Aesth Plast Surg
DOI 10.1007/s00266-008-9169-z

ORIGINAL ARTICLE

Effects of Pulsed Electromagnetic Fields on Postoperative Pain: A Double-Blind Randomized Pilot Study in Breast Augmentation Patients

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Received: 13 March 2008 / Accepted: 14 April 2008

Abstract
Background Postoperative pain may be experienced after breast augmentation surgery despite advances in surgical techniques which minimize trauma. The use of pharmacologic analgesics and narcotics may have undesirable side effects that can add to patient morbidity. This study reports the use of a portable and disposable noninvasive pulsed electromagnetic field (PEMF) device in a double-blind, randomized, placebo-controlled pilot study. This study was undertaken to determine if PEMF could provide pain control after breast augmentation.
Methods Forty-two healthy females undergoing breast augmentation for aesthetic reasons entered the study. They were separated into three cohorts, one group ($n = 14$) received bilateral PEMF treatment, the second group ($n = 14$) received bilateral sham devices, and in the third group ($n = 14$) one of the breasts had an active device and the other a sham device. A total of 80 breasts were available for final analysis. Postoperative pain data were obtained using a visual analog scale (VAS) and pain recordings were obtained twice daily through postoperative day (POD) 7. Postoperative analgesic medication use was also followed.
Results VAS data showed that pain had decreased in the active cohort by nearly a factor of three times that for the sham cohort by POD 3 ($p < 0.001$), and persisted at this level to POD 7. Patient use of postoperative pain medication correspondingly also decreased nearly three times faster in the active versus the sham cohorts by POD 3 ($p < 0.001$).
Conclusion Pulsed electromagnetic field therapy, adjunctive to standard of care, can provide pain control with a noninvasive modality and reduce morbidity due to pain medication after breast augmentation surgery.

Keywords Breast augmentation · Pulsed electromagnetic field therapy · Pain reduction

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Apprehension about postoperative pain is sometimes an important contributing factor in otherwise motivated patients for postponing or avoiding aesthetic surgical procedures. During consultations for breast augmentation it is common to hear patients express great concern about possible intense postoperative pain. With new surgical techniques and development of effective pain management programs, the postoperative experience after breast augmentation has been substantially improved throughout the last decade [1]. Adding local anesthesia, even during procedures performed under general anesthesia, considerably reduces postoperative pain long term [2]. A careful, sharp surgical technique and avoidance of blunt dissection after a submuscular breast augmentation further contributes to minimizing postoperative discomfort. Nevertheless, discomfort can be quite considerable for a patient after a breast augmentation procedure [3]. Identifying innovative technologies for improving postoperative comfort is important here, as it is for all types of surgical procedures.

This is particularly so in this age of ambulatory breast augmentations wherein the immediate and long-term side effects from the use of pharmacologic analgesics in the home setting can contribute to patient morbidity [4].

There is accumulating and substantial clinical evidence that pulsed electromagnetic field (PEMF) therapy can have physiologically significant effects on tissue repair. PEMF devices have been cleared by the US Food and Drug Administration (FDA) for the relief of acute and chronic pain and the reduction of edema, all symptoms of wounds from postsurgical procedures. PEMF therapy has also been cleared for the treatment of recalcitrant fractures and is now part of the standard armamentarium of the orthopedist [5]. A meta-analysis [6] performed on randomized clinical trials using PEMF on soft tissues and joints showed that PEMF was effective in accelerating healing of skin wounds [7–11] and in the treatment of pain associated with connective tissue injury and joint-associated soft tissue injury [12–15].

As good scientific data that demonstrate increasing efficacy for specifically configured PEMF signals continue to emerge, the present study was designed to clinically assess the effect of a PEMF signal designed to modulate Ca^{2+} binding to calmodulin (CaM) [16, 17], an early step in the anti-inflammatory cascade involving the signaling molecule nitric oxide (NO) [18], on pain reduction post breast augmentation surgery. Indeed, analgesics containing NO donors have shown promising clinical results on acute pain reduction [19, 20]. Tuning the drug-free PEMF signal for the NO cascade provides an immediate stimulus independent of pharmacokinetics because the time-varying magnetic field appears instantaneously in all compartments of the target tissue [17]. These technologic advances have allowed economical, light-weight, and disposable PEMF devices to become available. Given all of the above, this pilot study was designed to determine if PEMF treatment, given in addition to standard of care, could further minimize postoperative discomfort and morbidity after a breast augmentation.

