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Low Intensity Pulsating Electromagnetic Field as an Adjunctive Therapy for Bone Regeneration around Fractures, Dental Implants and Orthodontic Therapy-A Clinical Update

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ABSTRACT

Pulsed Electromagnetic Field (PEMF) is a non invasive, therapeutic form of low field magnetic stimulation that has been used for several years to supplement bone healing. It is known to generate pulsating magnetic frequencies within the body that accelerate the process of healing and reduce postoperative pain. The survival rate of dental implants over a 10-year observation has been reported to be higher than 90%. Success of dental implant therapy depends on the quality and quantity of available bone in which they are inserted. Implants with poor early or primary stability frequently may require additional time for osseointegration or may sometimes fail. Development of procedures which accelerate osseointegration of dental implants, reduce the period of healing, and lead to an early rehabilitation of the patient are required for successful oral rehabilitation. The potential for bone repair can be stimulated through non invasive adjunctive treatments such as application of pulsating electromagnetic field therapy, Low-Intensity Pulsed Ultrasound (LIPUS), and Low-Level Laser Therapy (LLLT). These methods of biophysical stimulation of bone union were developed initially to enhance the healing of fractures, healing of bony non unions and have been hypothesised to improve implant osseointegration. This study sought to report latest trends in PEMF Therapy stimulations in oral tissues and its use to enhance the bone repair and regeneration. Pulsed electromagnetic field stimulation to induce bone regeneration mandates a broad range of settings that include magnetic field intensity, frequency, type of signals and duration of application etc. The present study analyses these clinical settings in published human trials and is expected to serve as a treatment guide for the clinicians to bring into their clinical use these strategies to improve bone regeneration and implant osseointegration in deficient and osteoporotic bone.

Keywords: Biophysical stimulation, Bone healing, Magnetic field therapy, Osseointegration

INTRODUCTION

The background and history of surrounding Pulsed Electromagnetic Field (PEMF) demonstrates scope for an extensive research, development, and clinical applications. There are a few non invasive treatment modalities used adjunctively that trigger and stimulate the intrinsic potential of the body for bone repair and regeneration. They include application of pulsating electromagnetic field therapy, Low-Intensity Pulsed Ultrasound (LIPUS), and Low-Level Laser Therapy (LLLT) [1]. These methods which are based on biophysical stimulation of bone union were developed initially to enhance the healing of fractures, healing of bone non unions and have been hypothesised to improve implant osseointegration. The use of PEMF has been tagged as a safe modality of treatment by the United States Food and Drug Administration (US FDA) in non union of bone [2].

Biophysical stimulation with PEMF is an emerging field that introduces physical stimuli to aid in healing and proliferation seen in bone cells [3]. PEMF is a non invasive, therapeutic form of low field magnetic stimulation that has been used for several years to supplement bone healing. It shows extraordinary amount of bone growth and proliferation especially noted in patients postoperatively and enhance the vascular flow as well leading to rapid recovery [4]. It is known to generate pulsating magnetic frequencies within the body that accelerate the process of healing and reduce postoperative pain and promote faster tissue swelling. Pulsed electromagnetic field utilises a broad range of settings that includes the magnetic field intensity, frequency, signals and duration of application etc.

Apart from these factors, there exist two different waveforms which may or may not be used in combination during therapy and function to treat abundant musculoskeletal conditions [5]. These multiple PEMFs settings present as a hurdle for defining better treatment protocols for wider clinical applications and mandates extensive clinical trials and research. This review aimed at examining bone-implant union and the current trends surrounding the enhancement of this union using PEMF for biophysical stimulation. It also is expected to act as a guide for clinicians and researchers in this field to introduce these strategies for clinical use for improving implant osseointegration in inadequate and osteoporotic bone.

