

Original article

Effects of pulsed electromagnetic field on knee osteoarthritis: a systematic reviewSeo Ryang We¹, Yun Hyung Koog¹, Kwang-Il Jeong² and Hyungsun Wi¹**Abstract**

Objective. Many reviews have been previously published on the efficacy of pulsed electromagnetic field (PEMF) in the management of knee OA. However, their results regarding pain and function yielded conflicting conclusions. Therefore this study was conducted to determine the efficacy of PEMF as compared with a placebo.

Methods. We reviewed randomized, placebo-controlled trials using electronic databases. We also manually reviewed sources to identify additional relevant studies.

Results. Fourteen trials were analysed, comprising 482 patients in the treatment group and 448 patients in the placebo group. When the efficacy of PEMF in treating pain was investigated, no significant effects were observed at any of the time points considered. However, when trials employing high-quality methodology were analysed, PEMF was significantly more effective at 4 and 8 weeks than the placebo. When the efficacy of PEMF was evaluated for function, a significant improvement was observed 8 weeks after the treatment initiation, with a standardized mean difference of 0.30 (95% CI 0.07, 0.53). No significant association was found between the use of PEMF and the occurrence of adverse events, as indicated by a relative risk of 1.47 (95% CI 0.67, 3.20). However, three (21.4%) trials applied electromagnetic field intensity over the levels recommended by the International Commission on Non-Ionizing Radiation Protection.

Conclusion. The present study provided suggestive evidence supporting PEMF efficacy in the management of knee OA. Our results further raise the need for more well-controlled trials, employing adequate methodology, to conclusively evaluate the efficacy of PEMF.

Key words: pulsed electromagnetic field, knee osteoarthritis, systematic review, randomized placebo-controlled trials.

Introduction

OA is a degenerative synovial joint disease involving cartilage loss, synovial inflammation, subchondral bone lesions and meniscus extrusion [1, 2]. Knee OA is the most common form of joint disease [3] and the major cause of pain and physical disability among middle-aged and elderly people [4]. Therefore, current treatment strategies aim to alleviate joint pain, reduce physical disability

and limit the progression of joint damage [5]. Although it is important to establish treatment guidelines for knee OA, basic efforts to establish the efficacy of treatments currently available are still ongoing [5–7].

Among the treatments available, pulsed electromagnetic field (PEMF) is a controversial treatment modality. In 2000, the panel of experts responsible for the recommendations of the European League Against Rheumatism (EULAR) did not analyse the efficacy of PEMF [8]. However, PEMF had been used with increasing frequency over the prior two decades [9]. Furthermore, numerous randomized trials showing the potential of PEMF to improve OA symptoms were published [10, 11]. After this situation was pointed out in the literature [12], a later version of the EULAR recommendations finally recognized PEMF as a good treatment option for knee OA [13]. Nonetheless, PEMF was not mentioned by the

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International Multidisciplinary Committee of experts appointed by the Osteoarthritis Research Society International [5–7].

The results were conflicting even among systematic reviews evaluating the efficacy of PEMF compared with placebo. In recent years, three such reviews [14–16] were published. One review reported no beneficial effect on pain and function measurements 6 weeks after the initiation of treatment [14]. Another reported a significant alleviation of pain 0–4 and 8 weeks after the treatment initiation [15]. The third review reported only a significant improvement in knee function 3–10 weeks after the beginning of treatment [16].

To reduce the confusion surrounding the usefulness of PEMF, we conducted a systematic review to determine its efficacy in the management of knee OA. PEMF is an empirically based therapy for which the exact mechanism of action is largely unknown. Thus, a study of the time course of its efficacy is required from a clinical viewpoint. For this aim, we attempted to demonstrate PEMF efficacy using randomized, placebo-controlled trials, because placebo-controlled trials can control the potential influence of confounding factors on PEMF efficacy [17].

Methods

Search strategy and study selection

Studies were identified through various searching methods. First, we searched MEDLINE (PubMed), SCOPUS and the Cochrane Central Register of Controlled Trials from their inception to December 2011. We used the terms (knee arthritis OR knee osteoarthritis OR gonarthrosis OR gonarthrosis) with limits to randomized controlled trials and humans in MEDLINE. We used the same terms with limits to article title, abstract or keywords and medicine in SCOPUS and the same terms with a limit to title, abstract or keywords in the Cochrane Register of Controlled Trials. Secondly, we searched systematic reviews on PEMF and related comments. Thirdly, we manually searched the *Journal of Rheumatic Diseases* (<http://www.jrd.or.kr/>) indexed in the National Research Foundation of Korea (<http://www.nrf.re.kr/html/kr/>). No language restriction was applied in the searches performed. Randomized, placebo-controlled trials comparing PEMF with placebo in the management of knee OA were then independently selected by two of the authors (S.R.W. and Y.H.K.).

