A Double-Blind Trial of the Clinical Effects of Pulsed Electromagnetic Fields in Osteoarthritis

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ABSTRACT. Objective. **Further evaluation of pulsed electromagnetic fields (PEMF), which have been observed to produce numerous biological effects, and have been used to treat delayed union fractures for over a decade.**

Methods. **In a pilot, double-blind randomized trial, 27 patients with osteoarthritis (OA), primarily of the knee, were treated with PEMF. Treatment consisted of 18 half-hour periods of exposure over about 1 month in a specially designed noncontact, air-coil device. Observations were made on 6 clinical variables at baseline, midpoint of therapy, end of treatment and one month later; 25 patients completed treatment.**

Results. **An average improvement of 23–61% occurred in the clinical variables observed with active treatment, while 2 to 18% improvement was observed in these variables in placebo treated control patients. No toxicity was observed.**

Conclusion. **The decreased pain and improved functional performance of treated patients suggests that this configuration of PEMF has potential as an effective method of improving symptoms in patients with OA. This method warrants further clinical investigation.** (*J Rheumatol 1993;***20:456–60**)

Key Indexing Terms:
OSTEOARTHRITIS
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Pulsed electromagnetic fields (PEMF) have been widely used in the treatment of delayed union fractures for over a decade, and there is a growing body of literature concerning the biological and clinical effects of such low frequency, nonionizing forms of energy.

Clinical responses have been reported in longstanding nonunion of fractures[1], failed arthrodeses[2], avascular necrosis of hips in adults[3,4], and Legg-Perthes's disease in children[5]. Similar devices are being evaluated in the treatment of osteoporosis. A device to generate PEMF installed in a body brace increased the success rate of lumbar fusions in a double blind control study[6]. There are also reports of augmentation of peripheral nerve regeneration and function and promotion of angiogenesis[7]. Patients with persistent rotator cuff tendinitis, refractory to steroid injection and other conventional measures, showed significant benefit compared with placebo treated patients[8]. In clinical studies done over 17 years in over 200,000 patients treated safely with PEMF, no toxic effects have been reported[9].

One of us (RM) developed a unique delivery system of extremely low frequency (ELF) pulsed waves, consisting of a magnetic field generator with an electronic interface to a freely moving air coil. Two delivery systems have been developed, one for peripheral joints and one for the axial skeleton. The most effective magnetic field configuration delivered by these devices was established empirically by treating groups of 20 patients with rheumatic conditions, varying the field variables until the optimal configuration was determined. Uncontrolled observations were then carried out in Europe in 861 patients with various painful rheumatic conditions; data suggested improvement of symptoms in 70-80% of treated patients. Therefore, a carefully controlled, double blind pilot study of possible therapeutic effects of this device was undertaken.

MATERIALS AND METHODS

Patients. All patients met the criteria for the diagnosis of osteoarthritis (OA) published by Altman[10]. Radiographs were available in all but one of the patients with OA; severity grading was done by the criteria of Brandt[11].

We followed the approach to data gathering and analysis suggesting that the impact of a new drug or device on chronic arthritis is best determined by the patients' accounts of their joint pain and their ability to perform activities of daily living (ADL)[12-14].

Patients were required to be older than 18 years of age with persistent arthritic symptoms of at least one year duration, incompletely relieved by conventional treatment including nonsteroidal antiinflammatory drugs (NSAID), other analgesics, and physical therapy modalities. Patients who

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had started any new form of treatment, including NSAID, within one month were also excluded from the investigation. The single most symptomatic peripheral joint was studied (knee in 21, the first carpometacarpal (MCP) or interphalangeal group of joints of the hand in 5 and posttraumatic OA of the ankle in 1.) Patients with OA of isolated MCP or single proximal interphalangeal (PIP) joints, or OA of the spine were not accepted for the study.

All women of child bearing age had to agree to use contraceptives. Other exclusions included the use of a cardiac pacemaker or the presence of any serious, unstable medical illness. Informed consent for entry into a double blind trial was obtained.

Patients who were taking stable daily doses of NSAID were instructed not to change their usual medications during the study period; the use of medications was checked by history at each evaluation point, but no pill counts were done.

