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REVIEW

Electromagnetic Field Therapy: A Rehabilitative Perspective in the Management of Musculoskeletal Pain – A Systematic Review

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Abstract: Electromagnetic fields (EMFs) provide a non-invasive, safe, and easy method to treat pain with respect to musculoskeletal diseases. The purpose of this systematic review was to describe the use of electromagnetic therapy in the rehabilitation field by investigating the efficacy in acute and chronic pain in the musculoskeletal disorders. A database search was conducted using the following resources: PubMed, Cochrane, PEDro, SCOPUS, and WoS. The following MESH terms were used: [Electromagnetic field AND/OR Rehabilitation], [Electromagnetic field AND/OR Pain], [Pulsed Magnetic field AND/OR Rehabilitation] and [Pulsed Magnetic field AND/OR Pain], [Pulsed Electromagnetic field AND/OR Rehabilitation] and [Pulsed Electromagnetic field AND/OR Pain], per the guidelines of the PRISMA statement. Articles published between January 1, 2009 and December 31, 2018 were included as assessment of musculoskeletal pain conditions, randomized clinical trial including crossover and prospective design studies, full English text available, population age > 18 years; instead were excluded neurological randomized clinical trials, transcranial magnetic stimulation application, neuropathic pain, animal/in vitro studies, and articles without English abstract or English full text. Three independent investigators (AMC, NG, and LP) retrieved all the information. Twenty-one RTC (N=21) were considered for the inclusion and exclusion criteria. The results showed as pulsed magnetic fields at low intensity and frequency (from 1 Hz up to 100 Hz) are commonly used with efficacy in resolving musculoskeletal pain. EMFs therapy is a well tolerated, effective with no negative side effects, which can be integrated with rehabilitation for the treatment of chronic and acute pain in musculoskeletal diseases, but further studies are needed to examine the use of more standardized protocols.

Keywords: pulsed electromagnetic fields, rehabilitation, physical medicine, magnetic therapy, pain

Introduction

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.[1]

Musculoskeletal diseases comprise several conditions that are characterized by pain and limitations in mobility, dexterity and functional ability, reducing people's ability to work and participate in social roles with associated impacts on mental wellbeing. The most common and disabling musculoskeletal diseases are osteoarthritis, back and neck pain, tendinopathy, fibromyalgia and myofascial pain. Among the clinically relevant pain conditions treated in rehabilitation, pain with respect to

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the musculoskeletal system is most frequent and has a major impact on people's quality of life.[2] Chronic low back pain (CLBP) has a significant impact on musculoskeletal pain with a prevalence increases linearly from the third decade of life on, until the 60 years of age, being more prevalent in women.[3–5]

The use of electromagnetic fields (EMFs) and in particular of the magneto-therapy has had a notable increase in the last decade in rehabilitation treatment and provides a non-invasive, safe, and easy method to directly treat the site of injury, the source of pain and inflammation, and other types of disease.[6–8] Magnetic field therapy was applied to promote bone healing, treat osteoarthritis and inflammatory diseases of the musculoskeletal system, alleviate pain, enhance healing of ulcers and reduce spasticity[9] and, also, extremely low frequency (ELF) magnetic fields in the pico tesla and milli tesla ranges are aimed at improving neurotransmission and correcting local immune pathology, respectively.[10] An analgesic and anti-nociceptive efficacy, similar to the opioid analgesic effect respect of pulsed electromagnetic field (PEMF) is reported by scientist literature but the clear biological and biochemical mechanism of the effect of magnetic therapy on pain remains unknown.[11] Also, some studies have shown that short-term exposure to electromagnetic fields influences several inflammatory cellular and neurological processes, such as patterns of cortical activation and inhibition and the activity of various neurotransmitters.[12]

Above all, the magneto-therapy recognizes an important use in the field of both chronic and acute pain in musculoskeletal disorders using protocols with specific intensities and frequencies: magnetic fields applied in magneto-therapy for pain, in line with the criteria generally accepted in physical medicine, have the frequency below 100 Hz and magnetic flux density in the range between 0.1 mT and 30 mT.[13] When used alone, the PEMF seems to have a good effect in reducing the pain intensity in low back patients, independently of the low-back pain condition. However, when added to other standard therapies (such as standard physiotherapy or analgesic therapy) seems to do not add any additional effect.[14–16]

Furthermore, the efficacy of magnetotherapy compared to some forms of chronic pain such as fibromyalgia (FM) still remains debated.[17,18] Moreover, also in neurological pathology, ELF magnetic field was revealed to induce a significant improvement in functional and mental status in brain stroke patients and clinical parameters had positive correlation with the level of enzymatic antioxidant protection.[7]

Thus, surely, the efficacy of magneto-therapy is related to the type of electromagnetic fields used and in the rehabilitation field there are today very different treatment protocols: certainly, in the last decade, the use of ELF magnetic fields has been on its increase. Innovative and still experimental approaches concern, for example, the use of cyclotronic resonance (CR), a kind of specific ultra-weak pulsed electromagnetic fields, in low back pain:[19] the theory of the CR considered that the endogenous electromagnetic forces generated by the activity of the cells of the human body are of infinitely low intensity. Then, the effect of ELF fields, however, does not depend directly on their very low frequency and intensity, but more on the fact that if they are structured with a correct form, intensity, frequency and sequence, they synchronize with the frequencies of the biological system that disturb, triggering an effect. CR involves electrically charged ions and molecules that oscillate at specific harmonic frequencies, within a continuous feedback system with the cells themselves. This mechanism of interaction between ELF magnetic fields, the earth's magnetic field, and living organisms has been called Cyclotron Resonance (CR) by Liboff.[20]

Despite the widespread use of magneto-therapy in rehabilitation field it is difficult to find standardized treatment protocols especially when aimed at treating musculoskeletal pain, be it chronic or acute.

Musculoskeletal pain often develops over time resulting in more hyperalgesia and larger pain areas. Peripheral and spreading sensitizations are probably important mechanisms for the translation of acute local pain to chronic musculoskeletal pain conditions. The transition from acute to chronic musculoskeletal pain is not well understood.[21] Acute pain is a direct outcome of the noxious event and is reasonably classified as a symptom of underlying tissue damage or disease. Chronic pain may not be directly related to their initial injury or disease condition, but rather to secondary changes including some that occur in the pain detection system itself. Thus, the mechanisms underlying chronic or persistent pain may be quite different from acute pain.[22] The distinction between acute and chronic pain is sometimes determined by an arbitrary interval of time since onset; the two most commonly used markers being 3 months and 6 months since onset, though some theorists and researchers have placed the transition from acute to chronic pain at 12 months.