Data extraction

Two authors (S.R.W. and Y.H.K.) independently extracted data for pain from either the visual analogue scale (VAS)-related measurement or the pain subscale of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Data on function were obtained from either the WOMAC function subscale or the Lequesne Algofunctional Index. In trials that assessed more than one outcome measure for pain or function, the outcome measure most frequently reported in the eligible trials was selected for the present study. We noted data involving

changes from baseline. When the required values were not available in the text, we estimated them based on the *Cochrane Handbook for Systematic Reviews of Interventions* [18]. Data regarding assessments performed at ≥ 2 and < 6 weeks after the treatment initiation were used to analyse the 4-week efficacy, and those regarding assessments at ≥ 6 and < 10 weeks after the beginning of treatment were used to analyse the 8-week efficacy. Data relating to assessments at ≥ 10 and < 14 weeks were used to analyse the 12-week efficacy, and finally, those concerning assessments performed at ≥ 14 and < 18 weeks after the treatment initiation were used to analyse the 16-week efficacy. Pain was considered to be the primary outcome of this study.

Three authors of this study also extracted information on applied doses (K.I.J.) and safety outcomes (S.R.W. and Y.H.K.). To check whether the electromagnetic field applied in each trial could induce potential hazard to therapists and patients, we calculated the reference levels according to the guidelines issued by the International Commission on Non-Ionizing Radiation Protection (ICNIRP) [19]. All disagreements between the independent data selections and extractions were resolved through open discussion.

Quality assessment

Two authors (S.R.W. and Y.H.K.) independently evaluated all trials for methodological quality using the Physiotherapy Evidence-Based Database (PEDro) rating scale [20]. To obtain the PEDro scores, one point was awarded to each of the following items: (i) performed randomization; (ii) concealed allocation; (iii) similar baseline characteristics of the two groups; (iv) patients blinding for the treatment applied; (v) therapists blinding for the treatment applied; (vi) assessors blinding for the treatment applied; (vii) attrition rate of $< 15\%$; (viii) performed intention-to-treat analysis; (ix) comparison of the two groups using statistical analysis; and (x) reported point measures and variability. Since previous studies [21, 22] reported that $> 50\%$ of the raters responded yes in 5 of the 10 items, we considered trials with scores of ≥ 6 as having high quality and trials with scores of ≤ 5 as having low quality.

Data synthesis and analysis

For pain and function, the standardized mean difference (the Hedge's g effect [23]) was calculated as the difference between the improvement change from baseline in the PEMF and placebo groups divided by the pooled s.d. of the improvement change of the two groups. For the safety outcome, the relative risk was calculated as the ratio of the number of patients reporting adverse events to the total number of patients in the PEMF group divided by the same ratio in the placebo group. The summary estimate was then calculated using a random effects model [24]. The I^2 test was used to measure heterogeneity [25].

Further analyses were performed on the primary outcome, when at least four trials were analysed within

each time window. To explore sources potentially altering the significance of the results, we conducted a sensitivity analysis using the following factors: each item of the PEDro scale, trial quality (<6 PEDro scores vs ≥ 6), ICNIRP reference levels (values below vs values above these levels), administration of non-standardized analgesics (yes vs no), co-interventions (yes vs no), region where the trial was published (English-speaking country vs non-English-speaking country) and PEMF-related firm funding (yes vs no). Since the results may depend on the quality scale used [26], we also compared trials meeting all the Jadad scale-related items (i.e. randomization, allocation concealment, patient and therapist blinding and intention-to-treat analysis [27]) and trials not meeting these items. To explore possible sources of the heterogeneity of the results, we performed a heterogeneity analysis using the factors above. We also performed a meta-regression against continuous outcomes (i.e. mean age, female proportion, baseline pain intensity and total treatment time). To control for type 1 error, a mixed-effects model in which the random between-studies variance component was estimated by maximum likelihood estimation was used [28]. As many items were tested, we present only statistically significant data. Finally, we performed Egger's regression test [29] and constructed a funnel plot for each time window, to detect small study effects. The Comprehensive Meta-Analysis software version 2.0 (Biostat, Inc., Englewood, NJ, USA) was used to perform all the statistical analyses.

