ENHANCED FRACTURE HEALING WITH PULSED ELECTROMAGNETIC FIELD

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ABSTRACT

Our study was designed to examine the effect of pulsed electromagnetic field (PEMF), capacitative technique, on the healing of fractures at different stages. Forty-four patients were included in the study. They were divided into three groups. The first group comprised twenty-three patients who were subjected to PEMF after application of plaster cast (early treatment group). The second included six patients who received PEMF after removal of the cast at 8 weeks (late treatment group). The third group comprised fifteen patients who were only treated with fixation in plaster cast and served as a control group.

The three groups were investigated using cross-sectional osteocalcin level at the start and at 8 and 12 weeks. Plain x-rays were done every 2 weeks and bone mineral density (BMD) was assessed with the quantitative CT of periosteal callus and expressed as F (fracture) / N (normal) % at 8 and 12 weeks. Laboratory and radiological data were statistically analyzed.

We concluded that PEMF accelerates bone healing as there was a statistically significant difference in osteocalcin level between early treated patients and controls at 8 weeks and a highly significant difference at 12 weeks for patients who continued treatment. Late treatment patients were found to have increased osteocalcin level too. Radiological results confirmed the laboratory results for the positive effect of PEMF on bone healing. We recommend the use of PEMF for enhancement of fracture healing in cases of delayed union and in old age.

INTRODUCTION

Non-union and delayed union are common problems that may be encountered in the management of fractures especially at certain sites where there are no vascular foramina or in old age. Numerous animal studies suggested a role of pulsed electromagnetic field in fracture healing based on light and electron microscopic studies *(Aaron, 1989 and Ottani et al., 1991).*

Few clinical studies have demonstrated a positive effect on fracture healing using X ray assessment. Most of them used inductive technique *(Whlestorm, 1982; Marcer et al., 1984; Borsalino et al. 1988 and Mammi et al., 1991).* The capacitative technique was used by *Brighton and Pollack (1985).* Assessment of bone mineral density with quantitative computed tomography and measurement of markers of bone formation have been recently introduced for follow-up of fracture healing.

The aim of our study:

To evaluate the role of pulsed electromagnetic field (capacitative technique) on fracture healing through using sensitive markers of bone formation as bone gala protein (osteocalcin) and by estimation of bone mineral density by quantitative computed tomography.

PATIENTS AND METHODS

Forty-four patients with fracture radius, ulna or humerus were included in the study. Patients with pathological fractures, endocrinal diseases, osteoporosis, internal fixation and aged patients >60 were excluded from the study.

Patients Were Divided Into 3 Groups:

Group I (Early PEMF treated):

Twenty-three patients received PEMF *(Level magnetic system, Italy)* at the Rheumatology & Rehabilitation Department of Ain Shams University Hospitals. PEMF was applied to the fracture site over the plaster cast within the first week of the onset of the fracture for 18-30 sessions (3-5 sessions/ week for 6-8 weeks with an intensity of 100 gauss, frequency 50 Hz and duration 30-40 minutes). Five of them (having incomplete healing by X-ray and QCT) continued the treatment for another 4 weeks after removal of the cast.

Group II (late PEMF treated):

Six patients received the same treatment for four weeks after removal of the cast (started PEMF 8 weeks from the onset of the fracture).

Group III (Control):

Comprised 15 fractured patients treated only in a plaster cast.

All the patients were subjected to the following:

Laboratory Investigations:

The following investigations were done at the beginning of the study to ensure proper patient selection.

- Hb % and CBC were done with Coulter estimation.

- Renal function tests (creatinine and blood urea) were measured to exclude renal osteodystrophy.

- Total serum calcium was estimated with timed end-point color reaction *(Minchoylova et al., 1971)* and was corrected according to the level of serum albumin.

- Serum phosphorous was done with a timed end-point color reaction *(Dryer & Routh, 1963).*

- Follow-up for all patients was done through estimating serum osteocalcin using osteocalcin I^{125} RIA kit *(Incstar corporation, Stillwater, Minnesota, USA)* that was measured at the start of the study, 8 weeks and 12 weeks later.

Radiological investigations:

- Plain X ray AP and lateral views every 2 weeks: The presence of periosteal bone callus was evaluated and scored 1- 4 according to *Mammi et al. (1991)* with grade four representing the maximum healing of bone.