Thus, the aim of this systematic review was to investigate the scientific evidence over the last decade with

respect to the use of electromagnetic therapy in the rehabilitation field by investigating the efficacy in acute and chronic pain in the musculoskeletal disorders.

Materials and Methods

Search Strategy

A systematic review of the literature was performed using the following search engines: PubMed, Cochrane, PEDro, SCOPUS and Web of Science (WoS), per the guidelines of the PRISMA statement.[23] In order to perform the search, the following algorithm was developed, based on the PICO acronym,[24] to evaluate the effects of electromagnetic fields respect the reduction of pain (acute and chronic) as the primary outcome in musculoskeletal diseases.

These keywords were used (MESH terms): [Electromagnetic field AND/OR Rehabilitation], [Electromagnetic field AND/OR Pain], [Pulsed Magnetic field AND/OR Rehabilitation] and [Pulsed Magnetic field AND/OR Pain], [Pulsed Electromagnetic field AND/OR Rehabilitation] and [Pulsed Electromagnetic field AND/OR Pain].

Reference lists of most relevant studies were scanned for additional citations; country, author, affiliated institutions, and enrollment periods were extracted and reviewed to identify and exclude duplicate publications from the same cohort.

Study Criteria and Selection

Inclusion criteria were: (1) articles published between January 1, 2009, and December 31, 2018, (2) assessment of musculoskeletal pain conditions, (3) randomized clinical trial including crossover and prospective design studies, (4) full English text available, (5) population age > 18 years.

Exclusion criteria were (i) neurological randomized clinical trials, (ii) transcranial magnetic stimulation application, (iii) neuropathic pain (iv) animal/in vitro studies, and (v) articles without English abstract or English full text.

Data Extraction

Three independent investigators (AMC, NG, and LP) retrieved all the information. The main outcome of interest was the quantification of intensity of pain in musculoskeletal diseases. The secondary outcomes were the recovery of function and quality of life with respect to the disability in musculoskeletal diseases. Thus, after the application of the eligibility criteria and the included studies were determined, the studies were analyzed based on sample demographics, study's aim, statement of conflict of interest, study duration and follow-up (period of time and percentage), EMF devices used, evaluation time, intervention protocol, and outcome parameters assessed (clinical and functional).

Methodology Quality and Risk of Bias Assessment

Establish a quality assessment of each study using the PEDro scale (Physiotherapy Evidence Database, 1999): this scale has shown good reliability for scoring RCTs.[25] The PEDro scale consists of 11 items related to scientific rigor. The scale's items 2 to 11 contribute to internal validity, and the study is given 1 point for each of these items that are met. The first item relates to external validity and is not included in the final score. The quality assessment was performed independently by the three reviewers, and any disagreement was discussed until consensus was reached. We considered trials with scores of ≥6 as having high quality and trials with scores of ≤5 as having low quality.

The assessment of the risk of bias was done independently by the same three authors (AMC, NG, and LP), and was assessed according to the Cochrane Collaboration's domain-based evaluation framework.[26] Main domains were assessed in the following sequence: 1) selection bias (randomized sequence generation and allocation concealment); 2) performance bias (blinding of participants and personnel); 3) detection bias (blinding of outcome assessment); 4) attrition bias (incomplete outcome data, eg, due to dropouts); 5) reporting bias (selective reporting); 6) other sources of bias. The scores for each bias domain and the final score of risk of systematic bias were graded as low, high, or unclear risk.

Results

The PRISMA flow-diagram showing the selection of studies is given in Figure 1.

Twenty-one articles (N=21) satisfied the inclusion criteria and were considered in the review: 8 articles treated pain of the knee for osteoarthritis (OA),[27–34] 2 articles treated Shoulder Impingement Syndrome (SIS),[35,36] 5 articles treated spine pain, of which 1 study about chronic mechanical neck pain (CNP),[37] and 4 studies were about low back pain (LBP),[14,16,38,39] 3 articles treated Fibromyalgia Syndrome