Materials and Methods

Before the start of this study, a sample size analysis, assuming a 30% (±25% SD) increase in pain reduction from PEMF treatment, suggested 12 patients per group were needed. It was decided to use 14 per cohort to account for dropouts. Thus, 42 healthy women, aged 20–55 years, who elected breast augmentation for aesthetic reasons, were admitted to this double-blind, placebo-controlled, randomized study. Silicon breast implants (Allergan Style 410) were used for all patients. There were three cohorts in this study: bilateral, wherein 14 patients received active devices on both breasts (both coils delivered a PEMF signal); contralateral, wherein 14 patients received one active or one sham coil on each breast; and 14 patients received sham devices on both breasts (neither coil delivered a PEMF signal). All PEMF devices were assigned according to a random list generated on the basis of the devices' serial numbers. All personnel in the study with patient and/or data contact remained blinded until after the final patient completed treatment. The ethics committee of the Karolinska Institute, Stockholm, approved this study. All patients signed informed consent forms. The only addition to standard of care was PEMF treatment for all patients.

The PEMF signal utilized in this study was a 2-ms burst of 27.12-MHz sinusoidal waves repeating at 2 bursts/s (SofPulse^{TM}, Ivivi Technologies, Northvale, NJ), which induced an average electric field of 32 ± 6 mV/cm in each breast. The PEMF signal is inductively coupled and can thus be applied through clothing or dressings, requiring no contact with the skin. PEMF was delivered from a small (2.5 cm diameter, 1 cm thick) battery-powered generator to a single-turn 15-cm-diameter electrical coil. Two such devices were placed within a specially modified compression bra (Marena Group, Inc, Lawrenceville, GA), one for each breast (see Fig. 1, left). The device-equipped bra was placed on the patient as part of normal postsurgical procedure and the signal was activated before the patient left the operative theatre. Once active, the PEMF device automatically provided a 30-min treatment according to the following regimen: every 4 h for the first 3 days postop; then every 8 h for the next 3 days; and every 12 h until the follow-up visit, normally at postoperative (POD) 7. All patients were treated for a total of 8 days. Sham devices were activated in exactly the same manner as the active devices but produced no electromagnetic field in the target breast tissue. PEMF signal amplitude and configuration was checked for each device at the beginning and end of PEMF treatment with a calibrated field probe (model FCC-301-1-MR1, Fischer Custom Communications, Torrance, CA) connected to a calibrated 100-MHz oscilloscope (model 2358, Tektronix, Beaverton, OR). Measurement of the PEMF signal distribution in a tissue phantom and in air provides an accurate map of the signal in tissue [21, 22]. Such plots revealed the amplitude dose of the electromagnetic field in the treated breast from active devices was uniform to within ±20%. For the contralateral cohort, signal mapping also showed the PEMF signal in the adjacent sham-treated breast was 40–60% of the field in the active breast because of field capture by the sham coil on the contralateral breast.

Since the completion of this study, the PEMF device has been made more economical and simpler to use by incorporating two coils with a single generator, as shown in the right panel of Figure 1.

