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NARRATIVE REVIEW

Potential Use of Pulsed Electromagnetic Field in Musculoskeletal Disorders: A Narrative Review

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ABSTRACT

Numerous studies conducted in the last few years have produced figures showing that the incidence of musculoskeletal issues is continuously rising and that a variety of treatment options are available. Musculoskeletal illnesses, including fractures, arthritis, and osteoporosis, are increasingly treated with electromagnetic fields (EMFs). As a non-invasive, secure, and efficient treatment tool with no apparent side effects, Pulsed Electromagnetic field (PEMF) are well recognized. The present study aims to evaluate the literature by reviewing the data already available on PEMF's effectiveness in the treatment of different musculoskeletal disorders. For locating the literature, articles published in English language on various musculoskeletal diseases treated by PEMFs were included. Information was looked for in the databases of PubMed, Google Scholar, Cochrane, and SCOPUS. The result of the study shows that due to its great efficacy and few risk considerations, PEMF has a lot of potentials to become a separate or complementary treatment strategy for treating numerous musculoskeletal disorders. The present study concludes that numerous issues are still unresolved. Further research from well-designed, high-quality studies are required to standardise therapy parameters and identify the most effective process for healthcare decision-making prior to widespread clinical application. In this study, we aim to provide up-to-date details on the therapeutic applications, mechanism of action, and ethical issues surrounding PEMFs in musculoskeletal disorders.

Keywords: Electromagnetic Field, Low Back Pain, Musculoskeletal Diseases, Osteoarthritis.

INTRODUCTION

Musculoskeletal disorders such as osteoarthritis (OA), chronic mechanical neck pain (CMNP), shoulder impingement syndrome (SIS), fibromyalgia (FM), low back pain, lumbar myalgia, patellofemoral pain caused around 1.3 billion incidences, 121.3 thousand fatalities, and 138.7 million disability-adjusted life years lost (DALYs) between 1990 and 2017, according to statistics from the Global Burden of Disease (GBD) research, which was undertaken in 195 nations and territories. The prevalence of musculoskeletal problems was found to be greater in females than in males, and it increased with age. Low back pain had the greatest prevalence rate of all musculoskeletal conditions in 2017, representing 36.8% of all cases, followed by other musculoskeletal diseases (21.5%), neck pain (18.4%), OA (19.3%), rheumatoid arthritis (RA) (1.3%), and gout (2.6%).[1]

In the 21st century magnetic therapy and electromagnetic fields have emerged as very effective physical means of management that are alleviating numerous health issues even when the conservative way of management has failed. Magnetotherapy offers a comfortable and hazard-free method that precisely acts on the site of injury, and works on the main causative factor of pain and inflammation, as well as many illnesses and associated pathologies.[1]

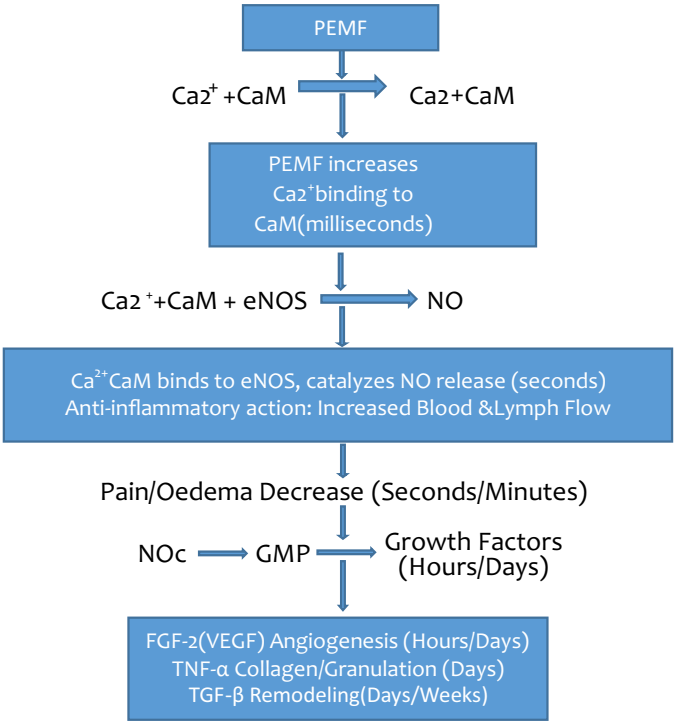
Pulsed electromagnetic fields (PEMF) are one of the significant modalities in magnetotherapy. Initially, various types of electromagnetic signals were used at the time of II World War, and after that electromagnetic fields started to be used in the management of various medical conditions.[1] In the 1953, Yasuda *et al*. established that an unrealized electric ability exists in bones, comprising of uniform-state potential and stress-induced potential. After this kind of invention, the researchers develop an interest in investigating the function of electrical energy in the development of bone and the healing of fractures.[2] A variety of appliances have been developed which produce electromagnetic fields and stimulate bone formation.[3] Bassett *et al*. published their findings in 1964 confirmed that electric current has beneficial effects on the

