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THERAPEUTIC POTENTIALS OF ELECTROMAGNETIC FIELDS IN OSTEOPOROSIS: A COMPREHENSIVE REVIEW

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Abstract:

Background and Objective: *Pulsed electromagnetic fields (PEMFs) in low frequencies and intensities have been reportedly effective in osteoporosis treatment and prevention. Preclinical and clinical studies have shown PEMFs alter the osteoblast and osteoclast processes, enhance bone mineral density (BMD), and reduce bony pain in osteoporosis patients. The well-design studies in this field are in early stages and no definitive dose-response has been determined. The present study aims to comprehensively review the therapeutic efficacies of PEMFs in osteoporosis treatment and prevention*

Methods: *The databases of Web of Sciences (1970-2017), PubMed (1980-2017), Embase (1980-2017), Google Scholar (1980-2017) and additional resources were searched using the key words "pulsed electromagnetic fields" OR "electromagnetic fields" AND "osteoporosis". The abstracts of the retrieved records to select the relevant records for full review. Considering the variances in the study design and stimulation parameters we conduct a comprehensive review aiming the therapeutic efficacies oo PEMFs in osteoporosis treatment and physiological effects.*

Results: *Current evidence on the efficacy of PEMFs in osteoporosis is moderate and further studies need to be conducted. The PEMFs have preventive and therapeutic effects on osteoporosis. To yield the therapeutic effects, relatively long treatment period ranging two to three month of daily 30-40 min stimulations are required. The main effects of PEMFs for osteoporosis treatment are reducing chronic bony pain, increasing BMD and osteoblast, bone strength and enhancing bone metabolism.*

Conclusion: *Low-frequency PEMFs relieves the pain of primary osteoporosis quickly and efficiently, enhances bone formation and increases BMD of secondary osteoporosis. But the effects of PEMFs on bone mineral density of primary osteoporosis and bone.*

Keywords: *Electromagnetic fields, Osteoporosis, Treatment, Prevention*

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INTRODUCTION:

Osteoporosis is the most common chronic and progressive disease that created due to a reduction in the volume of bone tissue. The most important consequence resulting of this condition is an increased risk of skeletal fractures, thus prevention and treatment of this disease is of great important (1-3). Electromagnetic fields (EMFs) are a new class of new non-invasive modality for treatment as well as preventing or slowing down the osteoporosis progression that have shown beneficial therapeutic effects in treating primary and secondary osteoporosis is (4, 5). The main characteristic that has dramatically developed the applications of EMFs in bone related disorders is the intrinsic electromagnetic features of bone so that make the bone acts as piezoelectric compound (6, 7). Applying electrical forces on the bone induces mechanical stress and vice versa that is the underpinning of most of physiological effects (7, 8). Moreover, different cellular and molecular processes involving in the osteoblast and osteoclast, and bone cellular metabolism are modulated by external electric and magnetic fields. The EMFs can change the treatment management of such patients through reducing the treatment costs and drug medication side effects. Several double-blind and controlled prospective studies have confirmed the biological effectiveness of this method in bone healing (9-12). Results of the preclinical and clinical studies have shown regenerative and analgesic effects of variable magnetic fields with therapeutically parameters. Several experimental and animals studies was proved the influence of EMFs on enzymatic and hormonal activity. It has also shown effectiveness on dielectric and rheological properties of blood, protein, and lipid metabolism (13-17). Clinical studies have also shown high therapeutic efficacy of EMFs in the treatment of abnormal ossification, osteoporosis, osteoarthritis, and fractures healing (6, 18-22). The findings have confirmed that the use of EMFs as a noninvasive method is associated with considerably less risk and cost (23-27).
However results of the number of publications on these topics have shown and determined that EMFs have significant therapeutic effects in musculoskeletal disorders and bone healing process, but pertinent mechanisms of action and finding an optimal therapeutic protocol are disputed and controversial. Therefore, further studies is needed for determination and elucidation the exact mechanisms of action and introduce an optimal protocol for each particular musculoskeletal diseases.

