REVIEW

Pulsed electromagnetic field therapy for osteoporosis

Aroona Devi Mudoo, YU Le-hua

[**Abstract**] Osteoporosis is becoming a great social and medical problem due to the elderly population . Various forms of prevention and treatment are needed to deal this problem . It has been found that pulsed electromagnetic field therapy is safe and effective in treating osteoporosis . This review thus concentrates on the progress of recent studies done so far on pulse electromagnetic therapy in the treatment of osteoporosis .

[**Key words**] osteoporosis ; pulsed electromagnetic field

INTRODUCTION

Osteoporosis is a state in which the bone becomes fragile due to decreased bone mass per unit volume in otherwise normal bone. It can be classified into primary and secondary osteoporosis. Primary osteoporosis being the one in which no specific etiologic mechanism is known. Osteoporosis is typically a "silent disease" until fractures occur. Secondary osteoporosis is mainly due to chronic medical conditions, medications and nutritional deficiencies[1]. Osteoporosis is becoming a major health problem worldwide due to the increasing elderly population[2]. Thus so far several studies have been conducted to find the best way to treat this systemic skeletal disease. Among these studies pulsed electromagnetic field therapy (PEMF) has been one of medical doctors' interests because of it being safe and effective.

PEMF has been in use in orthopaedics for treating non-union and delayed fracture healing[3] for the past thirty years or so. It has now been found that the weak electromagnetic fields can initiate several healing processes[4]. This type of therapy was first conducted following the observation that physical stress on bone causes the appearance of tiny electric currents (piezoelectric potentials) that are believed to be the mechanism of transduction of physical stresses into a signal that promotes bone formation[5,6]. Bone metabolism is affected both *in vivo* and *in vitro* on application of electromagnetic fields. Bone mineral density (BMD) and biomechanical properties are increased whereas the bone resorption process is slowed *in vivo*. Both pathways of bone metabolism are affected, *in vitro*, it helps the process of osteoblast while decreases the formation of osteoclast thus shifting the balance towards osteogenesis[3]. The purpose of writing this review is mainly to observe the recent progress in the studies conducted on pulse electromagnetic magnetic fields in the treatment of osteoporosis.

BASIC RESEARCH

Pathological Test

To begin with several studies were done to prevent osteoporosis in ovariectomized female rat models[7~10]. Low frequency electromagnetic fields were used to find their effect on osteoporosis and serum prostaglandin E 2 concentration in bilaterally ovariectomized rats. One study[7] consisted of thirty-five, three month old female Sprague-Dawley rats which were randomly divided into several groups including a control group. Bilateral ovariectomy was performed on them sparing the control group. The experiment showed that PEMFstimulation increased and restored proximal tibial metaphyseal

Centre of Rehabilitation Medicine and Physical Therapy, The Second affiliated Hospital of Chongqing Medical University, Chongqing 400010, China
Correspondence to YU Le-hua, Centre of Rehabilitation Medicine and Physical Therapy, The Second affiliated Hospital of Chongqing Medical University, Chongqing 400010, China
E-mail: yulehuadoc@ yahoo. com

trabecular bone mass and architecture after 30 days of exposure in the PEMF exposed groups. PEMF exposure also attenuated the higher serum PGE 2 concentrations of the ovariectomised rats and restored it to the level of the control group. This experiment thus showed that PEMF exposure can decrease loss of trabecular bone and restore the trabecular bone structure. So this study clearly states that osteoporosis can be prevented by using PEMF.

Another study[11] using a canine tibial model to show the effects of PEMF on late bone healing phases of its osteotomy gap was performed. Twelve adult mixed-breed dogs on which transverse mid-diaphyseal osteotomy with 2 mm gap was done unilaterally and stabilized with external fixation. They were divided into two groups randomly and were treated with PEMF for one hour daily during eight weeks excluding the control group. It was found that the periosteal callous area increased at six weeks and thereafter following surgery and that of the control group at eight and ten weeks after surgery. Histomorphometric analyses showed greater new bone formation in the osteotomy gap tissue and increased mineral apposition rate and decreased porosity in the cortex adjacent to the osteotomy line in the PEMF group. Thus this study revealed that PEMF did enhance callous formation and the maturation in late phase of bone healing.

