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Original Article

Effectiveness of pulsed electromagnetic field therapy in the management of complex regional pain syndrome type 1: A randomized-controlled trial

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ABSTRACT

Objectives: This study aims to investigate whether pulsed electromagnetic field (PEMF) therapy in addition to a conventional rehabilitation program is effective on pain and functioning in patients with type 1 complex regional pain syndrome (CRPS-1) of the hand.

Patients and methods: Between March 2013 and January 2015, a total of 32 patients (16 males, 16 females; mean age: 50.1±13.1 years; range, 25 to 75 years) were included. The patients were randomly allocated into two groups. The control group (n=16) received a conventional rehabilitation program consisting of physical modalities, exercises, and occupational therapy, whereas the PEMF group (n=16) received additional PEMF (8 Hz, 3.2 mT) to the affected hand. The primary outcome measure was pain intensity using the Numeric Rating Scale (NRS). Secondary outcome measures were grip and pinch strength, hand edema, hand dexterity, and hand activities. All patients received 20 therapy sessions (five sessions/week, four weeks in total) and were evaluated before and after the therapy and at the first-month follow-up.

Results: Both groups showed significant improvements in primary and secondary outcomes ($p<0.05$) after the therapy and at follow-up. When the groups were compared in terms of improvements in assessment parameters, no statistically significant difference was found between the two groups in any of the outcomes ($p>0.05$).

Conclusion: The PEMF in addition to conventional rehabilitation program did not provide additional benefit for pain and hand functions in CRPS-1. Future studies using different application parameters such as frequency, intensity, duration, and route may provide a better understanding of the role of PEMF in CRPS-1 treatment.

Keywords: Complex regional pain syndrome, physical therapy, pulsed electromagnetic field, rehabilitation, ultrasonography.

Complex regional pain syndrome (CRPS) is characterized by persistent regional pain that is disproportionate in time or degree to the usual course of any known trauma or other lesions.[1] The pain is regional, not in a specific nerve territory or dermatome, and usually has a distal predominance of abnormal sensory, motor, vasomotor, sudomotor, trophic findings.[1] The syndrome is divided into two different types CRPS-1 and CRPS-2 according to the absence or presence of peripheral nerve damage, respectively.[2] The pathophysiology remains unclear and appears to be multifactorial. Exaggerated inflammation to an inciting stimulus leads to increased nociceptor activation and subsequent allodynia and hyperalgesia.[3] Increased release of inflammatory mediators can lead to overactivation of sympathetic activity which results in autonomic abnormalities such as changes in skin color, edema, osteopenia.[4,5] Motor

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dysfunction can be added to the clinical findings. All these findings result in debilitating consequences in functioning, interfering with the quality of life (QoL). Any treatment that can control the inflammatory microenvironment is quite important for decreasing pain and improving functioning and QoL in patients with CRPS-1. Management of CRPS-1 requires an interdisciplinary multimodal approach, including both pharmacological and non-pharmacological treatment. Rehabilitation is the cornerstone and consists of physical and occupational therapy combined with appropriate exercises.[1]

Pulsed electromagnetic field (PEMF) therapy is an innovative physical therapy modality that involves the application of electromagnetic energy to tissues. Its effect on biological tissues is due to its anti-edema and analgesic effects through regulating gene expression by influencing voltage-gated ion channels.[6] It also modulates the inflammatory process through the regulation of pro-and anti-inflammatory cytokine secretion during different stages of the inflammation.[7] The effectiveness of PEMF in the control of pain and edema after surgery/injury,[8] fracture and ligament healing,[9] and nerve regeneration[10] have been demonstrated. However, further studies demonstrating the efficacy of PEMF in patients with CRPS-1 whose main findings are also pain, edema, and soft tissue inflammation are limited.

In the present study, we hypothesized that PEMF in addition to conventional rehabilitation program might provide extra benefit on pain and functioning of the hand in patients with CRPS-1. In the literature, there is only one study investigating the effects of PEMF on pain and edema in patients with CRPS-1;[11] however, no study has assessed its effects on functional outcomes such as grip strength, hand dexterity, or hand activities to our knowledge. In the present study, we aimed to investigate whether PEMF prescribed in addition to conventional rehabilitation program had an effect on pain and the functioning of the hand in patients with CRPS-1.

