeks, then to group 1 or 2 (only five patients) Treatment time: 32–72 h; current density: unknown	Positive trend Healing rate/week (estimated from a graph): 27, 19, 11 and 14% in Gp 1, 2, 3 and 4, respectively, although without statistical significance Stratified data (patients requiring more than 8 d of treatment and applying ES at least 30 min/d): when combining data from Gp 3 and Gp 4, Gp 1 showed significantly faster healing rate (27.0 ± 4.0%) than combined control group (17.3 ± 2.7%), while Gp 2 (16.4 ± 6.1%) did not Mean healing time (% healed): unknown Adverse events were not reported
Lundeberg *et al*.[28]	64 patients with diabetic leg ulcers (no information about duration) Gp 1: 32 Unclear type NMES or TENS Gp 2: 32 “sham” ES 13 dropouts	Gp 1: square-wave biphasic PC, amplitude to evoke paresthesias, 1 ms pulse duration, 80 Hz, a pair of 4 × 6 cm electrodes placed just outside the ulcer, changing polarity after each treatment, 20 min, 2 times/d, (7 d/week),1 week + 11 weeks at home Treatment time: 56 h; current density: unknown	Positive Healing rate/week (calculated): 5.1% in Gp 1, and 3.4% in Gp 2 ($P < 0.05$) Mean healing time (% healed): 12 weeks (42% in Gp 1; 15% in Gp 2; $P < 0.05$), similar difference if analyzed as ITT Withdrawals for similar reasons in both groups
Atalay and Yilmaz[23]	173 patients with post-mastectomy skin flap Gp 1: 86 TENS Gp 2: 87 standard care only	Gp 1: rectangular, symmetrical, biphasic PC, 2 mA, 0.2 ms pulse duration, 70 Hz, 1 h/d, 5 consecutive days (starting from the first operative day), a pair of 5 × 4 cm electrodes placed 5 cm above and below incision Treatment time: 5 h; current density: 0.1 mA/cm^2.	Positive 15% with flap necrosis for Gp 1 vs. 42% for Gp 2 ($P < 0.0001$). Mean area of flap necrosis of 85.2 ± 35.9 for Gp 1 vs. 252.5 ± 64.1 for Gp 2 ($P = 0.024$). 21% of patients with flap ecchymosis for Gp 1 vs. 43% for Gp 2 ($P < 0.002$). Mean area of flap ecchymosis of 105.5 ± 49.8 for Gp 1 vs. 172.9 ± 49.9 for Gp 2 ($P = 0.34$) No complications attributable to TENS were found
Lundeberg *et al*.[31]	24 patients with ischemic skin flaps Gp 1: 14 Unclear type NMES or TENS Gp 2: 10 “sham” ES	Gp1: square-wave biphasic PC, amplitude set to three times the threshold to tingling sensation, 0.4 ms pulse duration, 80 Hz, two electrodes 3 × 5 cm on the base of the flap, 2 h/d until achieving an improvement on capillary refilling, edema or stasis or for 7 d Treatment time: up to 14 h; current density: unknown	Positive After 6th session 86% improved at least in one measure in Gp 1 vs. 20% in Gp 2 (the other 8 became necrotic). ES was better ($P < 0.05$) than “sham” ES reducing ischemia. Patients from Gp 1 had a significantly ($P < 0.01$) higher blood flow Two patients had an allergic skin reaction to the adhesive tape
Finsen *et al*.[30]	52 patients – 51 finally (33 below-knee amputees) Gp1: AL-TENS Gp 2: “sham” ES and medication Gp 3: “sham” ES only Unequal distribution of levels of amputation	Gp 1: 0.09 ms pulse duration, 100 Hz, 2 bursts at amplitude just below discomfort level, 30 min, 2 times/d, (7 d/week), 2 weeks. Two pairs of electrodes over the femoral and sciatic nerves Treatment time: 14 h; current density: unknown	Positive trend Stratified data (below-knee amputation) Healing rate/week: unknown Mean healing time (% healed): 9 weeks (80% in Gp1; 61% in Gp 2; $P < 0.05$) The re-amputation rate was lower among patients at Gp 1 (1) than among patients at Gp 2 and Gp 3 (5), although failed to reach statistical significance Adverse events were not reported