- Quantitative computed tomography (QCT): Bone mineral density (BMD) at the fracture site was measured with QCT at the 8th and 12th weeks. A series of 3-6 scans of 3 mm slices were obtained perpendicular to the long axis of the callus and corresponding site of normal bone on the other side. The results were expressed, as F/N % where F is BMD at the fracture site and N is the BMD at the normal side. The roentgen absorption *(in Housfield units per pixel)* within periosteal callus was used as a measure of bone density. The radiation

dose was adjusted to 85 kilovolt/ peak and 140 milliampere / sec *(Husby et al., 1989)*.

Statistical Analysis:

The clinical and laboratory data were analyzed with "Microstat Version 2.0" to obtain descriptive data (mean X, standard deviation SD, and range). Wilcoxon rank sum test was used to compare variables between the two groups and Wilcoxon signed rank test was used to compare values before and after treatment in the same group.

RESULTS

A non-significant statistical difference was observed between the treated (group I) and the untreated (group III) as regards age, basal serum calcium and phosphorous levels. Comparison of osteocalcin levels between groups I and III on the fracture day i.e. 0 week, 8 weeks and 12 weeks and the change in osteocalcin 0-8 weeks and 8-12 weeks were analyzed with Wilcoxon sum test. Osteocalcin showed a non-significant difference between the two groups at 0 week and a statistically significant difference at 8 weeks and a highly significant difference at 12 weeks. Also the change of osteocalcin level at 0-8 and 8-12 weeks were highly significant.

Table 1: Comparison between groups I and III as regards osteocalcin level.

Osteocalcin	Group I	Group III	Z or t value	p value	Statistical significance
At fracture time (0)	14.5 $\pm$ 5(23)	11.9$\pm$ 5.3(15)	1.837	> 0.05	NS
After 8 weeks	18.36 $\pm$ 5.4(23)	13.92 $\pm$ 5.1(15)	0.836	< 0.05	S
Difference between 0 & 8	5.5 $\pm$ 1.69	2.0 $\pm$ 0.6	4.94	< 0.01	HS
At 12 weeks	15.7 $\pm$ 1.39(5)	11.7 $\pm$ 0.7(6)	3.317	< 0.001	HS
Difference between 8 & 12	2.23 $\pm$ 1.2	0.27 $\pm$ 0.1	3.317	< 0.001	HS
BMD (F/N%) at 8 wks	68 $\pm$ 17.8	38.1 $\pm$ 10.3	3.677	< 0.001	HS

Table (1) shows the comparison between group I (patients receiving PEMF) and group III (control) as regards osteocalcin level (OC) at fracture time, 8 weeks and 12 weeks. Osteocalcin difference 0 & 8 and 8 & 12 weeks was also compared. The comparison between BMD (bone mineral density of the 2 groups at 8 weeks was also shown.

Comparison between osteocalcin levels at 8 and 12 weeks in group I patients who continued PEMF (n= 5) and patients in group II who started

PEMF lately at the 8th week (n= 6) revealed a significant positive effect of PEMF in both groups (table 2).

Table 2: Comparison between osteocalcin level at 8 weeks and 12 weeks in patients who continued PEMF (group I) and those who started it lately at 8 weeks (group II).

	Osteocalcin 8 weeks	Osteocalcin 12 weeks	Z value	p value	Statistical significance
Group I (5 patients)	14.72 + 0.9	15.7 + 1.39	2.023	< 0.05	S
Group II (6 patients)	12.15 + 1.39	15.23 + 1.07	2.201	< 0.05	S

Radiological results:

Plain x-rays:

Twenty one patients of the PEMF early treated group (91.3%) were in the third radiological category fracture healing and 2 patients were in the second category (8.7%) according to *Mammi (1991)* while in the untreated group 5 patients 33.4 % were in the third category fracture healing and ten patients (66.6 %) were in the second category fracture healing.

Quantitative computed tomography:

Comparison of BMD (F/N%) of groups I and III at 8 weeks revealed a highly significant difference between both groups $p < 0.001$ (table 1). Comparison of BMD (F/N%) of groups I and II at 12 weeks revealed a significant difference between both groups ($p < 0.05$) with BMD 82.6 + 4.0 % in group I as compared to 60.5 + 14.8 in group II.