In the following study[12] rabbits were used as models to investigate the effect of PEMF during consolidation phase of limb lengthening. Mid-tibial osteotomy was performed on eighteen adult New Zealand White rabbits. External fixators were applied to stabilize the limbs. The animals were divided into a control and a treatment group randomly. The tibiae were distracted 0.5 mm every 12 h for 10 days after a 7-day latency period. During 20 days the treatment group received PEMF for one hour. Radiographs were taken regularly every week. At the end of 3 weeks radiographic analysis showed no obvious difference in regenerate callous area between the 2 groups. But there was significant positive difference in mineral apposition rate between the groups during the interval 1 ~ 2 weeks post-distraction. There was increased osteoblastic activity in the cortical bone adjacent to the distraction site.

Biochemical Tests

In one study[13] the effect of whole body exposure to magnetic fields on calcium level of bone and blood was carried out. In all 50 Guinea pigs were divided into 5 groups (A, B, C, D and E) randomly. Group E being the control group and groups A, B, C and D were exposed to 50 Hz, 0.2 mT magnetic field for 30 days. Group A was euthanized immediately after exposure, group B was left for 15 days, group C was given the drug Centrum for 15 days after exposure while group D got the drug Centrum during the exposure. After the experiment both the level of calcium in blood and bone were analysed. It was shown that there was a significant increase in blood calcium level in the exposed animals compared to the control group. There was a significant decrease in bone calcium concentration level in group A and an increase in bone calcium level in group C and D respectively, thus indicating the role of trace element as a compensatory agent of magnetic field damage and as a radio-protecting agent during the exposure period.

A bioassay[14] using neonatal rat calvarial bone was used to determine the early effects of PEMF exposure *in vivo* and *in vitro* on bone metabolic calcium exchange. Whole body exposed animals (0 ~ 4 h) showed a long exposure time-dependant average increase in net calcium uptake in the 0% ~ 50% range in the bone discs. They also showed a decrease in serum calcium and there was no increase in serum calcium even after administration of exogenous parathyroid hormone. Untreated rats' bone discs exposed to PEMF *in vitro* showed increase in net calcium uptake in a similar magnitude and refractory to the calcium releasing effect of parathyroid hormone. Unexposed bone discs responded normally to parathyroid hormone by decreasing net calcium uptake. On treating the calvarial bone discs with calcitonin or acetazolamide, both of them inactivate osteoclasts, it made the bone refractory thus further increasing calcium uptake by PEMF. These results show that PEMF exposure produces parathyroid hormone-refractory osteoclastics and has a relatively rapid effect on increasing net bone calcium uptake, putatively due to a decrease in parathyroid hormone or paracrine-mediated bone resorption.

Experiment was done to investigate the preventive effects of low frequency (50 Hz), low- intensity (1 mT) and long duration (6 weeks) EMF on bone loss in ovariectomised rats[8]. Eighteen female albino Wistar rats were used. Ten of them were exposed to EMF and the rest served as the control group. The mineralization and the morphology of the tibia were analysed in both groups. It was found that the cortical thickness of the tibia was increased in the EMF exposed group. Also the level of sodium and potassium in the tibia were significantly increased in the rats exposed to EMF. An increase in blood alkaline phosphatase was as well noted in the treated group. These findings support the idea that EMF proves to be an effective method in the treatment of osteoporosis and other abnormalities related to bone.