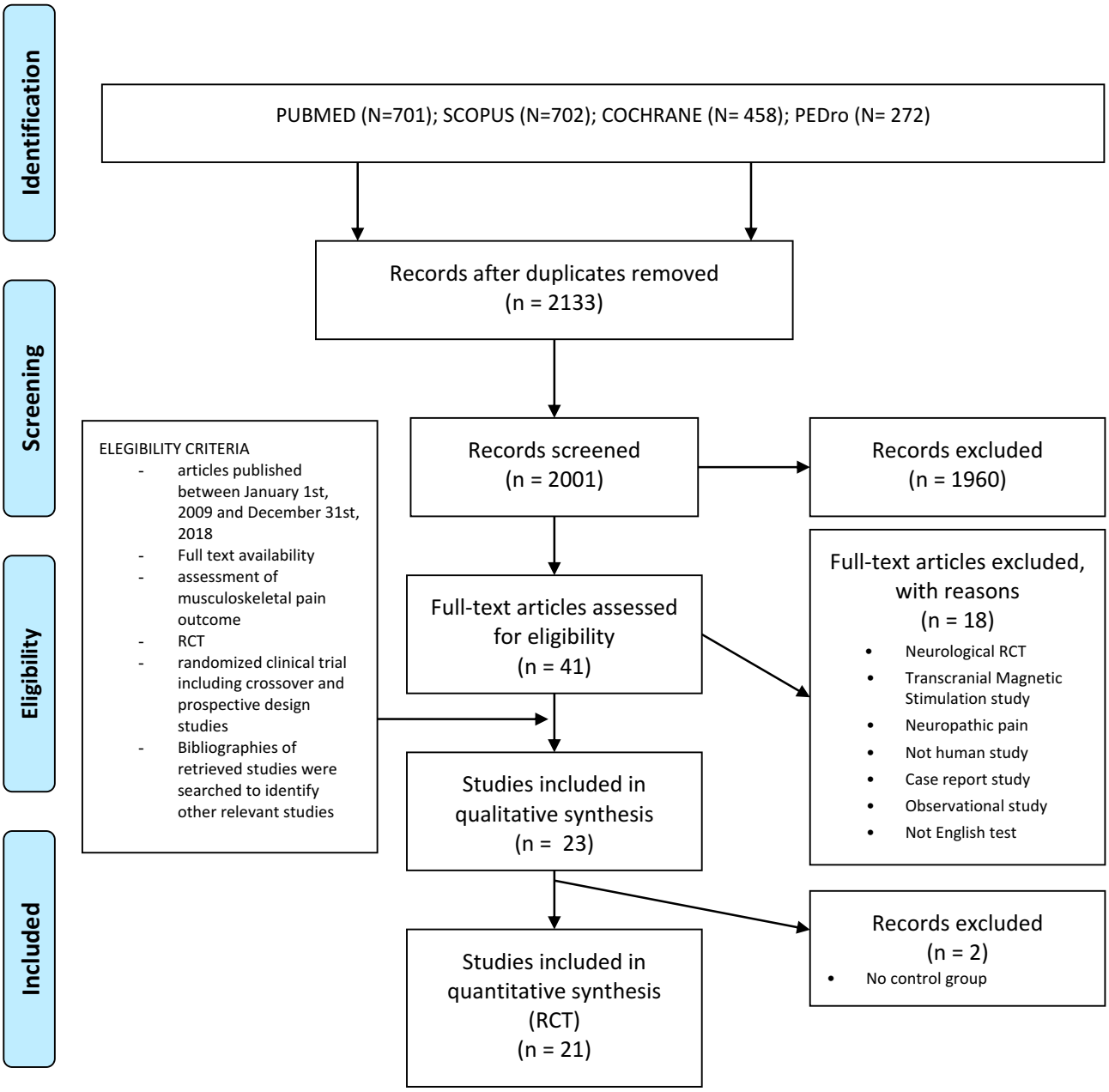

Figure 1 Flowchart of the included studies in the review according to the PRISMA 2009 guidelines.

(FM),[17,18,40] then 1 article showed the effect of EMF respect of patellofemoral pain (PFP),[41] 1 article treated Plantar fasciitis (PF),[42] and 1 article treated Hand osteoarthritis (HO).[43] The PEDro score values and other characteristics of the included studies were shown in Table 1: the methodological quality of the twenty-one included articles, according to the PEDro scale, with averaged between 4/10 and 10/10, averaged 7.57/10 and only 4 studies have a PEDro score ≤5 indicating low quality. Furthermore, in Table 2 were specified type of magnetic field and parameters used in the individual studies included in our review. In detail, 15 studies have used Pulsed Electromagnetic Field (PEMF),[14,16,17,27-29,31,33-35,37,38,40,41,43] one study has used Extremely low-frequency magnetic field (ELF-MF),[18] 2 studies have used Pulsed Radiofrequency Electromagnetic Field (PRFE),[30,42] one study has used Electromagnetic transduction therapy (EMTT),[36] and another one has used Pulsed electromagnetic energy (PEME),[39] and Gökşen et al[32] have used Magnetic resonance treatment. Lastly, the risk of bias was considered High for 4 studies,[31,33,34,38] Unclear for 2 studies[14,43] and Low for fifteen studies (see Table 3). The most frequent source of potential bias was the performance

Table 1 PEDro Score Values and Other Characteristics of the Included Studies

Author (Year Published) [Ref.]	Diagnosis	N (M/F) Mean± SD Age (Years)	Study	N TG (Mean± SD Age) CG (Mean± SD Age)	Intervention	Outcome Parameters	Evaluation Time	Conclusions	PEDro Score
Ay et al (2009)[31]	OA	N=55 (15/40)	RCT	TG=30 (58,9±8,8) CG=25 (57,7±6,5)	TG: PEMF, hot pack, TENS and exercise program; CG: sham-PEMF, hot pack, TENS and exercise program	VAS: pain; Likert pain scale: pain; LI: function	T0: baseline T1: 3 weeks	VAS: TG=CG LI: TG=CG	6/10
Bagnato et al (2016)[30]	OA	N=60 (43/17) y=67,7 ±10,9	RCT	TG=30 (68,6±11,9) CG=30 (66,9±10)	TG: PRFE CG: placebo	VAS: pain; WOMAC: function, pain, disability SF-36: QoL	T0: baseline T1: 1 month	VAS, WOMAC: TG>CG SF-36:TG=CG	9/10
Brook et al (2012)[42]	PF	N=70 (18/52)	RCT	TG=42 (53,2±14,7) CG=28 (49,7±15,2)	TG: PRFE CG: sham-PRFE	VAS: pain	T0: baseline T1: 1 day T2: 2 days T3: 3 days T4: after 4 days T5: 5 days T6: 6 days T7: 7 days	VAS: TG>CG	8/10
Dündar et al (2016)[34]	OA	N=40 (11/29)	RCT	TG= 20 (56.8 ±14.5) CG= 20 (57.6 ±13.8)	TG: hot pack, ultrasound, TENS, isometric knee exercise and PEMF CG: hot pack, ultrasound, TENS, isometric knee exercise and sham-PEMF	VAS: pain WOMAC: function, pain Ultrasonographic effusion of the knee Serum YKL-40 a novel biomarker of osteoarthritis	T0: before treatment T1: 1 month	WOMAC: TG=CG VAS: TG=CG	5/10
Galace de Freitas et al (2014)[35]	SIS	N=56 (20/36) y=50,5 ±8,9	RCT	TG=26 (50,1±8,2) CG=30 (50,8±9,6)	TG: PEMF and exercises; CG: placebo and exercises	VAS: pain; CMS: function; UCLA: function; Handheld dynamometry: strength	T0: baseline T1: 3 weeks T2: 9 weeks T3: 3 months	VAS, UCLA, CMS, Dynamometry: TG>CG	9/10

(*Continued*)

Table 1 (Continued).