PATIENTS AND METHODS

This single-blind, randomized-controlled study was conducted at Ankara University Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Hand outpatient clinic between March 2013 and January 2015. Adult patients who were referred to our clinic with pain, swelling, and edema in hands were screened. Patients who fulfilled the Budapest diagnostic criteria for CRPS-1 according to the International Association for the Study of Pain[12] were included in the study. Exclusion criteria were as follows: having acute deep arterial/vein thrombosis in the upper extremity, history of arterial/venous injuries or repair operations, being at the post-acute rehabilitation phase of tendon repair, diagnosed as CRPS-2 according to the Budapest diagnostic criteria, having comorbid conditions (decompensated heart failure, chronic renal failure, malignancy) that may impair the individual's functioning and health-related QoL, and presence of comorbid diseases affecting the hand functions (rheumatoid arthritis, psoriatic arthritis, or other inflammatory disease involving the hand). Patients with metal implants in the hand-wrist region were also excluded. Of 55 patients evaluated for inclusion, 20 patients were excluded as they did not meet the inclusion criteria, and three patients declined to participate. A total of 32 patients (16 males, 16 females; mean age: 50.1±13.1 years; range, 25 to 75 years) were recruited and 16 were randomized to each group. All participants in each group completed the study. The study flow chart is shown in Figure 1. A written informed consent was obtained from each patient. The study protocol was approved by the Ethics Committee of the Ankara University Faculty of Medicine (Date/no: 09.12.2013/18-701-13). The study was conducted in accordance with principles of the Declaration of Helsinki. Reporting of this trial was conducted according to the Consolidated Standards of Reporting Trials (CONSORT) checklist.[13]

Interventions

Eligible participants were randomly allocated to receive either a conventional rehabilitation program (control group) or PEMF plus a conventional rehabilitation program (PEMF group). Conventional rehabilitation program, including physical modalities, exercises, and occupational therapy was administered to both groups for four weeks, five days a week, 75-95 min/day. The PEMF group received PEMF therapy in addition to the conventional rehabilitation program. The PEMF therapy was applied to the affected hand and wrist at 3.2 mT and a frequency of 8 Hz, for 20-min/day with the magnetotherapy device named PMT Quattro Pro.

The content of the conventional rehabilitation program is described below:

Contrast bath therapy: The involved extremity was repeatedly immersed in hot water (nearly 38°C) for

