Initial Exploration of Pulsing Electromagnetic Fields for Treatment of Migraine

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Two studies were conducted during which 23 patients with chronic migraine were exposed to pulsing electromagnetic fields over the inner thigh. In an open study, 11 subjects kept a 2-week headache log before and after 2 to 3 weeks of exposure to pulsing electromagnetic fields for 1 hour per day, 5 days per week. The number of headaches per week decreased from 4.03 during the baseline period to 0.43 during the initial 2-week follow-up period and to 0.14 during the extended follow-up which averaged 8.1 months. In a double-blind study, 9 subjects kept a 3-week log of headache activity and were randomly assigned to receive 2 weeks of real or placebo pulsing electromagnetic field exposures as described above. They were subsequently switched to 2 weeks of the other mode, after which they kept a final 3-week log. Three additional subjects in the blind study inadvertently received half-power pulsing electromagnetic field exposures. The 6 subjects exposed to the actual device first showed a change in headache activity from 3.32 per week to 0.58 per week. The 3 subjects exposed to only half the dose showed no change in headache activity. Large controlled studies should be performed to determine whether this intervention is actually effective.

Key words: migraine headache, pulsed electromagnetic fields, treatment

Abbreviation: PEMFs pulsing electromagnetic fields

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Most adults in the United States have at least occasional headaches. Headache is now the leading medical cause of lost days of work and costs billions of dollars per year to treat. The Nuprin Pain Report found that 157 million workdays per year were lost due to this problem alone. Numerous surveys of the general population have indicated that about 65% of males and 78% of females reported having had at least one headache within the past year.[1] About half of men and 65% of women report having at least one headache per month. About 30% of males and 44% of females reported that these were severe, with about 15% having headaches severe enough to affect daily activities. Among young adults, severe headaches lasted about 6 hours for men and 8 hours for women with 8% of men and 14% of women losing a day or more of work per month due to headaches.[2] About 6% of people attending civilian general medical practices request treatment for headaches as their primary reason for coming. About 7% of males and 17% of females reporting headaches requested treatment within the previous year.[3] A survey of over 20 000 typical Americans (with a response rate of over 60%) showed that about 17% of women and 6% of men had at least one headache per year which met the International Headache Society's criteria for migraine (eg, vomiting, unilateral or pulsatile pain with photophobia or phonophobia, visual or sensory aura before the headache). About 59% of females and 50% of males reported at least one headache per month. These headaches caused moderate to severe disability in about 47% of the females and 43% of the males.[4]

Pulsing electromagnetic fields (PEMFs) have been in use as therapeutic modalities for at least 40 years. One of the well-recognized, standard uses of PEMF generators is in enhancing the rate of healing of un-united fractures.[5] The investigators were treating a patient for such a knee condition when she mentioned a long history of weekly migraine headaches with auras (classic migraines) which had stopped shortly after PEMF treatment began. She reported that the visual auras had continued to occur as usual, but the subsequent headache did not follow. Her headaches did not return for months following treatment. This effect led us to wonder how exposure

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to PEMFs at the upper leg could have an effect on headaches presumably centered in the head.

The PEMF units used in our clinic (Diapulse model D103; Diapulse, Inc, New York, USA) are set to produce pulsed, high-frequency, high peak power, electromagnetic energy at a frequency of 27.12 MHz in 65-microsecond bursts occurring in 600-pulse-per-second sequences at 975 watts peak. This is sufficient power to light a 60-watt bulb placed in the field. The field extends about 12 cm from the unit's head in a conical pattern. The head of the unit is placed just above the area to be exposed and turned on for a set amount of time. Units from other manufacturers differ slightly in a variety of ways such as the exact shape of the wave, rise and fall times, and power. The device looks like a floor-mounted hair drier from the 1950s, has a relatively loud fan, a ticking timer, and sufficient knobs, lights, and a meter, etc to be quite impressive. This impression has to be considered when attempting to differentiate actual from placebo effects.

Exposure to PEMFs of the type described above appears to result in at least a temporary increase in peripheral blood flow. For example, Erdman[6] recorded peripheral blood flow from 20 normal subjects using both a temperature probe and volumetric measurements while they were being exposed to pulsing electromagnetic-generated fields. He found a high correlation between the amount of energy produced by the device and peripheral blood flow, with increases beginning within about 8 minutes and plateauing by 35 minutes. Pulse rate and rectal temperature did not change. This relationship has been confirmed in basic studies of blood flow in rabbit ears.[7] Ross[8] recently reviewed the basic science and animal studies, as well as some of the clinical studies, showing the effectiveness of PEMF generators in increasing blood flow and wound healing. Cameron[9] demonstrated increased rates of healing in experimentally induced wounds in dogs. Goldin et al[10] found similar results among humans in a double-blind study using changes in fibroblast concentration, fibrin fibers, and collagen in the wound sites and in swelling. The increased rate of wound healing was ascribed to increased blood flow. Thus, it is very likely that exposure to this device does result in increased peripheral blood flow, at least while exposure is in progress.