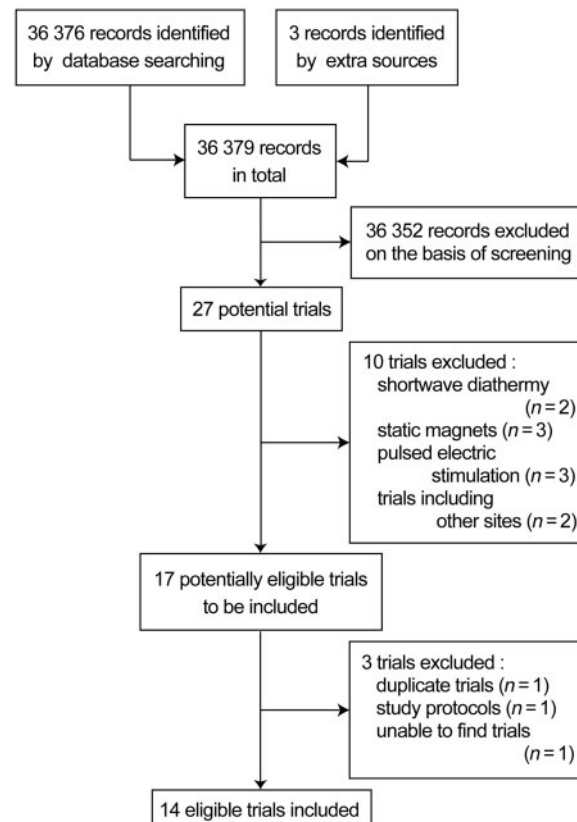
Results

A total of 36 379 studies were identified: 1646 from MEDLINE, 32 246 from SCOPUS, 2484 from Cochrane Registered Trials and 3 from other sources (Fig. 1). Of these, 14 trials [11, 30–42] were eligible for inclusion in the final analysis. One trial [43] was excluded because we could not obtain a copy of the study. Three other trials [44–46] were excluded because the pulsed electrical stimulation used in those trials is considered as a type of transcutaneous electrical stimulation by the US Food and Drug Administration [47].

Trial characteristics

Table 1 describes the characteristics of the 14 trials included in this study. Five trials [30, 31, 34, 35, 38] scored <6 on the PEDro scale and the remaining trials scored ≥ 6 . All trials, except one [31], involved small samples (<50 patients in each group). In total, 482 patients underwent the PEMF treatment, and 448 patients received the placebo. The median age of patients was 63.0 (range 60.0–73.0) years. The median proportion of female patients was 72.3 (range 50–88.1) years in all trials but two, which included only 27.5 [32] and 9.8% [35]. The Kellgren–Lawrence radiological score of these patients ranged from 2.3 to 3.3, with a median of 2.7. Regarding the type of placebo administered, four trials [30, 31, 38, 40] used a switched-off PEMF, three [33, 39, 42] a switched-on PEMF without output, one [41] a PEMF of near zero intensity and one [36] a PEMF with a constant

Fig. 1 Study flow diagram.



current. The remaining trials [11, 32, 34, 35, 37] provided no full description of the placebo. Table 2 describes the characteristics of the PEMF treatment applied in each trial. Although PEMF was applied for 6 weeks in most of the trials, frequency and pulse length of the electromagnetic field emitted varied across trials.

Efficacy of PEMF

Fig. 2 shows the efficacy of PEMF in the reduction of knee pain 4, 8, 12 and 16 weeks after the initiation of the treatment. When summary estimates were calculated, PEMF was not more effective than placebo at any of the time points. The degree of heterogeneity derived for the time points assessed was low to severe. Fig. 3 shows the efficacy of PEMF in improving knee function 4, 8, 12 and 16 weeks after the beginning of the treatment. When summary estimates were calculated, PEMF was more effective than the placebo only at 8 weeks, with a standardized mean difference of 0.30 (95% CI 0.07, 0.53). The degree of heterogeneity derived for the time points assessed was low to moderate.