development of bones in vivo, and then they established the role of PEMF in inherited and developed pseudarthroses and non-union of fractures in humans beings in 1977.[4] The application of PEMF also considered safe for the management of fractures non-union.[5] Modalities using PEMF are constructed on low-frequency fields with certain waveforms and amplitudes low-frequency fields that are varying from 6 and 500 Hz and revealed to produce non-thermal and nonionizing effects. PEMF uses a high rate of changes in bioelectric currents (Tesla/s) in tissues, building distinct biological effects. Usage of electromagnetic fields medical treatment generally have magnetic flux and low-frequency less than 100 Hz densities ranging from 0.1 mT to 30 mT.[6] The various types of distinct waveforms such as asymmetrical, biphasic, sinusoidal, trapezoidal, and quasi-rectangular are used in PEMF. However, the PEMF's mode of action at the molecular and cellular levels remains unknown.[7] There is no consistent set of treatment protocols or justification for the selection of parameters.[8] The objective of this review was to provide up-to-date information about the therapeutic uses, PEMFs mechanism of action and several points of view in musculoskeletal illnesses.

Mechanism of PEMFs

Several researches have been conducted throughout the years to investigate the underlying mechanisms of PEMFs on living organisms. One of the accepted theories for the beneficial effects of electromagnetic fields on the body is how they affect cellular membrane potential. The operation of ATPases concurrently delivering proteins and ions to channels causes ionic concentration gradients through the cell membrane, which create and initiate the membrane potential. Therefore, the low resistance route of the wounded cells serves as the source of the residual flow of ionic current if damage of any type compromises the integrity of the tissue. Ionic currents that move between healthy and damaged tissue are crucial to the healing processes that are required to restore the tissue's ability to function normally. The healing process is aided by electromagnetic current because of its capacity to penetrate deeply. It is anticipated that the magnetic field will modify signal/transduction pathways because the energy employed is below the thermal threshold level.[13]

The binding agents, distribution, and activity of several membrane receptors, including as insulin, parathyroid hormone, Interleukin-2, low-density lipoprotein and Insulin-like growth factor 2 were observed to change as result of PEMF exposure, altering transmembrane signalling. It is reported that PEMFs work as an agonist of adenosine A2A and A3 receptors to significantly reduce inflammation in the joint. In the most recent review, the main signalling pathways of PEMFs for bone repair were summarised as Ca2+, Wnt/-catenin, mitogen-activated protein kinase (MAPK), fibroblast growth factor (FGF), and vascular endothelial growth factor (VEGF), as well as insulin-like growth factor (IGF),transforming growth factor (TGF)-/bone morphogenetic proteins (BMP) and PGE2 are examples of growth factors produced exposure to PEMF has a similar effect on mechanisms that promote the formation of extracellular matrix (ECM) proteins and accelerated tissue healing.[3,4,11] However, PEMFs are still a relatively new form of treatment. The mechanism of action of PEMFs remains unclear despite much research. Therefore, more investigation is needed to validate the PEMF's fundamental mode of operation. A Figure illustrating the flowchart of mechanism of action PEMF is shown in figure 1.