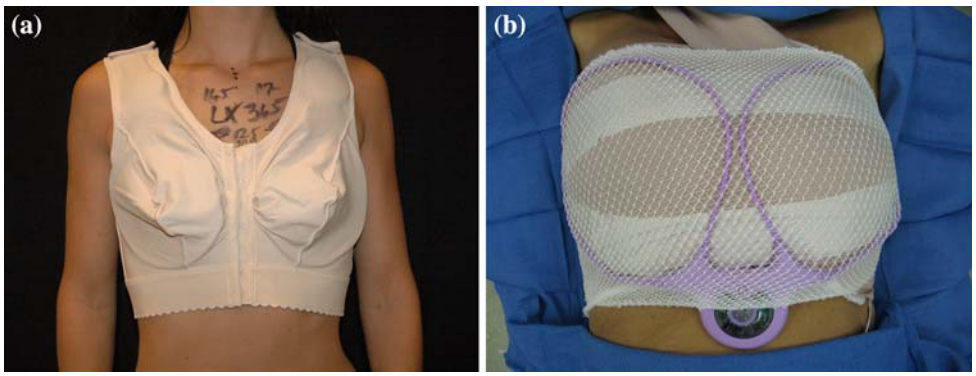

Fig. 1 *Left* PEMF device in place on a breast augmentation patient before the operation to check for correct sizing. Coil around the breast can be seen in the support bra. The circular coil around each breast delivers active or sham treatment. The bra containing coils remains in place for 24 h a day so the treatment regimen may be followed. *Right* PEMF device in current use to control postoperative pain following breast surgery (courtesy A. Gabriel, MD)

The primary outcome measure in this study was the effect of a PEMF signal on the rate of postoperative pain reduction. Pain data for each breast was obtained using a visual analog scale (VAS) for pain which was recorded twice daily starting 30–60 min and again 3–5 h after surgery and on the following postoperative days upon awakening and at approximately 12 p.m. Patients were asked to place a cross line on an unmarked horizontal scale labeled "No Pain" at 0 mm and "Worst Possible Pain" at 100 mm. A separate VAS assessment was used for each time point and for each breast. The use of the VAS scale for postoperative pain has been validated [23, 24].

Postoperative pain medication was also monitored for each patient. Twelve of 14 patients in the active cohort, 13 of 14 patients in the sham cohort, and 12 of 14 patients in the contralateral cohort (35 of 42, 83%) were prescribed an analgesic plus mild narcotic mixture (500 mg paracetamol/30 mg codeine) to be taken as required.

All data were collected and patient compliance with the PEMF protocol was monitored by a senior research nurse who remained blinded throughout the study.

Statistical Analyses

The primary outcome measure was the rate of reduction in postoperative pain, measured as daily changes in mean VAS score with respect to the mean initial pain reading 3–5 h after surgery. These data were analyzed using SigmaStat 3.0 (SPSS, Chicago, IL). Data that passed the Kolmogorov-Smirnov normality test allowed parametric statistical analyses to be used. In this case, mean VAS pain scores were compared for all cohorts using Student's unpaired t test, the paired t test, and one-way analysis of variance (ANOVA), as appropriate. The mean slopes of the daily pain decrease for the PEMF and the sham-treated cohorts were also compared using the nonparametric test for two independent groups, the Mann–Whitney test. As a secondary outcome, the mean percent difference in rate of decrease in dose (pill count) of postoperative pain medication for all patients from POD 1 to POD 7 for PEMF and sham-treated groups was compared using the Mann–Whitney test. All results are expressed as mean ± SEM. All tests were two-sided and $p < 0.05$ was taken as statistically significant.

Results

The PEMF devices were well tolerated and no adverse events were noted. Forty patients completed the study. Complete VAS data were not obtained from two patients in the bilateral sham group. This left 14 patients in the bilateral active group, 12 in the bilateral sham group, and 14 in the contralateral group, with 80 breasts available for analysis. The overall mean VAS pain score differences versus initial postoperative pain from POD 1 through POD 7 was compared for both breasts in all cohorts. It was also of interest to ascertain whether the difference in rate of pain decrease in the active versus sham groups from POD 1 to POD 7 persisted throughout the PEMF therapy. For the latter, the slope of daily VAS pain score differences from initial VAS score versus time in the bilateral active group was compared to that in the bilateral sham group. First-order regression was used to evaluate the slope of pain versus time. Contralateral patients were analyzed separately because PEMF dosage for the sham breast was substantially different than that for patients assigned bilateral sham devices.