PULSED ELECTROMAGNETIC FIELD THERAPY (PEMF)

The use of PEMF was approved by the Food and Drug Administration (FDA) in 1979 and has been used clinically for over 40 years following convincing evidence that electric currents can accelerate bone formation. It was discovered that everyday bone movements during physical activity produces endogenous electrical currents in bone that could modulate bone cell activity (Wolff's law) [3]. Pulsed electromagnetic field is a non invasive, therapeutic form of low field magnetic stimulation that has been used for healing bone non unions and various fractures [4,5]. It is known to generate pulsating magnetic frequencies within the body that accelerate the process of healing and reduce postoperative pain and promote faster tissue swelling [6].

The early devices were based on animal studies [7-9] and used implanted and semi-invasive electrodes delivering direct current to the fracture site.

Bassett CA et al., reported a significant increase in endosteal bone formation around the cathode of insulated battery implants whose electrodes were implanted in the femurs of 12 dogs [6]. Jansen JHW et al., showed that PEMF exposure of human bone marrow-derived stromal cells induced differentiation and enhanced the mineralisation of bone, which supports the theory that PEMF induces an osteogenic response in-vivo and may therefore stimulate fracture healing [7]. Tabrah F et al., noted a positive effect in the improvement of the bone mineral density of osteoporotic women which increased significantly in the immediate area of the field during the exposure period and decreased during the following 36 weeks [8]. Results demonstrated a significant increase in the bone mineral density in the midshaft region of forearm after 12 weeks of exposure.

PEMF USE IN MAXILLOFACIAL REGION

1. Fractures

Abdelrahim A et al., evaluated the effect of a PEMF on the healing of mandibular fractures [9]. Out of the two groups taken, the group that received PEMF exposure showed an increase of 10.2% in bone density compared to density found at 15th postoperative day. A significantly greater increase in the percentage of changes in bone density in the test group was also noted at 30 days postoperatively. This might have been due to enhanced osteogenesis, because PEMF has been shown to increase osteogenesis in-vitro and the maturation of callus in-vivo [10].

Refai H et al., studied radio densitometric assessment of the effect of PEMF stimulation and Low Intensity Laser Irradiation (LILI) on mandibular fracture repair [11]. Their study comprised of eighteen patients who were divided into three groups. Group A received PEMF at fracture sites for 2 hours for 12 days, group B received LILI on 10th and 12th postoperative day and Group C were taken as controls. The results found that at 2nd postoperative week, the mean bone density at the fracture sites decreased by 4.74%, 6.6% and 27.89% in PEMF, LILI and control group respectively. The period from the 2nd to the 4th postoperative weeks showed an increase in the bone density by 1.49%, 1.95% and 14.12% in the three groups respectively. Their finding was somewhat in accordance with those of Abdelrahim A et al., who also found an increased clinical stability of the segments 14 days postoperatively [9].

Mohajerani H et al., studied the effect of PEMF on mandibular fracture healing in a randomised control trial [12]. A total of 32 participants were enrolled in the study and divided into two groups (16 each) i.e, experimental and controls group. The experimental group received PEMF in addition to conventional therapy while the control group received only conventional treatment. They found no significant difference in the mean bone density values between the two groups (p-value >0.05). However, the percentage of changes in bone density of the two groups revealed that the experimental group had insignificant decreases at postsurgery day 14 and a significant increase at postsurgery day 28 compared with the control group (p-value <0.05). They concluded that PEMF therapy application postoperatively leads to an increase in bone density, faster recovery, increased formation of new bone, increased mouth opening and decreased pain.

2. Implant Osseointegration

Gujjalapudi M et al., placed twenty tidal spiral implants and used safer magnet (Neodymium Boron Iron) on 10 patients between 50 to 75 years of age at two sites on edentulous mandible with D1 and D2 bone type with one site as a control [13]. Both the implants were compared for stability using Resonance Frequency Analyser (RFA) at days 0, 30, 60 and 90. The results reflected that the average Implant Stability Quotient (ISQ) value measured for implants at 0 day in the B and D regions of implant site was 68.6 and 68.7, respectively. The mean ISQ values at day 30, 60 and 90 were 73.25, 76.05 and 78.95, respectively on the magnetic side. The non magnetic side recorded values at 30th day, 60th day and the 90th day as 68.45, 72.05 and 74.45, respectively. The ISQ values seen on the magnetic side were remarkably higher than on the non magnetic side.