Table 3. Summary of studies included

Reference	Problem, subjects and groups	Parameters used	Results
	between groups. Two below-knee dropouts		
Case series			
Debreceni *et al*.[32]	24 individuals (10 diabetic) with chronic ischemia of the lower extremities complicated by ulceration and necrosis of the toes AL-TENS	Spike-wave, biphasic PC, 20 min/d daily,1–2 Hz at an amplitude to obtain rhythmic, painless muscle contractions, usually 15–30 mA, an electrode between the tibia and the head of the fibula, and the other between the first and second metatarsal bones Treatment time and current density: unknown.	Positive Healing rate/week: unknown Mean healing time (% healed): 8–52 weeks (83% regression or complete healing) Adverse events were not reported.
Kaada[33]	10 patients with lower-extremity chronic ulcers of various etiologies AL-TENS	Square-wave PC, at amplitude up to muscle contraction (usually at 15–30 mA), 100 Hz, 2 bursts, 20–45 min, 3 times/d, from 4 to 22 weeks, the cathode on the web space between first and second metacarpal bones and the anode at the ulnar edge Treatment time: 28–346 h; current density: unknown.	Positive Near 100% healing at different periods of time; only one patient without complete healing. This patient had 10 ulcers and eight of them healed, but two were not solved Adverse events were not reported
Kaada and Emru[34]	40 leprosy patients with lower leg and foot chronic ulcers AL-TENS 21 dropouts, 13 of them followed for at least 2 weeks	Square-wave PC, at an amplitude of 25–50 mA, 0.1–0.2 ms pulse duration, 100 Hz, 2 bursts, 30 min, 2 times/d for 5 d/week and one more time for 6th day of the week, until healing, 3 × 4 cm electrodes on one hand, but sometimes applied locally Treatment time: unknown; Current density: 2.08–4.16 mA/cm^2	Positive trend Healing rate/week: 1.0 cc Mean healing time (% healed): 5.2 weeks average healing time (48%) Similar healing index to comparable patients in 11 of 13 patients that discontinued TENS Adverse effects were not reported
Karba *et al*.[35]	17 patients with chronic wounds most frequently from amputation, 14 geriatric patients with chronic pressure ulcers and 32 patients with chronic wounds of vascular origin NMES	Square balanced asymmetrical, biphasic PC at amplitude to achieve minimal contraction (from 15 to 25 mA), 0.25 ms pulse duration, 40 Hz, 50% duty cycle (4 s on/4 s off), 60 min/d, electrodes on healthy skin at the edge of the wound Treatment time and current density: unknown	Positive Healing rate/week: 1.02 ± 0.26 for post-traumatic wounds, 0.83 ± 0.33 for pressure ulcers and 0.47 ± 0.09 for vascular wounds (exponential) Mean healing time (% healed): 4.5 weeks average healing time for post-traumatic wounds; over 5.5 weeks in pressure ulcers; over 10 weeks in vascular wounds. 63 ulcers healed and three ulcers failed Adverse effects were not reported

AL-TENS, acupuncture-like transcutaneous electrical nerve stimulation; DC, direct current; ES, electrical stimulation; Gp, group; LIPDC, low-intensity pulsed direct current; NMES, neuromuscular electrical stimulation; PC; pulsed current.
Treatment time in hours is calculated by intended minutes per day × number of sessions; current density is calculated by amplitude/electrode size in cm^2. Healing rate/week is the % of decrease in ulcer surface per week reported or calculated from provided data.
[a] The authors described it as 85 ms, but that must be 85 μs according to the type of stimulation.

Case series

There were four studies,[32-35] dealing with different types of wounds (Table 3).

Discussion

Very little research has been found on the effect of bidirectional currents on wound healing. Many studies have been limited to pressure ulcers. All the studies except one trial have found a positive effect or a positive trend. A lack of statistically significant differences may be due to the quality of the studies and inconsistency in treatment techniques. The review has shown high variability in stimulation parameters and methods for data analysis. The majority of the trials did not use blinding and concealed allocation or intention-to-treat analysis and were biased on prognostic variables. Only one study expressed current density and whole time of treatment.[23] It was not possible to estimate a common measure of energy delivered and compare it among the studies.

Despite these shortcomings, three of four small low-quality controlled clinical trials suggest a benefit associated with biphasic PC compared with standard care or "placebo" stimulation on pressure ulcers.[24, 26, 27] The patients treated in these three trials were spinal cord injured, and a NMES-type current was supplied using an asymmetrical biphasic PC, with electrodes placed locally. One of them found a significant difference in the main measure.[24] The mean healing rate per week was 38% for the NMES group, 21.8% for the LIDC group, and 15.5% for the control group, which means bidirectional currents improved healing at a slower speed than reported by Kloth and Feedar[36] (44.8%) but at a higher speed than that reported by Houghton *et al*.[37] (5.8%), Franek *et al*.[38] (14.2%), and Griffin *et al*.[39] (28%), all of them using HVPCs. Despite the absence of statistically significant differences, Jercinovic *et al*.[27] found a linear healing rate per week of 15.4% for the NMES group and 10.5% for the control group. This means healing occurred at a higher or similar speed than that reported by Adegoke and Badmos[40] (5.6%), Wood *et al*.[41] (10.5%), Feedar *et al*.[42] (14%), Mulder[43] (14%), and Carley and Wainapel[44] (17.9%), all of them using unidirectional currents (monophasic and LIDC). Moreover, healing rates with bidirectional currents are above the control rate calculated by Gardner *et al*.[2] for pressure ulcers (3.3%) and chronic wounds (9.1%), and above the values found for control groups by different researchers,[36-38, 40-44] ranging from negative values (meaning increased size)[36] to positive values of 9%.[44] Only Griffin *et al*.[39] and Baker *et al*.[26] found a higher rate for the control group at 18.2 and 32.7%, respectively. In this last study,[26] a higher healing rate (36.4%) was obtained for the asymmetrical biphasic PC group, although it failed to reach statistical significance. The only trial that did not find any positive effect used AL-TENS to treat geriatric patients with electrodes placed at acupuncture points and did not present the ulcer duration.[22] Cukjati *et al*.[29] included ulcers of different etiology but mainly pressure ulcers due to spinal cord injury. They found significant positive results with asymmetrical biphasic NMES. Two case series studied patients with pressure ulcers among other etiologies and reported positive findings of AL-TENS and NMES.[33, 35] All the studies used amplitude to achieve contraction except Baker *et al*.,[26] who set amplitude just below contraction. In summary, there is limited level 2 evidence to suggest that asymmetrical biphasic PC is associated with size reduction of pressure ulcers, at least for spinal cord patients.