The mean starting VAS pain score for all breasts ($N = 80$) in all cohorts was 53 ± 3 mm on the VAS pain scale used (0–100 mm). There was no significant difference in starting VAS pain score for all groups ($p = 0.387$). Comparison of pain decrease for left and right breasts by POD 7 in the bilateral cohorts showed no significant

difference within each cohort. This allowed the results for both breasts to be combined for analysis of active and sham groups. By POD 3 pain had decreased in the treated group for both breasts ($n = 28$) to 28.5 ± 4 mm (87%, $p < 0.001$ versus the postoperative pain score) and in the sham group ($n = 24$) to 40.2 ± 3.5 mm (32%, $p < 0.001$ versus the postoperative pain score). These results show that PEMF therapy caused a statistically significant decrease in pain in the treated versus sham groups by approximately 2.7 times by POD 3 which persisted throughout the course of PEMF treatment. The results for the bilateral cohorts at POD 3 are summarized in Figure 2. Comparison of the daily rate of pain decrease in the active and sham groups reveals that mean daily VAS pain score differences for patients receiving bilateral PEMF therapy was consistent throughout the course of PEMF therapy starting at POD 3 ($p < 0.001$). For all slopes r^2 was greater than 0.95, indicating that first-order linear regression was justified. These data are shown in Figure 3. For comparison, there was no significant difference in the slope of cumulative daily VAS pain score decreases from left to right breast in either the active group ($p = 0.825$), or the sham group ($p = 0.704$).

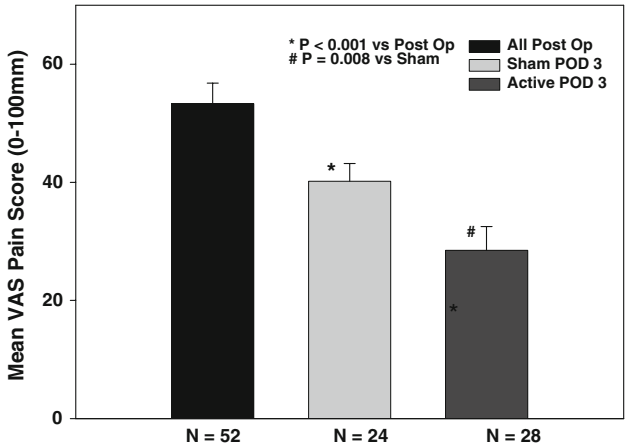

Fig. 2 Effect of PEMF therapy on postoperative pain from breast augmentation. Bars represent the mean VAS pain score at POD 3 vs initial postoperative VAS score. Mean postoperative VAS score was 53 ± 3 mm for all groups. Mean VAS decreased to 28.5 ± 4 mm in the treated group (87%, $p < 0.001$ vs. postop) and to 40.2 ± 3.5 mm in the sham group (32%, $p < 0.001$ vs. postop), representing a clinically meaningful reduction in pain by approximately 2.7 times, which persisted through POD 7 (see Fig. 3)

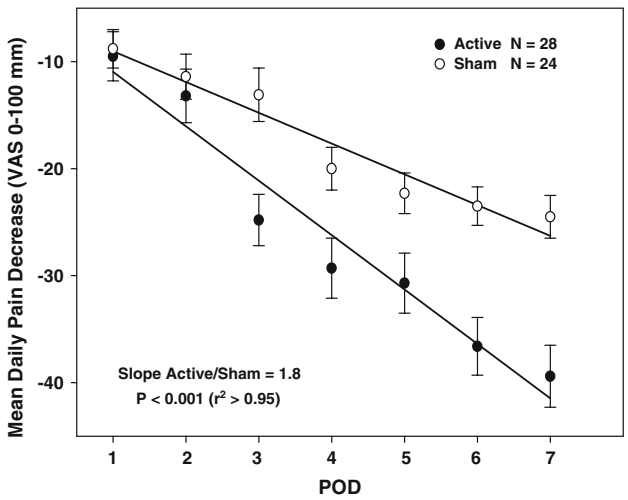

Fig. 3 Effect of PEMF therapy on postoperative pain from breast augmentation. Data are presented as the mean reduction in daily VAS pain from after surgery to POD 7 compared to the initial postoperative VAS pain score. As may be seen, the rate of pain decrease in the treated group was consistently higher than that in the sham group throughout PEMF therapy by nearly a factor of 2

