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A retrospective study of clinical and radiological outcomes of fracture nonunion and delayed union treated by low frequency pulse-electromagnetic field therapy (PEMF).

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Abstract

Background: Pulsed electromagnetic field therapy (PEMF) has gained popularity because of its non-invasive nature. The present study measured the clinical and radiological outcomes of pre and post-PEMF therapy to establish its efficacy in preventing surgical procedures for early diagnosed delayed union and nonunion fractures.

Methods: A retrospective study with a self control design was conducted, involving 122 patients with signs of delayed union or nonunion fractures. The patients under went PEMF as per their treatment plans and were followed up for 2–4 years. Radiological and clinical assessment was done during each visit.

Results: A high proportion of patients (81.14%) displayed radiological union after the final follow-up. A significant reduction in pain was reported at rest (Wilcoxon Signed Ranked Test (W): 5.306, $p<0.05$) and after moderate activity after PEMF therapy (W: 9.745, $p<0.05$). Further, 83.6% of patients exhibited full functional status after 6 months of therapy.

Conclusion: PEMF stimulation is an effective and affordable non-invasive method for addressing delayed union patients. Early treatment with PEMF therapy can significantly reduce morbidity, offering pain relief, improved functional status, and improved quality of life.

Keywords: Delayed Union, Electromagnetic, Osteogenesis, Nonunion, Pulsed Electromagnetic Field Therapy (PEMF), Radiological

Introduction

Regardless of improvements in fracture management, delayed union and nonunion remain resolute impediments following surgical fixation of long-bone fractures, which can adversely affect the wellbeing of patients and cause considerable morbidity. Approximately 5-10% of all fractures show compromised healing (1,2). Delayed union and nonunion refer to a slowed or absent progression of callus formation and osseous healing in a fracture from three to six months and beyond six months, respectively (3). There are multiple etiologies for a fracture going into nonunion, including fracture complexity, amount of soft tissue injury, infection at fracture, initial strategy for fracture fixation, and use of anticoagulants, steroids, anti-inflammatory drugs, or radiotherapy. Patient-related factors for nonunion include nutritional deficiencies (mainly calcium and vitamins C and D), addictions like smoking, tobacco chewing, and alcoholism, which impair the normal bone healing process (4). Non-invasive treatment options for delayed union and nonunion include pulsed electromagnetic field (PEMF), low-intensity pulsed ultrasound (LIPUS), and extracorporeal shock wave therapy (5). PEMF, introduced in the 1970s as a supportive tool for fracture healing, has gained popularity among medical practitioners because of its non-invasive characteristics and satisfactory results (6,7). Studies suggest that PEMF involves numerous characteristics of fracture healing —promoting mineralization and angiogenesis, increasing DNA synthesis, and modifying the cellular calcium content in osteoblasts (8–12). The present study aimed to measure the clinical and radiological outcomes of pre- and post- PEMF therapy to establish its efficacy in preventing surgical procedures for early diagnosed delayed union.

Materials And Methods

A retrospective study was performed involving 122 patients taking PEMF treatment for the management of fracture delayed union or fracture nonunion. The patients were followed up and assessed for around 2 years from March 2015 to March 2019. The patients were skeletally mature, with long and non-long bone fractures. The patients with a non-traumatic fracture, active osteomyelitis, fracture gap of >10 mm, pregnancy, and pacemaker were excluded from the study. The patient inclusion and exclusion criteria are summarised:

Inclusion Criteria

1. Patients aged between 18-67 years
2. Patients with fracture delayed union or fracture non-union
3. Patients who underwent PEMF therapy

Exclusion Criteria

1. Patients with a non-traumatic fracture
2. Patients with active osteomyelitis
3. Patients with fracture gap of >10 mm
4. Patients with pregnancy
5. Patients with pacemaker

Materials

A PEMF bone growth stimulator was used that was designed explicitly for the body area requiring physical and field strength treatment. The instrument was used at a 3-mA electric current with 20 Hz frequency and was applied daily once for 30-45 min.

Method

The study used a self-control design where the pre PEMF status of the patients was compared with their post PEMF status. Initial surgical or conservative intervention in all the patients was carried out at the institute. The patients were then called for regular follow-up and advised on an appropriate individualized PEMF treatment plan. The clinical and radiological evaluation was recorded at the time of enrolment, at PEMF initiation, and 6 weeks, 12 weeks, 6 months, and 2 years following PEMF.

The patient's demographic data, including their comorbidity, long-term medications, and addictions, was noted on initial evaluation. Furthermore, fracture site, fracture pattern, either long bone fracture (LBF) or non-long bone fracture (NLBF), Gustilo Anderson classification, type of fixation, duration of immobilization after fixation were noted. The time between injury and initiation of PEMF therapy was also recorded. All the patients underwent daily PEMF therapy for 2–4 months.