Author (Year Published) [Ref.]	Diagnosis	N (M/F) Mean± SD Age (Years)	Study	N TG (Mean± SD Age) CG (Mean± SD Age)	Intervention	Outcome Parameters	Evaluation Time	Conclusions	PEDro Score
Giombini et al (2013)[37]	CNP	N=45 (14/31)	Prospective RCT	TG=15 (44.0±9.6) CG1=15 (40.5±7.4) CG2=15 (43.0±9.4)	TG: PEMF CG1: neck balance system CG2: neck balance system with negligible balancing	VAS: pain NDI: disability NPDS: QoL	T0: baseline; T1: end of 8 week T2: after follow-up 12 weeks	VAS: CG1>TG>CG2 NDI: CG1>TG>CG2 NPDS: CG1> CG2 > TG	8/10
Gökşen et al (2016)[32]	OA	N=97	RCT	TG=49 (54.02 ±6.79) CG= 48 (54.92 ±7.5)	TG: magnetic treatment CG: sham-magnetic treatment	VAS: pain WOMAC: function, pain, disability SF-36: QoL	T0: baseline; T1: end of 2 week T2: follow-up after 12 weeks	VAS, WOMAC, SF-36: TG=CG	9/10
Kanat et al (2013)[43]	HO	N= 50	RCT	TG= 25 (64±2.6) CG= 25 (62±2.4)	TG: PEMF + exercise CG: sham PEMF + exercise	Likert scale: pain at rest, pain at motion, joint stiffness SF-36: QoL Duruöz: function AUSCAN: pain, stiffness and disability HG and PG: strength	T0: baseline T1: after treatment T3: follow-up one month after treatment	SF-36: TG>CG Duruöz: TG>CG AUSCAN: TG>CG HG: TG=CG, PG: TG=CG	7/10
Klüter et al (2018)[36]	SIS	N=86 (41/45)	RCT	TG=44 (50,21±8,5) CG=42 (49,21±7,3)	TG: EMTT/ESWT; CG: sham-EMTT /ESWT	VAS: pain; CMS: function	T0: baseline T1: 6 weeks T2: 12 weeks T3: 24 weeks	VAS: TG>CG CMS: TG>CG	9/10
Krammer et al (2015)[39]	LBP	N=40 (20/20)	RCT	TG=20 (35,7) CG=20 (30,2)	TG: PEMF and physiotherapy treatment; CG: sham -PEMF and physiotherapy treatment	NRS: pain ODI: disability PSFS: function	T0: baseline T1: 1 week T2: 4 weeks	NRS, ODI, PSFS: TG=CG	8/10
Külcü et al (2009)[33]	OA	N=45	RCT	TG =15 (65.8 ±10.3) TG1 = 15 (63.1±13.6) CG =15 (62.0±6.0)	TG: PEMF TG1: US CG: control	VAS: pain WOMAC: function, pain, stiffness	T0: baseline T1: end of three weeks	VAS, WOMAC: TG, TG1>CG	5/10

Multanen et al (2018)[17]	FM	N=108 y=47±10	RCT (cross-over)	TG=57 CG=51	TC: PEMF CG: sham-PEMF	VAS: pain, stiffness FIQ: QoL and disability	T0: baseline T1: end of 12 week T2: after washout 16 week T3: end of 28 week	VAS: TG= CG FIQ: TG= CG	10/10
Nelson et al (2013)[27]	OA	N=34	RCT	TG=15 (55.5±2.5) CG= 19 (58.4±2.5)	TG: PEMF CG: Sham-PEMF	VAS: pain	T0: baseline T1: end of day 3 T2: end of day 14 T3: end of day 29 T4: end of day 42	VAS: TG>CG	10/10
Oke et al (2013)[38]	BP	N=16 (9/7) y= 26.00 ± 8.62	RCT	TG=8 CG=8	TG: PEMF + FANS CG: FANS	NRS: pain Functional Activity Scale	T0: baseline T1: end of treatment (after 5–9 days)	NRS, Functional Activity Scale: TG>CG	4/10
Omar et al (2012)[14]	LBP (Unilateral Radicular Pain)	N=40	RCT	TG=20 (37.5±8.5) CG= 20 (40.0±8.3)	TG: PEMF CG: sham-PEMF	VAS: pain OSW: disability SSEPs: nerve conduction	T0: baseline T1: end of 8 week T2: after follow-up 12 weeks	VAS, OSW, SSEPs: TG>CG	5/10
Özgüçlü et al (2010)[28]	OA	N=40	RCT	TG=20 (60.55±7.7) CG= 20 (62.15 ±8.1)	TG: isometric knee+ hot pack+ therapeutic ultrasound+ PEMF exercise CG: isometric knee+ hot pack+ therapeutic ultrasound+ sham PEMF	VAS: pain WOMAC: function, pain, disability	T0: baseline T1: end of 2 week	VAS, WOMAC: TG=CG	6/10
Paolucci et al (2016)[18]	FM	N=37 (F) y=50.33 ±10.94	RCT (cross-over)	TG1=16 (49.5 ±9.38) TG2 =17 (51.12±12.47)	TG1: ELF/sham-ELF TG2: sham-ELF/ELF	VAS: pain FAS: pain, fatigue and quality of sleep FIQ: QoL and disability HAQ: QoL and daily activities	T0: baseline; T1: end of 1 treatment cycle T2: beginning of 2 treatment cycle (after a 1-month washout) T3: end of 2 treatment cycle T4: follow-up after 1 month	VAS, FAS: T1:TG1<TG2 T3:TG2<TG1 FIQ, HAQ: T1: TG1<TG2 T3: TG2<TG1	8/10

(*Continued*)

Table 1 (Continued).

Author (Year Published) [Ref.]	Diagnosis	N (M/F) Mean± SD Age (Years)	Study	N TG (Mean± SD Age) CG (Mean± SD Age)	Intervention	Outcome Parameters	Evaluation Time	Conclusions	PEDro Score
Park et al (2014)[16]	LM (Lumbar Myalgia)	N= 38 (11/27) y=31.95 ±12.30	RCT	TG=19 (33.00 ±11.06) CG=19 (30.89 ±13.66)	TG: PEMF CG: placebo	VAS: pain ODI: function SF-36, EQ-5D: QoL BDI: depression RMDQ: disability	T0: baseline T1: after the 6th treatment T2: follow-up after 1 week	VAS, RMDQ: TG>CG ODI, SF-36, EQ-5D, BDI: TG=CG	9/10
Servodio Iammarrone et al (2016)[41]	PFP	N= 31 y=22.5	RCT	TG: 13 (21±7) CG: 17 (24±8)	TG: PEMF, Home exercise program CG: Home exercise program	VAS: pain VISA: pain, functional mobility, QoL	T0: baseline T1: 2 months T2: 6 months T3: 12 months	VISA T1: TG=CG VISA T2-T3: TG>CG VAS: TG<CG	6/10
Sutbeyaz et al (2009)[40]	FM	N=56	RCT	TG=28 (42.96 ±9.57) CG=28 (40.89 ±6.88)	TG: PEMF CG: sham-PEMF	VAS: pain FIQ: QoL and disability BDI: depression SF-36: QoL PGART: patient's global assessment	T0: baseline; T1: end of 3week T2: follow-up after 12 weeks	VAS: TG>CG FIQ, SF-36: TG >CG BDI: CG>TG PGART: debated	8/10
Wuschech et al (2015)[29]	OA	N=57	RCT	TG=44 (63.4±12.1) CG=13 (55.5±10.8)	TG: PEMF CG: placebo	VAS: pain WOMAC: function, pain, disability	T0: baseline; T1: end of 18 days	VAS, WOMAC: TG>CG	9/10

