Effects of Pulsed Electromagnetic Fields on Skin Microvascular Blood Perfusion

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ABSTRACT: Pulsed electromagnetic fields (PEMF) are potentially useful as therapy for pain and edema management in some post surgical patients. The present study was undertaken to determine if skin blood perfusion changes occur during PEMF use and could thereby possibly be related to its reported therapeutic effects. Using a commercially available device (Magnetic Resonance Therapeutics, Inc.) the right forearms of seven female and two male healthy subjects (age 34 to 54 years) were exposed to maximum field excitation for 45 minutes while the subjects were seated and in a temperature controlled room. During this interval, and for 20 minutes prior to PEMF activation, local skin blood perfusion (LaserFlo, Vasamedics, Inc.) and temperature were monitored on both forearms. Changes in skin perfusion during the activation interval (expressed as a percentage of the pre–activation baseline values) were determined for each arm and used to access the presence and extent of the effect of field excitation on skin blood perfusion. Baseline levels of blood perfusion were not significantly different ($p = 0.29$) between arms although the control arms tended to have a greater perfusion than the treated arms with mean ± being respectively 1.05 ± 0.61 vs 0.78 ± 0.32 volts. Baseline skin temperatures were nearly identical (32.1 ± 1.0 vs. 32.0 ± 1.0, $p = 0.84$). Post–excitation data, analyzed using a 2–way anova with repeated measures, revealed a significant treatment–time interaction (multivariate $p = 0.03$) with a significantly ($p = 0.01$) elevated perfusion ($29 \pm 24\%$) in the treated arms after 40 minutes of treatment. No perfusion increase was present in the control arms. These findings point to the presence of a potentially useful EMF—blood flow interaction which is manifest after adequate field exposure. Possible mechanisms involved in this interaction and potential links to perfusion augmentation and other facets of PEMF treatment are discussed.

WOUNDS 1992;4(5):197-202

The following are proceedings from a presentation given at the **Symposium on Advanced Wound Care** and **The Medical Research Forum on Wound Repair**, April 23 – 25, 1992, New Orleans, LA.

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Electro–magnetic stimulation as a therapeutic modality has a long and tortuous history.[1] Modes of administration have included various combinations of faradic,[2] capacitive and inductive coupling to the tissue with different patterns of pulsation and frequencies.[3,4] The induction mode using a pulsed radio frequency has the attractive feature of not requiring patient contact nor the need for return electrodes. Its efficacy in the management of certain types of refractory bone

healing has been advocated and is fairly well established[5,6] although certain contraindications to electrical stimulation have been described.[7] Pulsed electromagnetic fields (PEMF) have been recently approved for the management of post operative pain and edema and both old and more recent reports suggesting its effectiveness have appeared in the literature.[8,9]

The mechanism of action of PEMF is claimed to be different from standard diathermy-like action,[8,10] in that when operated with low average power and short duty cycles it is suggested that the results obtained with this modality are likely athermal in origin.

Reports, both recent and of a more vintage variety, have alluded to the potential use of PEMF as an aid in wound healing,[9,11-18] although the absence of effects in some animal models have also been reported.[12-13]

Important questions concerning the mechanism whereby this modality might aid in these processes remain unanswered. Since nutrient blood flow deficits are often present in patients with delayed and nonhealing wounds, we wondered if PEMF treatment was associated with detectible changes in blood circulation and via this effect could possibly be related to its indicated benefits. Indirect evidence suggests that PEMF therapy could augment peripheral blood flow via reflex vasodilation following epigastric application in normal subjects[19] and in patients with intermittent claudication.[10] However, there have been no direct measurements of PEMF effects on blood flow at the site of application which ultimately would be the target of potential wound healing interventions.

Thus the present study was undertaken specifically with the limited experimental objective to determine if and to what extent treatment with PEMF affects skin blood perfusion in the treated region.

