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EFFECT OF PULSED RADIO FREQUENCY STIMULATION ON WOUND HEALING: A DOUBLE-BLIND PILOT CLINICAL STUDY.

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INTRODUCTION

Chronic pressure ulcers are a well recognized problem in persons with spinal cord injury, stroke, the elderly and other individuals who may be bedbound or wheelchair bound. The National Pressure Ulcer Advisory Panel estimates the prevalence of pressure ulcers to be between 2.7% and 29.5% in acute care facilities, between 2.4% and 23% of patients in skilled care facilities and nursing homes and between 7% and 12% of patients in the home care setting[1]. Various studies estimate the cost to heal an ulcer range from $5,000 to more than $25,000 and the total financial cost runs over $5 billion annually[2].

A variety of treatment interventions are used to facilitate healing of chronic pressure ulcers[3]. One method that is well documented to accelerate the rate of wound healing involves the use of EMF to deliver small electric currents into periwound tissues. Clinical trials by Kloth and colleagues[4-6] were among the first contemporary studies to show that chronic wound healing can be accelerated with EMF stimulation that delivers between 250 and 500 µC into wound tissue. A recent double-blind study by Salzberg et al.[7] further confirmed that small electric currents induced into chronic pressure ulcers by RF energy resulted in a significant increased rate of healing with a greater percentage of healing at one week than occurred in a control group. These studies confirm that EMF of the proper charge, density and total energy causes dramatically improved healing of dermal wounds. Based on numerous human and animal efficacy studies one would expect a beneficial outcome from a therapy that could decrease edema, debride necrotic tissue, attract neutrophils and macrophages, stimulate receptor sites for growth factors, stimulate growth of fibroblasts and granulation tissue, increase blood flow, stimulate neurite growth, induce epidermal cell migration, prevent post-ischemic oxygen radical-mediated damage, inhibit bacteria, and reduce numbers of mast cells.

This double-blind, placebo-controlled, prospective clinical pilot study was aimed at determining the effect of pulsed radio frequency (PRF) stimulation on the healing of chronic wounds in spinal cord injured patients. Based on other reports that invasively applied electric currents accelerate wound healing[4-6], it was hypothesized that an electric current having similar parameters induced non-invasively into wound tissues by a radio frequency electromagnetic field would have a similar effect.

METHODS

In this double-blind, placebo-controlled pilot study the goal was to determine the effect of PRF treatment on healing of pressure ulcers in spinal cord injured patients. Two groups of five male patients with pressure ulcers were enrolled in the study. The ulcers of one group were treated with an active PRF device for 30 minutes, Monday through Friday for four consecutive weeks. Ulcers of the second group were treated with a sham PRF device for 20 days over the same time period. Both groups received a standard saline moist gauze dressing to their wounds between daily treatments. A baseline tracing of each patient's wound opening was made and four subsequent tracings were made at weekly intervals. Tracings were digitized by computer to determine wound area dimensions in cm^2.

Patients could be included in the study if they met the following criteria: i) a complete or incomplete spinal cord transection and insensate skin surrounding a stage III or IV pressure ulcer located in the pelvic /buttock /hip or lower extremity area and in existence longer than 30 days; ii) the ulcer area could not be less than 4 cm^2 or greater than 100 cm^2 in area; iii) be cooperative and willing to participate for the entire study and willing to sign an Informed Consent Statement; iv) all patients selected for the study had to have their pressure ulcer treated for the first 30 days with moist wound therapy (saline - moist gauze). After this control period, only ulcers that had not shown improvement toward healing were selected for entry into the study; v) when necrotic ulcer tissue required removal, debridement was performed prior to the patient entering the study.

Patients were excluded from the study for the following reasons: a) presence of cardiac pacemakers, electronic stimulators or other implanted or external electronic devices; b) excessively obese; c)negative nitrogen balance or serum albumen less than 3.5 g/dl; d) younger than 18 years; e) active osteomyelitis underlying the ulcer; f) adhesive strapping or moist dressings where the PRF was to be applied; g) patients receiving long term radiation, steroid or chemotherapy, or who were terminally ill; h) poorly controlled diabetes mellitus; i) wounds that hemorrhaged easily, had heavy exudation, or were totally occluded by eschar.

All patients in the active treatment group were treated with a PRF device which delivers a 65 ☞sec burst of high frequency sinusoidal waves (27.12 MHz, in the short wave band) repeating at 600/sec to the treatment area. The peak magnetic field in tissue was approximately 2 Gauss (1 Gauss = 10^{-4} Tesla). This corresponds to a peak induced electric field of 1 V/cm and current density of 1 mA/cm^2 in a typical wound target, similar to that delivered by high voltage galvanic stimulators (HVGS) clinically utilized for edema reduction and wound healing[2,3]. The signal is applied via a 23 cm diameter applicator, containing a pancake coil, placed within 0.5-1 cm of the external surface of skin, bandages, slings, casts, or ice packs (in contrast to HVGS devices which utilize skin (or wet dressing) contact electrodes. PRF dose was monitored via magnetic field measurements using a calibrated probe[8,9]. The sham unit had the same operational outward appearance and was applied in the same manner as the active unit, but did not broadcast an RF signal to the wound tissue. Both groups received a standard saline moist gauze dressing to their wounds between daily treatments.