Abbreviations: OA, knee osteoarthritis; PF, plantar fasciitis; SIS, shoulder impingement syndrome; CNP, chronic mechanical neck pain; HO, hand osteoarthritis; LBP, low back pain; FM, fibromyalgia; BP, back pain; LM, lumbar myalgia; PFP, patellofemoral pain; PPS, parallel prospective study; RCT, randomized controlled trial; TG, treatment group; CG, control group; PEMF, pulsed electromagnetic fields; PRFE, pulsed radiofrequency electromagnetic field therapy; US, therapeutic ultrasound; EMTT/ESWT, electromagnetic transduction therapy/extracorporeal shockwave therapy; VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; RMS, Roles–Maudsley score; CMS, Constant–Murley scale; UCLA, University of California/Los Angeles; SF-36, Short-Form 36 version-2; NDI, Neck Disability Index; NRS, numerical rating scale; LI, Lequesne algofunctional index; FIQ, Fibromyalgia Impact Questionnaire; FAS, Fibromyalgia Assessment Scale; HAQ, Health Assessment Questionnaire; BDI, Beck Depression Inventory; PGART, patient's global assessment rating scale; NPDS, neck pain disability scale; OSW, Modified Oswestry Low Back Pain Disability Questionnaire; SSEPs, somatosensory evoked potentials; FSS, Fatigue Severity Scale; MFIS, Modified Fatigue Impact Scale; ROM, range of motion; VISA, Victorian Institute of Sport Assessment score; AUSCAN, Australian Canadian Osteoarthritis Hand Index; Duruöz, Duruöz Hand Index; HG, hand grip; PG, pinch grip; ODI, Oswestry Disability Index; EQ-5D, EuroQol-5 Dimension; RMDQ, Roland-Morris Disability Questionnaire; PSFS, Patient Specific Functional Scale.

Table 2 Type of Magnetic Field and Parameters Used in the Included Studies

Author (Year Published) [Ref.]	Diagnosis	Magnetic Fields	Frequency	Intensity	Duty Cycle	Wave's Type	Duration of Singles Session/Number of Sessions of Treatment Group
Ay et al (2009)[31]	OA	PEMF	50 Hz	105 μT	NA	NA	30 min/5 per week/3 weeks
Bagnato et al (2016)[30]	OA	PRFE	27,12 MHz (pulse rate of 1000 Hz and a 100 μs burst width)	NA	NA	NA	Nightly/11,3± 0, 8 h/day/4 weeks
Brook et al (2012)[42]	PF	PRFE	27,12 MHz (pulse rate of 1000 Hz and a 100 μs burst width)	NA	NA	NA	Nightly for 7 days
Dündar et al (2016)[34]	OA	PEMF	50 Hz	100 μT	NA	NA	20min/5 per week/4 weeks
Galace de Freitas et al (2014)[35]	SIS	PEMF	50 Hz	20 mT	NA	NA	30 min/3 per week/3 weeks
Giombini et al (2013)[37]	CNP	PEMF whole body	5–25 Hz	5–70 μT	NA	Sinusoidal wave	2 hours/twice a day/8weeks
Gökşen et al (2016)[32]	OA	Magnetic Treatment	17–85 kHz	NA	NA	NA	1 hour/5 per week/2weeks
Kanat et al (2013)[43]	HO	PEMF	NA	3.5–25 mT	NA	NA	20 min/once a day for 10 days
Klüter et al (2018)[36]	SIS	EMTT	3 Hz	80 μT	NA	NA	20 min/2 per week/4 weeks
Krammer et al (2015)[39]	LBP	PEME	27.12 MHz (1000 pulses/s)	0.03 mT	NA	NA	For 7 days
Külcü et al (2009)[33]	OA	PEMF	2–100–25 Hz consecutively	2–10 mT	NA	NA	35 min/5 per week/3 weeks
Multanen et al (2018)[17]	FM	PEMF whole body	33,3Hz	0–150μT	NA	Sinusoidal half-wave	8 min twice a day/12weeks
Nelson et al (2013)[27]	OA	PEMF	6.8 MHz	NA	NA	Sinusoidal wave	15 min/twice a day/2 weeks
Oke et al (2013)[38]	BP	PEMF	NA	NA	NA	NA	2 hours per session; 4 per day for 5–9 days
Omar et al (2012)[14]	LBP (Unilateral Radicular Pain)	PEMF	7–4000 Hz	5–15 G	NA	NA	20min/once a day/3 weeks
Özgüçlü et al (2010)[28]	OA	PEMF	50 Hz	30 G	90-s interval	NA	30min/5 per week/2 weeks
Paolucci et al (2016)[18]	FM	ELF-MF whole body	1–80Hz	100 μT	NA	NA	30 min/3 per week/4 weeks
Park et al (2014)[16]	LM (Lumbar Myalgia)	PEMF	8.56 kHz	820 mT	NA	NA	10 min/3 per week/2 weeks
Servodio Iammarrone et al (2016)[41]	PFP	PEMF	75 Hz	1.5 mT	10%	Square waveform	4 h per day/6 weeks
Sutbeyaz et al (2009)[40]	FM	PEMF whole body	0.1–64Hz	40 μT	NA	NA	30 min/twice a day/3 weeks
Wuschech et al (2015)[29]	OA	PEMF	4–12 Hz	105 mT	NA	NA	5 min/twice a day/18 days

Abbreviations: OA, knee osteoarthritis; PF, plantar fasciitis; SIS, shoulder impingement syndrome; CNP, chronic mechanical neck pain; HO, hand osteoarthritis; LBP, low back pain; FM, fibromyalgia; BP, back pain; LM, lumbar myalgia; PFP, patellofemoral pain; PEMF, pulsed electromagnetic field; PRFE, pulsed radiofrequency electromagnetic field; ELF-MF, extremely low-frequency magnetic field; EMTT, electromagnetic transduction therapy; PEME, pulsed electromagnetic energy.