The radiological characteristic appropriate scoring system was used to calculate the union score for each visit— Radiographic Union Score for tibial (RUST) for tibia (13), Radiographic Union Score for Hip (RUSH) for the femur (14), and Radius Union Scoring System (RUSS) for radius (15). The region's fractures other than these were measured by cortical bridging present in anteroposterior and lateral X-rays. Union was considered positive when the bridging callus was observed for 3 out of 4 radiographic cortices on X-rays; patients demonstrated full weight-bearing status and confirmed no pain at rest or moderate activity. Treatment was terminated once the union was achieved, or no progress to union was seen for 3 consecutive months.

Clinical evaluation included fracture pain, weight-bearing status, and functional assessment during each visit. The patients' pain intensity was described using a Visual Analog Scale (VAS), ranging from 1 to 10, with 1 indicating no pain and 10 indicating maximum pain at the fracture site. VAS score was noted at rest and after activity. During the initial 3 months, a fracture site ultrasound assessed the bridging callus formation for radiological evaluation (16). Moreover, X-rays in anteroposterior and lateral views were obtained and saved digitally at each visit. X-rays were reviewed to study peculiarities, including the presence of bridging callus across Anterior/posterior/medial/ lateral surface, a continuation of the cancellous bony bridge at fracture, and the presence or absence of fracture line. After a total assessment, outcomes were interpreted based on radiological union measured using an appropriate scoring system, patients' functional status at final follow-up, and pain at the fracture site.

Results

The study retrospectively involved 132 patients with long bone and non-long bone fractures. Two patients were excluded from the study as they reported being diagnosed with osteopetrosis and osteogenesis imperfecta. Four patients lost to follow-up after a few weeks of initial treatment; hence were not included in the study. The other 4 patients were excluded as they opted for alternate treatment option. Finally, 122 patients(78males and 44 females) met the required criteria (Figure 1).

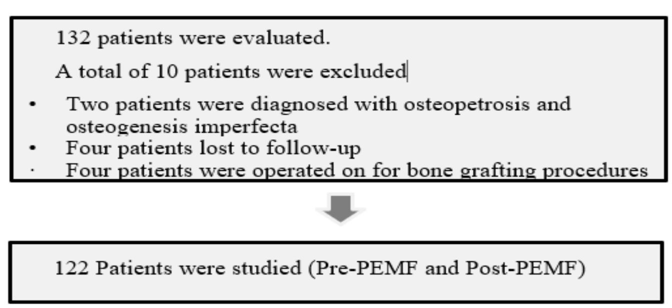

Figure 1. Patient Flow Chart

As summarised in Table 2, the patient age ranged from 18–67yearswith a median age of38 years. Of 122 patients, 106 had long bone fractures, and 16 had nonlong bone fractures. Long bone fractures included humerus, radius ulna, femur, tibia, and fibula fractures (upper limb: 30 and lower limb: 76). Nonlong bone fractures included scaphoid, metacarpal, and metatarsal fractures.

Table 1: Characteristics of patients evaluated in the study.

Characteristics	Patients (N=122)
Median Age	38 years
Gender	
Male	78
Female	44
Type of Fracture	
Long Bone	106
Non long bone	16
Patients with delayed union	97
Patients with non-union	25

Ninety-seven patients-initiated treatment in the delayed union phase, while 25 had established nonunions.

Moreover, 14 patients were conservatively treated by appropriate immobilization, and 108 (98 out of 106 long bone and 9 out of 16 nonlong bone fractures) patients were surgically operated by Closed reduction and internal.

Ninety-seven patients-initiated treatment in the delayed union phase, while 25 had established nonunion. Moreover, 14 patients were conservatively treated by appropriate immobilization, and 108 (98 out of 106 long bone and 9 out of 16 nonlong bone fractures) patients were surgically operated by Closed reduction and internal fixations (CRIF), Open reduction, and internal fixation (ORIF), or External Fixator. The mean duration of PEMF therapy to the patients was 12 weeks (8–16 weeks). Removal of the implant was done in 8 patients.

Failure of treatment was seen in 6 patients in whom future surgical intervention had to be done.

Radiological Outcomes

The study revealed that 99 patients (81.14%) with delayed union and nonunion showed union, confirmed by the roentgenogram findings at the fracture site. Figure 2 captures X-ray images demonstrating the efficacy of PEMF therapy in radius fracture of one of the patients.