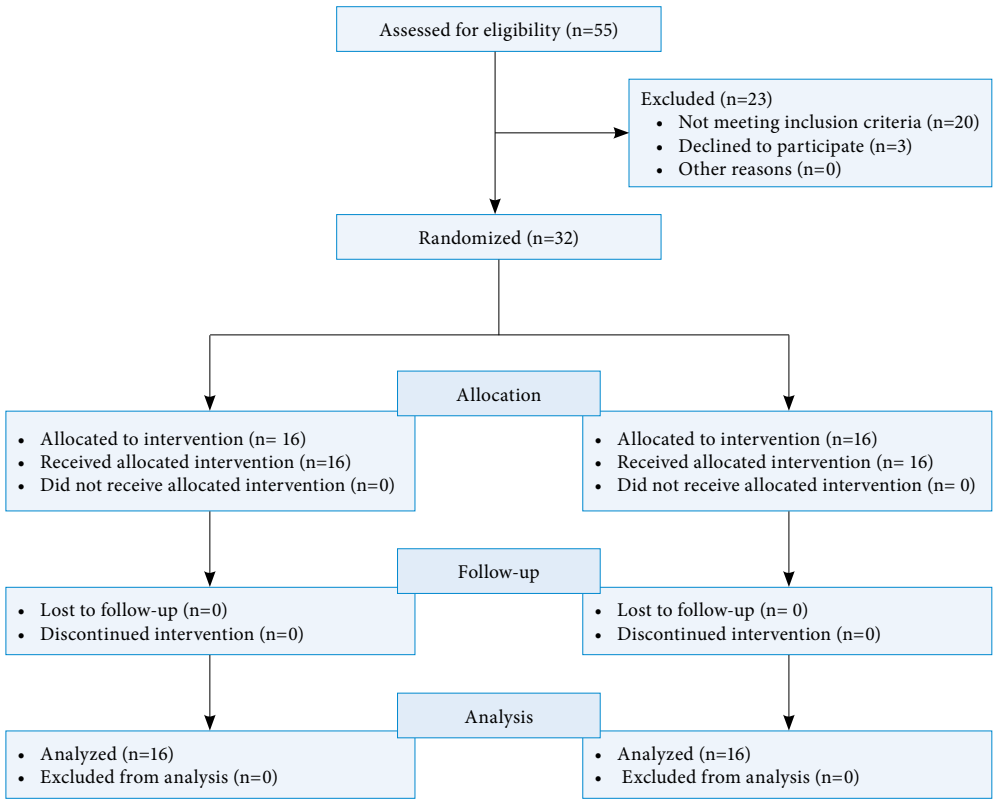

Figure 1. Study flow chart.

4 min, followed by cold water (nearly 15°C) for 1 min for an overall duration of 15 min.[14]

Hot pack: Hot pack was applied to the soft tissues of the wrist and hand for 20 min before exercise.

TENS: Conventional TENS (Intelect Advanced Brand; USA) was applied for 20 min over the hand and wrist by two electrodes with a frequency of 100 Hz, pulse duration of 40 microsec, and amplitude that creates a feeling of numbness and tingling that does not create muscle contraction.[14]

Desensitization: Gradual increasing tactile stimulus was applied to the hypersensitive hand area for 5-10 minutes starting with the softer and progressing to the more irritating material (plain, coarse, rough, cotton, paper towels). Retrograde massage was applied to reduce edema and sensitivity.

Exercise Program: First, active-assisted and/or active joint range of motion exercises, slow flexibility, and isometric strengthening exercises were performed. Then, stress loading exercises and gentle stretching at the pain limit were initiated. Within the scope of loading exercises, activities such as brushing and carrying bags to improve lateral grip were performed. At the third step, isotonic strengthening exercises (bow, ball, dough squeezing exercises) and different comprehension activities to improve coordination and hand skills were administered. Also, occupational therapy was applied to improve their activities of daily living such as dressing, feeding, personal hygiene, house- and/or work-related activities. The daily exercise program lasted for 20-40 min according to the patients' condition.

All patients were prescribed 90 to 120 mg/day of oral acemetacin for anti-inflammatory effect for four weeks without any difference between the two groups in this respect.

Outcome measures

The primary outcome measure was pain severity which was evaluated with the Numeric Rating Scale (NRS) where scores ranged from 0 (no pain) to 10 (most severe pain). Secondary outcome measures were grip and pinch strength, hand edema, hand dexterity, and hand activities. Grip strength was measured with a Jamar dynamometer by setting at the third handle space, with the shoulders adducted, elbows flexed

at 90°, forearm neutral positioned, and wrist 0-30° dorsiflexed.[15] Pinch strength was measured with a pinch meter by placing the pad between the thumb and the lateral surface of the index finger as lateral pinch. All measurements were done with the maximum effort of the patient and the best score among the three measurements was recorded.

Hand edema was assessed by measuring the hand circumference with a tape at the wrist (radius and styloid process of ulna) and the third metacarpophalangeal joint (MCP) level. Ultrasonographic subcutaneous tissue thickness was measured separately at the level of the affected dorsum of the wrist and the third MCP joint by placing the probe transverse to the ulnar and radial styloid process and perpendicular to the metacarpus respectively (Toshiba Aplio 80; Japan). Each measurement was done three times and the average was recorded.

Hand dexterity was evaluated by Moberg Pick-Up Test (MPUT). This test includes holding and picking up 12 small metallic objects on the table (paperclips, safety pin, ring, coins, wing/small nuts, key, screws) and placing them in the box.[16] The participants were instructed to do this task with the injured hands and the time, until they put all the materials in the box was recorded.