The analyses of sensitivity and heterogeneity revealed that besides the Jadad scale-related items and the ICNIRP reference levels, no other factors affected the summary estimate of the 4-week efficacy (Fig. 4). When the summary estimate was calculated over trials that

TABLE 1 Characteristics of included trials

Trial	Age, years	Female, %	Kellgren-Lawrence score ^a	PEDro score		Patient number		
				10 items ^b	Total	PEMF group	Placebo group	Description of placebo
Trock <i>et al.</i> [11]	67.5	69.8		1 111 011 011	8	42	44	Indistinguishable machine
Jezek <i>et al.</i> [30]	60.1	76.7		0010 000 001	2	30	30	Switched-off PEMF
Jacobson <i>et al.</i> [31]				1 001 011 010	5	101	74	Switched-off PEMF
Piptone and Scott [32]	63.0	27.5		1 001 111 111	8	34	35	Indistinguishable machine
Nicolakis <i>et al.</i> [33]	67.9	59.4		1 011 111 011	8	15	17	Disconnected PEMF without output
Tejero Sanchez <i>et al.</i> [34]	67.7	88.1	2.7, 2.7	1 110 000 011	5	33	34	Same PEMF, but no further explanation
Lee <i>et al.</i> [35]	64.9	9.8		1 011 000 011	5	26	25	Same PEMF, but no further explanation
Thamsborg <i>et al.</i> [36]	60.0	54.2	2.5, 2.8	1 011 011 111	8	45	45	Same PEMF with constant currents, thus yielding no pulsed field
Fischer <i>et al.</i> [37]	60.2	71.8		1 011 111 011	8	35	36	Indistinguishable machine
Laufer <i>et al.</i> [38]	73.0	78.5		0 001 011 011	5	32	33	Switched-off PEMF
Callaghan <i>et al.</i> [39]	60.9	50.0	3.3, 3.3	1 110 010 011	6	9	9	Switched-on PEMF without output
Ay and Evcik [40]		72.7	2.4, 2.3	1 010 011 111	7	30	25	Switched-off PEMF
Ozgüçlü <i>et al.</i> [41]			2.6, 2.3	1 011 011 110	7	20	20	Same PEMF of near zero intensity
Fukuda <i>et al.</i> [42]	62.5	100.0		1 101 011 111	8	30	21	Switched-on PEMF without output (i.e. standby mode)

^aThe former value is for the PEMF group, and the latter for the placebo group. ^bTen items of the PEDro scale [20]: (i) randomization performed?; (ii) allocation concealed?; (iii) baseline characteristics similar?; (iv) patients blind?; (v) therapists blind?; (vi) assessors blind?; (vii) attrition rate <15%?; (viii) intention-to-treat analysis performed?; (ix) statistical analysis performed?; and (x) point measures and variability reported?

satisfied the Jadad scale-related items or the ICNIRP guidelines, PEMF provided more pain relief than placebo. In contrast, patient blinding, therapist blinding, assessor blinding, attrition rate <15%, trial quality and the ICNIRP reference levels all affected the summary estimate of the 8-week efficacy (Fig. 4). For trials that had sufficient patient blinding, adequate therapist blinding, appropriate assessor blinding or an attrition rate of <15%, PEMF was significantly more effective in reducing pain than the placebo. For trials with a PEDro score ≥ 6 , PEMF was also more effective than the placebo. When trials that satisfied the ICNIRP guidelines were analysed, PEMF significantly alleviated knee pain. In the meta-regression tests, no factors were found to be associated with the 4- or 8-week efficacy.

In the tests aiming to detect small study effects, no bias could be depicted for either the 4- or the 8-week efficacy study. The Egger's regression tests detected no small study effects, with coefficients of -1.98 (95% CI $-9.45, 5.48$; $P=0.56$) at 4 weeks and 2.15 (95% CI $-6.84, 11.13$; $P=0.57$) at 8 weeks. In addition, the funnel plot showed no signs of bias (supplementary Fig. S1, available as supplementary data at *Rheumatology* Online).

Safety

Two trials [32, 36] reported adverse events of the treatment. In the trial performed by Piptione *et al.* [32], two patients in the PEMF group reported increased knee pain and feet numbness, and four patients from the placebo group reported increased knee pain, paraesthesia of the foot and tenderness in a sternoclavicular joint. In the trial carried out by Thamsborg *et al.* [36], 10 patients in the PEMF group reported uncomfortable sensations, 2 patients in the PEMF group reported increased knee pain, 5 patients in the placebo group reported uncomfortable sensations and 1 patient in the placebo group reported increased knee pain. The relative risk across two trials was 1.47 (95% CI 0.67, 3.20). Calculation of the reference levels for the electromagnetic field used in each trial revealed that in three trials [34, 35, 41], this was over the reference levels recommended by the ICNIRP (Table 2).

