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Early Effects of Combined Ultrasound and Electric Field Stimulation on Chronic, Recalcitrant Skin Ulcerations

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Abstract

The authors evaluate a Combined Ultrasound and Electric Field Stimulation Device (CUSEFS) on chronic recalcitrant wounds. Patients chosen for the study suffered from Diabetic Foot Ulcers (DFU's) or Venous Leg Ulcers (VLU's). Twice weekly use of the CUSEFS for fifteen minutes a session was performed for one week on patients whose wound had shown no improvement in the previous two weeks. 96% of the subjects showed some response. The majority of these recalcitrant wounds closed between 8-20% in the first week of treatment with CUSEFS.

Keywords: Diabetic foot; Chronic wounds; Ultrasound and electrical stimulation

Introduction

Diabetic foot wounds result in substantial morbidity, reduced quality of life, and increased mortality in individuals with diabetes. Several studies have confirmed that intermediate wound reduction is a predictor of final healing in venous stasis, pressure, and neuropathic foot ulcerations [1-3]. Attinger [4] recommended that wound area should reduce by 10–15% per week. Lavery evaluated the predictive value of percent healing at one week on total closure at sixteen weeks [5].

Wound healing phases include inflammation, proliferation, and tissue remodelling, including an abundance of cell types. Soluble mediators, keratinocytes, nerve cells, fibroblasts, extracellular matrix components, and a variety of leukocytes are some of the cell types included in wound healing [6]. In chronic wounds, cellular and subcellular activities are decreased. Treatment of chronic wounds benefits from ultrasound therapy by increasing local blood flow in the wound and periwound area, stimulation of angiogenesis, increased vascular permeability, cellular protein synthesis, and improved collagen substance and configuration [7,8]. Electrical stimulation therapy assists in wound healing by affecting the electrochemical wound process. Chronic wounds lose the electrical currents and, hence, have decreased healing. Electrical stimulation therapy reintroduces the currents and assists with the healing process [9,10]. Ultrasound and electrical stimulation have proven effective in treatment of chronic ulcerations. Davis and Ovington [11] noted these modalities can be beneficial in various types of wounds.

The BRH A-2 (BRH Medical, Jerusalem, Israel) is a combined Ultrasound and Electric Field Stimulation device. The two energy sources, acoustic and electric are combined in a proprietary method so that the combinations of the two enhance each other. Avrahami et al. have reported significant success with CUSEFS in the healing of both Diabetic Foot Ulcers (DFU's) and Venous Leg Ulcers (VLU's) [12].

The authors evaluate the effect of BRH A-2 and CUSEFS on initiating healing installed, recalcitrant ulcerations under conditions of expected treatment.

Methods

This was a multicenter retrospective analysis of the efficacy of CUSEFS on initiating wound healing in wounds that were recalcitrant to previous treatments. Patients were included in the analysis if they suffered from either a DFU or a VLU that has been present for a minimum of three months. The wounds would have had to show less than 5% change in the 30 days prior to initiation of CUSEFS. All treatments prior to initiation were included and the last treatment prior to initiation was continued during the first week of this study as long as it had been in use for a minimum of 14 days.

Subjects were treated using the BRH A-2 protocol which included treating the wound with CUSEFS twice weekly for fifteen minutes per treatment. As per the protocol, patients were treated for two minutes with just electric stimulation followed by eleven minutes of CUSEFS, followed by another two minutes of just electric stimulation. Patients had their wounds measured with the built in BRH A-2 digital planimetry system and the measurements were reviewed by an independent investigator. Measurements were compared after one week of treatment as compared to the baseline measurement

Results

415 patients from six centers were evaluated. All of the patients' wounds had no change in measured area in the fourteen days leading up to the trial initiation. Figure 1 shows the results of the study. 96.39% had some effect in the first week of treatment. 49.4% had between

1-10% wound closure, and 32.5% had between 10-30% wound closure. Figures 2 and 3 shows the breakdown of the 1-10% and 10-30% response group respectively. 146 (35.18%) patients had between 8-20% responses.

The results of having any effect on wound closure were statistically significant ($p<0.01$). The result of having a significant change in wound size as being more than 10% in the week was also statistically significant ($p<0.05$).

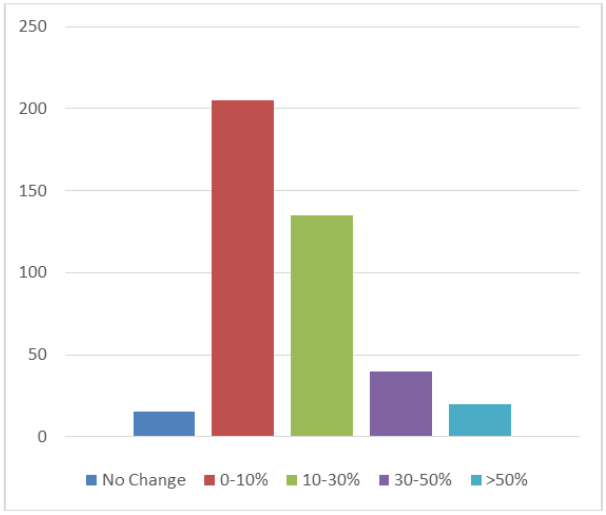

Figure 1: Overall results of the study.