The activity limitations of the hand were evaluated by Duruöz Hand Index (DHI) which consists of 18 items related to hand activities of daily living, including ability in the kitchen, dressing, personal hygiene, office tasks, and other activities. Each item is scored between 0 and 5, and the overall score is 0 and 90, higher score indicating more hand-related disability.[17]

Demographic and clinical characteristics of participants such as age, sex, etiology, history, and duration of immobilization, and operation were recorded.

Sample size

The sample size was calculated based on the primary outcome variable, that is, ΔPain (change) score (0-10 NRS). Group sample sizes of 16 and 16 achieve 81% power to detect a difference of 2.5 in terms of ΔPain[18] between the null hypothesis that both group means are 4.5 and the alternative hypothesis that the mean of group 2 is 2.0 with estimated group standard deviations of 2.5 and 2.5 and with a significance level of 0.05 using a two-sided Mann-Whitney U test.

Randomization and allocation concealment

All participants were randomly allocated to two groups: PEMF and control group. A block randomization with a size of two was used by a computer-generated random allocation schedule (Random Allocation Software). Concealment was provided by closed envelopes which were numbered and opened in a sequence-based computed generated random numbers table.

Blinding

The study was conducted as a single-blind trial. The physician performing the clinical assessments and the radiologist performing the ultrasonography were blinded to the treatment allocation. The administration of study interventions was performed by the hand therapists in the hand rehabilitation unit of the department.

Statistical analysis

The R programming language version 4.1.1 was used for statistical analyses. Descriptive data were expressed in mean ± standard deviation (SD), median (min-max) or number and frequency. The Student t-test and Mann-Whitney U test were used to evaluate difference between two groups for continuous variables and non-normally distributed variables, respectively. Differences between the two groups for categorical variables were analyzed using the chi-square test. The Friedman two-way analysis of variance by ranks was used to test difference among three repeated measurements. When the p-value from the Friedman test was statistically significant, the Dunn test was used to identify which measurement differed from others. The Bonferroni correction was used to control type I error rate. A p value of <0.05 was considered statistically significant.

RESULTS

The mean ages of the control (n=16) and PEMF groups (n=16) were 49.5±14.2 and 50.6±12.3 years, respectively. The CRPS-1 etiology was mainly distal radius fracture in both groups. More than half of the patients in both groups had a history of operation, and almost 90% had a history of immobilization. All patients were in the acute phase of their CRPS-1. No significant difference with respect to demographic and clinical variables was observed between the two groups at baseline (Table 1).

TABLE 1
Demographic and clinical characteristics of patients

	PEMF group (n=16)					Control group (n=16)					
	n	%	Mean±SD	Median	IQR	n	%	Mean±SD	Median	IQR	*p*
Age (year)			49.5±14.2	53.5	24.5			50.6±12.3	52.0	17.5	0.812[a]
Sex											
Female	8.0	50.0				8.0	50.0				1.000[c]
Dominant hand (right)		100.0		16.0			93.8		15.0		1.000[c]
Etiology											0.558[c]
Distal radius fracture	10.0	62.5				10.0	62.5				
Other upper extremity fracture	2.0	12.5				2.0	12.5				
Rotator cuff lesion	1.0	6.25				1.0	6.25				
Tendon repair	3.0	18.75				1.0	6.25				
Other	0.0	0.0				2.0	12.5				
History of immobilization		93.8		15.0			87.5		14.0		1.000
Duration of immobilization (day)			31.7±8.3	35.0	14.0			33.4±16.3	36.0	25.8	0.745[a]
History of operation		62.5		10.0			56.3		9.0		0.719[c]
Time since injury (day)			60.0±31.5	49.0	46.3			58.8±31.8	55.0	33.23	0.910[b]

PEMF: Pulsed electromagnetic field; SD: Standard deviation; IQR: Interquartile range; a: Student t-test; b: Mann-Whitney U test; c: Chi-square test.