Methods

Study population. Seven female and two male subjects between the ages of 34 and 54 years who were free of any known vascular disease participated in this study which was approved by our Institutional Review Board. Each subject was instructed as to the nature of the study and signed an informed consent form prior to participation.

Protocol. All testing was done in a temperature controlled room (23 to 24° C) with the subject seated on a comfortable easy chair. On each arm a non-metallic laser Doppler probe (Vasamedics, Inc.) was affixed with double-sided tape to a medial forearm site approximately 5cm distal to the antecubital space. A temperature sensing thermistor for surface temperature measurements was placed approximately 1cm distal to the outer edge of the probes and secured with tape. A towel was draped over each forearm to diminish the direct effects of any circulating air currents. With the subject resting comfortably, the skin temperature of each arm was monitored. During this monitoring interval the actuator head containing the excitation coil for producing the PEMF (Magnetic Resonance Therapeutics, Inc., MRT) was positioned directly above the Laser Doppler probe of the right forearm at a vertical distance of approximately 2cm from the skin surface. When the monitored skin temperature reached a steady state value, the data acquisition phase was begun. This consisted of a 20 minute baseline interval followed by a 45 minute interval in which the MRT unit was activated to its maximum power and pulse repetition levels.

Data acquisition. Skin temperature was recorded at five minute intervals during the entire protocol. Skin blood perfusion signals as determined with the Laser Doppler Flowmeter (LDF) were continuously displayed on a chart recorder and simultaneously acquired by a computer following analog to digital conversion. The LDF signals were time averaged by the computer during each contiguous five minute interval of measurement to produce a single averaged perfusion value for each interval. At the end of the procedure the relative magnetic field strength at the skin site was measured with a 2.5 cm diameter loop which was coupled to a special designed and calibrated metering system.

Field and power levels. The MRT unit produces a pulsed electromagnetic field with a fixed radio frequency carrier of 27.12 MHz and a fixed pulse duration of 65 microseconds. The duty cycle, which is the ratio of pulse on time to the total period, is adjustable by controlling the pulse repetition frequency (PRF). In the present study the PRF was set at 600 pulses per second and the associated duty cycle was 0.039.

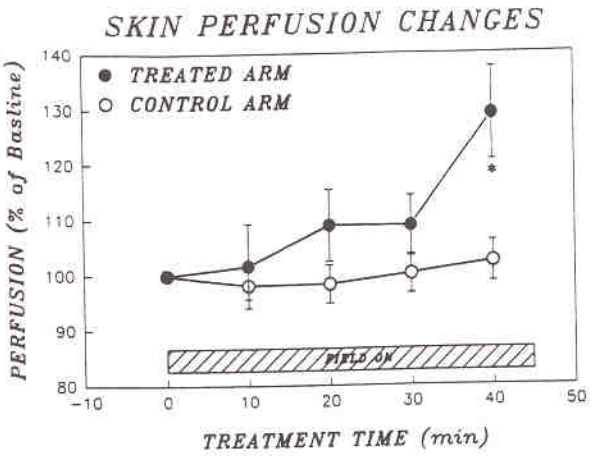

*Figure 1. Forearm skin blood perfusion during PEMF treatment. Values are expressed as a percentage of the pre-treatment perfusion (mean ± sem) for the nine subjects evaluated. *= p = 0.01.*

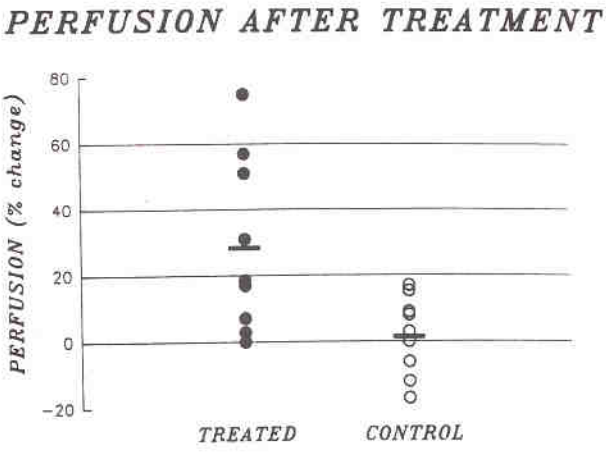

Figure 2. Forearm skin blood perfusion for each subject as measured after 40 minutes of treatment. Values are the percentage change from pre-treatment.