There was no significant difference in the daily pain decrease between the active or sham-treated breasts in the contralateral group ($p = 0.707$). In this cohort, by POD 3 mean VAS pain scores were 29.3 ± 3.8 mm in the treated breasts and 28.5 ± 3.4 mm in the sham breasts, which were not significantly different from each other ($p = 0.854$), but which were significantly different from the mean VAS scores in the bilateral sham cohort, 40.2 ± 3.5 mm ($p < 0.001$). For comparison, mean VAS pain in the active group was 28.5 ± 4 mm at POD 3, which was not significantly different from that for both breasts in the contralateral group ($p = 0.694$).

There was no significant difference in pain medication (mean pill count) for all cohorts immediately after surgery ($p = 0.248$). Pill count in the active cohort decreased from 6.2 ± 0.4 to 3.1 ± 0.3 ($p < 0.001$), and in the sham cohort to 4.9 ± 0.5 ($p < 0.001$) by POD 3. This represents a decrease in use of pain medication in the active group versus the sham group by a factor of approximately 2.9, which persisted to POD 7 and closely followed the PEMF effect in this study. Pill count in the contralateral cohort (3.2 ± 0.4) was not significantly different from that in the active cohort by POD 3 ($p = 0.629$).

Discussion

The results of this pilot study suggest adjunctive PEMF therapy can significantly reduce postoperative discomfort, pain, and patient morbidity. As further expanded studies confirm these results, PEMF therapy for postoperative care may also lead to significant reductions in healthcare costs. Such prospects would apply to all types of wound healing and surgical procedures. When it comes to aesthetic procedures such as breast augmentation, the prospect of even further reductions in postoperative discomfort and pain may also further increase patient acceptance of the procedure and the use of ambulatory facilities. Obviously, modalities that can minimize postoperative discomfort and

improve wound healing have to be cost effective and must be user friendly and simple to use. The PEMF devices utilized in this study appear to satisfy these criteria. The equipment can be placed in the wound-healing area over the dressings directly following the procedure. Once activated, the unit delivers the PEMF regimen automatically, requiring minimal patient involvement. In breast augmentation surgery the equipment may easily be placed in a compression or sports bra and worn for the first postoperative week. The device was well tolerated and no adverse events were noted, further attesting to the clinical applicability of this new noninvasive technique.

It is interesting to note that the mean VAS scores for the active and sham-treated breasts in the contralateral group were not significantly different from those for the bilateral active group ($p = 0.847$). This was expected because of the presence of the sham coil on the untreated breast that captured up to 60% of the signal from the active coil. There may, of course, also be a systemic contribution from the anti-inflammatory actions of the PEMF signal. In any case, both breasts in this contralateral cohort experienced essentially the same increased rate of pain relief from PEMF as the bilateral cohort patient with active devices on both breasts, suggesting that the dose chosen a priori on the basis of a Ca/CaM transduction pathway was well within the expected range for this clinical outcome.

It is also interesting to note that mean starting VAS pain score for all breasts in all cohorts was 53 ± 3 mm on the VAS pain scale used (range = 0–100 mm). In the first author's personal experience, pain after breast augmentation was considerably more pronounced 10–20 years ago. Most patients needed to be admitted for the first postoperative night for pain medication; a common complaint was that the pain intensity was similar to or worse than that felt durng childbirth. In modern breast augmentation surgery in the 21st century, it is the first author's experience that these pronounced levels of pain are hardly ever encountered. Most patients in our unit are dismissed within 4 h after the procedure with acceptable pain levels. This is well illustrated by the initial VAS scores in this study. The explanation for this relatively low level of pain intensity is probably related to a much more atraumatic surgical technique without blunt dissection, the addition of local anesthesia to the surgical field, and, in the first author's experience, early activation with arm movements clasping hands on top of the head directly at wakeup. Despite these clinical improvements, we noted a significantly faster pain reduction throughout the postoperative period with pulsed electromagnetic field treatments. It is possible that the differences between treated and nontreated groups would be even more pronounced if the procedures were of greater magnitude or more traumatic to the patient as in breast reconstruction or in post-bariatric remodeling procedures.