There was no significant difference between the two groups in terms of baseline primary and secondary outcome measures (Table 2). There was a statistically significant improvement in both groups after the treatment and at the first month follow-up compared to baseline in terms of pain, grip and pinch strength, hand circumference measured at the third MCP joint level, ultrasonographic subcutaneous thickness, dexterity, and hand activities (Table 3). When the two groups were compared in terms of change from baseline to both time points, none of the outcome measures in the PEMF group showed superiority over the control group (Table 4).

DISCUSSION

The results of our study showed that PEMF administered in addition to the routine rehabilitation program for CRPS-1 of the hand did not provide

TABLE 2
Baseline outcome measures

	PEMF group			Control group			
Parameter	Mean±SD	Median	IQR	Mean±SD	Median	IQR	*p*
Pain (NRS)	5.9±2.1	5.0	1.0	6.1±1.4	6.0	2.0	0.244
Grip strength (kg)	3.9±5.4	1.5	5.5	5.8±5.2	5.0	9.5	0.231
Pinch strength (kg)	1.8±2.1	1.5	2.5	2.7±1.7	2.5	1.0	0.139
Edema							
Hand circumference (cm)							
Wrist	17.7±2.8	17.5	2.3	17.9±1.6	17.8	1.8	0.909
MCP 3rd	19.1±4.5	19.8	3.2	19.7±1.3	19.8	2.4	0.940
Subcutaneous thickness (mm)							
Wrist	10.8±2.5	10.7	5.1	10.9±2.2	12	3.8	0.806
MCP 3rd	5.8±2.9	4.6	2.7	5.0±1.6	4.9	1.4	0.692
MPUT (s)	80.6±73.0	45.5	144.0	45.3±44.9	33.0	33.0	0.180
DHI (0-90)	59.8±26.0	67.0	37.8	57.1±18.5	53.0	32.0	0.462

PEMF: Pulsed electromagnetic field; SD: Standard deviation; IQR: Interquartile range; NRS: Numeric rating scale; MCP: Metacarpophalangeal joint; MPUT: Moberg pick up test; DHI: Duruöz Hand Index; Mann-Whitney U test.

TABLE 3
Comparison of outcome measures within each group by therapy

Parameter	PEMF group				Control group			
	Mean±SD	Median	IQR	*p*	Mean±SD	Median	IQR	*p*
NRS				<0.001				<0.001
Before	5.9±2.1	5.0[a]	1.0		6.1±1.4	6.0[b]	2.0	
After	2.0±1.8	2.0	3.0		3.1±2.1	3.0	3.7	
First month	1.0±1.2	0.5	2.0		1.5±2.0	0.0	3.0	
Grip strength				<0.001				<0.001
Before	3.9±5.4	1.5[c]	5.5		5.8±5.2	5.0[d]	9.5	
After	10.5±7.9	7.8	9.7		11.7±8.0	13.5	11.5	
First month	12.2±8.9	9.0	11.3		14.2±8.6	15.5	11.9	
Pinch strength				<0.001				<0.001
Before	1.8±2.1	1.5[e]	2.5		2.7±1.7	2.5[a]	1.0	
After	4.9±2.0	4.3	3.3		4.7±2.1	5.0	2.6	
First month	6.4±3.4	5.8	5.4		5.7±2.3	6.0	8.0	
Hand circumference (cm)				0.114				
Wrist								0.255
Before	17.7±2.8	17.5	2.3		17.9±1.6	17.8	1.8	
After	17.8±2.2	17	2.5		17.7±1.4	17.5	2.4	
First month	17.6±1.9	17	2.8		17.5±1.3	17.5	1.9	
MCP 3rd				0.012				<0.001
Before	19.1±4.5	19.8[f]	3.2		19.7±1.3	19.8[g]	2.4	
After	19.6±1.5	19.7	2.7		19.3±1.3	19.3	2.2	
First month	19.1±1.9	19.0	2.4		19.0±1.2	19.0	2.0	
Subcutaneous thickness (mm)				0.004				
Wrist								<0.001
Before	10.8±2.5	10.7	5.1		10.9±2.2	12.0	3.8	
After	9.1±2.0	9.3	1.9		9.8±2.0	10.0	3.3	
First month	7.9±1.5	8.1[h]	1.4		8.3±1.8	8.4[i]	2.5	
MCP 3rd (mm)				0.005				0.003
Before	5.8±2.9	4.6[j]	2.6		5.0±1.6	4.9[k]	1.4	
After	4.6±0.9	4.6	1.2		4.3±0.8	4.3	1.4	
First month	4.2±1.0	4.1	0.9		4.2±1.3	3.7	1.6	
MPUT (s)				<0.001				<0.001
Before	80.6±73.0	45.5[l]	144.0		45.3±44.9	33.0[d]	33.0	
After	24.8±16.8	19.4	10.6		24.8±14.4	21.5	12.5	
First month	18.2±6.7	16.6	6.0		21.4±13.3	17.0	9.8	
DHI				<0.001				<0.001
Before	59.8±26.0	67.0[m]	37.7		57.1±18.5	53.0[e]	32.0	
After	22.2±17.3	17.5	34.2		29.7±23.8	27.5	35.5	
First month	13.1±15.0	6.0	23.0		18.1±14.6	18.5	19.0	