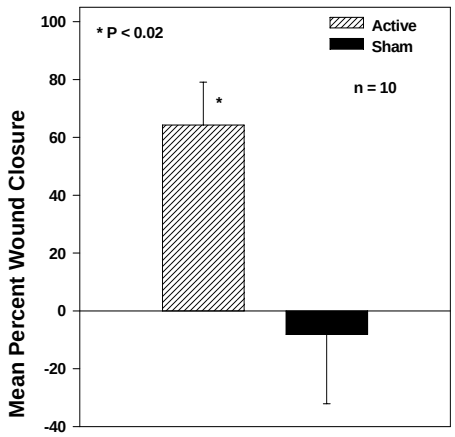
A baseline tracing of each patient's wound opening was made. Tracings were digitized by computer to determine wound perimeter dimensions. The wound surface area was evaluated from the measured length and width dimensions prior to the start of treatment, and after 4 weeks. Mean wound area ratio was computed from these measurements and compared for the active and sham groups. This was defined as percentage healing. Significance was assessed using an unpaired Student's t test. The analysis of variance F test confirmed there was no significant difference in the variances for all comparisons. The Kolgomorov-Smirnov test confirmed all data sets were normally distributed. Significance was accepted for $P \leq 0.05$.

RESULTS AND DISCUSSION

Comparison of the wound area prior to the start of PRF treatment revealed that initial mean wound opening area was not significantly different for the PRF sham and active groups. In contrast, after 4 weeks of PRF therapy, wounds treated with PRF were 64 ± 15% healed (wound closure) vs -8 ± 24%, or no change i.e., wound progression was identical to that prior to study entry, in the sham treated group, $P = 0.016$ ($t = 2.57$, unpaired t test). These results are summarized in the figure.

The results from this study substantiate those from a double-blind study using a similar PRF signal

on pressure ulcers in the same patient population[8]. Although the number of patients treated with PRF was small, the results obtained in this pilot study suggest that RF therapy may be beneficial as an adjunct treatment for chronic wounds. Certainly the results are similar to those obtained with high voltage pulsed current[4-6], with the added clinical advantage of a non-contact application and dosimetry relatively independent of the wound state.



Effect of PRF therapy for 30 min daily after four weeks on pressure ulcers in spinal cord injured patients. Treated wounds were 64% closed vs essentially no change in opening area in the sham treated group, i.e., the sham group continued as prior to entry in study.

The RF signal utilized in this study has been reported to reduce pain and edema in several double-blind clinical studies[10-13]. Chronic inflammation is associated with pressure ulcers due to the continual presence of necrotic tissue. Inflammation is an essential phase in the healing process, however, during this phase the body often responds by creating excessive amounts of tissue fluid resulting in edema that distends interstitial spaces causing pain, delayed healing and increased morbidity. For soft tissue and musculoskeletal injuries, as well as post-surgical, post-traumatic and chronic wounds, suppression of edema buildup and/or existing edema are pre-requisite therapeutic goals for the acceleration of healing[14,15]. It is therefore possible that the PRF signal energy utilized in this study reduces inflammation (edema) in the wound, thereby speeding the healing process.

The mechanism of action of RF for the reduction of edema is not known. Animal studies, wherein direct skin contact electrodes (HVPC) have been used to deliver mono- or bi-phasic rectangular pulses of relatively high voltage (just below motor response) and long duration (10-1000 μsec), report edema reduction immediately post treatment[16]. In contrast, when RF was employed for 20-30 minutes for ankle sprains, edema reduction persisted[12,13]. It has been suggested RF modulates sympathetic outflow thereby restricting the movement of blood constituents from vascular to extravascular compartments at the injury site[17]. Recent studies at the molecular and cellular level suggest the transmembrane voltage changes induced by the RF signal utilized in this study are sufficient to affect ion binding and/or transport with resultant modulation of relevant biochemical cascades[18,19]. Thus, RF affects the phosphorylation rate of myosin, a contractile protein, by modulating Ca^{2+}-calmodulin interactions[20]. Such ion-protein interactions regulate a variety of cellular processes basic to the physiological response to injury, including the release of cytokines. In this manner the RF signal may directly reduce extracellular fluid production and/or affect osmotic capabilities at the injury site.

CONCLUSIONS

The outcome of this pilot study further supports the findings of many other clinical trials that have reported enhanced healing of chronic wounds with PRF stimulation. When wounds do not show evidence of healing with standard wound treatment, PRF treatment is a cost saving intervention that can stimulate the

endogenous bioelectric tissue repair processes. In addition, acceleration of tissue healing also reduces the pain and suffering experienced by individuals afflicted with chronic wounds. For patients with pressure ulcers, relative immobility in bed as a means of reducing pressure is often required by caregivers. Extended periods of recumbency may have detrimental effects on the patient's cardiovascular and musculoskeletal systems, which may lead to complications such as orthostatic hypotension, muscle atrophy or joint contractures. Thus, accelerated healing of chronic wounds with PRF will enable patients to return to functional activities sooner so undesirable complications do not develop. Further research is needed to determine if results similar to those obtained in this pilot study may be obtained in a larger homogeneous population of chronic wounds.

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