The mechanism of action of PEMF signals on tissue growth and repair is not completely known at this time. Nonetheless, it is well demonstrated that PEMF signals can accelerate growth factor production in the various stages of tissue repair [25]. Recent animal studies have reported that specific targeted PEMF signals produced a statistically significant several-fold increase in neovascularization, suggesting an important clinical application for increased flap survival [26, 27]. In addition, there is recent evidence that PEMF signals can modulate anti-CD3 binding at lymphocyte receptors, suggesting that PEMF can reduce the nflammatory response [28]. If these PEMF effects exist in this postsurgical application, accelerated healing could occur, from both a reduction of time in the inflammatory phase of healing and acceleration of, e.g., collagen production in later healing phases. Indeed, advanced PEMF signals, configured a priori assuming a Ca/CaM transduction pathway, as in this study, accelerated wound repair in a rat cutaneous wound model by approximately 60% as measured by tensile strength [29]. A similar PEMF signal also increased Achilles' tendon repair in a rat model by approximately 70% [30].

Perhaps most directly relevant to this work are studies that show that PEMF can enhance nitric oxide (NO) release via effects on Ca^{2+} binding to CaM [31, 32] which, in turn, activates the constitutive nitric oxide synthases (NOSs). NO is a short-lived signaling molecule that is known to be involved in anti-inflammatory cascades. Several studies report PEMF effects via the NO pathway [33–38]. It is interesting to speculate that the short-term NO cascade was affected which, in turn, accelerated pain relief through the normal anti-inflammatory process of vasodilatation and by inhibition of proinflammatory pathways such as those producing endothelin-1 and IL-1. Studies are currently underway to address these possibilities by examining postsurgical wound exudates for the effect of PEMF on the presence of cytokines and growth factors.

The accelerated pain decrease reported in this pilot study is characteristic of all reported PEMF effects on tissue repair. For example, PEMF modulates bone repair by accelerating return to intact breaking strength, and therefore function [5]. Sham-treated fractures reach the same biomechanical endpoint, as expected, but require more time. Thus, PEMF treatment could accelerate healing, which can reduce morbidity. One of the most important observations of PEMF therapy is that an effect on normal resting tissue has never been reported[5, 6, 17], which is certainly at least part of the reason for the lack of any known side effects.

In view of the above, the effects of pulsed electromagnetic field treatment may, in any surgical intervention, have positive effects on wound healing that goes beyond postoperative pain relief. For breast augmentation surgery such

a problem is obviously the formation of a capsular contraction. Indeed, a recent study demonstrated that electrical stimulation could prevent capsule formation in an animal model [39]. The first author has anecdotally noted significant and positive effects of PEMF on established capsular contracture. There have been no controlled clinical studies thus far. However, the clear anti-inflammatory effects of PEMF signals suggest they would be important to determine whether postsurgical PEMF treatment could reduce the incidence of periprosthetic capsular contracture after breast augmentation. It will be equally important to assess whether PEMF could effectively treat established capsular contracture, possibly reducing the necessity for repeated surgeries. In fact, in a broader multisite study designed to further elucidate the effects reported here, provision could be made for long-term patient follow-up to assess whether the incidence of capsular contraction is affected.

Conclusion

In conclusion, this randomized, placebo-controlled, double-blind pilot study suggests that noninvasive treatment with pulsed electromagnetic fields can significantly reduce postoperative pain after breast augmentation with concomitant reduction in the use of postperative pain medication. The postoperative use of PEMF using disposable economical devices could help decrease postsurgical patient morbidity in many surgical procedures. The technique is clinically simple to use and may possibly also contribute to reduced costs for healthcare, particularly for more complex surgical procedures. It is also interesting to speculate that as experience is gained with PEMF therapy, patients may require less pharmacologic intervention with associated side effects for postsurgical pain relief.

Acknowledgments The authors sincerely thank Anneli Gustavsson Jonsson for her invaluable clinical help and Ivivi Technologies, Inc., Montvale, NJ for the generous donation of the PEMF units used in this study.

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