Nayak BP et al., studied 19 subjects (40 implants in total) and randomly divided them into the PEMF group and control group [14]. An activated Miniaturized Electromagnetic Device (MED) was placed as a healing cap in the PEMF group while the control group received a sham healing cap. Radio Frequency Analysis was performed to record implant stability quotient values soon after the procedure, and then post two, four, six, eight and 12 weeks. Radiographic qualitative analysis was conducted at baseline, six and 12 weeks after the implant was placed. Proinflammatory cytokine evaluation in peri-implant crevicular fluid (PICF) was also done at baseline, six and 12 weeks. They reported that the PEMF (MED) group presented higher ISQ mean values when compared to the control group. In the first two weeks after implant placement which is the primary stability period the MED group depicted an increase in stability of 6.8%, compared to a decrease of 7.6% in the control group related to the baseline. An overall stability increase of 13% was reported in the MED treated group (p-value=0.02), in contrast, the overall stability in the control group decreased by 2% (p-value=0.008). Tumour Necrosis Factor-α (TNF-α) concentration during the first four weeks was lower in the MED treated group. It was concluded that a continuous PEMF generated by a miniature device attached to an implant may enhance the primary stability of the dental implant.

3. Orthodontic Tooth Movement

Showkatbakhsh R and Jamilian A, analysed canine retraction in 10 patients where canines of one side were exposed to PEMF of 1 Hz. The canine of the contralateral side was unexposed and retraction on both sides was performed via Coil springs. The study was basically a randomised clinical trial with five male and five female participants. The side exposed to PEMF achieved a retraction of canine by of 1.53±0.83 mm more than the unexposed side with (p-value <0.001) [15].

Jung JG et al., conducted a pilot study to assess how PEMF impacted the pain caused by initial tooth movement during fixed orthodontic treatment. The sample size included 33 female patient of average age 16 years, who had no history of dental pain and had a healthy periodontium. The patients were divided into experimental and placebo group where the placebo group had PEMF device with inversely positioned battery. It was observed that there was a significant decrease in pain experienced after placement of the PEMF device in the experimental group with (p-value <0.01) [16].

DISCUSSION

New biophysical approaches that promote healing and enhance the regenerative capacity of all oral and dental tissues can be extremely enticing due to their non consumable nature, accessibility to oral wounds, and efficacy of promoting the endogenous healing process. This would over all reduce frequent patient visits along with reducing cost of treatment [17].

Numerous studies such as the ones conducted by Jiang Y et al., and Li J et al., over the past decades have hypothesised that biophysical methods such as pulsating electromagnetic fields and biomodulation have the potential to affect osteoblastic behaviour both in-vivo and in-vitro and hence, can be a potential tool to improve the clinical outcome of several regenerative and prosthetic therapies in orthopedics and dentistry [18,19]. The bio modulation of physiological processes by PEMF depends upon: (i) the physiological state of the injured tissue; (ii) effective dosimetry of the applied PEMF at the target site [20].

Studies (both in-vitro and in-vivo) have shown that, biophysical stimulation induces: (i) an increase in osteoblast differentiation, promoting the production of collagen and of the main matrix glycoproteins osteocalcin and osteopontin; (ii) stimulates the mineralisation process; and (iii) plays an inhibitory role in the process of osteoclast differentiation and exerts a protective action against osteolysis [21-23]. Bone matrix induction by PEMF is similar to those induced by growth factors such as Bone Morphogenetic Proteins (BMPs), Transforming Growth Factor beta (TGF-β 1), Insulin-like Growth Factors I (IGF-I), indicating that the effects induced by a biophysical stimulus are of significant medical importance [24]. Many previous studies have analysed the effects of biophysical stimulation on osteoblast proliferation and have highlighted a dose-response effect for the following parameters: (i) signal waveforms; (ii) PEMF intensity, frequencies; and (iii) exposure times [25,26].