Although some patients with other forms of arthritis were evaluated, data are presented here only for the patients who met the published criteria for the diagnosis of OA, since too few patients with other diagnoses were studied to allow conclusions to be drawn.

Treatments. Treatments were administered by the device described above, which produces an extremely low frequency (less than 30 Hz.), varying, pulsed electromagnetic field averaging 10-20 gauss of magnetic energy at a coil current of up to 2 amperes drawn from a power source of 120 volts AC. The pulse phase duration was 67 ms, including 15 micropulses with a pause duration of 0.1 s. The wave duration varied according to the frequency used. The patients rested the joint being treated on a pillow, encircled by the air coil which did not contact the skin. Treatments were given for 30 min; 3-5 sessions were given each week for a total of 18 treatments, the entire treatment period extending over about one month.

The magnetic therapy system used comprised 3 components: the magnetic field generator (MFG), the electronic interface and the air coils of varying dimensions as described above. The MFG produces a low voltage, DC current. The gating circuits employed CMOS logic integrated circuits. The electronic interface carried the current to the air coil, forming a flexible link between the fixed MFG and the air coil. The winding geometry employed in the air coil is formed with a specially designed jig to produce a pure DC homogeneous magnetic field.

The air coil produced a uniform homogeneous magnetic flux throughout the x, y and z axes. The joint under treatment was positioned eccentrically in the air coil, completely within the magnetic field flux. Since the device applied a pure magnetic field through the air coil, no heat was generated, nor did the patients feel any sensation during the treatment.

The magnetic field flux engulfed the joint area; it can penetrate the entire joint area since neither the skin nor other tissues present a barrier to magnetic energy. Since the field consisted of a uniform (homogeneous) flux density, the size of the body part (joint) treated did not affect the quality or quantity of magnetic energy delivered. Therefore, there was little or no variability of dosage to various joints or body parts treated.

Randomization. Upon entry to the study, patients were randomized to receive active PEMF or placebo using a table of 1,000 random digits. A coded master record sheet was kept by an office administrator, and a trained PEMF therapist activated the coil energy of the PEMF device and timed each treatment to 30 min. The ON/OFF control of the MFG was in the "ON" position with the associated red light for all of the patients in both the active and placebo groups during treatments. The PEMF device produces no noise or sensation and therefore the placebo therapy was applied by not energizing the air coil; all patients kept the affected joint in the air coil for the same 30 min period signalled by a laboratory timing clock placed on the generator. In this way, both the patient and the examining physician remained blinded as to whether active PEMF or placebo was being given.

Data collection. A case report form was prepared for each patient which recorded their enrollment eligibility criteria, pertinent clinical history, baseline medications, and examination. Baseline hematocrit and white blood cell counts (WBC), serum electrolytes, creatinine, and an erythrocyte sedimentation rate (ESR), as well as a urinalysis, were done to exclude any concurrent illness and to monitor for any changes. These tests were repeated at the end of the treatment period. A radiograph of the joint to be treated was taken unless one had been obtained within the preceding 4 months.

Evaluations by the patient and the physician observers were made at 4 points during the study: baseline, midway through the treatment series, at the end of the treatment period, and 4 weeks after treatment was completed. At each evaluation the patient's opinion about joint symptoms was recorded along with the physician's assessment of the patient's symptoms and clinical signs. Data were collected for overall severity of pain, difficulty performing the activities of daily living (ADL) identified as the most troublesome by the patient before therapy was begun, pain generated by those specific activities of daily living, and the worst discomfort experienced by the patient in the previous week. A standard visual analog pain scale was marked by the patient to indicate the total amount of pain, pain with ADL and worst discomfort in the past week; the scale had no markings but was 100 mm long and the patient's mark was measured from the zero point. The difficulty in performing the specific ADL identified as most troublesome were quantitated on a scale of 1 to 5 using explanatory adjectives of "none, slight, moderate, severe, or extreme" to assist patients in their evaluations.