Table 3 Risk of Bias Summary of 21 Included Studies

		Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting	Other Bias
Ay et al (2009)[31]	High	–	?	–	+	+	–	–
Bagnato et al (2016)[30]	Low	+	+	+	+	+	–	?
Brook et al (2012)[42]	Low	+	+	+	+	+	+	?
Dündar et al (2016)[34]	High	?	–	–	+	–	+	?
Galace de Freitas et al (2014)[35]	Low	+	+	+	+	+	+	?
Giombini et al (2013)[37]	Low	+	+	–	–	+	+	?
Gökşen et al (2016)[32]	Low	+	+	+	+	+	+	?
Kanat et al (2013)[43]	Unclear	?	?	+	–	+	–	?
Klüter et al (2018)[36]	Low	+	+	–	+	+	+	?
Krammer et al (2015)[39]	Low	+	+	+	+	–	–	?
Külcü et al (2009)[33]	High	+	–	–	–	–	+	?
Multanen et al (2018)[17]	Low	+	+	+	+	+	+	–
Nelson et al (2013)[27]	Low	+	?	+	+	+	–	?
Oke et al (2013)[38]	High	?	–	–	–	–	+	?
Omar et al (2012)[14]	Unclear	?	–	?	?	–	+	?
Özgüçlü et al (2010)[28]	Low	+	–	+	?	–	+	?
Paolucci et al (2016)[18]	Low	+	+	+	+	–	+	–
Park et al (2014)[16]	Low	+	+	+	+	+	+	?
Servodio Iammarrone et al (2016)[41]	Low	+	+	+	–	–	?	?
Sutbeyaz et al (2009)[40]	Low	+	+	+	+	+	+	?
Wuschech et al (2015)[29]	Low	?	+	+	+	–	?	?

Notes: The "+" means low risk of bias; the "–" means high risk of bias; the "?" means unknown risk of bias. Trials involving three or more high risks of bias were considered as poor methodological quality.

bias related to incomplete outcome data, due to not mentioning adverse events, and the inadequate blinding participant and personnel. Furthermore, the articles analyzed share the same contraindications to the use of magnetotherapy as patients with pacemakers (or other electrical devices) and/or with cancer or in pregnant women.

Outcomes of Interest

Regarding the primary outcome, acute and chronic pain, in the included studies, the Visual Analogue Scale (VAS)[44] was the main evaluation tool, except for Kanat et al,[43] which presented 10-point Likert Scale to quantify pain at rest and at motion of the hand. Also, Oke et al[38] used the numeric rating scale for pain (NRS).[45]

Regarding the evaluation of the recovery of function, the authors use specific scales depending on the musculoskeletal diseases. In fact, to evaluate the patients with OA was administrated the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC),[46] or Lequesne Algofunctional index of knee (LI).[47]

Instead, to measure pain in SIS[35,36] was used the Constant–Murley Scale (CMS)[48] and University of California/Los Angeles scale (UCLA);[49] in addition, to evaluate the hand's function was used Duruöz and Auscan Hand Osteoarthritis Indexes (AUSCAN).[50,51] The evaluation of function in neck and low-back pain was assessed with the Neck Disability Index (NDI),[52] the Modified Oswestry Low Back Pain Disability Questionnaire (OSW),[53] the Korean version of Oswestry Disability Index (ODI)[54] and Modified Version Functional Activity Scale.[38] The Fibromyalgia Assessment Status scale (FAS)[55] and the Fibromyalgia Impact Questionnaire (FIQ)[56] have been administered specifically in FM to quantify pain and the secondary outcomes like recovery of function, disability and quality of life. Last, the Victorian Institute of Sport Assessment score (VISA)[57] was used to quantify mobility and function in patellofemoral pain.

Finally, in order to evaluate the increase in quality of life (QoL) perceived by patients, five studies[16,30,32,40,43] used the 36-item Medical Outcomes Study Short-Form 36

(SF-36);[58] then the Health Assessment Questionnaire (HAQ)[59] or the EuroQol-5 Dimension (EQ-5D).[60]

Discussion

The purpose of this systematic review was to investigate the scientific evidence of the last decade regarding the use of EMF in rehabilitation about its efficacy of acute and chronic pain in musculoskeletal disorders. The results suggest as EMF therapy is an optional treatment in the management of musculoskeletal pain disease that can reduce pain intensity and improves function.

Our review shows that PEMF are the most widely used magnetic fields, particularly in knee OA.[27–34] Among non-pharmacological treatments, PEMF have beneficial therapeutic effects on knee joint tissue.[61] PEMF signals modulate calmodulin (CaM)-dependent nitric oxide (NO) signaling cascades in articular chondrocytes and other cells, as demonstrated by a previous study that used CaM antagonists and NO downstream inhibitors.[62,63] This mechanism could promote the resolution of pain by accelerating the removal of inflammatory substances. PEMF stimulates chondrocyte proliferation, differentiation, and extracellular matrix synthesis through the release of anabolic morphogens, such as bone morphogenetic proteins and anti-inflammatory cytokines, by adenosine receptors $A2_A$ and A3: in clinical translational study, a beneficial effect was observed in improving function in knee OA.[64] In 4 studies dealing with knee OA,[27,29,30,33] there were good results in the reduction of pain and improvement of function compared to the control group. In detail, Nelson et al[27] proposed a short protocol of 2 weeks (15 mins per session, twice daily) with 6.8 MHz and an intensity of 30 Gauss in OA: patients in the PEMF group had a mean self-reported maximum daily VAS pain score at baseline of 6.85 ±0.33 and 4.19±0.71 at the end of treatment, compared with 7.18±0.31 and 6.11±0.54 for the sham group. Thus, PEMF effects significant and rapid reductions in pain in early knee OA (p=0.036). Also, in Wuschech's et al[29] study, a PEMF portable device was used and a total of 57 patients were enrolled, 44 patients randomly assigned to the treatment group but only 13 patients to placebo group. At the end, the PEMF group showed a great improvement in pain, disability and function. Another study[33] compared PEMF respect of therapeutic ultrasound (US) and authors suggested as PEMF and US were more effective than no treatment and PEMF may be a good alternative to other physical therapies in the management of knee pain in the osteoarthritis. A further study to the efficacy of the PEMF in knee OA was a double-blind, placebo-controlled, randomized clinical trial by Bagnato et al[30] randomly allocated 60 patients with OA of the knee into 2 groups (treatment PEMF and control placebo-PEMF), reporting a decrease in pain but not in the quality of life (SF-36 in the PEMF group) after 12 hrs/daily for 1 month of treatment. The results showed a decrease in pain in the PEMF group but quality of life (SF-36) did not change in a statistically significant way in the two groups.