Discussion

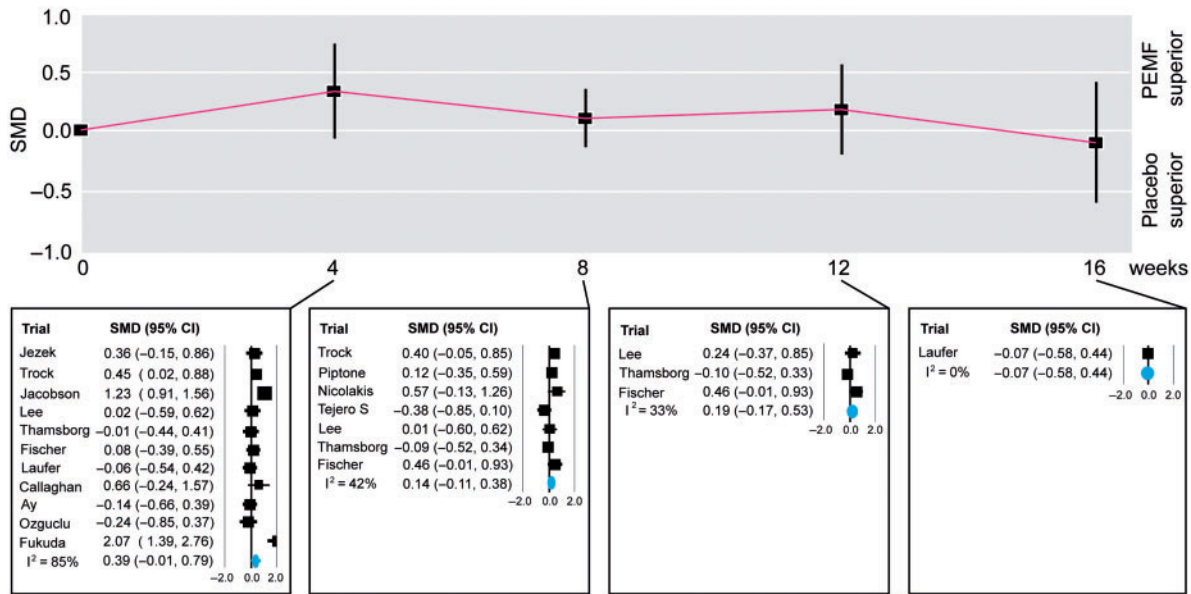
We analysed the efficacy of PEMF therapy in the management of patients with knee OA. The current results indicate that PEMF was not more effective than placebo in

TABLE 2 Characteristics of applied PEMF

Trial	Treatment regimen	PEMF regimen							
		Machine-operating frequency, MHz	Pulse frequency	Pulse length	Electrical field strength	Magnetic flux density, G	Mean power, W	Total energy per day, kJ	ICNIRP reference levels ^a
Trock <i>et al.</i> [11]	30 min a day, 18 sessions, 4 weeks		5–12 Hz			10–25			20.8–80 G
Jezek <i>et al.</i> [30]	20 min a day, 15 sessions, 3 weeks		12.5 Hz			0.276			20 G
Jacobson <i>et al.</i> [31]	6 min 8 times a day, 8 sessions, 2 weeks		1–8 Hz			$0.34\text{--}2.74 \times 10^{-9}$			31.3–2000 G
Piptone and Scott [32]	10 min 3 times a day, daily, 6 weeks		3–7.8 Hz	10 μ s		<0.5			32.9–222 G
Nicolakis <i>et al.</i> [33]	30 min twice a day, daily, 6 weeks		1–3000 Hz			0.4			0.307–200 G
Tejero Sanchez <i>et al.</i> [34]	30 min a day, daily, 20 sessions		15–50 KHz			52–69			0.307 G
Lee <i>et al.</i> [35]	30 min a day, 18 sessions, 6 weeks		12 Hz			25			20.8 G
Thamsborg <i>et al.</i> [36]	2 h a day, 30 sessions, 6 weeks		50 Hz	6 ms	1 V/m				10^4 V/m
Fischer <i>et al.</i> [37]	16 min a day, daily, 6 weeks		10–300 Hz			0.034–0.136			0.83–25 G
Lauer <i>et al.</i> [38]	20 min a day, 9 sessions, 3 weeks	27.12	300 Hz	300 μ s			18	21.6	–
Callaghan <i>et al.</i> [39]	20 min a day, 6 sessions, 2 weeks	27.12	400 Hz	400 μ s			20	24	–
Ay and Evcik [40]	30 min a day, 15 sessions, 3 weeks		50 Hz			1.05			5 G
Ozgülü <i>et al.</i> [41]	30 min a day, 10 sessions, 2 weeks		50 Hz			30			5 G
Fukuda <i>et al.</i> [42]	19 min a day, 9 sessions, 3 weeks	27.12	145 Hz	400 μ s			20	16.53	–