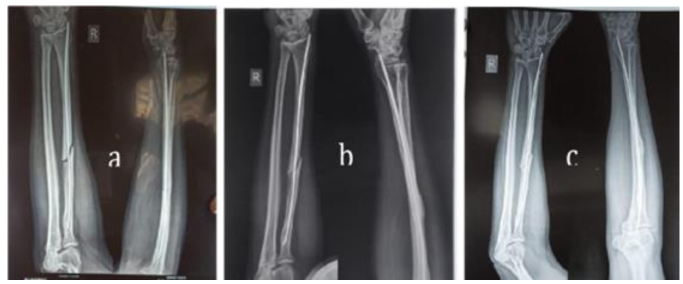

Figure 2: X-ray images of right-side shaft radius fracture under PEMF therapy: a. At the initiation of PEMF therapy; b. 3months post-PEMF; c. 6months post-PEMF

The radiological outcomes measured as RUST scores for 40 patients with tibia fractures are captured in Table 3. There was a significant increase in number of patients showing higher RUST score, 6 months after PEMF therapy ($p<0.05$).

Table 2: Comparison of RUST scores

RUST scores	No of patients At the initiation of therapy	No of patients 6 months post-therapy
4-6	30	2
7-9	8	5
10-12	2	33

* Chi-square – 52.649 (p<0.05)

of 6 patients with femur fractures with the delayed union, 5 patients exhibited a final RUSH score between 25–30 after 6 months. Out of 6 patients with radius fractures, 5 patients showed a RUSS score of 6–8 after 6 months. All other patients had an overall 81.14% union rate.

While ultimate success of therapy was union on roentgenogram, USG served as a prognostic evaluation tool in the early period. We studied ultrasonography images to demonstrate callus formation at fracture site after PEMF therapy till 3 months. After which ultimate union was based on roentgenographic finding only.

Clinical Outcomes

Weight-bearing status of the 76 patients having lower limb fractures, 70 patients had either antalgic gait or were using walker support at the initiation of treatment. After 3 months of therapy, 69 patients started partial weight-bearing with a walker or 4 stick. On 6 months follow-up after therapy, 62 patients could bear weight entirely. Similarly, 40 out of 46 patients with upper limbs and NLB fracture gained routine functional activity at 6 months post-therapy. Conclusively, 102 out of122 patients had complete functional status post 6 months of therapy. Figure 3: Captures full functional activity for one of the patients at the end of therapy.

Figure 3. Clinical images showing full functional activity at the end of therapy, in the patient with shaft radius fracture. The average VAS score at rest at the initiation of treatment was 1.25±2.32, which lowered to 0.23±0.86 after 3 months of PEMF therapy (Table 4). A significant difference of 1.03 at treatment initiation and 3 months post-therapy was noted at rest pain (W= 5.306, p<0.05) (Wilcoxon Signed Ranked Test).

Likewise, the average VAS score after activity was 3.69 ± 2.34, which reduced to 0.34±1.11after 12 weeks.

So average difference between scores at treatment initiation and 3 months post-therapy was 3.34 (W = 9.745, p <0.05). Out of 122 patients, 103 reported no pain at the fracture site 6 months post-PEMF therapy.

Table 3: VAS scores observed at day 1 and after 12 weeks of PEMF treatment.

VAS score at rest*		VAS score after activity*	
Average VAS Score at Day 1 (control)	Average VAS Score after 12 weeks of PEMF	Average VAS Score at Day 1 (control)	Average VAS Score after 12 weeks of PEMF
1.25±2.32	0.18±0.83	3.69±2.34	0.34±1.11

*N=122

Success parameters

The PEMF therapy showed a good success rate as mentioned below.

- 99/122 (81.14%) showed full union in radiological outcomes.
- 102/122 (83.6%) demonstrated full functional recovery.
- 103/122(84.5%) patients confirmed no pain after 6 months of PEMF.

Discussion

The present study analyzed the benefit of PEMF therapy in fracture delayed union and nonunion by measuring the radiological and clinical outcomes of the therapy. The radiological characteristic appropriate scoring system (RUST, RUSS, and RUSH) used to calculate the union at the fracture site by employing roentgenogram which showed promising results. Ultrasonography, a low-cost and non-invasive procedure with no associated ionizing radiation, served as a better modality for evaluating callus formation as early as 3 weeks. It was used as a prognosticating tool in the early phase where callus formation was seen after starting the therapy which led to appearance of mineralised callus on x-rays. Figure 4 shows an illustration of how the callus formation is seen on fracture site USG and how it consolidates further forming a bony bridge across the fracture site. However, success in our study based on union was assessed from x-ray scores only.

