

Johnson, et al. 2008. Modulation of carrageenan-induced paw edema and hyperalgesia in the rat with pulsed magnetic field therapy. Bioelectromagnetic Society Meeting, June 2008. San Diego, CA.

Background: Post-operative acute inflammation continues to affect a significant percentage of surgical patients. Current anti-inflammatory agents rarely cause a decrease in recovery time, and harbor several potential side effects and adverse drug interactions. Non-invasive pulsed electromagnetic field therapy (PEMF) has been shown to reduce inflammation and modulate pain in a number of wound healing and pain modulation studies. A study of PEMF treatment with a blinded, randomized design is described in this report, using a validated rat model of acute inflammation induced by paw injection of microgram amounts of carrageenan. The results indicate the efficacy of a pulse modulated sinusoidal PEMF signal in reducing edema and preventing a decrease in pain tolerance, both indicators of acute inflammation in this animal model.

Methods: Inflammation was induced in the left hind paw of Harlan Sprague-Dawley rats (200-340g) by injection of 100 μ L of a 3.5mg/mL sterile phosphate buffered saline-based carrageenan solution into the footpad using a 30 gauge tuberculin syringe. The carrageenan dose was carefully calibrated to produce a mild, controllable form of inflammation that could be evaluated for rate of onset. Edema was determined using a plethysmometer volume displacement transducer system and pain tolerance was evaluated using a Randall-Selitto paw pressure analgesia instrument (both devices from Stoelting Company, Wood Dale, IL). Edema and pain tolerance were measured pre-carrageenan injection and at 1, 4 and 8 hours post-injection. Rats were exposed to either the PEMF signal or a control, untreated experimental coil configuration for 15 min. An experimental 8" coil system was used to provide PEMF exposures at 0.25, 2, 4 and 8 hours post-injection (SofPulse, Ivivi Health Sciences, Inc., Montvale, NJ). The system delivers a 2 msec burst of 2 MHz sinusoidal waves repeating at 2 bursts/sec, and inducing 1 V/m electric field at a target diameter of 2 cm. This PEMF signal was configured a priori to modulate Ca²⁺ binding in a calmodulin (CaM) transduction pathway. Data were analyzed with SigmaStat 3.0 software (SPSS, Chicago, IL) using Student's unpaired t-test and one way ANOVA, as appropriate. Differences were also compared using the Mann-Whitney test for two independent groups. Significance was accepted at $P \leq 0.05$.

Results: The results showed a pre-injection pain threshold for both groups that was not significantly different ($P = 0.568$), nor was hind limb volume ($P = 0.433$). There was no significant difference between active or sham groups in mean pain tolerance pre-injection ($P = 0.880$), or at 1 hour ($P = 0.688$). In contrast, mean pain tolerance decreased by $51 \pm 8\%$ at 4 hours and $52 \pm 10\%$ at 8 hours in the sham cohort ($P < 0.009$), compared with no significant difference in pain tolerance at 1 hour ($P = 0.797$), at 4 hours ($P = 0.878$), or at 8 hours ($P = 0.566$) in the active cohort. Mean edema volume in the sham treated animals was $33 \pm 7\%$ greater at 1 hour post-injection ($P = 0.037$), $41 \pm 8\%$ greater at 4 hours ($P =$

0.005), and 47 ± 9 % greater at 8 hours ($P = 0.009$) than edema volume in the PEMF treated animals at these time points.

Conclusions: Data from these experiments confirmed the hypothesis that a PEMF signal, configured a priori to modulate Ca/CaM- dependent anti-inflammatory cascades, possibly involving the signaling molecule nitric oxide, can inhibit both pain and edema resulting from tissue trauma or injury. Previous reports have indicated a reduction in Visual Analog Scale for human post-surgical pain with similarly configured PEMF signals. Injected carrageenan produces localized irritation and inflammation of short duration in a rat paw model. By downregulating these in vivo indicators of inflammation, we have demonstrated the analgesic potential of SofPulse PEMF therapy using objective corollary determinations in a randomized, blinded animal study.