Cellular effects

Electromagnetic fields have effects on the interaction of receptors of cell membrane through change permeability of the cell membrane. They

also change orientation of the dipole molecules and affects ion balance. EMFs have shown abilities to modifying the extracellular matrix, improve oxygenation and metabolism in tissues, (4, 28-31). In vitro and experimental studies provided further basic data to augment the therapeutic application of PEMF stimulation on bone and cartilage disorders. Sakaki et al. investigated the effects of pulsing electromagnetic fields (PEMFs) on cultured cartilage cells. They evaluated the effects of PEMFs on cell proliferation and glycosaminoglycan (GAG) synthesis on rabbit costal growth cartilage cells and human articular cartilage cells. Protocol in this study was 6.4 Hz frequency and 0.4 mT magnetic field strength. The results showed that intermittent PEMF stimulation is more effective than continuous stimulation on both cell proliferation and GAG synthesis of cartilage cells. They maintained that the stimulation could related effects by the cellular membrane-dependent mechanism (32). Aaron et al. in an in vivo study examined the effect of PEMF with certain configuration on the extracellular matrix and calcification of endochondral ossification. They stimulated the experimental endochondral ossification by low energy pulsing electromagnetic fields. The results indicated that PEMF can change the composition of cartilage extracellular matrix and help to improve other processes of endochondral ossification (33). PEMF stimulation have also shown effectiveness on osteoblast cell activities (34). Shen et al. investigated the effects of PEMF on bone mineral density (BMD) and local factor production of rats with disuse osteoporosis (DOP). They measured the BMD, interleukin-6 (IL-6) concentration and serum transforming growth factor-beta 1 (TGF-β1) in 1, 2, 4, and 8 weeks after treatment. The BMD and serum TGF-β1 concentration were increased in the PEMF group after 8 weeks. The results demonstrated that PEMF stimulation can prevent bone mass loss and through promoting TGF-β1 secretion and inhibiting IL-6 expression may can affect bone remodeling process (35). Results of in vitro studies have been reported that EMF stimulation promotes osteogenesis and increasing the proliferation of osteoblasts and also it causes to increasing bone matrix through inhibiting osteoclast formation (11). Chang et al. investigated the effect of PEMF on osteoclastogenesis, bone resorption, Osteoprotegerin (OPG), receptor activator of NFkappaB-ligand (RANKL) and macrophage colony-stimulating factor (M-CSF) concentrations. Their results confirmed that PEMFs stimulation with different intensities affects osteoclast formation through regulate of osteoprotegerin, RANK ligand and macrophage colonystimulating factor (36).

Effects on Primary and Secondary Osteoporosis

The main objective of all therapeutic modalities in primary and secondary osteoporosis is bone loss prevention. The most common symptom in patients with primary osteoporosis (OP) is chronic bony pain that affects their quality of life. PEMF have shown the analgesic effect (37-39). Results of several randomized controlled trials demonstrated that PEMFs therapy can reduce pain in the most patients with primary osteoporosis after 30-60 days treatment (23, 40-42). They have also reported that this analgesic effect can persistent for two or three days after therapy and it depends to the number of therapies significantly (40, 43). The activity of bone formation and bone resorption depend to the metabolites include biochemical markers that this process of bone metabolism produced by osteoblast and osteoclast (10). The main markers of osteoblastic activity are serum osteocalcin and alkaline phosphatase. These biochemical markers can determine the expression of bone remodeling, identify metabolic bone diseases early, monitor bone loss and fractures and informant pharmacological effect. Studies showed that PEMFs effected on biochemical markers of bone metabolism for primary osteoporosis and increased the level of serum osteocalcin after treatment (40, 44). The balance between osteoblast and osteoclast cyclic process plays an important role in the process of osteoporosis. Keeping balance between osteogenic and adipogenic differentiation of bone marrow mesenchymal stem cells is also important. The results of recent studies have suggested that EMFs have a positive impact on the balances (45).

Weng et al. analyzed effectiveness of PEMF in treating pain in 126 patients with primary osteoporosis. Their results reported pain reduction mainly in the legs and low back. PEMFs had also shown more effective on bone pain relief for female type I than type II primary osteoporosis patients. They confirmed that PEMFs as a safe and effective method can use for the treatment of osteoporotic pain (27). Giordano et al. in a single-blind, randomized pilot study investigated the effects of PEMFs on bone mineral density and biochemical markers of bone turnover in osteoporosis. In this study 20 outpatients with postmenopausal osteoporosis were exposed to 100 Hz PEMFs, 60 minutes per day, 3 times a week for 3 months. The results reported that PEMFs therapy increase the serum osteocalcin and serum procollagen type I C-terminal propeptide but there was not observed a significant increase in BMD. They suggested that PEMFs can stimulate osteogenesis through increasing osteoblastic activity in women with postmenopausal osteoporosis (46).