CaM - Calmodulin
NOS - Nitric oxide synthase
eNOS - Endothelial nitric oxide synthase
GMP - Guanosine Monophosphate
TNF - Tumor Necrosis Factor
TGF - *Transforming Growth Factor*

Figure 1: Mechanisms of action of pulsed electromagnetic field on the cell [9-12]

Medical uses for PEMFs

Osteoarthritis: OA is a very common condition of aging that extremely influences the quality of a patient's life. The knee joint is most frequently affected and OA knee

is one of the major causes of disability in old age. Numerous treatments are available for the management of OA knee, comprising non-pharmacological management, anti-inflammatory drugs, and final option for advanced OA is complete knee replacement.[14] New treatment strategies have been developed to lessen pain, lessen disability, and stop the progression of joint degeneration. Numerous research are currently concentrating on the advanta-geous benefits of PEMF treatment on preventing the onset and progression of OA, however the results are still debatable.[15] PEMF treatment has been shown to accelerate chondrogenic differentiation and stem cell proliferation. PEMF has been identified to modify the cyclic guanosine monophosphate (cGMP) /calmodulin (CaM) - dependent nitric oxide (NO) signalling pathway which has the capacity of decreasing pain in primary knee OA.[15] However, a randomized, controlled trial found that using PEMFs for 10 sessions over the course of two weeks each lasting 30 minutes-had a no significant and additional impact in patients with primary OA knee.[8] The inconsistent outcomes may be because of dissimilar types of study designs and small sample sizes. Recent research confirms PEMF as a good supplemental therapeutic option for treating knee OA.[14]

Chronic mechanical neck pain: CMNP is a non-specific disorder in the general population; mostly it is aggravated with movements of the neck and is resistant to common therapeutic interventions. This condition influences approximately 45% to 54% of the population at some phase of their lives and can cause severe discomfort, pain, and disability. The cause of symptoms in CMNP is not well recognized but has been assumed to be associated with several anatomical structures such as muscles, ligaments, and vertebral joints of the cervical spine even though the signs of degenerative disease are absent. Several etiological factors had been suggested related to CMNP like postural abnormalities, traumas, psycho-emotional stresses, and altered neuromuscular control of the cervical muscles.[16] A randomized, controlled study suggested that PEMF at 5-25Hz frequency and 5-70 μT intensity twice a day for 2 hours for 8 weeks does not show any considerable effect on the reduction of disability and pain in the study.[16]

Shoulder Impingement Syndrome: SIS frequently produces pain in the upper extremity and can cause a reduction in the function of this joint and a decline in the quality of life. It influences almost 20 % of the population and its incidence increases with aging. As the chief complaints of patients suffering from SIS are stiffness, joint pain, and functional deficit, nonsurgical management is concentrated on relief in symptoms and enhanced functions.[17] However, a randomized, controlled study recommended that a combination of PEMF at 50 Hz frequency, 20mT intensity for 30 minutes 3 sessions per week for 3 weeks along with exercises of the shoulder are helpful in the recovery of functions, muscle strength, and decreases pain in patients with SIS. But the outcomes of PEMF in shoulder pain patients are presently controversial.[17]

Fibromyalgia: FM is a persistent pain condition that primarily affects females and is characterised by acute muscular pain, exhaustion, discomfort, and disturbed sleep, and other associated symptoms. Although the specific aetiology and pathophysiology of FM are unclear, they may involve aberrant neurotransmitter levels in the peripheral and central neurological systems, inadequate hypothalamic-pituitary-adrenal axis regulation, or nitric oxide/oxidative stress. Since there is no unique management strategy for FM, the current therapeutic approaches are focused on easing FM symptoms. Exercises, antidepressants, and painkillers are typically used to reduce symptoms.[18] Sutbeyaz *et al*. found that when PEMF is applied at a frequency of 0.1–64Hz, an intensity of 40 μT for 30 min twice a day for 3 weeks improves pain, weakness, and overall functional status in patients with FM and could offer a possible beneficial adjunct to present FM therapies in the future.[19] Multanen *et al*. demonstrated that low-energy PEMF therapy at 33.3 Hz and intensity 0–150μT with the sinusoidal half wave was not effective in decreasing pain and stiffness or the recovery of functions in females with FM.[20]