In the RCT study of Ay et al[31] 55 patients have been recruited and randomly assigned to PEMF group and placebo-PEMF group. Both groups have carried out hot pack, transcutaneous electric nerve stimulation (TENS) for 20 mins and isometric quadriceps exercise program. PEMF was applied for 30 mins, treatment consists of 15 sessions, 5 times/week for 3 weeks. After the treatment period both groups improve their symptoms (pain and functional capacity) but without statistically significant difference in two groups. Only morning stiffness and daily living activity have shown a statistical difference in the two groups in favor of the treatment group. Also, in Özgüçlü's study[28] forty patients with OA were randomized into two groups: both groups received 20-min hot pack, 5-min therapeutic ultrasound instead treatment group underwent also PEMF therapy for 30 mins. A bias was that patients could take the acetaminophen as needed. Their results conclude that PEMF did not show additional effect on reducing knee pain. This study showed that were no statistically significant differences between groups in WOMAC pain, stiffness, and physical function scores after treatment (p = 0.906, p = 0.855, p = 0.809, respectively).

Only one study of Dundar et al[34] provide a measure of a YKL-40, a serum marker made in OA by chondrocytes and neutrophils in inflamed joints. Forty patients were included and randomized into two groups: group 1 (PEMF) and group 2 (sham-PEMF). Both groups receive a physical therapy consist of therapeutic US, TENS, hot pack and isometric exercise five-session/week for 4 weeks. Each patient underwent to knee ultrasound to assess the knee effusion and has compiled a VAS score and WOMAC questionnaire at baseline and at the end of the treatment (1 month). A venous blood sample was collected for each patient before and after the protocol period to measure YKL-40 serum marker. Results showed no effect or additional result from PEMF therapy with conventional therapy. Also, there was a significant improvement in both groups for VAS and WOMAC. The only significant

correlation among these parameters was between delta-VAS and delta-WOMAC (r = 0.512, p = 0.001). Moreover, YKL-40 level was not correlated with the change in VAS, WOMAC questionnaire scores, as well as knee effusion. In conclusion, PEMF therapy had no additional effect on knee OA when associated with other physical therapy, but this study still has a low risk of bias but a Pedro score of 5. In fact, Vavken et al[65] in their review suggested that PEMF has clinical relevance as a successful adjuvant option in the management of OA rather than a stand-alone therapy.

While being a magnetic field therapy method, Gökşen et al[32] used the effects of magnetic resonance therapy (MRT) in OA versus placebo-MRT with a high frequency of 17–85 kHz. They enrolled 100 patients and randomized them equally into 2 groups (MRT and placebo-MRT). The treatment consisted of magnetic fields, 1 hr per day 2 two weeks. Their results did not show positive effects in favour of the treatment group, because both groups improved significantly regarding pain after 2 and 12 weeks: thus, MRT was safe but not superior to placebo.

Conversely, Brook et al[42] analysed a pulsed radiofrequency electromagnetic field device in treating plantar fasciitis, noting positive results with respect to morning pain; however, this study had several limitations, such as the lack of long-term follow-up and the lack of interceptor analysis.

Kanat et al[43] evaluated the efficacy of magnetotherapy in hand osteoarthritis. In this study, the treatment group received magnetotherapy with flux intensity from 3.5 to 25 mT, 450 pulse/s, and 5–80 G, for 10 days, 20 min/day, combined with exercises for the hand. The control group received sham-magnetotherapy for 20 min/day for the same duration, combined with the same exercises. Pain and quality of life for SF-36 scale improved in favour of the treatment group.

Servodio-Iamarrone et al[41] assessed whether the combination of a home exercise program with PEMFs was more effective than the program alone in patellofemoral pain syndrome, concluding that PEMFs improve the reduction of pain favouring the earlier start of the exercise the therapeutic exercises, accelerating the recovery and reducing pain in this condition.

Other groups have reported the use of PEMFs at frequencies of 50 Hz,[35] reporting good results in SIS, as with standard physical therapy, with no negative effects. Patients in the treatment PEMF group showed a higher level of function and less pain at all follow-up time frames compared with baseline. On the contrary, the placebo-PEMF group had increased function and reduced pain only at the 9-week and 3-month follow-ups that is, after performing the associated exercises. Instead, in Klüter et al[36] 86 patients with SIS were randomized to undergo 3 sessions of extracorporeal shock wave therapy in combination with 8 sessions of electromagnetic transduction therapy or sham-electromagnetic transduction therapy. Therefore, the two treatment modalities seem to have a synergetic effect and electromagnetic transduction therapy can be useful to improve the results after extracorporeal shock wave therapy. For example, a study compared PEMF and therapeutic ultrasound (US),[33] suggesting these modalities are more effective than no treatment and that PEMF is a good alternative to other.

Other groups have proposed very-high-frequency treatment protocols of 27.12 MHz,[30,39,42] because in 1947, the Federal Communications Commission assigned 3 frequencies at the short end of the radiofrequency band for medical use. McGaughey et al[66] underline that pulsed electromagnetic energy encloses the terms pulsed short-wave diathermy, pulsed electromagnetic field (PEMF) and diapulse, but if we move on frequencies of 27.12 MHz, then we considered diathermy effect related to therapy. Energy is emitted in a sequence of impulses with the "off" period much longer than the "on" period which entails a lower dose that is given to the patient and any heat produced is dissipated by the circulation.[67] For this reason, Goats et al suggest that "pulsed electromagnetic energy therapy cannot correctly be called diathermy because little or no heating of the tissue occurs".[67] An electric field is influenced by a magnetic field and vice versa, for this reason, an exogenous electromagnetic field influences many biologic processes which are important for therapeutic interventions.[68] Markov et al[68] in their work they showed that the magnetic and electromagnetic fields that are used today can be classified as follows: permanent magnetic fields (created by several permanent magnets or by passing a direct current through a coil); electromagnetic fields from low-frequency sine waves; pulsed electromagnetic fields usually low-frequency and forms of looking specific signal; pulsed radiofrequency fields with selected frequencies in the radiofrequency range and short but intensive magnetic pulses for transcranial magnetic stimulation.[68] In literature, other studies report the efficacy of other forms of energy that are based on magnetic fields in rehabilitation for shoulder pain that exploit other clinical effects of magnetic fields

but equally effective. For example, short-wave diathermy utilizes electromagnetic waves to convert energy to deep heat, and diathermy is thought to exert its therapeutic effects by both thermal and nonthermal mechanisms. The primary nonthermal mechanism associated with the use of therapeutic short-wave diathermy occurs via vibration induction of tissue molecules when exposed to radio waves. By changing the characteristics of the shortwave applicator, the therapist can target the specific type of tissue he or she wants to heat.[69,70]