Signal waveforms

The waveforms associated with PEMF exist as different types including quasi-square/rectangular asymmetrical, biphasic, sinusoidal, and trapezoidal. The FDA approved the quasi-rectangular and quasi-triangular PEMF as the most efficacious ones for treatment for fractures [5]. Galli C et al., in their review of the use of PEMF on titanium implants, the authors highlighted that most animal studies have used the quasi square/rectangular and trapezoidal signal waveforms [22].

Magnetic field intensity and frequency

It has been shown that atleast 3 amplitude windows exist: at 50-100T (5-10 Gauss), 15-20 mT (150-200 Gauss), and 45-50 mT (450-500 Gauss) [24], the maximum response that was observed within the range of 10-100 mT. The electromagnetic fields that are applied in clinical treatment have a frequency less than 100 Hz and the magnetic flux density varies between 0.1 mT and 30 mT [5]. The response of PEMF to different cells and tissues with titanium devices for orthopaedic or dental use has been studied using a wide range of PEMF approaches, but aside from few minimal attempts in the early 2000s with 100 Hz PEMF pulses at very low intensities, around 0.2 mT [22].

Matsumoto H et al., in their study demonstrated PEMF application at different intensities, duration of application and length of treatment in weeks. Their study concluded that the bone contact ratio and bone area ratio of the 0.2 mT- and 0.3 mT-treated femurs were significantly larger than the respective value of the 0.8 mT-treated femurs of Japanese rabbits (p-value <0.001) [27]. No crucial difference was highlighted in bone contact ratio or the bone area ratio whether PEMF was applied for 4 or 8 hours per day. Although, a remarkably greater amount of bone had been deposited around the implant of the femurs treated for 2-weeks than the 1-week treated femurs. Also, no significant difference was noted between the 2-week and 4-week treated femurs. This study highlighted the importance to select the proper magnetic intensity, duration per day, and length of treatment. Most recent studies have used 15 Hz-75 Hz trapezoidal stimuli, with higher intensity, around 1-2 mT.

Apart from one in-vitro animal study of Grana DR et al., that used a higher intensity of 72 m T most animal studies have used intensities in the range of 0.2 to 2 mT [19,28]. Broader screening studies testing across a spectrum of amplitudes and frequencies are still missing with the purpose of establishing better and more reliable clinical protocols [13] reported in a human trial reported an increase in primary stability of commercially available dental implants by using 0.5 mT continuous electromagnetic field application for 12 to 15 hours. Nayak BP et al., stated that continuous PEMF generated by a miniature device generation 0.5 mT attached to an implant stimulated the stability of the implants at the early healing period [14].

Exposure times

Most studies involving fracture unions have supported a finding that an increase in the average daily “dose” of PEMF stimulation was associated with acceleration in the rate of fracture healing [13,14,27].

Matsumoto H et al., in their study demonstrated PEMF application at different intensities, duration of application and length of treatment in weeks [27]. No discernible difference in bone contact ratio or bone area ratio was noticed on PEMF use for 4 or 8 hours per day. Even though two weeks treated femurs had considerably more bone around the implant than the one week treated femurs, there really was no notable change between the two weeks and four weeks treated femurs. The two human studies of Gujjalapudi M et al., and Nayak BP et al., also reported improved early healing and primary stability of dental implants when applied for a continuous or 12 to 14 hours in a two week period after implant placement [13,14].

Despite the positive results of PEMF treatment as reported in several in-vivo and in-vitro studies, more defined and better controlled/monitored treatment methods are still needed. Various factors such as the use of different animal species in different studies, different implantation sites (trabecular or cortical bone, intramedullary), different biomaterials (ceramic or metallic), and different stimulation intensity, frequency, signal waveform, and duration can all be attributed to the varied observations and effects. Because of the need for a wide variety of settings, including magnetic field intensity, frequency, and duration of application, a multicentric trial with the participation of engineers, biophysicists, biologists, and medical practitioners needs to be conducted to further investigate and develop PEMF use. To test and validate effectiveness, well-controlled randomised clinical trials would be required at different PEMF settings.