Tabrah et al. in a clinical trial determined the effect of PEMF on bone density of osteoporosis-prone women. The protocol of the study was 72 Hz PEMF, 10 hours daily exposure for 12 weeks. The results showed that BMD increased in the critical areas during the exposure period. But results of follow up in 36th weeks reported reduction in BMD. They remeasured their assessment after eight years and the results reported no long-term changes on these women. They suggested that further studies are designed alone and in combination with exercise and pharmacologic agents for demonstrate effect of PEMF on enhancing the bone density (47).

Garland et al. in a human study investigated the effect of PEMF on osteoporosis at the knee. They evaluated 6 males with complete spinal cord injury. The BMD was measured at initiation, 3 months, 6 months, and 12 months. In each case, 1 knee was stimulated for 6 months and the opposite knee served as the control At 3 months BMD decrease in the control knees 6.6% and increased in the stimulated knees 5.1%. After 6 months the BMD of two groups returned to near baseline values and in 12th months both knees had lost bone at a similar rate to below baseline. They concluded that although the PEMF stimulation appeared useful in prevention of osteoporosis, the significant decrease in the control and treatment knees at 6 months is suggested more complex underlying mechanisms than originally anticipated (48).

Skerry et al. in an animal study investigated the effect of PEMFs on bone loss associated with disuse. After 12 weeks bone loss on PEMFs group was significantly reduced to 9% and 23% in control group. Any new bone formation on the periosteal surface was not reported in treated or untreated fibulae (49).

Effect on Prevention of Osteoporosis

One of the most common health problems in the elderly and in menopause women is osteoporosis. Some treatment methods are offered till now but they have been showed infliction serious side effects. Recently, EMF has been introduced as a new method and promising candidate for better treatment of osteoporosis (27, 45, 50).

Sert et al. in an animal study investigated the preventive effects of low-frequency EMF on bone loss in ovariectomized rats. The protocol of this study was 50 Hz frequency, 1 mT intensity for 6 weeks. Their assessments were examination the mineralization and the morphology of the tibia in EMF-exposed and control group. The cortical thickness, blood alkaline phosphatase (ALP) and the levels of Na and K of the tibia were significantly increased in EMF-exposed rats. The levels of Ca, Mg, Li, or creatine had no significant differences between the exposed and unexposed groups. The results showed that EMF therapy can consider as an effective treatment method for osteoporosis and other anomalies related to bone loss (50).

Rubin et al. in an animal model examined the effect of PEMF to prevent the osteoporosis. Their applied protocol is induced at a physiological frequency and intensity for one hour per day. The maximum osteogenic effect was observed between 0.01 and 0.04 tesla per second as an osteogenic dose-response. More or less than these pulse power levels showed less effective.

The results suggested that short daily periods of exposure of PEMF in advisable protocols can determine beneficially effect on cell populations which have role and responsible for bone-remodeling. They also observed and discussed about an effective window of induced electrical power (51).

Chang et al. investigated the effect of PEMF on osteoporosis and serum prostaglandin E(2) (PGE(2)) concentration in bilaterally ovariectomized rats. The results showed that PEMF stimulation increased hard tissue percentage, bone volume percentage, trabecular number, trabecular perimeter, trabecular thickness, and decreased trabecular separation. They demonstrated that PEMF stimulation can enhance proximal tibial metaphyseal trabecular bone loss and restored trabecular bone structure in bilateral ovariectomized rats. They also concluded that PEMF may be beneficial in the prevention of osteoporosis by virtue ovariectomy (52).

CONCLUSION:

This study reviews the therapeutic efficacies of PEMFs for treatment and prevention of osteoporosis based on the preclinical and clinical studies. Different protocols of PEMFs have been used for bone related disorders and the findings despite of controversial were promising (11, 17, 34, 36). Several studies have evaluated the effects of PEMFs on bone formation and remodeling but the obtained results were ambiguous and equivocal. Clinical studies confirmed that PEMF stimulation showed the beneficial therapeutic efficacy on relieve chronic bony pain and bone mineral density of patients with primary and secondary osteoporosis (40, 43, 50-52). However, the effects of PEMFs to enhance the BMD in patients with osteoporosis are still controversial. In addition, the mechanism through which EMFs influence on the bone cells behavior is poorly understood. In this regard, further studies with well-designed methodology and large sample size are needed to determine the mechanism of actions of PEMFs on bone mineral density as well as to determine exact dose-response for efficient treatment protocols for each type of osteoporosis.

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