Comparison of the BMD (F/N%) difference 8-12 weeks in group II (late treated) and group III (untreated) showed that BMD increased by 25.57 + 10.7% in PEMF treated group as compared to 10.5 + 8.2 in the untreated group. The difference was statistically significant $p < 0.05$.

Comparison of BMD in patients with perfect reduction and those with displaced fractures revealed a statistically significant increase in healing power in those with perfect reduction ($p < 0.05$) as compared to those with displaced fractures among patients of the three groups.

Correlation studies revealed that osteocalcin level negatively correlated with the age of the patient (r= - 0.54049) and positively correlated with the number of sessions of PEMF (r= 0.57051).

Also osteocalcin difference on weeks 0 and 8 correlated with BMD (F/N %) at 8 weeks (r= 0.5914).

DISCUSSION

Our data indicated that serum osteocalcin (0-8) correlated with BMD F/N%. The values showed marked increase at 8 week and were normalized at 12 weeks. These findings are in agreement with *Oni et al. (1989)* who stated that as long as serum osteocalcin remains at higher level than initially, there is still an increased osteoblastic activity, probably caused by the incomplete consolidation of the callus. On the other hand *Mallmin et al. (1993)* showed an increase all through the 16 week study period. We can explain the early normalization of osteocalcin level in our study by the earlier healing of our patients as they were younger in age than Mallmin's group.

Cross sectional study of osteocalcin level in PEMF treated patients showed a significant increase in osteocalcin level that was not observed in the untreated group. This significant increase could be explained by the stimulating effect of PEMF on osteoblastic activity and bone healing. The highly significant difference of osteocalcin level between 0 & 8 and 8 & 12 weeks and also the highly significant increase in BMD F/N % proved by laboratory and radiological evidence that PEMF is a useful therapeutic tool for enhancement of fracture healing. This effect was observed to be cumulative as there was a positive correlation between the number of sessions of PEMF and osteocalcin levels.

The positive correlation between osteocalcin difference 0 & 8 weeks and bone density of the periosteal callus F/N % indicates that osteocalcin is a good marker of bone healing. It can be used for frequent monitoring of fracture healing as it is a simple and easy method for evaluation of bone healing.

The significant negative correlation between age and osteocalcin level at 8 weeks reveals that healing power decreases with aging. This indicates the need for modalities such as the PEMF for enhancing fracture healing in old age.

Few studies were done to evaluate the effect of PEMF on the healing of fresh fractures in humans *(Wahlestrom, 1982; Macer et al., 1984; Borsalino et al., 1988 and Mammi et al., 1991).* Most of them used the inductive technique of PEMF and all concluded that PEMF is useful in promoting bone healing and osteogenesis in humans. Only *Brighton (1985)* studied the effect of PEMFs (capacitative technique) on non-united

fractures. The average duration of non-united fractures in the study was 3.3 years. The results showed a satisfactory osseous healing in 77.3%.

Roentgen graphic studies for treated patients revealed that 72.2 % showed third and fourth grade healing as compared to 26.3 % of the controls. The higher % in our treated group reaching third grade healing 91.3% is due to the younger age in our study and the chronicity of the condition in Brighton's group. The stimulating effect of PEMF on bone growth was supported by the finding of *Chang (1991)* who stated that the electricity induced in the fractured bone by capacitatively coupled electric field stimulation may produce not only a cell membrane coupling process such as specific and nonspecific absorption, but a cell membrane mediated response such as calcium influx, adenylate response synthesis and / or activation. Therefore, the electrical signal is the first messenger to the osteogenitor and mesenchymal cells.

The growth and remodeling processes are supposed to be mediated by a potent local hormone, prostaglandin E_2. The electrical signal then acts as the first messenger to stimulate the synthesis of prostaglandin E_2 to activate the adenylate cyclase. The latter stimulates a series of physiological responses in the osteogenitor and mesenchymal cells to induce the differentiation of these cells to form fibro cartilaginous callus. This is then replaced by bony callus to enhance healing of the fracture *(Chang et al., 1991)*.

Histo-morphometric studies indicate that the maturation of bone trabeculae is also promoted by PEMF stimulation. These results indicate that a specific PEMF can change the composition of cartilage extracellular matrix in vivo. *Aaron (1989)* suggested that exposure to PEMF increases the formation of cartilage via modulation of proteoglycan synthesis by a fixed population of chondrocytes or whether the chondrocyte population is increased by recruitment, proliferation or differentiation.