Data were also recorded for a rheumatologist's evaluation of pain on joint motion and tenderness of the joint being treated to firm palpation. At each observation after baseline, the physician made an "overall assessment of improvement" on a 5-point scale (worse or no change = 1, slight but insignificant change = 2, moderate improvement = 3, excellent improvement = 4, and complete disappearance of symptoms in affected joint = 5).

Statistical methods. Data were analyzed for change from baseline to each observation point for each patient by nonparametric matched pair 2-tailed t tests using the Wilcoxon signed rank test, for both treated and control groups. Instat (Graphpad Software Co.) was used for statistical calculations. The physicians' overall assessment of improvement was analyzed at the end of the treatment period and one month later, comparing treated and placebo groups, also using 2-tailed t tests.

RESULTS

Fifteen patients with OA were randomized into the active treatment group, 12 into the placebo treatment group. Two patients, after agreeing to randomization, withdrew from the study before the start of active treatment and asked for unblinded, active treatment; one (randomized to active treatment) withdrew because of transportation difficulties; one (randomized to the placebo group) was hospitalized because of a hernia; both of these patients had been evaluated at baseline, but not after treatment had begun and were not included in the data analysis. Five patients did not appear for the evaluation one month after completion of treatment; 4 had received active treatment, one, in the placebo group, had been hospitalized for community acquired pneumonia. All data for each patient were included in the analysis, including the last observation point; the numbers evaluated at each point are given in Table 1.

The 2 groups of patients did not differ significantly in respect to age, sex, race, body weight, or number of years with symptoms. The active treatment group included 11 with OA of the knee, 3 of the hand (PIP and MCP joints); 1 had OA of the ankle. The placebo group included 10 with OA of the knee, 2 of the hand. The dropouts all had OA of the knees.

At baseline there were no significant differences between

Table 1. *Numbers of patients with OA observed at each phase of the study*

	Numbers of Patients	
	Treated	Placebo
Entered into study	15	12
Evaluated at middle of treatment	14	11
Evaluated at end of treatment	14	11
Evaluated at one month followup	10	10

the active treatment and the placebo groups in any of the subjective patient variables or the physician examination variables evaluated.

Improvement occurred in each variable followed in the treated group, and data analyzed as matched pairs showed significant differences for the data for each variable at the midpoint of treatment, the end of treatment and one month after treatment. The patients who were followed showed continued improvement during the month after completion of treatment (Table 2A).

The placebo treated group showed some improvement from baseline in each variable, the change not reaching statistical significance for any of the observations (Table 2B).

The actively treated group averaged 34% improvement in the mean value for each variable evaluated at the midpoint of therapy, and 36% at the end of treatment; by one month after treatment ended, improvement averaged 47%; Figure 1A shows the percentage improvement in each of the 6 variables observed for the treated patients. Among the patients in the placebo group, improvement averaged 8% at the midpoint, 10% at the end of treatment, and 14% one month later (Figure 1B).

The overall assessment of improvement by the physician observer at the midpoint, end of treatment and one month after completion of treatment for treated and placebo groups is shown in Table 3.

The degree and frequency of improvement for upper extremity and lower extremity joints was similar.

No patient reported any increase in the use of their usual medications during the period of observation. Two patients, both in the treatment group, reported discontinuation of usual medications (ibuprofen, 800 tid in one, and pentazocine, 50 mg prn in the other); no placebo patient reported any change in medication.

Laboratory data at the end of treatment showed no changes in any tests including CBC, ESR, serum electrolytes, BUN, creatinine, and tests of liver status. No patient reported symptoms suggestive of toxicity nor was any toxicity observed by the physician evaluators.