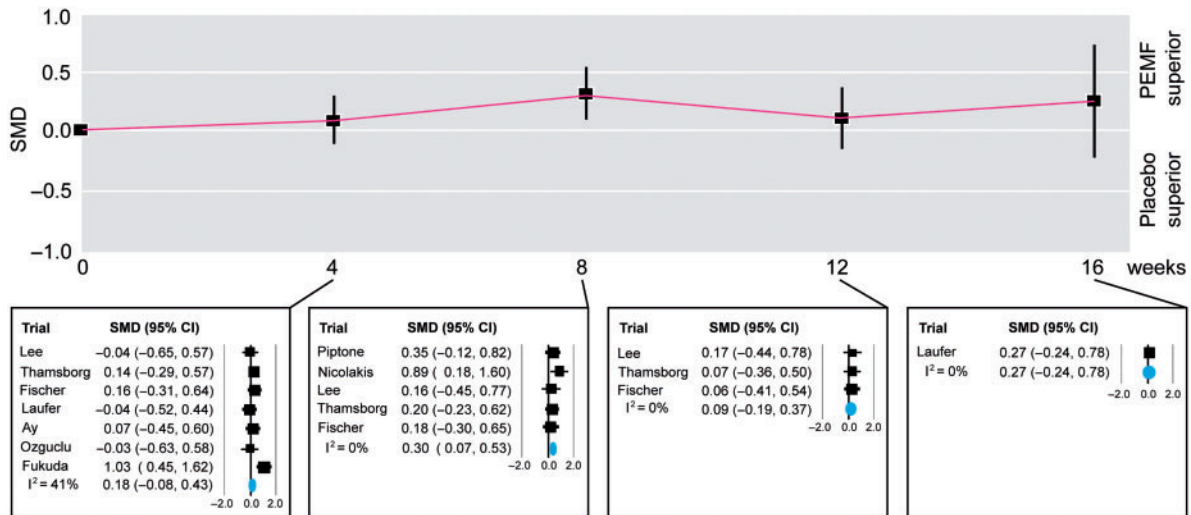
^aValues were calculated from a report [19] on the guidelines of the ICNIRP.

Fig. 2 Efficacy of PEMF on knee pain.



Data are expressed as the standardized mean difference (SMD) with 95% CI.

Fig. 3 Efficacy of PEMF on knee function.