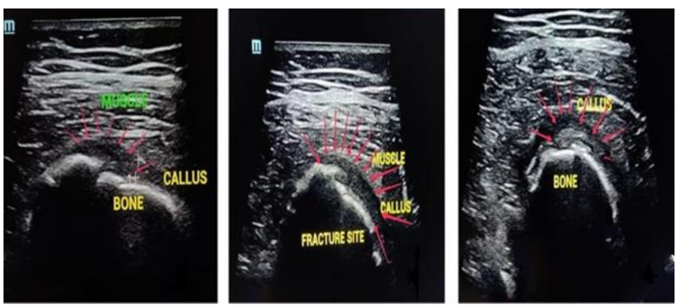

Figure 4: Ultrasonography showing callus formation at fracture site after PEMF therapy: a. 3 months post-PEMF; b. 6 months post-PEMF; c. 2 years post-PEMF.

The study revealed that 81.14%of the patients with delayed union and nonunion showed union, making it evident that PEMF therapy effectively treats these fractures. This might be attributed to the tendency of PEMF to promote osteogenesis by simulating the natural endogenous streaming potentials in bone (17). The similar physiological frequencies (8–30 Hz) and the voltage difference across the cell membrane caused by natural muscle contractions and induced electric fields activate L-type voltage-gated transcellular calcium channels. The activated calcium channels increase calcium influx into the intracellular space, leading to early stages of proliferation and differentiation of human bone marrow stem cells, ultimately resulting in osteogenesis (18,19).

Moreover, PEMF increases the cell membrane density of Adenosine receptors A2A and A3 on chondrocytes, synoviocytes, and osteoblast, which modulates pro and anti-inflammatory processes and helps osteogenesis at the fracture site (20). Additionally, PEMF stimulates the Wnt/β-catenin signaling pathway, thus improving the trabecular microarchitecture of bone (21). Likewise, PEMF activates osteogenic differentiation of osteoblastic cells through the Wnt signaling pathway and upregulates members of transforming growth factor (TGF)-β and bone morphogenetic proteins (BMPs) 2 and 4 gene family, resulting in increased synthesis of corresponding proteins (22).PEMF can also mark fracture site angiogenesis by increasing fibroblast growth factor -2 (23). Figure 5 depicts the different mechanism of actions of PEMF therapy at cellular level.

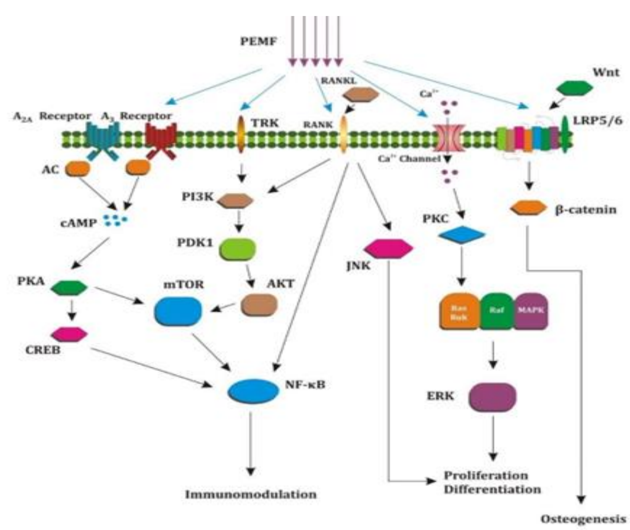

Figure 5: Mechanism of actions of PEMF therapy at

cellular level. Adapted from Hu H, et al.. Biomedicine and Pharmacotherapy. 2020;131:110767.

Our results agreed with previous studies that demonstrated the efficacy of PEMF treatment on delayed unions. A prospective clinical study demonstrated fracture union success in 77.3% of patients with non-infected tibial union abnormalities (5). Another follow-up study in 1382 patients examining the in-practice results of PEMF therapy in managing nonunion fractures reported an overall success rate of 89.6% (24).

The pain relief was measured using the VAS score, a reliable self-reporting measure of pain intensity (25). Results show a significant decline in the VAS Score of patients post PEMF therapy compared to pre-PEMF status, both at rest and after activity. These results support the radiological outcomes of the study. Overall, 81.14%of patients showed radiological union after final follow-up, along with 83.6% patients achieving full functional status and 84.5% patients reporting no pain at the fracture site.

Conclusion

PEMF stimulation is an effective implant compatible, non-invasive, and affordable method for addressing delayed union patients. The early application of PEMF treatment can reduce significant morbidity, provide pain relief, and improve functional status, thereby improving one’s quality of life. This technique accelerates the process of bony union and hence can be used as an effective alternative invasive procedure such as bone grafting.

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