The study was not designed for crossover analysis of an active treatment phase for the placebo treated patients; at the completion of observations, however, placebo patients were informed of the nature of their "treatment" and offered the opportunity to have active treatment in an unblinded fashion, and 7 did so. New baseline and followup observations were

Table 2. *Observations on actively treated and placebo-treated patients at each point. Figures are numbers of patients observed at each point (n) mean for groups*

Table 2A. Actively treated patients

	Baseline	Midpoint	End of Treatment	1 mo Later
n =	15	14	14	10
Overall severity of pain (scored on 10 cm visual analog scale)				
Mean	7.65	4.28	3.80	3.55
SEM (±)	0.6405	0.88	0.82	1.08
p =		0.0215	0.0023	0.0052
Difficulty score with most troublesome ADL (scale: 1 to 5)				
Mean	4.27	3.25	3.07	2.80
SEM (±)	0.20	0.25	0.31	0.29
p =		0.0098	0.0020	0.0078
Pain with most troublesome ADL (scale: 1 to 5)				
Mean	3.90	2.89	3.14	2.40
SEM (±)	0.12	0.22	0.29	0.27
p =		0.002	0.0313	0.0078
Worst discomfort in previous week (scored on 10 cm visual analog scale)				
Mean	8.14	5.36	5.03	4.03
SEM (±)	0.58	0.74	0.83	0.94
p =		0.0046	0.0009	0.0059
Pain on joint motion by MD exam (scale: 1 to 5)				
Mean	3.47	2.07	2.29	1.85
SEM (±)	0.21	0.29	0.38	0.26
p =		0.002	0.0195	0.0117
Joint tenderness by MD exam (scale: 1 to 5)				
Mean	3.57	2.29	2.00	1.40
SEM (±)	0.33	0.29	0.29	0.22
p =		0.0034	0.0024	0.0039

Table 2B. Placebo-treated patients

n =	12	11	11	10
Overall severity of pain (scored on 10 cm visual analog scale)				
Mean	8.07	7.23	7.32	7.10
SEM (±)	0.75	0.55	0.47	0.35
p =		> 0.3	> 0.6	> 0.5
Difficulty score with most troublesome ADL (scale: 1 to 5)				
Mean	3.88	3.77	3.59	3.65
SEM (±)	0.15	0.18	0.24	0.26
p =		> 0.6	> 0.4	> 0.6
Pain with most troublesome ADL (scale: 1 to 5)				
Mean	3.92	3.77	3.50	3.45
SEM (±)	0.15	0.23	0.20	0.26
p =		> 0.6	> 0.2	> 0.2
Worst discomfort in previous week (scored on 10 cm visual analog scale)				
Mean	8.18	7.16	6.65	6.82
SEM (±)	0.59	0.63	0.79	0.82
p =		> 0.4	> 0.3	> 0.3
Pain on joint motion by MD exam (scale: 1 to 5)				
Mean	3.25	2.86	2.82	2.60
SEM (±)	0.28	0.38	0.42	0.42
p =		> 0.3	> 0.4	> 0.2
Joint tenderness by MD exam (scale: 1 to 5)				
Mean	3.00	2.73	2.95	2.45
SEM (±)	0.44	0.36	0.32	0.26
p =		> 0.8	> 0.9	> 0.8

SEM = standard error of the mean, and p value is for change from baseline for that variable.