Bone Mineral Density

Bone mineral density (BMD) being a very important factor in diagnosing osteoporosis, many studies have been conducted till now to show the effect of PEMF on BMD. In one such recent study[15] the authors showed how PEMF stimulation affects BMD and local factor production of rats with disuse osteoporosis. To perform this experiment, 80 4-month old female Sprague-Dawley rats were used. They were randomly divided into the control group, the disuse osteoporosis group, the calcitonin-treated group and the PEMF stimulated group. The control group was left intact whereas others had their right hind limbs immobilised by tibia-tail fixation. Calcitonin was injected daily in the calcitonin-treated group while the PEMF group was exposed to PEMF. At the end of first, second, fourth and eighth week the BMD, serum transforming growth factor-beta 1 (TGF-beta 1) and interleukin-6 (IL-6) concentration were analysed. It was found that BMD and TGF-beta 1 concentration increased significantly after the eighth week in the PEMF group. IL-6 concentration was found to be elevated in the disuse osteoporosis group while it was significantly lower in the PEMF group. Thus showing that bone mass loss can be prevented by PEMF stimulation. And eventually by promoting TGF-beta 1 secretion and inhibiting IL-6 PEMF can affect bone remodeling process. In one study[3,16] the authors tried to compare the effect of estrogen therapy and estrogen combined with PEMF and PEMF alone on the bone mineral density of patients with postmenopausal osteoporosis. The experiment was carried out for three months on a random basis. It was noted that the bone mineral density of the patients increased in the combined group, estrogen therapy group and the PEMF alone group but no comparison was made between the groups. Other experiments[3,17,18] were performed using calcitonin alone and combined with PEMF. The results were positive but with no equivalent test.

There were few observations about the long term effects of PEMF on bone mineral density of osteoporosis patient. In one such study[3,19] the patients were given PEMF treatment during 30 days for 3 times. It was found that the bone mineral density had been increased significantly 2 ~ 6 months after the therapy. In another similar study[3,20] it was found that the bone mineral density was higher than the control group 3 ~ 4 months after 30 days of therapy. So it can be concluded that after PEMF therapy the increased bone mineral density can last for at least 3 ~ 4 months implying that osteoporosis patient need not be treated daily. Most of the studies have used low frequency PEMF and the duration of therapy being approximately 30 days to increase bone mineral density in osteoporosis patient[3].

CLINICAL APPLICATION OF PEMF FOR PATIENTS

Till date many[5] scientific and clinical studies have proved that PEMF help in bone unification; reduce pain, oedema and inflammation; increase blood circulation; stimulate immune and endocrine system. PEMF[21] have also been useful in treating chronic pain associated with connective tissue (cartilage, tendon, ligaments and bone) injury and joint associated soft tissue injury. Basically[22,7] there are two ways to stimulate PEMF non-invasively on biological systems: capacitive or inductive coupling. In capacitive coupling, opposing electrodes are placed within a conducting medium for example in contact with the skin overlying the tissue concerned. Inductive coupling does not need direct contact with skin or biological system. It is the time-varying magnetic field of PEMF that induces an electric field, thus producing a current in the body's conductive tissue. PEMF[5] signals have a variety of designs for its clinical use. That is the sine wave type signals, the rectangular type of signals and the pulsed signals. Most of the EMF signals used in research and as therapeutic modalities have been chosen in some arbitrary way. Very few studies examined the clinical and the biological value of different signals by comparing the physical or biophysical dosimetry and biological or clinical outcomes. There are at least two ways of using these signals, mainly by building an elliptical or spherical coil that can move around the patient body and by applying a magnetic field on the upper or lower limbs. New magnetotherapeutical devices are being designed using the computer technology. Modern medicine[23] has started using magnetic energy for treating physical and mental disorders. NASA found that in order to maintain bone density and normal health for the early astronauts it is mandatory to install magnetic field generators in manned space ships. MRI is one of the most important ways of using magnetic energy in conventional medicine. Other approved devices are the EEG, MEG and SQUID diagnostic equipment. A special form of[23,24] electromagnetic therapy, repetitive transcranial magnetic stimulation (RTMS) have shown promise in the treatment of Parkinson's disease, auditory hallucination schizophrenia, obsessive compulsive disorder, tinnitus, eating disorders, migraines, pain management and other mood disorders. It has also been found that[4] nighttime magnetic field therapy can stimulate the production of melatonin which is an anti-stressful, anti-aging and anti-infectious hormone and it thus induces sleep and relaxes the brain and the body.