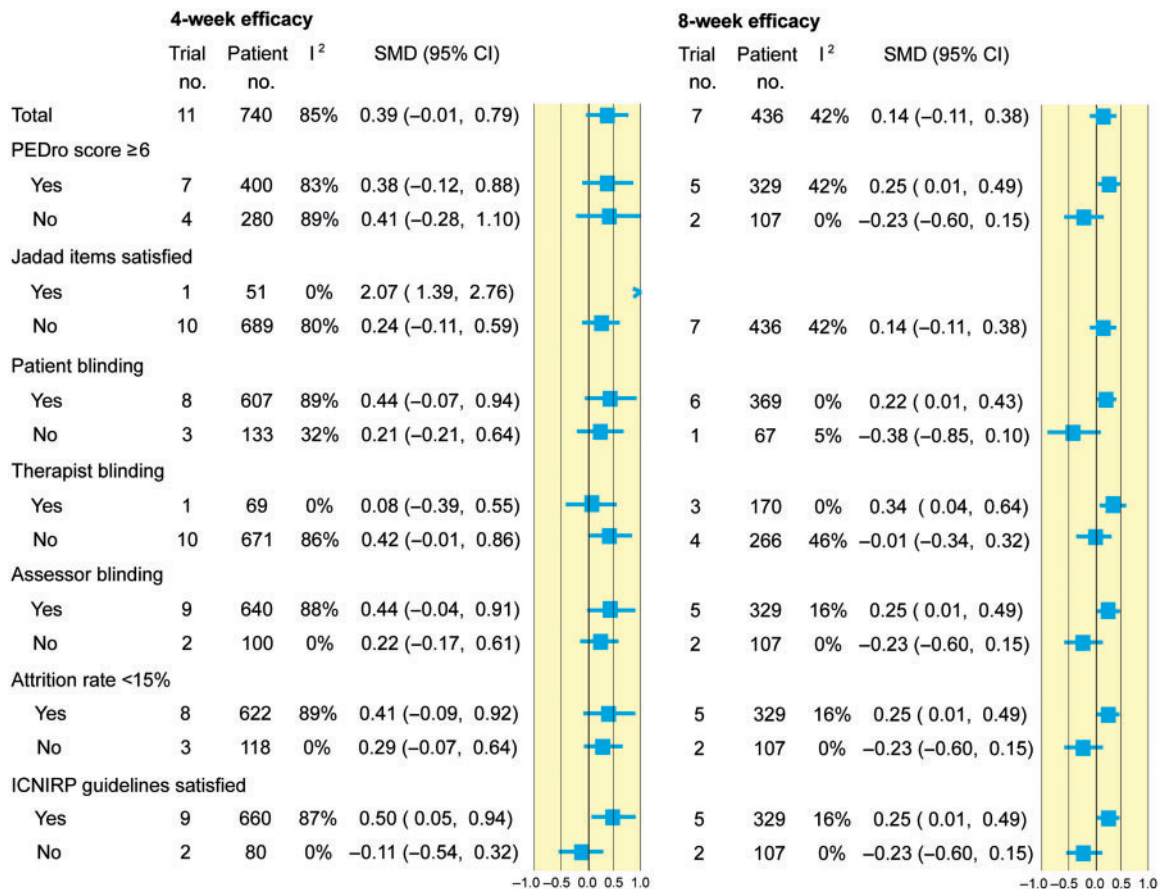
Data are expressed as the standardized mean difference (SMD) with 95% CI.

treating pain at any of the time points. However, when the analysis was restricted to trials using high-quality methodology, PEMF was significantly more effective in alleviating pain 4 and 8 weeks after the treatment initiation. For trials that met the ICNIRP reference levels, PEMF also alleviated knee pain at 8 weeks. The current results also indicate that PEMF was more effective in improving function 8 weeks after the start of the treatment. Regarding safety, no significant differences in the number of adverse

events reported were found between the PEMF and placebo groups. However, when the ICNIRP reference levels were examined, we found that three trials utilized magnetic fields above the levels permitted by the ICNIRP guidelines.

The efficacy of PEMF was previously analysed in a series of systematic reviews [14–16]. One earlier review completed by McCarthy *et al.* [14] reported that PEMF provided no benefits with respect to either knee pain or

Fig. 4 Subgroup analyses of efficacy on pain.



function. The results of our study do not support the conclusions of their review. The discrepancy appears to be due to the different sets of trials included in the review. First, the authors did not include five trials [30, 31, 33–35] published in non-English-speaking countries and may thus have introduced a selection bias [48]. Secondly, they included one trial [49] in which hip and knee OA was investigated simultaneously. A previous study [50] showed that patients with knee OA experienced greater improvement with naproxen than those with hip OA, as measured by the WOMAC and SF-36 domains. It was also argued that because anatomy, physiology and risk factors are different for hip and knee, analysing hip and knee OA in the same study might be misleading [51]. Therefore, including such a trial might have produced less favourable results for PEMF.

Another review presented by Bjordal *et al.* [15] reported that PEMF alleviated knee pain from 0 to 4 weeks and 8 weeks after the initiation of treatment. In contrast, our study found that PEMF was not effective at 2–6 weeks. Although both studies analysed different sets of trials, the discrepancy appears to be derived from the methods used for data extraction. Interestingly, the authors only

extracted data from the period in which the largest efficacy was shown, from 0 to 4 weeks. If a study only utilizes data demonstrating the greatest efficacy of a particular intervention, the results will be skewed in favour of the intervention. Therefore, the results of this review might be misleading.