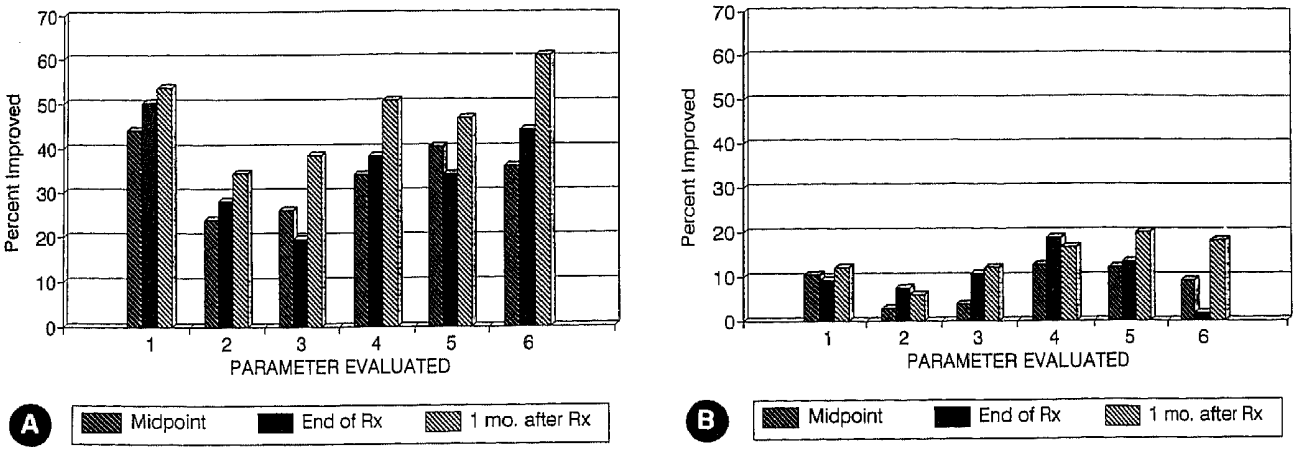

Fig. 1. Percent improvement, defined as difference between baseline value and value at each specific observation point, divided by baseline value (times 100). Numbered observations shown included (1) Overall severity of pain. (2) Difficulty performing ADL identified as the most troublesome by the patient before therapy was begun. (3) Pain generated by the most troublesome ADL. (4) The worst discomfort experienced in affected joint area in the past week. (5) Pain on motion of the treated joint detected by the examining physician. (6) Tenderness of study joint detected by the examining physician. 1A: Treated patients; 1B: Placebo patients.

Table 3. *Assessment of improvement by observing physician at midpoint of treatment, end of treatment and one month after completion of treatment. p Value is for difference between treated and placebo groups*

	Midpoint	End of Treatment	1 mo Later
Treated patients			
Mean	2.71	2.71	3.30
SEM (±)	0.27	0.37	0.45
Placebo patients			
Mean	1.73	1.86	1.75
SEM (±)	0.27	0.47	0.34
p =	0.0175	0.1611	0.0134

made on these patients. As a group, these patients showed improvement during the active treatment phase but, in view of the small numbers involved, statistically significant changes that occurred did not occur in all of the variables followed.

Radiographs were graded as to severity of the OA. There were too few cases in the treated group to permit meaningful statistical analysis of the response according to radiological criteria of severity. It is possible to say, however, that 5 patients with radiologic grade 3 and 4 disease obtained good or excellent responses according to physician assessment at the last observation, and thus that advanced disease does not preclude symptomatic benefit from this form of therapy.

DISCUSSION

The results of our prospective double blind study of PEMF treatment show beneficial effects in the amelioration of symptoms, subjective improvement in functional ability and decrease in objective findings in a small group of patients with OA. The benefit seemed to continue for at least the first month after completion of treatment. Furthermore, no toxicity was observed.

This application of PEMF therapy is not similar to other physical modalities of treatment, such as ultrasound, TENS, diathermy, moxibustion, etc. The PEMF generated by the device used in our study differs from the device used in the treatment of unhealed fractures in that it generates a lower frequency (<30 Hz vs 72 Hz), as well as differing in pulse and wave form characteristics. The extremely low frequency pulsed magnetic fields used in these studies, as well as those used in laboratory experiments, are too weak to work through a mechanism such as thermal effect, dielectric breakdown, particle displacement or electrophoresis. Mechanisms which have been suggested include some form of induced resonance of outer shell electrons, an effect on cell membrane receptors or on other endogenous processes, such as an effect on ion flux, but these suggested mechanisms lack experimental substantiation[15-18]. Evidence exists that pulsed magnetic fields can modulate the actions of hormones, antibodies, and neurotransmitters at surface receptor sites of a variety of cell types[15]. Effects on fibroblast, chondrocyte and osteocyte metabolism and lymphocyte functions have been reported. Augmentation of mRNA and protein synthesis has been reported in several tissue culture symptoms[16,17,19-25].

Since the factors responsible for the pain in patients with OA are varied and often uncertain in an individual patient, an attempt to delineate the mechanism of pain relief brought about by this form of therapy in relation to known biological effects of pulsed magnetic fields would be purely speculative.

This form of nonionizing radiation is not known to have

any deleterious clinical effects, despite the variety of metabolic changes that have been demonstrated in laboratory experiments. On the basis of the findings in this pilot study, further investigation of clinical effects of pulsed magnetic fields in OA is warranted.

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