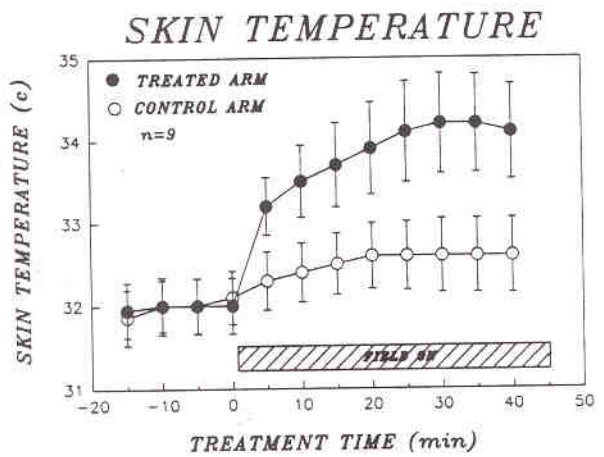

Figure 3. Forearm skin temperature prior to and during PEMF treatment.

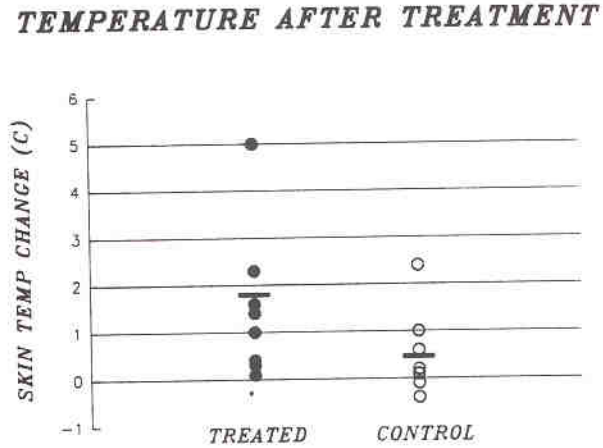

Figure 4. Forearm skin temperature for each subject as measured after 40 minutes of treatment. Values are the absolute change in temperature from pre-treatment.

The total output power as measured at the surface of the actuator was set at its maximum level for all tests herein reported. The power level was measured under these conditions using a large loop connected to an RF power meter. Values obtained were 35 watts which was within 10% of the theoretical maximum (38 watts) stated by the maufacturer.

Relative magnetic and electric field strength measurements at varying vertical distances below the actuator surface were made using magnetic and electric field probes coupled to a high frequency oscilloscope. At a vertical distance of 3 cm, the magnetic and electric fields were reduced respectively to 58% and 30% of their maximum values.

Data handling. For each subject the baseline perfusion for the treated arm and the control arm was determined as the average during the 20 minute baseline interval. Subsequent perfusion values, following the start of PEMF treatment, was expressed as a percentage of this baseline. Comparison between the treated and control arms were done using analysis of variance with arm (treated vs. control) as the grouping variables and with time as a repeated measure.

Results

Figure 1 summarizes the time course of the perfusion change found during treatment for the nine subjects studied. Analysis shows significant treatment-time interaction ($p = 0.03$) with a significantly ($p<0.01$) elevated blood perfusion in the treated arm after 40 minutes of field activation. The absolute values of baseline perfusion (mv) did not differ between control and treated arms, being respectively (mean ± sd) 1050 ± 610 and 780 ± 320. Analysis of covariance with the baseline perfusion in absolute units (mv) as the covariate also shows an overall difference between treated and control arms ($p<0.01$).