Hand Osteoarthritis: Hand Osteoarthritis (HO) is a very common joint disorder that influences almost 15%-20% of the adult population including wear and tear of cartilage which leads to painful joint movements The proximal and distal interphalangeal joints of the second and third fingers, as well as the carpometacarpal joint of the first finger, are the most often affected joints in OA of the hands. Finger mobility limitation, significant discomfort, and decreased muscular power in the hands may occur, causing difficulties with daily tasks.[17] The effectiveness of magnetotherapy in HO was examined by Kanat *et al*. Magnetotherapy was used in the treatment group in this study for 20 minutes each day for 10 days with flux 3.5 to 25 mT intensities, 450 pulses per second, and 5-80 G, combined with hand exercises. Along with the same exercises, the control group also received sham magnetotherapy for 20 minutes each day for 10 days. Quality of life, pain, and SF-36 scale scores were greater in the treatment

group.[21]

Lumbar radiculopathy: Lumbar radiculopathy usually occurs due to intervertebral disc herniation of the lumbar region, it is one of the most common reasons for radicular pain. A maximum number of patients are treated conservatively, while considerable minorities undergo discectomy. PEMF's efficacy in the conservative treatment of low back pain (LBP) was evaluated in a small number of trials, and preliminary results indicated great results in patients with lumbar disc herniation with and without radicular symptoms.[22] According to Omar *et al*. PEMF treatment can help with the conservative management of lumbar radiculopathy caused by lumbar disc prolapse, when administered at a frequency of 7-4000 Hz and an intensity of 5-15 G for 20 minutes once a day for three weeks. The improvement in somatosensory evoked potentials (SSEP) characteristics following therapy demonstrates that PEMF may be helpful in reducing nerve root compression in addition to the reduction in clinically noticed radicular symptoms.[22]

Back Pain: Back pain is a very common musculoskeletal problem faced in clinical practice. The associated deformities and vast financial loss among the involved individuals lead them to continuously explore economical treatment modalities that are non-invasive and are with least side effects. Research was done by Oke *et al.* to evaluate the therapeutic efficacy of a PEMF method for treating back pain and obtained the results that PEMF therapy is effective in decreasing pain and disability in patients with back pain if applied for 4 times a day, for 5-9 days, 2 hours every session.[23]

Lumbar Myalgia: Lumbar Myalgia is a most frequent form of back pain is lumbar discomfort. It is estimated that between 70% and 80 % of persons may experience lumbar discomfort at some point in their lives. One of the main factors limiting the activities of the people over the age of 45 is chronic low back pain, according to research.[24] Myalgia is one of these and suggests signs of muscular discomfort. Clinically, it is the situation in which there is a strong pain in soft tissues other than joints that has an unknown cause and is not accompanied by any obvious symptoms or abnormal test results. Lumbago is classified into four kinds based on the cause of myalgia and its clinical features: muscle deficit, muscular spasm, muscle tension, and myofascial pain syndrome. Research performed by Park *et al.* revealed that PEMF is an appropriate treatment for relieving lumbar myalgia.[24]

Patellofemoral Pain: Patellofemoral pain and patellofemoral pain syndrome is a highly prevalent disorder in young people that produces recurring or chronic knee discomfort, most commonly in the retropatellar area. The exact cause is unknown; however numerous variables such as anatomical anomalies, muscle imbalance, or joint overuse are thought to be involved. Exercise treatment, including home exercise regimens, has been shown to have positive effects. Joint inflammation can be detected when there is a clear development of chondromalacia and is caused by an increase in pro-inflammatory cytokines in the synovial fluid. Chondrocyte activity that is anabolic and anti-inflammatory has been found to be increased by use of PEMF. Iammarrone *et al*. stated that PEMFs having a square waveform, a duty cycle of 10%, a frequency of 75 Hz, and an intensity of 1.5 mT were used to reduce pain if given for 4 hours per day for 6 weeks.[25]