PEMF: Pulsed electromagnetic field ; SD: Standard deviation; IQR: Interquartile range; NRS: Numeric rating scale; MCP: Metacarpophalangeal joint; MPUT: Moberg pick up test; DHI: Duruöz Hand Index; Friedman's two-way analysis, Dunn test; a: Different from both after (p=0.001) and first month (p<0.001); b: Different from both after (p=0.018) and first month (p<0.001); c: Different from both after (p=0.006) and first month (p<0.001); d: Different from both after (p=0.040) and first month (p<0.001); e: Different from both after (p=0.011) and first month (p<0.001); f: Different from first month (p=0.018); g: different from first month (p=0.001); h: Different from both before (p=0.006) and after (p=0.040); i: Different from before (p<0.001); j: Different from first month (p=0.004); k: Different from first month (p=0.002); l: Different from both after (p=0.004) and first month (p<0.001); m: Different from both after (p=0.008) and first month (p<0.001).

an additional benefit in terms of pain, edema, grip and pinch strength, dexterity, and hand activities. All outcome parameters improved by therapy in both groups; however, the PEMF group showed no superiority over the control group.

The anticipated effect of PEMF on CRPS-1 is expected to be through its analgesic, anti-edema, and anti-inflammatory effect. The experimental and preclinical evidence support that PEMF alleviates pain and post-traumatic edema[19,20] by regulating nitric oxide (NO) cascades. Pulsed electromagnetic field therapy can be configured to modulate calcium-binding kinetics to calmodulin. This binding activates NO synthase which results in an increase in NO and leads to an anti-inflammatory response