PEMF[25] has been shown to be effective in healing non-union fractures and stimulating the formation of new bone thus helping osteoporotic and patients with arthritis. In very short time periods it has been found that there has been significant increase of bone density. Thus decrease in pain, healing of existing fractures and preventing further fractures as bone density is restored. Bone density has been documented to increase by 5.1% in three months in one study.

EXPLANATION FOR THE MECHANISM

Several cellular studies have shown the effects of electromagnetic field on signal transduction pathways. The cellular membrane acts as a primary target for magnetic field action[26]. It has been found that selected magnetic fields can affect the signal transaction pathways via alteration of ion binding and transport. Calcium ion is the main player in such alterations. A series of studies[5] conducted by Markov et al. on calcium-calmodulin dependant myosin phosphorylation demonstrated that specific static magnetic fields, PEMF and 27.12 MHzpulsed radiofrequency electromagnetic field could modulate Ca^{2+} binding to CaM to a twofold enhancement in Ca^{2+} binding kinetics in a cell-free enzyme preparation.

There is also the[5] concept of "biological windows" which has been in use for the past three decades. It is said that during evolution Mother Nature created preferable levels of recognition of signals from exogenous magnetic fields. The "biological windows" could be identified by amplitude, frequency and their combinations. It has been found that at least three amplitude windows exist: at 50 ~ 100 microT (5 ~ 10 Gauss), 15 ~ 20 mT (150 ~ 200 Gauss) and 45 ~ 50 mT (450 ~ 500 Gauss). By using cell-free myosin phosphorylation to study a variety of signals, Markov *et al.* showed that the biological response depends strongly on the parameters of applied signals and thus confirming the validity of the last two "windows".

CONCLUSION

Till date, bone density indeed increases in animal models and patients who are prone to osteoporosis after exposure to pulsed electromagnetic fields. Thus it can be implied that pulsed electromagnetic field therapy can become one of the important methods to treat osteoporosis and other related bone diseases. It can be used as a first line of treatment in these conditions. It provides a noninvasive, safe and easy method to directly treat the site of the body concerned and can save many people from undergoing surgery. The only side effect if any that has been reported till now is hypotension. But then there is still room for further studies in concerned with the frequency, intensity which needs to be standardized. Due to lack of equivalent tests in some of the studies performed it is difficult to give a strong statement about its effect. More controlled, randomized and double-blind studies are needed to evaluate the effect of pulsed electromagnetic field for the best treatment.