Two clinical trials studied the effect of bidirectional currents (likely NMES) on diabetic ulcers. Baker *et al*.,[25] in a six-point quality-scored study, only found statistical effects when compliant patients requiring more than eight days of treatment were selected and both control groups were combined. Lundeberg *et al*.,[28] in a five-point quality-scored study, found positive results in the number of healed ulcers and in reducing ulcer area. The main known differences between them are relative to pulse duration and duty cycle. Lundeberg *et al*.[28] used longer pulses and seem to have omitted information about periods of rest (duty cycle). As Baker *et al*.[25] hypothesized, due to the neuropathy frequently seen in the distal extremities of this type of patient, a longer pulse duration and proximal placement of the electrodes within a dermatomal pattern may provide better recruitment of sensory nerve fibers and, therefore, better results. A case series treating ischemic ulcers (nearly half of them due to diabetes) found a positive effect of AL-TENS.[32] Bidirectional ES trials[25, 28] showed a healing rate per week of 5.1 and 27%, while the control rate from chronic wounds calculated by Gardner *et al*.[2] is 9.1%. The values from two unidirectional studies[45, 46] were 7.2 and 11%. Consequently, there is very limited level 2 evidence that asymmetrical biphasic ES makes a significant difference in treatment of diabetic ulcers.

A case series studied patients with venous ulcers, among other etiologies, and reported positive findings of AL-TENS.[33] Furthermore, there is very limited level 4 evidence of a beneficial effect from TENS on venous ulcer healing.

Two RCTs studied the effect of biphasic ES on skin flaps. One TENS study[23] (a high-quality RCT) used a symmetrical biphasic wave, while in the probable NMES trial[31] this information was not provided. A positive trend was reached with TENS while significant results were found with NMES. In the latter study, higher amplitude (three times the tingling threshold), longer pulse duration, and length of session were used. There is very limited level 1 evidence showing that symmetric biphasic ES has a beneficial effect on flap survival.

One low-quality trial analyzed the effect of AL-TENS on amputation. The electrodes were placed on the nerve and suggested to improve healing at least for below-knee amputees. There is very limited level 2 evidence of faster healing in below-knee amputees when using AL-TENS placed following the nerve.

Regarding which type of current is more beneficial to healing, results were unclear as one TENS,[23] two likely NMES,[28, 31] and two NMES[24, 29] controlled trials found a positive effect on healing. The NMES studies used a balanced asymmetrical biphasic wave, and the TENS trial used a symmetrical wave. When both types of waves were compared, the asymmetrical wave was more effective.[25, 26] The amplitude of the trials that reached significant differences varied from 2 mA[23] to level of contraction,[24, 29] so there is no clear trend. However, studies on blood flow suggest that it is necessary to reach muscle contraction in order to improve circulation.[4, 6, 13, 16] All of them used low-frequency or burst TENS, but Indergand and Morgan[11] did not find any effect with high-frequency TENS at the motor level. Thus, another important parameter may be frequency employed. Several studies found that at the same intensity, low-frequency TENS had more influence on blood flow than high-frequency

TENS.[5, 9] Scudds *et al*.[15] only found some positive effects on skin temperature with low-frequency, high-amplitude TENS vs. high-frequency, low-amplitude TENS. Tracy *et al*.[17] found that 50 Hz NMES increased blood flow more than lower frequencies did. In this review, trials with positive results employed frequencies from 40 to 80 Hz; however, they were mainly NMES currents. In all the studies that found significant differences, the electrodes were placed locally on the edges of the wound.

Only two original studies reported information about adverse effects. Atalay and Yilmaz[23] did not find complications attributable to TENS, while Lundeberg *et al*.[31] reported only allergic skin reaction to the adhesive tape for two stimulated patients. Because clinicians must check before for contraindications and because no electrochemical reaction occurs on bidirectional currents, no important adverse effects should be detected.

Conclusions

In general, bidirectional currents appear to increase wound healing rates and reduce wound size of skin wounds, particularly in skin flaps, pressure ulcers, and diabetic ulcers. However, there is a lack of well-designed studies on biphasic and alternating stimulation, and there is a need for improvement in parameters description and in nomenclature uniformity. More research is needed to know which type of wave is better for healing and if an amplitude to achieve contraction and higher periods of treatment are necessary to find positive effects. The investigators must report the adverse effects of the bidirectional currents or state that they did not occur, in order to confirm their safety and advantages over unidirectional currents.

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