The third review completed by Vavken *et al.* [16] reported that PEMF did not alleviate knee pain, but improved knee function 3–10 weeks after the treatment initiation. The authors did not include four trials [30, 31, 34, 35]. However, considering that all trials were evaluated as low-quality trials in our study, the results of Vavken *et al.* are in good agreement with our findings on the improvement of knee function. Nevertheless, they are not consistent with the results of the present study on the efficacy of the PEMF therapy in reducing knee pain. Although the authors included several trials [10, 49] dealing with other OA sites in their review, this discrepancy may be explained by the fact that their analysis involved the use of different measurement units between trials. Indeed, for the calculation of the weighted mean difference, the authors combined data from the VAS (100 mm) and the WOMAC pain subscale (20 points) without prior

transformation of the values. This flaw may have distorted the conclusions of their review.

Our study further detected several aspects of concern that have not been raised by the previous reviews [14–16]. First, none of the eligible trials reported the rationale for the selection of the dosage applied. Since PEMF has been empirically utilized in clinics, there is a need for the use of clear, standardized treatment protocols tested in pilot studies and supported by concrete evidence. For example, in one study [52], the successful effects of PEMF were largely confined to the application of dosages of >40 kJ of energy per day for the management of acute tissue injury. Therefore, the power output (i.e. total energy per day) may be clinically more relevant to the assessment of PEMF efficacy. However, most trials provided no details on the dosage applied, and thus we could not estimate the power output.

Secondly, three (21.4%) trials [34, 35, 41] applied electromagnetic fields over the levels recommended by the ICNIRP. Although these guideline limits should not be taken as a precise delineation between safety and hazard, it is known that the potential risk to human health gradually increases with higher exposure levels [53]. At present, the threshold between cure and risk of the electromagnetic fields is unknown. Therefore, from a conservative viewpoint, we believe that the ICNIRP guidelines should represent a minimum standard to be followed in PEMF studies. Moreover, our data also showed that electromagnetic fields below the levels permitted by the ICNIRP guidelines significantly alleviated knee pain.

Thirdly, most of the trials did not fully describe the type of placebo used. To accurately address the efficacy of the treatment, the placebo should mimic the PEMF in appearance and should be physiologically inert [54]. However, even for the trial [39] that used the most credible placebo (i.e. switched-on PEMF without output), we could not determine whether this placebo was adequate to the study because the authors provided no description of working conditions. In addition, some trials [36, 41] used a PEMF that emitted an electromagnetic field as a placebo. Although of low intensity, at present it is not possible to exclude likely beneficial effects of this level of intensity in knee tissues. To exactly determine the efficacy of PEMF, the use of optimal placebos as control is thus essential.

Although we showed that PEMF was effective in improving function at 8 weeks and, for high-quality trials, in treating pain at 4 and 8 weeks, the results should be interpreted with caution. Selection bias may have been introduced in our study [48]. While we attempted to identify eligible trials using three main electronic databases encompassing most of the specialized literature, the searches failed to identify a list of all eligible trials. For example, when we manually searched a Korean peer-reviewed journal, one trial [35] was identified that was not retrieved by other searches. In addition, we were unable to obtain a copy of one study [43] identified by the literature searches. Likewise, possible correlations between results obtained for the different time points were not determined [55]. The reasons for this were the limited

number of eligible studies and the sparsity of data available for the time points analysed [56]. Finally, our subgroup analyses were largely dependent on the PEDro scale. Even though the reliability of the PEDro scale is acceptable for consensus ratings [57], it is possible that the results would be different if another team rated the same trials. Indeed, the scores of the PEDro database were slightly different from those adopted in the present study. Despite this, when the analyses conducted depended on the scores of the PEDro database, PEMF efficacy still varied according to the trial quality.

In conclusion, the present study indicates that although PEMF was not more effective than placebo in treating knee pain, it was more effective in improving knee function 8 weeks after treatment initiation. However, the results of the present study, restricted to trials using high-quality methodology, provide suggestive evidence supporting the efficacy of PEMF in pain alleviation. Therefore, there is a need for more well-controlled randomized trials employing adequate methodology to conclusively evaluate the efficacy of PEMF.

Rheumatology key messages

- Analysis of high-quality trials suggests that PEMF is effective in treating pain and improving function.
- More well-controlled trials employing adequate methodology are needed to conclusively evaluate PEMF efficacy.

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Supplementary data

Supplementary data are available at *Rheumatology* Online.

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