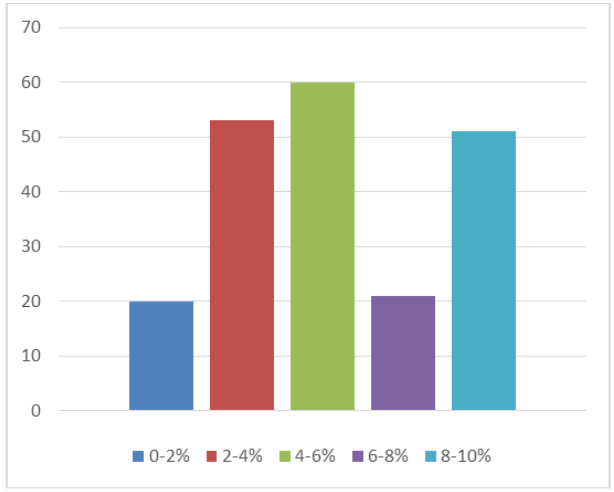

Figure 2: Breakdown of the response group of >0-10%.

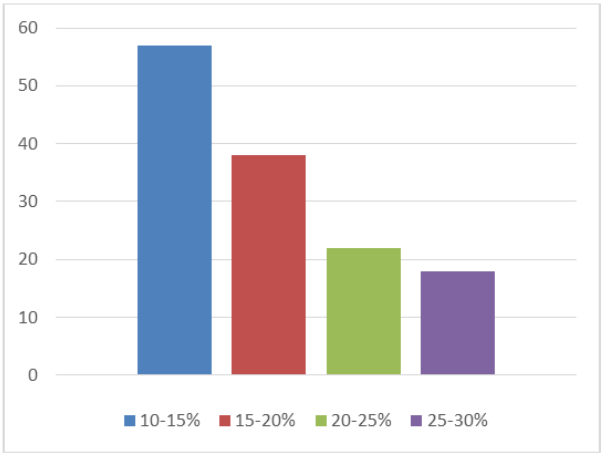

Figure 3: Breakdown of the response group of 10-30%.

Discussion

Cellular senescence is an essentially irreversible form of cell-cycle arrest that can be triggered by a variety of cellular damage or stress, including DNA damage, chromatin disruption, oncogene activation, oxidative stress, and telomere dysfunction [13]. Senescent cells remain viable and metabolically active, but are refractory to mitogenic stimulation. Another important feature of senescent cells is the expression of the Senescence-Associated Secretory Phenotype (SASP) or the Senescence Messaging Secretome (SMS) [13,14], characterized by the increased expression of inflammatory cytokines/chemokines (e.g., IL1, IL6, IL8, MCP2, MCP4, MIP-1a, MIP-3a) and ECM degrading enzymes (e.g., matrix metalloproteinases [MMPs]), and downregulated expression of ECM components (e.g., collagen) [15].

Senescence in cutaneous wounds is controlled by CCN1 (also known as CYR61), a matricellular protein dynamically expressed at sites of inflammation and wound healing [16].

Ultrasound and Electric Stimulation and their combination CUSEFS have a mechanical effect on the cells, reversing the pathway towards senescence [17,18]. The micromovement generated by the modalities causes an immediate effect, with the two distinct wave types having a cellular affect both individually and combined.

This study looked at the immediate effect of CUSEFS on wound healing. The wounds evaluated all exhibited clinical signs of senescence, with little to no cellular effect occurring and allowing for healing. With application of CUSEFS, the mechanical and chemical environment of the cells in the wound are altered. The results of this study showed a significantly positive effect according to Attinger's [5] statement that 10% weekly healing is predictive of healing. The wounds included in this study all exhibited signs of senescence and no healing for a prolonged period of time. CUSEFS was effective in causing a stimulation in more than 99% of the wounds.

The biggest drawback to this study was that it was not a randomized controlled trial. The number of subjects reviewed, and the individual controlled build of the study, whereby the patients had no change prior

to initiation, and the only change to their treatment regimen was CUSEFS, makes this a controlled trial with significant results.

Conclusion

CUSEFS has shown to be effective in initiating wound healing in chronic, stagnant, recalcitrant ulcers. The modality is easy to use, and has a place in the wound care armamentarium. Further studies to qualify and quantify the effect of CUSEFS are called for.

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