REFERENCES

1. Prevention and treatment of osteoporosis. Randall L. Braddom, Physical medicine and Rehabilitation, third edition.
2. Electromagnetic field treatment for osteoporosis. Ben Philipson. Curatonic Ltd. Page 1-12
3. Huang Li-Qun, HE Hong-Chen, HE Chengqi, Chen Jian and Yang Lin. Clinical update of pulsed electromagnetic fields on osteoporosis. Chinese Medical Journal, 2008, 121 (20): 2095 – 2099.
4. Marko S. Markov. Pulsed electromagnetic field therapy history, state of the art and future. Environmentalist, 2007
5. Serap Tomruk Sutbeyaz. Nebahat Sezer Belma Fusum Koseoglu. The effect of pulsed electromagnetic field in treatment of cervical osteoarthritis: a randomized, double-blind, sham-controlled trial. Rheumatol. Int., 2006, 26: 320-324
6. David H. Trock. MD. Electromagnetic fields and magnets. Complementary and alternative therapies for Rheumatic diseases II. 2000, 26, 1 : 51 – 62
7. Chang K, Chang WH. Pulsed electromagnetic fields prevent osteoporosis in an ovariectomised female rat model: a prostaglandin E2-associated process. Bioelectromagneics, 2003
8. Sert C, Mustafa D, Duz MZ, Aksen F, Kaya a. The preventive effect of bone loss of 50 Hz, 1 mT electromagnetic field in ovariectomised rats. Journal of Bone and Mineral Metabolism, 2002, 20, 6: 345 – 349
9. Huang L, Wang W, Xiao D, Yang L, Lei Z, He C. Effect of Pulsed electromagnetic field of different time treatment on bone mineral density of femur in ovariectomised rats.
10. Yang YH, He CQ, Yang L, Wang W, Lei ZJ. Effects of different intensity Pulsed electromagnetic field on serum estradiol of ovariectomised rats.
11. Inoue N, Onishi I, Chen D, Deitz LW, Schwardt JD, Chao EY. Effect of Pulsed electromagnetic fields on late phase osteotomy gap healing in a canine tibial model. USA. J ortho Res, 2002, 0 (5): 1106 – 1114
12. Taylor KF, Inoue N, Rafiae B, Tis JE, Mc Hale KA, Chao EY. Effect of Pulsed electromagnetic field on maturation of regenerate bone in a rabbit limb lengthening model. J. Orthop. Res, 2006, 24(1): 2 – 10.
13. Hanafy E, Elhafez S, Aly F, Elazhary M. Loss of bone calcium in exposure to 50 Hz magnetic fields. Faculty of Physical . Biol. Med, 2008, 27(4): 402 – 408
14. Spadaro JA, Bergstrom WH. In vivo and in vitro effects of Pulsed electromagnetic field on net calcium flux in rat calvarial bone. Calcif Tissue Int, 2002, 70(6): 496 – 502
15. Shen WW, Zhao JH. Pulsed electromagnetic field stimulation affects bone mineral density and local factor production of rats with disuse osteoporosis. Bioelectromagnetics, 2009.
16. Huang S, Meng P, Cai HW. Effect of Pulsed electromagnetic field combination with estrogen on post menopausal osteoporosis. Chin J Clin. Rehabilitation (chin), 2003, 7: 1399 – 1400
17. Chen LD, Yang SL, Wang SZ, Tao J, Zhang B, Guo XL. Clinical observation of PEMF on patients with osteoporosis long in bed. J Fujian coll Trad Chin Med (chin), 2006, 16: 43 – 44
18. Gao Y, Zhang Y. Treatment of PEMF on primary osteoporosis. J Med Forum (chin), 2006, 27: 50 – 60
19. Zhou QW, He PY, Chen WX, Li XB, Wu XH. Curative effects of PEMF on senile osteoporosis patients. Fujian Med J (China), 2006, 28: 20 – 21
20. Liu L, Dong LP, Li XX. Clinical analysis of PEMF on osteoporosis. Chinese Journal Rehabilitation Medicine (china), 2007, 22: 555
21. Markov MS. Magnetic and electromagnetic field therapy: Basic principles of application for pain relief. In Rosch, P J, & Markov, M S (Eds.), Bioelectromagnetic medicine, NY: Marcel Dekker, 2004, 251 – 264.
22. Naomi M Shupak. Therapeutic uses of PEMF exposure: A review. Radio Science Bulletin, 2003, 307, 9 – 32.
23. Magnetic therapy today-home. latest information on magnetic therapy and magnets, 1 – 5
24. A brief history of pulsed electromagnetic therapy, 1 – 7
25. Bioelectromagnetic therapy. April 2008, volume 07, issue 02. David Rindge, DOM, L. Ac., RN
26. Adey, W R. Potential therapeutic application of non-thermal electromagnetic fields. Ensemble organization of cells in tissue as a factor in biological tissue sensing. In P J Rosch & M S Markov (Eds.), Bioelectromagnetic medicine, New York: Marcel Dekker, 2004, 1 – 15.

(Editor LEE)