CONCLUSION(S)

Pulsed electromagnetic field stimulation for various ailments and identifying suitable treatment protocols need further investigation. It is also anticipated to pave way for doctors and researchers in this field as they implement these techniques in the clinic to optimise bone tissue healing and implant osseointegration in deficient and osteoporotic bone.

REFERENCES

[1] Kim YD. Biophysical therapy and biostimulation in unfavorable bony circumstances: Adjunctive therapies for osseointegration. J Korean Assoc Oral Maxillofac Surg. 2012;38(4):195.
[2] Cadossi R, Massari L, Racine-Avila J, Aaron RK. Pulsed electromagnetic field stimulation of bone healing and joint preservation: Cellular mechanisms of skeletal response. J Am Acad Orthop Surg Glob Res Rev. 2020;4(5):):e1900155.
[3] Massari L, Benazzo F, Falez F, Perugia D, Pietrogrande L, Setti S, et al. Biophysical stimulation of bone and cartilage: State of the art and future perspectives. Int Orthop. 2019;43(3):539-51.
[4] Fiani B, Kondilis A, Runnels J, Rippe P, Davati C. Pulsed electromagnetic field stimulators efficacy for non invasive bone growth in spine surgery. J Korean Neurosurg Soc. 2021 Jul;64(4):486-94.
[5] Hu H, Yang W, Zeng Q, Chen W, Zhu Y Bin, Liu W, et al. Promising application of Pulsed Electromagnetic Fields (PEMFs) in musculoskeletal disorders. Biomed Pharmacother. 2020;131:110767.
[6] Bassett CA. The development and application of pulsed electromagnetic fields (PEMFs) for ununited fractures and arthrodeses. Clinics in Plastic Surgery. 1985;12(2):259-77. PMID: 3886262.
[7] Jansen JHW, Van Der Jagt OP, Punt BJ, Verhaar JAN, Van Leeuwen JPTM, Weinans H, et al. Stimulation of osteogenic differentiation in human osteoprogenitor cells by pulsed electromagnetic fields: An in-vitro study. BMC Musculoskelet Disord. 2010;11:01-11.
[8] Tabrah F, Hoffmeier M, Gilbert F, Batkin S, Bassett CAL. Bone density changes in osteoporosis-prone women exposed to pulsed electromagnetic fields (PEMFs). J Bone Miner Res. 1990;5(5):437-42.
[9] Abdelrahim A, Hassanein HR, Dahaba M. Effect of pulsed electromagnetic field on healing of mandibular fracture: A preliminary clinical study. J Oral Maxillofac Surg. 2011;69(6):1708-17.
[10] Fu YC, Lin CC, Chang JK, Chen CH, Tai IC, Wang GJ, et al. A novel single pulsed electromagnetic field stimulates osteogenesis of bone marrow mesenchymal stem cells and bone repair. PLoS One. 2014;9(3).
[11] Refai H, Radwan D, Hassanien N. Radiodensitometric assessment of the effect of pulsed electromagnetic field stimulation versus low intensity laser irradiation on mandibular fracture repair: A preliminary clinical trial. J Maxillofac Oral Surg. 2014;13(4):451-57.
[12] Mohajerani H, Tabeie F, Vossoughi F, Jafari E, Assadi M. Effect of pulsed electromagnetic field on mandibular fracture healing: A randomised control trial, (RCT). J Stomatol Oral Maxillofac Surg. 2019;120(5):390-96.