Freedman[11] has reviewed the effect of temperature biofeedback on peripheral blood flow. Numerous double-blind studies with 5- to 15-year follow-up have demonstrated that training patients with migraine to increase peripheral blood flow, through such techniques as temperature biofeedback from the finger, results in sustained decreases in all aspects of headache activity among a large percentage of people who successfully learn the techniques.[11] Thus, whatever other mechanisms come into play, a technique which is aimed solely at increasing peripheral blood flow, frequently results in decreased headache activity.

Synthesis of this background material led us to believe it was possible that application of a PEMF directed only to the thigh, with its significant vascular supply, could produce sufficient increases in peripheral blood flow to affect headache activity for as long as the effect on blood flow continued. The following explorations were attempts to begin testing that hypothesis.

METHODS

Twenty-three patients (19 women, 4 men; mean age 46.4 ± 14.9 years, range 20 to 73 years) having multiyear histories of headaches (mean 17.9 ± 9.9 years, range 2 to 40 years) were recruited from among the patients at a large military medical center. All of the subjects met the normally accepted criteria for migraine set out by the International Headache Society.[12] Several of the subjects had mixed headaches because they reported headaches meeting both the criteria for migraine and those for tension headache. After listening to an explanation of the study, each was given a consent form approved by the institutional review board of the center to read and sign. Two different pilot studies, one open and one double-blind, placebo-controlled, were performed. Demographic and diagnostic data for the participants in the open study are presented in Table 1, while those for participants in the controlled study are presented in Table 2.

Open Study.—Each of the 11 patients kept a 2-week diary of headache activity before and after being exposed to PEMFs. Several studies reviewed by Blanchard et al[13] indicate that 2 weeks should be sufficient time to determine the actual baseline level of activity in this population. The structure of the open study was essentially an "ABA" design with nonexposure periods surrounding a single exposure period. Prophylactic medications were stopped abruptly during the weekend between the end of the 2-week initial log and the start of the treatment period. Thus, any rebound effect should have developed by the end of the treatment period and have been observed during the last week of treatment or the 2 initial posttreatment weeks. During the exposure period, patients were exposed to between 2 and 3 weeks of PEMF treatments for 1 hour per day, 5 days per week at a power of 975 watts with 600 pulses per second. The PEMF was applied to the medial thigh. Headache activity during treatment was reported to the therapist every day. The PEMF unit utilized in the study was described in the introduction. Additional follow-up data beyond the 2-week "posttreatment" log period were collected telephonically for all of the subjects.

Double-Blind, Placebo-Controlled Study.—Twelve subjects kept a 3-week log of headache activity and two kept a 6-week log. They were then randomly assigned to receive 2 weeks of real or placebo PEMF exposures as described above. The log was extended from 2 to either 3 or 6 weeks to insure an adequate representation of baseline stability. Randomization was performed by picking a sealed envelope from a basket. The letter "A" or "B" was on a folded card inside the envelope. This determined which device they were exposed to for the first 2 weeks. The placebo machine was identical to the functioning machine both in looks (lights, dials, etc) and sounds (fan, timer noise, etc). The only difference was that several crucial tubes had been removed so it produced no field. As subjects could not sense the field, there was no way for them to know which machine was actually functioning. The ma-

chines were randomized by the senior author, who was not involved in working with the subjects, so the therapist working with the subjects was also unaware of which machine was which. At the end of 2 weeks, the subjects were switched to 2 weeks of the other device after which they kept a final 3-week log. Additional follow-up data beyond the 3-week "posttreatment" log period were collected telephonically and by a mail response survey for all of the subjects. At the end of each 2-week exposure period, each subject rated how likely they felt they had just been in the real exposure period on a scale of 0 to 10 (10 being certain they received the real exposure).

During 7 weeks of this study, the machine which was to provide the actual exposure partially failed, so three subjects inadvertently received half-power PEMF exposures for their 2 weeks of "actual" exposure. This happened because the senior author, who was supposed to calibrate the device twice per week, went on two trips and forgot to calibrate the device for several weeks. As "Murphy's law" dictates, it was during this period that the device partially failed and the signal strength was reduced by half.

The data were analyzed using repeated measures analyses of variance to determine whether there was an overall difference in headache activity between pretreatment, posttreatment, and follow-up periods. Paired *t* tests were used to determine whether there were differences between any two periods when the analysis of variance was significant. The data met the entrance criteria for the tests. Because very few people agreed to cross over from actual to placebo exposure, we used a pretreatment-to-posttreatment analysis rather than a cross-over analysis.