Non-union: Non-union of fractures or delayed fracture healing was indicated in 5–10 % of cases of fractures. The biological effects produced by PEMFs are due to molecular mechanisms. PEMF stimulation is found to influence cell proliferation, differentiation, and modulation in the immune system and inflammatory response using various molecular mechanisms.[26] Delayed union of bone fractures causes patients to experience on-going pain and impairment, as well as significant social and economic costs.[26] Surgery is now the best treatment option for fracture non-union and delayed union, however possibly might cause severe complications like infection, implant-related problems, and neurovascular damage.[27] PEMF therapy as a substitute is drawing the attention of experts now a days; it has the capability of reducing the threats of these complications.[7]

The use of PEMF in the management of fracture non-union has been mentioned in several reviews, also found to enhance the rate of healing varying from 68 % to 90 % by boosting growth factors, and helps the bone healing process, according to earlier in vitro and in vivo research. However, the sources differ on the role of PEMF in the treating of non-union fractures. A maximum investigator recommends that PEMF therapy should not be applied till a confirmed non-union is identified. Additionally, some other researchers advise using PEMF when the late stage of delayed union has occurred, more especially six months after the fracture.[28]

Osteoporosis: Osteoporosis is a chronic bone metabolic disorder is described as having bone mass loss, deterioration of microarchitecture, and increased bone fragility.[29] The prevalence rate of osteoporosis significantly rises with the ageing population. Researchers claim that in industrialised nations, half of those over 60 years will be diagnosed with osteo-

porosis in the upcoming years, with postmenopausal women making up roughly 80% of this group. In certain pathological disorders, the difference between the amount of bone reabsorption and bone formation plays a role in the abnormal bone remodelling and causes different types of osteoporosis.[6] Presently, several anti-osteoporotic medicines are available that help preserves strength and healthy bone mass but, the extensive usage of these medicines could cause several possible side effects; for example, upturn the chances of several types of cancers, osteonecrosis (ON) of the jaw, hypocalcaemia, atrial fibrillation, infections, and femoral fractures. PEMFs have been found to have a considerable impact on the treatment of osteoporosis. According to a randomised, active-controlled clinical research, treating postmenopausal osteoporosis with precise PEMF settings (40 minutes per day, six times per week, 8 Hz, 3.82 m T) in addition to alendronate (70 mg/week) provides the same therapeutic effect for a period of 24 weeks.[30] PEMFs can significantly reduce pain and enhance quality of life in people with primary osteoporosis.[31] Even so, it's still unclear how PEMFs affect patients with osteoporosis bone mineral density (BMD). Tabrah *et al* found no more effects of PEMFs (10 hours a day for 12 weeks at 72 Hz) on BMD over an 8-year follow-up.[30]

Osteonecrosis: ON is known to be as destructive condition that frequently comprises the involvement of the hip joint. The commonly mentioned risk factor for ON is the excessive dosage of corticoids. Various surgical treatments, such as non-vascularized bone grafting, are available to avoid collapse vascularized fibular grafting, core decompression, osteotomy, and joint arthroplasty. Although surgical techniques are beneficial, further attention should be paid to the risks and expenses associated with surgery. However, complete hip arthroplasty is the typical treatment if the head of the femur collapses.[30] In the young population, additional long-term consequences of joint replacement do not always appear to be favourable. There is presently no method to halt ON from advancing, hence ON treatment is essential for patients who require large doses of corticosteroid therapy. For the first time, 118 individuals with ON of the femoral head were successfully treated by Bassett and colleagues using PEMFs.[4] PEMFs may be helpful in the early stages of this condition, according to Massari *et al*. who performed a retrospective study on the effects of PEMF therapy on patients with femoral head ON (Ficat stages I and II).[32]