TABLE 4
Intergroup comparison of outcome measures (Change score (Δ) by therapy

	PEMF group Change score (Δ)			Control group Change score (Δ)			
	Mean±SD	Median	IQR	Mean±SD	Median	IQR	*p*
Pain							
Before-after	3.9±2.5	-3.5	3.0	-3.0±2.4	-4.0	3.7	0.619
Before-first month	-4.8±2.7	-4	2.7	-4.6±2.2	-5.0	4.5	0.879
After-first month	-0.9±2.0	-0.5	3.0	-1.6±2.4	-2.0	2.0	0.250
Grip strength							
Before-after	6.7±5.0	6.5	6.0	6.0±5.0	6.5	7.0	0.691
Before-first month	8.3±6.7	6.5	9.2	8.5±6.3	7.0	11.7	0.865
After-first month	1.7±4.7	2.0	6.1	2.5±3.8	2.0	2.8	0.776
Pinch strength							
Before-after	3.1±2.3	2.5	7.0	2.1±1.0	2.5	2.0	0.362
Before-first month	4.6±3.5	3.0	4.0	3.1±1.9	2.7	2.0	0.306
After-first month	1.5±2.3	0.7	2.4	1.0±1.5	1.0	2.0	0.569
Hand circumference							
Wrist	-0.2±2.7	-0.5	2.0	-0.2±0.9	-0.3	0.9	0.551
Before-after	-0.0±3.0	-0.5	1.0	-0.3±1.4	-0.6	1.5	0.529
Before-first month	-0.2±1.3	-0.3	2.0	-0.2±0.9	-0.3	0.5	0.893
After-first month							
MCP 3rd							
Before-after	-0.5±4.1	-.0.3	0.9	-0.3±0.6	-0.5	2.0	0.596
Before-first month	-0.0±3.8	-1.0	1.4	-0.7±0.5	-0.5	0.5	0.536
After-first month	-0.5±1.4	-0.8	1.9	-0.3±0.5	-0.5	0.9	0.357
Subcutaneous thickness							
Wrist	-1.6±2.5	-1.0	5.2	-1.1±1.3	-1.1	1.2	0.910
Before-after	-2.8±2.8	-2.3	5.4	-2.6±2.6	-2.0	3.3	0.985
Before-first month	-2.8±2.8	-2.3	5.4	-2.6±2.5	-2.0	3.3	0.558
After-first month							
MCP 3rd							
Before-after	-1.2±2.5	-0.6	1.1	-0.7±1.6	-0.3	0.7	0.533
Before-first month	-1.5±2.6	-0.6	1.6	-0.8±1.9	-0.5	1.4	0.597
After-first month	-0.4±0.7	-0.2	1.2	-0.2±1.7	-0.2	0.4	0.909
MPUT							
Before-after	-55.8±68.0	-17.4	106.0	-20.5±35.7	-9.5	16.7	0.090
Before-first month	-62.4±23.0	-22.9	140.0	-23.9±35.2	-15.0	25.3	0.163
After-first month	-6.6±14.0	-2.6	7.2	-3.4±5.1	-2.0	3.7	0.762
DHI							
Before-after	-37.6±23.8	-40.5	35.5	-27.3±18.6	-30.5	25.0	0.228
Before-first month	-46.6±29.7	-55.0	52	-38.9±20.4	-39.5	31.2	0.283
After-first month	-9.1±11.4	-8.0	13.2	-11.6±15.0	-11.0	18.7	0.664

PEMF: Pulsed electromagnetic field therapy; SD: Standard deviation; IQR: Interquartile range; MCP: Metacarpophalangeal joint; MPUT: Moberg pick up test; DHI: Duruöz Hand Index; Mann-Whitney U test.

via increased blood and lymph flow.[20] Nitric oxide also regulates guanosine 3',5'-cyclic monophosphate (cGMP) production and the relevant cascade increases angiogenesis, tissue repair, and remodeling.[20] Also, it has been reported that PEMF can influence C fibers and sensory neurons by changing the membrane potential leading to analgesia.[21] Several studies designed to assess PEMF effects on pain and edema in a carrageenan rat hind paw model have reported 100% inhibition of pain and 50% inhibition of edema.[22] In human studies, it has been shown that PEMF accelerates post-surgical pain relief and swelling following breast augmentation surgery.[23] In the light of these findings, we expected that the decrease in pain and edema in patients receiving PEMF treatment would be higher

in the control group; however, this was not the case in our study.

Different results were observed in clinical studies evaluating the effects of PEMF on musculoskeletal pain.[24] In some studies evaluating its effects in knee osteoarthritis by using sham-PEMF as control, PEMF was found to be effective in resolving pain compared to the control group.[25,26] However, a recent meta-analysis reported that PEMF did not have an advantage in treating pain and stiffness in knee osteoarthritis.[27] It was also shown that if other physical therapies, such as TENS, ultrasound, and hot pack were applied in addition to PEMF, no additive beneficial effect was observed on pain relief.[28,29] Our results are similar to the literature in this context that other treatment modalities (e.g., hot pack, TENS, exercise) that could affect pain and edema may have shaded the effect of PEMF in our study.