RESULTS

Open Study.—The results for each individual are presented in Table 1. The average number of headaches per week decreased from 4.03 (± 2.02) during the 2-week pretreatment baseline period to 0.43 (± 0.36) during the 2-week postexposure period (statistically different at $P=0.001$; paired $t=5.998$ with 10 *df*). Follow-up ranged from 1 week to 14 months with a mean of 8.1 months and a standard deviation of 3.09 months. The average number of headaches continued to decrease during the long-term follow-up period to an average of 0.14 (± 0.08) per week (statistically different at $P=0.001$; paired $t=5.77$ with 9 *df*). A one-way, repeated measures analysis of variance indicates that there was an overall difference between the periods ($P=0.0001$, $F=31.21$).

Before exposure, all 11 subjects took medications virtually every time headaches occurred. They used an average of 3.1 medications including Midrin®, Fiorinal®, Advil®, Toradol®, Tylenol®, Imitrex®, Cafergot®, and propranolol. After exposure, 8 had stopped using any medications at all, 1 had one visit to the emergency department where she was given Toradol, 1 took Midrin several times, and 1 said she used Premarin® several times.

Double-Blind Study.—The results for each individual are presented in Table 2. For the 6 patients who received actual exposure to PEMF first, the average number of headaches per week decreased from 3.32 (± 1.40) during the 3-week pretreatment baseline period to 0.67 (± 0.26) during the exposure period (statistically different at $P=0.003$; paired $t=5.56$ with 5 *df*). Follow-up ranged from 2 to 6 months with a mean of 2.94 months (± 1.29 months). The average number of headaches during the long-term follow-up period averaged 0.58 (± 0.80) per week (statistically dif-

Table 1.—Open Study: Patient Characteristics and Results

Patient	Age, y Sex	Headache History, y	2-Week Log of No. of Headaches per Week		Duration of Follow-up, mo - No. of Headaches per Week
			Pretreatment	Posttreatment	
Migraine With Nonvisual Precursors or Auras					
1	22 F	12	7	0.25	9 - 0.13
2	21 M	2	3	0.5	9 - 0.08
3	41 F	19	2	0.5	9 - 0.13
4	43 F	21	2	0	14 - 0.25
5	38 F	15	4	0.5	10 - 0.06
6	71 F	40	6	1	9 - 0.08
7	73 F	18	7	0	8 - 0.25
8	64 F	6	4.3	1	1 week
Migraine With Visual Auras					
9	20 F	2	2	0.5	8 - 0.08
10	39 F	11	2	0	7 - 0.25
11	38 M	25	5.3	0.5	5 - 0.13

ferent at $P=0.001$; paired $t=7.81$ with 5 *df*). A one-way, repeated measures analysis of variance indicates that there was an overall difference between the periods ($P=0.0001$, $F=35.67$).

receive actual exposure). After being crossed over to the actual exposure, these three subjects rated their certainty as 1, 5, and 7. The three patients who were inadvertently exposed to half

Table 2.—Double-Blind, Placebo-Controlled, Cross-Over Study: Patient Characteristics and Results

Patient	Age, y Sex	Headache History, y	3-Week Baseline	Actual Treatment First		Placebo Treatment First		3-Week Follow-up	Long-term Follow-up, mo - No. of Headaches per Week
				Actual	Placebo	Placebo	Actual		
Migraine With Nonvisual Precursor Symptoms									
1	63 F	20	6	—	—	4	5	6.5	3 - 6
2	33 F	8	3.5	0.5	Declined*	—	—	0.5	2.5 - 0.25
3	42 F	20	2	0.5	Declined	—	—	0	2.5 - 0.10
4	59 F	10	4.6	1	2	—	—	2	3 - 2
Migraine With Visual Aura Preceding Headache									
1	56 F	20	5.3	1	Declined	—	—	1	2.5 - 0.25
2	50 F	16	2	0.5	Declined	—	—	0	2 - 0.25
3	51 M	12	2.5	0.5	Declined	—	—	0	6 - 0.5
Modified Design With 6-Week Baseline									
1	63 F	33	4	—	—	3	1	2	5 - 2
2	40 F	20	2.8	—	—	3	1.5	2	None
Half-Power Treatment With No Visual Aura Preceding Headache									
1	49 F	35	2.5	2.5	2.5	—	—	2.4	2 - 2.5
2	42 F	30	4	—	—	4	4	5	1 - 4.3
Half-Power Treatment With Visual Aura Preceding Headache									
3	48 M	16	5	—	—	4	4	4.3	2 - 4.3

* Declined to cross over.
All values given as number of headaches per week.