Tendon disorders: Acute and chronic tendon injuries make up tendon diseases, which are usually diagnosed as musculoskeletal ailments and cause pain and impairment. Non-operative treatment, which includes NSAIDS, US, and physical therapy, is typically seen to be the primary line of care. The healing period for tendon diseases can be lengthy, and the effects are frequently minimal, this is logically because the tendons are avascular structures. In addition, insignificant opinions about the cellular and molecular events taking place in tendinopathy are the main reason for the obstruction in the development of new and effective management approaches. While current research repeatedly shows that a number of inflammatory events, including as inflammatory mediator excretion, lymphocyte and macrophage infiltration, and matrix metalloprotease activation, play an essential part in the aetiology of tendinopathies, other inflammatory events, such as the infiltration of lymphocytes and macrophages, are also implicated. Recently, several studies have evaluated the potential of using PEMFs to treat tendon problems. Girolamo *et al*. investigated the biotic effects of varying PEMF intensity, duration, and found exposure time that recurrent use of PEMFs at 1.5 mT had the greatest positive benefits.[33] Results from past research demonstrated that PEMF treatment on human tendons promotes IL-10 and VEGF synthesis, which can enhance the repair of the tendon, as well as collagen type I mobility.[33] PEMFs have a negligible effect on the proliferation of human tendon stem cells, but they do elevate the expression of stem cell markers, according to a controlled laboratory research. As a result, the use of PEMFs may represent a new perspective in tendon regeneration.

However, research on the use of PEMFs in the treatment of lateral epicondylitis, FM, degenerative disc disease, musculoskeletal chronic pain, and nerve regeneration has revealed that they are effective.[29,31] According to the results of various studies; the role of PEMFs in various musculoskeletal conditions will keep on rising with time and practice.

Limitations and undesirable effects: Though the usage of PEMFs illustrates adequate therapeutic outcomes in various musculoskeletal disorders, however, some matters persist unsolved. Primarily, many investigations have concentrated on the basic mechanism of action on which PEMFs work, however extensive mechanisms on which PEMFs works are still to be discovered.[15] However, there is no standard set of clinical principles or a rationale for parameter selection. Several experimental and clinical experiments used a variety of PEMF parameters, such as frequency, intensity, and exposure time.[15] The optimal dose parameters of PEMF treatment for certain illnesses are yet unknown. The precise PEMF settings should be

determined for each specific illness, much like the dosages of medications. Additionally, many research use small sample sizes, which remains a problem.[34] To determine the impact of PEMFs on patients suffering from a variety of musculoskeletal disorders, high-quality, large-scale randomised controlled trials with long-term follow-ups are necessary. When used properly, PEMFs are frequently recognised as a safe and useful therapeutic option for patients and research subjects.[35] It is yet unclear if PEMFs cause any health concerns to operators and patients during typical clinical use. Exposure to electromagnetic fields may be harmful to the brain, peripheral nervous system, cardiovascular system, cognitive function, and vestibular function, according to a variety of safety exposure recommendations and expert opinions from recognized organizations.[36]Additionally, past research found a link between utility workers' exposure to electromagnetic fields and their risk of depression, suicide, and neurodegenerative disorders.[36] Recent research has shown that deoxyribonucleic acid (DNA) damage from prolonged contact with artificial electromagnetic fields may contribute to an increased risk of cancer, syncope, seizures, and other neurological and reproductive disorders as well as cancer.[16]

CONCLUSION

PEMFs have been found to be beneficial in the literature and illustrate lots of possibilities to become a separate or complementary management method for treating various musculoskeletal conditions, due to their high efficacy and minimum risk factors. Substantially many studies have explored the primary consequences of PEMF stimulation on cellular and subcellular levels in different musculoskeletal conditions, revealing a molecular base for the clinical use of PEMFs. The absence of a precise dose and frequency in the application of the modality, however, is one of the important constraints that vary in various studies for different body areas in specific musculoskeletal issues. It would be useful to leverage the expertise of biologists and doctors to conduct out clinical and laboratory experiments with standard operating procedures and excellent quality methods in order to fully understand the effect of PEMFs in treating various musculoskeletal disorders. As a result, well-designed, high-quality research are essential before widespread clinical application to understand the underlying mechanisms, standardise therapy parameters, and evolve the most favourable protocol for application in varied musculoskeletal disorders. In brief, with appropriate patient selection, and suitable indications, in the future PEMFs might play a significant role in managing specific musculoskeletal conditions.

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