In the literature, there is only one study investigating the effects of PEMF in CRPS-1 in terms of pain and hand edema by comparing PEMF + calcitonin + exercise to calcitonin + exercise.[11] The authors concluded that PEMF, in addition to calcitonin and exercise, did not provide additional benefit on pain and edema. Our results on pain and edema are compatible with the aforementioned study; however, they did not evaluate hand functions. To the best of our knowledge, our study is the first to evaluate the effect of PEMF on hand functions in patients with CRPS-1. Although PEMF showed significant positive effects on hand functioning in terms of grip/pinch strength, hand dexterity, and hand activities, it was not superior to the control group.

Until now, a few studies in different diagnostic groups have evaluated the effects of PEMF on both pain and hand functions. In hand osteoarthritis, PEMF was found to be superior to sham-PEMF in improving pain, stiffness, and hand activities.[30] In another study, early addition of PEMF therapy during cast immobilization after distal radius fractures had beneficial effects on pain and hand/arm functioning.[31] When the clinical studies on PEMF are reviewed, it is notable that the dose, intensity, and frequency regimens of PEMF applications are quite heterogeneous.[31] Considering that the effect of PEMF depends on the characteristics of the applied magnetic field and tissue properties, the lack of a consensus on the standard application parameters (frequency, intensity, pulse characteristics) for various disorders makes it difficult to compare the clinical studies in the literature.[27-32] Our dose regimen had a frequency of 8 Hz and an intensity of 3.2 mT, as suggested by the manufacturer. It is usually accepted that PEMF applied for pain relief has a frequency below 100 Hz and magnetic flux density ranges between 0.1 and 30 mT.[24] However, the exact dosage schedule is not clear. In the study evaluating the effects of PEMF on CRPS-1, 100 gauss (10 mT) intensity and 50 Hz frequency, which slightly differed from our regimen was used.[11] Future studies would be helpful to determine the optimal frequency, intensity, and duration of PEMF therapy in the course of CRPS-1.

Central mechanisms may also play a role in the pathogenesis of CRPS-1, besides nociceptive pain.[33] It is reported that PEMF may improve pain in fibromyalgia where the development and maintenance of central pain hypersensitivity has a role in the pathophysiology.[34,35] This improvement is attributed to an alteration in pain perception, an increase in the pain threshold, and inhibition of inflammatory edema.[35] However, in the aforementioned study, PEMF was administered to the whole body, which differed from the application route in our study. Therefore, the application route in addition to the dose regimen may also be important for the effectiveness of PEMF on painful conditions having central neuroplastic changes, such as CRPS-1.

There are some strengths and limitations of this study. The main strength is that functioning of the hand in terms of grip and pinch strength, hand dexterity, and daily hand activities were also evaluated as outcome measures in addition to pain and edema. Another strength is that hand edema was evaluated by both ultrasonographic and conventional circumferential measurements. Hand edema is usually assessed by either the water displacement method with a volumetric meter or circumferential measuring.[36,37] While no change was observed in the wrist circumference after the treatment, detecting a significant decrease in the sonographic subcutaneous thickness in the same region suggests that ultrasonographic measurement may be a more useful method for the assessment of edema of the hand. Further studies are needed to investigate the sensitivity of this method.

The main limitation of the study is that sham-PEMF was not applied to the control group. Since there is only one PEMF device in our clinic and it is heavily used in various conditions, sham-PEMF could not be used in order not to occupy the device with inactive therapy. Second, other additional treatment modalities

did not allow us to evaluate the effectiveness of PEMF vigorously. However, it would be unethical to plan a study that includes only PEMF *vs.* sham-PEMF as a therapeutic modality without administering other conventional therapy modalities in acute CRPS-1 where early treatment is essential to avoid poor outcomes and irreversible disability.[4]

In conclusion, PEMF applied in addition to the conventional rehabilitation program did not provide an additional benefit in the treatment of CRPS-1 in terms of pain, edema, grip and pinch strength, dexterity, and hand activities. Future studies using different application parameters (frequency, intensity, duration), as well as using sham-PEMF as a control group may provide a better understanding of the role of PEMF in CRPS-1 treatment.

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