The subjects receiving actual exposure for the first 2-week period rated their certainty that they received the real treatment as an average of 8.6 with 10 being certain of having had actual exposure (three 8's, two 9's, and one 10). Only one of them agreed to cross over to the placebo exposure period. This person showed a decrease from 4.6 headaches per week during the baseline to one per week during actual exposure, and then an increase to two per week during placebo exposure which was sustained during follow-up. The three who received the placebo for the first 2 weeks rated their certainty that they had been exposed to actual PEMF as 0 (sure they did not power rated their certainty that they were receiving actual exposure as 1 or 0 after both periods.

There were no statistically significant differences in headache rates for the few subjects who did cross over from placebo to actual exposure. They were 4, 3, and 3 during placebo exposure and 5, 1, and 1.5 during the subsequent actual exposure ($t=0.64$ with 4 *df*; $P=0.557$). The baseline to follow-up period (6, 4, and 2.8 versus 6, 2, and 0) is also not significantly different ($t=0.63$ with 4 *df*; $P=0.561$).

There was no significant difference between the baseline headache rates of those who got

actual exposure first and those who got placebo exposure first (3.5, 2, 4.6, 5.3, 2, and 2.5 versus 6, 4, and 2.8 (t=.92 with 7 df; P=0.389). However, the headache incidence rates during initial exposure were different for the actual exposure first group (0.5, 0.5, 1, 1, and 5.5) than for the placebo exposure first group (4, 3, and 3) (t=-9.88 with 7 df; P=0.001).

COMMENTS

Most of the patients with a long history of vascular migraine headache, not initiated by other problems, who were exposed to adequate PEMFs showed a dramatic decrease in headache activity during the weeks of exposure and for months afterwards. It is possible that exposure to PEMFs did cause sufficient increase in peripheral blood flow to affect headache activity. This increase would have initiated some chain of psychophysiological events which actually caused the improvement. Of course, it is quite possible that exposure to the fields induced a currently unrecognized physiological effect, having nothing to do with blood flow, which somehow resulted in decreased headache activity. Interestingly, none of the patients who had aura preceding onset of their headaches reported a change in aura activity. The usual headache simply did not follow the aura.

The literature reviewed in the introduction shows considerable evidence that the particular PEMF generator used in this study has some ability to increase peripheral blood flow. The same body of evidence does not seem to exist for the weaker, battery-powered magnetic field generators which do not pulse, nor for the permanent magnets that people strap to themselves for a variety of reasons. If the working hypothesis (that increased peripheral blood flow has resulted in decreased headache activity) is correct, then devices incapable of increasing peripheral blood flow to a similar extent may not be effective. This is supported by the three patients who received half the normal exposure not showing any change in headache activity. Conversely, any device which can safely increase peripheral blood flow sufficiently, should be equally efficacious. Pulsing electromagnetic field units may produce increases in blood flow simply by heating the underlying tissues[14] rather than through any esoteric effects of their fields, so it is possible that diathermy units could also produce these effects.

It should be noted that the average number of headaches per week among our participants is higher than that usually reported by people with migraine. About half of our subjects had more than four headaches per week while most surveys report far lower rates.[2,4,13] Thus, we may have been working with a more complex population than usually encountered.

In spite of the impressive nature of the PEMF generator, the investigators do not feel that the major effects were due to placebo responses because (1) subjects in the placebo arm of the study did not show decreases in headache activity, (2) the participants each had multiyear histories of unsuccessful treatments with numerous highly touted therapeutic approaches, (3) the change in headache activity was much greater than would be anticipated due to a placebo response, (4) the decrease in headache activity has been maintained longer than the 6 months or so anticipated for a placebo effect, and (5) the rebound effect from stopping the prophylactic medicines should have hit sometime near the end of "treatment" and would have overwhelmed any placebo effect.

One of the staff who was responsible for exposing the subjects to PEMFs was also responsible for gathering the postexposure logs. As the results show that by the end of 2 weeks of exposure subjects had little difficulty differentiating between the real and placebo machines, it is possible that this staff person also realized which was the placebo device. Strong support for the study's "double-blind" integrity having been maintained, and thus avoiding a potential therapist expectation effect, is provided by the lack of improvement shown by all three patients who were accidentally exposed to half the normal dose due to partial machine failure. The therapist had no way to know that the "actual" machine had failed.

When we began these exploratory studies we had no idea that the headaches would not return shortly after exposures stopped, therefore, we used a cross-over design to help determine differences between responses to an actual and a placebo device. During the course of these studies, it became apparent that the headaches did not return within a short enough time for a cross-over design to be effective because there was no opportunity for any effects of the treatment to "wash-out" between the end of exposure to one device and start of exposure to the other. Further studies of this technique will require a parallel design.

Because of the powerful effects demonstrated in this trial, it is worth performing a large parallel-group controlled study to determine whether this intervention is actually effective and longitudinal studies to determine whether inexpensive, wearable pulsing magnetic field devices or other means of increasing peripheral blood flow can be used to keep the headaches from returning.

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