Figure 2 depicts the individual changes in perfusion as measured at 40 minutes of treatment and expressed as the percentage change from baseline. The group mean increase in the treated arm is 29% with a SD of 24% whereas essentially no perfusion change in the control arm was detected.

Figure 3 summarizes the time course of the measured skin temperatures. A rapid initial temperature increase on the treated arm is noted to occur within five minutes of treatment start. Thereafter, there is the appearance of a modest gradual increase and plateau at about 30 minutes. Statistical analysis shows that for the treated arm during treatment, all skin temperatures differ from baseline ($p<0.001$) but none significantly differ from each other. Thus the primary temperature increase indeed occurs within the first five minutes of treatment. Baseline skin temperature were nearly indentical in both arms (32.1 ± 1.0 vs. 32.0 ± 1.0).

Figure 4 depicts the skin temperature changes in individual subjects as measured at 40 minutes of treatment. The group mean increase in the treated arm is 1.8 degrees and in the control arm 0.5 degrees. It may be noted that in one subject the treated arm increased by five degrees. In the absense of this apparent outlier the mean temperature rise would have been less different between arms. The perfusion change for this subject was less than the mean.

Discussion

The main finding of the present investigational study is that PEMF treatment, when applied in the manner described to healthy volunteers, is associated with a significant augmentation in their resting forearm skin microvascular perfusion. This augmentation, which averages about 30% as compared with resting pre-treatment levels, occurs after about 40 minutes of treatment whereas no such augmentation is evident in the contralateral non-treated arm.

The mechanism responsible for this flow increase, though not the central issue of the present study, is worthy of comment. One obvious possibility is that the detected skin temperature elevation was in part involved. The time-changing current flowing in the coil of the device produces an electromagnetic field which penetrates the tissue being treated. The magnetic field is comprised of two components, one which is directed perpendicular to the loop and one which is directed radially in the plane of the loop. An associated circular electric field occurs in the tissue and gives rise to an induced electrical current in the treated tissue. Depending on the value of effective electrical conductivity of the tissue, a certain amount of the incident power will be absorbed by the field and be transformed into heat. In standard diathermy it is this heat that is sought for its therapeutic effects.

Under low-power and low-duty cycle operation as is the design of the device used in the present study, such heat generation is thought to be avoided. The rationale for this is in part based on the concept that energy absorbed during the short activiation pulse will have sufficient time during the off-time to be dissipated thereby preventing heat build-up during the treatment procedure. However, the possibility that rather than being completely prevented, heat build-up occurs at a much reduced rate. If so, the measured skin temperature rise may have been a manifestation of deep, low-level accumulated heating and the measured blood perfusion increase may have been attributable to normal thermal-regulatory vasodilatory processes when a certain threshold temperature was reached.

The observed magnitude and time course of the skin temperature change provides some, albeit limited, information on the likelihood that this thermal process was the principal mechanism. The largest fraction of the temperature rise occurred within five minutes of treatment yet the perfusion increase was not observed until about

40 minutes into treatment. This is clearly not fully consistent with the features of a primary thermally induced skin vasodilatory response. Indeed, the average 1.8 degree temperature rise herein measured at the site of application is similar to that reported in the epigastric application site and remote areas at the toe and foot dorsum.[10, 19]

An alternate possiblity needs to be considered. The measured skin temperature rise may have been induced by a PEMF related initial rapid increase in blood flow in the forearm muscle vasculature. Such a flow increase would occur in tissue which is well below the site of detectible skin perfusion measurement. The increased muscle flow would cause an increase in tissue temperature which would progress to the skin surface. This process could account for the observed initial skin temperature rise, being a consequence of an initially increased muscle blood flow, in the absence of an associated measured increase in skin perfusion at that time.

Arguing against this is the fact that in the skin, which as an electrical conductivity similar to that of muscle and is exposed to a greater field strength, no evidence of direct heating and corresponding flow increase was detected coincident with the early skin temperature rise. The questions then of the role of the temperature effect on skin perfusion per se in the present setting remains inconclusive.