Concerning LBP, four studies analysed the efficacy of electromagnetic fields.[14,16,38,39] Krammer et al[39] investigated PEMFs with the frequency 27.12 MHz for the treatment of LBP, generating uncertain results on the effectiveness of magnetic fields in combination with typical physiotherapy. To avoid the thermal effect, the analysed studies proposed a pulse rate of 1000 Hz and a 100-microsecond burst width. Also, Oke et al[38] assessed the efficacy of PEMF in the treatment of LBP without specifying the frequency, and their results were positive, as in Krammer et al.[39] Moreover, Park et al[16] performed a randomized-controlled trial to determine the efficacy of PEMFs in alleviating lumbar myalgia in acute LBP in 38 patients. All patients were treated on the lumbar muscle and acupuncture points, 3 times per week for 2 weeks with a frequency of 8.56 kHz; versus placebo, the PEMF group showed better results for pain but not quality of life. Also, Omar et al[14] have evaluated the effect of PEMF in the management of patients with LBP in 40 patients randomly assigned: 20 in a study group who received PEMF therapy, and 20 patients in a control group who received placebo treatment. The authors concluded that PEMF should be effective for conservative treatment of lumbar radiculopathy caused by lumbar disc prolapse and seems effective in reducing nerve root compression as evidenced by the improvement of somatosensory evoked potentials (SSEPs) parameters after treatment. The results are in line with the review by Andrade et al[15] in which the authors underline how PEMF can reduce pain and increase functionality in patients with different LBP conditions, when added to standard therapy, it seems not to add any beneficial effect.

Using a different approach, Giombini et al[37] randomized 45 patients to 3 groups with chronic neck pain. Groups A and B (control groups) used an NBS-DM2/RW (neck balance system-Del Monte 2/regular weight) and NBS-DM2/NW (neck balance system-Del Monte 2/negligible weight) helmet systems with balancing weight, respectively, whereas Group C (treatment group) underwent electromagnetic therapy with whole-body PEMF in supine position with a low frequency of 5–25 Hz and very low intensity of 5–70 μT. The authors concluded that PEMF therapy has no significant effect on reducing pain and disability in chronic mechanical neck pain. According to these results, Wu et al[71] showed that PEMFs are useless for reducing pain and improving function in cervical OA, as there is no evidence that PEMFs act on reducing the formation of osteophytes, which may induce nerve root compression that can lead to deterioration of pain and function.

Based on our review, PEMFs in whole-body mode have found innovative and unique use, especially in complex and widespread musculoskeletal chronic pain conditions, such as FM.

Multanen et al[17] analysed the effects on FM of low-energy PEMF therapy, with a signal that consisted of 5 sessions of pulses of half-wave-shaped sinusoidal variations, with a range of intensities of 0–150 μT and a frequency of 33.3Hz, in a sample of 108 women (47±10) who were randomized to 2 groups (TG, CG) in a crossover study. They found that treatment with an active device elicited no significant improvement in pain, stiffness, or FIQ index over sham treatment. Also, there was no correlation between the frequency of using the device and the decrease in pain with active ($r = -0.11$, 95% CI [−0.31, 0.10]) or sham treatment ($r = -0.10$, 95% CI [−0.31, 0.12]).

In contrast, Paolucci et al[18] described the efficacy of administering extremely-low-frequency magnetic fields (not pulsed ELF) to the entire body in FM patients in decreasing chronic pain. Thirty-seven (N=37) women (50.33±10.94) were randomized to 2 groups (TG1, TG2) in a crossover study. One group was first exposed to systemic ELF-MF therapy (100 μT, 1 to 80 Hz) and then sham therapy, and the other group received the opposite sequence of interventions. Regarding the primary outcome, ELF-MF treatment significantly lowered pain (p=0.001), which rose after the end of treatment but remained significantly lower than baseline levels (p=0.001) in both groups. Short-term benefits were also observed in terms of the secondary outcome measures, but the medium-term effects were less significant; FAS and FIQ scores generally declined by 40% for scores between pre-and post-ELF-MF versus sham treatment.

Also, Sutbeyaz et al[40] analysed the effects of PEMF on pain in 56 patients with FM, administered to the entire body using a mat with a mean intensity of 40 μT and

frequency that ranged from 0.1 to 64 Hz. For pain, VAS scores in the TG improved significantly from baseline (73.3±14.0) to after treatment (38.07±16.9) and at the follow-up (59.4±9.8). In contrast, in the CG, VAS scores improved significantly only from baseline (68.4±12.1) to after the treatment (63.4±13.8), not at the follow-up (67.4 ±11.8). Also, FIQ scores in the TG were enhanced at the end of therapy compared with baseline and were significant than in the CG at the end of therapy.

The three groups used very different protocols in FM: Paolucci et al[18] used a non-pulsed field, administered once per day, whereas Multanen et al[17] and Sutbeyaz et al[40] administered a pulsed-field twice daily. In addition, the results of Paolucci et al[18] and Sutbeyaz et al[40] should be interpreted with caution due to the small sample sizes in each treatment arm. However, there is evidence that exposure to electromagnetic fields affects pain, nociception, and opiate-mediated analgesia.[12] However, all three groups used frequencies lower than 100 Hz and very low intensities between 0 and 150 μT.

In the literature, the duration of disease in FM directly influences the efficacy of the treatment, because drugs and rehabilitation treatment are less sensitive to the placebo effect. This finding implies that the longer a person has FM, the more entrenched the condition becomes, the lower the patient expectancy is, and the harder it is to improve outcomes by active treatment or placebo or other factors that govern contextual responses.[72]

Conclusion

In conclusion, this systematic review suggests that electromagnetic field therapy relieves pain and improves function in patients with various pain musculoskeletal diseases. Electromagnetic field therapy is well tolerated with no reported negative side effects in the analyzed studies. Then, it could be a helpful component during drug therapy for chronic and acute pain in musculoskeletal disease. A limitation of our study is that the included studies analysed have high-level criticism about the standardized protocols especially with respect to the length and exposition time and Hz frequency of the magnetic field applied. PEMFs at the low weak intensity and low frequency (from 1 Hz up to 100 Hz) are the most commonly used and most effective in resolving pain, but when other physical therapies, such as TENS, US, and hot pack are added, no additive beneficial effect is observed.

Finally, further studies are needed to examine the use of more standardized protocols respect to the length and exposition time and frequency characteristics of the magnetic field, applied to specific pathologies to resolve with relatively safe and conservative treatment the musculoskeletal pain.

Disclosure

The authors report no conflicts of interest in this work.

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