[13] Gujjalapudi M, Anam C, Mamidi P, Chiluka R, Gautamkumar A, Bibinagar R. Effect of magnetic field on bone healing around endosseous implants- An in-vivo study. J Clin Diagnostic Res. 2016;10(10):ZF01-04.
[14] Nayak BP, Dolkart O, Satwalekar P, Kumar YP, Chandrasekar A, Fromovich O, et al. Effect of the pulsed electromagnetic field (PEMF) on dental implants stability: A randomised controlled clinical trial. Materials (Basel). 2020;13(7):01-09.
[15] Showkatbakhsh R, Jamilian A MS. The effect of pulsed electromagnetic fields on the acceleration of tooth movement. World J Orthod. 2010;11(4):e52-56.
[16] Jung JG, Park JH, Kim SC, Kang KH, Cho JH, Cho JW, et al. Effectiveness of pulsed electromagnetic field for pain caused by placement of initial orthodontic wire in female orthodontic patients: A preliminary single-blind randomised clinical trial. Am J Orthod Dentofac Orthop. 2017;152(5):582-91.
[17] Khan I, Arany P. Biophysical approaches for oral wound healing: Emphasis on photobiomodulation. Adv Wound Care. 2015;4(12):724-37.
[18] Jiang Y, Gou H, Wang S, Zhu J, Tian S, Yu L. Effect of pulsed electromagnetic field on bone formation and lipid metabolism of glucocorticoid-induced osteoporosis rats through canonical wnt signaling pathway. Evid Based Complement Alternat Med. 2016;2016:4927035; Available from: https://www.hindawi.com/journals/ecam/2016/4927035/.
[19] Li J, Zeng Z, Zhao Y, Jing D, Tang C, Ding Y, et al. Effects of low-intensity pulsed electromagnetic fields on bone microarchitecture, mechanical strength and bone turnover in type 2 diabetic db/db mice. Sci Rep. 2017;7(1):01-13. Available from: http://dx.doi.org/10.1038/s41598-017-11090-7.
[20] Singh S, Kapoor N. Health implications of electromagnetic fields, mechanisms of action, and research needs. Adv Biol. 2014;2014:198609.
[21] Varani K, Vincenzi F, Pasquini S, Blo I, Salati S, Cadossi M, et al. Pulsed electromagnetic field stimulation in osteogenesis and chondrogenesis: Signaling pathways and therapeutic implications. Int J Mol Sci. 2021;22(2):01-17.
[22] Galli C, Pedrazzi G, Mattioli-Belmonte M, Guizzardi S. The use of pulsed electromagnetic fields to promote bone responses to biomaterials in-vitro and in-vivo. Int J Biomater. 2018;2018:8935750.
[23] Diniz P, Shomura K, Soejima K, Ito G. Effects of Pulsed Electromagnetic Field (PEMF) stimulation on bone tissue like formation are dependent on the maturation stages of the osteoblasts. Bioelectromagnetics. 2002;23(5):398-405.
[24] Markov MS. Pulsed electromagnetic field therapy history, state of the art and future. Environmentalist. 2007;27(4):465-75.
[25] Zhou J, Wang JQ, Ge BF, Ma XN, Ma HP, Xian CJ, et al. Different electromagnetic field waveforms have different effects on proliferation, differentiation and mineralisation of osteoblasts in-vitro. Bioelectromagnetics. 2014;35(1):30-38.
[26] Oltean-Dan D, Dogaru GB, Apostu D, Mester A, Benea HRC, Paiusan MG, et al. Enhancement of bone consolidation using high-frequency pulsed electromagnetic fields (HF-PEMFs): An experimental study on rats. Bosn J Basic Med Sci. 2019;19(2):201-09.
[27] Matsumoto H, Ochi M, Abiko Y, Hirose Y, Kaku T, Sakaguchi K. Pulsed electromagnetic fields promote bone formation around dental implants inserted into the femur of rabbits. Clin Oral Implants Res. 2000;11(4):354-60.
[28] Grana DR, Aldana HJ, Marcos GAK. Pulsed electromagnetic fields as adjuvant therapy in bone healing and peri-implant bone formation: An experimental study in rats. Acta Odontol Latinoam. 2008;21(1):77-83.

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