If the measured perfusion increase is inferred to be produced by athermal processes then it is instructive to consider what the mechanisms may be. Though few if any hypotheses have been put forward in the literature there are several reports which bear on this issue. One of the central questions is with what entity is the field interacting? Grimes and co-workers,[20] using a highly sensitive superconducting magnetometer system, discovered the presence of small current loops of the order of 12 uA flowing within the normal leg. Though at present, neither the source or function of these current loops are known, their very presence provides for an identifiable entity with which the treatment field would interact. Some alteration of the intrinsic loop current would clearly be a consequence of such an interaction. But how might such an interaction lead to an increase in blood perfusion?

Basic data provided by Miura and Okado[21] may provide the necessary link. Direct observation of arterioles in the web membrane of the frog revealed that PEMF treatment caused them to dilate to 126% of their pre-treated value. This arteriolar vasodilation was observed in spite of the fact that the web was perfused with a solution maintained at 20° C whereas no vasodilation was observed in the absense of the field even when perfused at 30° C. Thus the possibility of a significant thermal effect is all but eliminated. Further, by altering the calcium ion concentration in the perfusate, these authors showed that the vasodilatory response was inversely related to calcium ion concentration and could be clocked by Methylene Blue which is an inhibitor of guanylate cyclase. Taken together, these findings suggest that the vasodilatory response is in some way related to either an increase in the outflow of calcium ion through vascular smooth muscle plasma membrane or an increase in the inflow into the sarcoplasmic reticulum. The time course of the response was similar to the findings of the present study in that the vasodilation proceeded very slowly and did not plateau until about 60 minutes of field application. Field related changes in calcium ion fluxes have also been implicated in DNA synthesis acceleration[22] and in fracture healing.[6]

Based on the results of the present investigation and on the key findings discussed above we are able to formulate a tentative working hypothesis concerning a potential athermal mechanism to explain the PEMF effect. In its simplest form this hypothesis would first suggest that the normal calcium ion flow associated with vascular smooth muscle tone regulation is a component of the detected tissue current loop.[20] And secondly, that the interaction of the field with this current loop is the initiating process which alters the calcium fluxes in a direction to produce vasodilation and hence the increase in skin blood perfusion as observed in the present study.

Though this theory must be viewed speculatively at present, its ramifications extend beyond PEMF related perfusion effects. It contains the seeds to help clarify other issues related to modalities in which electrical currents and fields are employed therapeutically. At a basic level, Nordenstrom[23] has long advocated the existence of "biologically closed electric circuits" as a fundamental property of normal tissue which, upon

tissue injury of various sorts, are altered and otherwise disturbed. For example, it is thought that currents generated by alterations in tissue polarization are associated with the control of the movement of leukocytes to and within injured tissue as well as affecting the liberation of substances which effect capillary permeability. Increases in vascular permeability, which are prominent features of edema formation, thus become linked to field-cell interactions. The precise mechanism whereby PEMF therapy for example, might act to reduce post-surgical edema is not known but the field-cell interaction concept provides a plausible basis for futher inquiry.

Extension of the preceding findings and concepts to account for the processes whereby electromagnetic interactions may aid in promoting soft tissue healing are clearly premature. The augmentation of skin blood perfusion may play a role, but this needs to be tested in patients with existing blood flow deficits and be correlated with wound healing success. It is the authors' opinion that more is involved. If one accepts the premise that repair of injured tissue is at least in part dependent on the presence of appropriate ionic currents, then the absence of healing may reflect an inadequate intrinsic self-driving system. It is conceptually easy to imagine that an external field may act to either trigger or entrain errant current loops toward normalization. It is a much more difficult task to describe with any reasonable degree of specificity, the details of how this occurs.

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Acknowledgement

The authors thank MaryBeth Regan, RN, MS, CNS for invaluable technical assistance and project coordination.