The second effect of PEMF on cells that affects trabeculae formation and remodeling is that PEMF increases endochondrial ossification, formation of cartilage and also enhances the maturation of subsequent trabeculae. It enhances the cellular calcium uptake and calcification of organic matrix. The study of *Ottani group (1991)* demonstrated by light and electron microscope that the PEMF accelerated the healing process by producing a sequence of morphological appearances identical to those of a normal fracture callus being the enhancement of osteogenesis produced by

an acceleration of preliminary ossification. The positive correlation between the number of sessions of PEMF and mineral density at the fracture site reveals a dose related effect, which was strongly supported by the positive correlation of osteocalcin difference and the number of sessions. This dose related effect was also supported by *Mammi et al. (1991).*

Comparison of bone mineral density in early and late treated patients at 12 weeks revealed a statistically significant difference. This emphasizes the value of early treatment with PEMFs in improving the healing power and accelerating fracture healing. This finding was supported by the experimental work of *Grace et al. (1998)* who found that PEMF enhances early vascular reaction and stimulates chondrogenesis and bone formation restoring normal trabecular structure. Grace concluded that PEMF treatment might be useful in advancing repair during the early proliferative stage. But later results of his experimental work suggested that prolonged use may have deleterious effects enhancing chondrogenesis beyond a point observed in normal repair and thus delay normal surface trabeculation.

The negative correlation between the bone mineral density at the fracture site and the age of the patient recommends the use of PEMF for enhancement of fracture healing in aged persons. The statistically significant difference in BMD between perfectly reduced fractures and displaced fractures and in those with displaced fracture ends, confirms the finding of *Sharrard (1990).* The latter author found that PEMF significantly influences the healing of tibial fractures with delayed union. However the data obtained by *Muhsin et al. (1991)* that the use of PEMF in the treatment of fractures of markedly displaced non-united fractures with soft tissue interposition have no beneficial role does not contradicts our finding or that of Muhsin's group as bony ends should be opposed to some degree for the stimulant action of PEMF to work as healing of fracture decreases with the increase of the degree of displacement.

We recommend the use of the capacitative technique of PEMF since it increases BMD at the fracture site significantly, being a non-invasive therapeutic modality. Also it does not require precise localization of the capacitator plates and it does not need long treatment time as the inductive technique.

Further studies should be done to find more applications for PEMF in stimulating osteogenesis in osteoporotic bones either in generalized or in localized forms as those with Sudek's atrophy.

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دور المجال المغناطيسي النابض في التئام الكسور

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أجريت الدراسة على 44 مريض بهدف دراسة تأثير التيار المغناطيسي النابض السعوي على التئام الكسور في مراحلها المختلفة. وتم تقسيم المرضى إلى ثلاث مجموعات: الأولى تضم 23 مريضاً بكسور حديثة تم علاجهم بالتيار المغناطيسي النابض منذ البداية والثانية ضمت ستة مرضى بدءوا العلاج بالتيار المغناطيسي عند الأسبوع الثامن من حدوث الكسر بعد إزالة الجبس أما المجموعة الثالثة والتي اعتبرت كمجموعة ضابطة فقد ضمت خمسة عشر مريضاً تم علاجهم بتثبيت الكسر في الجبس بدون استخدام التيار المغناطيسي.

وقد خضع جميع المرضى للفحص المعملي لقياس الأوستيوكالسين عند بداية الدراسة وعند الأسبوع الثامن و كذلك عند الأسبوع الثاني عشر.

كما تم إجراء أشعة عادية كل أسبوعين لمتابعة التئام الكسر. وكذلك أجرى قياس كثافة العظام عند موضع الكسر بالأشعة المقطعية الكمية وتم حساب كثافة العظام كنسبة مئوية بالمقارنة للموضع المناظر لموضع الكسر في الناحية المقابلة.

وأثبتت الدراسة أن التيار المغناطيسي النابض له تأثير إيجابي ذو دلالة إحصائية حيث أنه يساعد على سرعة التئام الكسور حيث وجد أن مستوى الأوستيوكالسين أعلى في مرضى المجموعة الأولى عن المجموعتين الثانية و الثالثة. كما أيدت ذلك نتائج الأشعة المقطعية الكمية. ولذا نوصى بالاستخدام المبكر للتيار المغناطيسي النابض في حالات الكسور خاصة في كبار السن أو عند تأخر التحام الكسور.