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Original article

Efficacy of acupuncture in fibromyalgia syndrome—a systematic review with a meta-analysis of controlled clinical trials

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Abstract

Objective. To systematically review the efficacy of acupuncture in fibromyalgia syndrome (FMS).

Methods. MEDLINE, PsychInfo, EMBASE, CAMBASE and the Cochrane Library were screened (through July 2009). The reference sections of original studies and systematic reviews for randomized controlled trials (RCTs) on acupuncture in FMS were searched.

Results. Seven RCTs with a median treatment time of 9 (range 6–25) sessions and 385 patients were included. Outcomes of interest were key symptoms of FMS, namely pain, fatigue, sleep disturbances, reduced physical function and side effects at post-treatment. Follow-up of two RCTs with a median follow-up of 26 weeks was available. Standardized mean differences (SMDs) comparing verum and control acupuncture were calculated. Strong evidence for the reduction of pain (SMD −0.25; 95% CI −0.49, −0.02; $P = 0.04$) was found at post-treatment. There was no evidence for the reduction of fatigue and sleep disturbances, or the improvement of physical function at post-treatment. There was no evidence for the reduction of pain and improvement of physical function at the latest follow-up. Subgroup analyses resulted in moderate evidence for a significant and small reduction of pain at post-treatment in studies with electro-stimulation and individualized acupuncture. Stratifying the type of controls (penetrating *vs* non-penetrating control acupuncture) did not change the results. Significant reduction of pain was only present in studies with risk of bias. Side effects were inconsistently reported.

Conclusion. A small analgesic effect of acupuncture was present, which, however, was not clearly distinguishable from bias. Thus, acupuncture cannot be recommended for the management of FMS.

Key words: Fibromyalgia syndrome, Acupuncture, Systematic review, Meta-analysis.

CLINICAL SCIENCE

Introduction

The main symptoms of fibromyalgia syndrome (FMS) are chronic widespread pain, fatigue and sleep disturbances/non-restorative sleep [1, 2]. Moreover, most patients suffer from additional somatic and psychological symptoms. Co-morbidity with inflammatory rheumatic diseases [3], other functional somatic syndromes such as irritable bowel syndrome [4], or mental disorders such as affective and anxiety disorders [5] are highly prevalent. FMS affects ~3% of the general population and occurs predominantly in women in clinical settings [6].

Treatment of FMS is symptomatic, aiming at the reduction of pain, fatigue and sleep disturbances, and the improvement of physical and psychological symptoms as well as social functioning.

Due to the high strain and impact on health-related quality of life (HRQOL) as well as the dissatisfactory treatment situation, a variety of different pharmacological and

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non-pharmacological therapies are employed [7, 8]. Acupuncture is one of the most frequently used complementary alternative medicine (CAM) intervention. The expression 'acupuncture' literally means to puncture with a needle. In the real treatment situation, needling combined with moxibustion—the burning on or over the skin of selected herbs—and may also involve the application of other kinds of stimulation, e.g. electrical stimulation, laser, pressure to or cupping at defined points on the surface of the skin [9]. Overall, 15–20% of FMS patients seek acupuncture treatment [7, 10].

In order to give patients and physicians an orientation within the continuously growing number of studies on the therapy of FMS [11–13], evidence-based guidelines on the management of FMS were published recently. With regard to evidence-based medicine, systematic reviews and meta-analyses are considered to ensure the highest quality as basis for specific recommendations [14]. However, the most recent qualitative systematic reviews on the efficacy of acupuncture in FMS did not provide consistent conclusions. While one review concluded that there is moderate evidence for the efficacy of acupuncture [15], a second one found that the evidence for acupuncture in the treatment of FMS is mixed [16]. Both reviews have some methodological limitations in that they did not consider all studies available and did not analyse all outcomes. A recent systematic review based on a meta-analysis concluded that there is no evidence for a beneficial effect of acupuncture compared with placebo acupuncture in FMS [17]. Since the authors searched the literature until January 2008 and did not conduct subgroup and sensitivity analyses, an update of the literature and a meta-analysis based on recent methodological recommendations [18] are needed in order to evaluate the significance of acupuncture in the management of FMS.

Materials and methods

Methods of meta-analysis

Meta-analysis was performed according to the quality of reporting meta-analyses guidelines [19] and the recommendations of the Cochrane Collaboration [18].

Study selection

In order to be included into the systematic review, studies were required to meet the following criteria.

(i) Type of participants: trials with adults diagnosed with FMS based on recognized criteria were included.
(ii) Type of studies: randomized and quasi-randomized study designs were included. Quasi-randomized studies are those that do not strictly adhere to randomized methods of allocation, e.g. allocation by order of admission, date of birth or some other method that is not truly random. Data were required to be published as a full paper.
(iii) Types of interventions: for the present purposes, three types of acupuncture were defined. Chinese acupuncture: stimulation of traditional meridian points, usually with the intention of influencing energy flow in the meridian. Additional tender points may also be used; Western acupuncture—the use of tender or trigger points only with no named acupuncture points; and Japanese acupuncture—superficial needling in the area of the pain. Acupuncture points should be stimulated by needle insertion or laser. We labelled these kinds of acupuncture 'verum acupuncture'. Methods of stimulating acupuncture points by acupressure, transcutaneous electrical nerve stimulation, infrared light for verum acupuncture were excluded. Trials comparing verum acupuncture with the following control interventions were included: sham acupuncture (penetration of the skin with and without stimulation of non-acupuncture points) and simulated acupuncture (simulated non-penetrating stimulation of the skin at acupuncture or non-acupuncture points).
(iv) Types of outcome measures: at least one key symptom of FMS, namely pain, fatigue, sleep disturbances and physical function was required as outcome measure. Secondary outcome measures were adverse events.

Data sources and searches

The electronic bibliography databases screened included MEDLINE, PsycINFO, PUBMED, EMBASE, CAMBASE, The Cochrane Central Register of Controlled Trials (CENTRAL) and Cochrane Library Systematic Reviews (until July 2009). The search terms 'fibromyalgia' and 'acupuncture' and their variations were used with the following strategy.

To locate FMS:

#1 fibromyalgia [MeSH]
#2 fibromyal* [tw]
#3 fibromyalgia syndrome [tw]
#4 RCT [tw]
#5 or/1–4

To locate acupuncture interventions:

#6 acupuncture [MeSH]
#7 acupuncture therapy [MeSH]
#8 acupuncture points [MeSH]
#9 body acupuncture [tw]
#10 electroacupuncture [MeSH]
#11 electro-acupuncture [tw]
#12 electrical acupuncture [tw]
#13 ear acupuncture [MeSH]
#14 auricular acupuncture [tw]
#15 scalp acupuncture [tw]
#16 or/6–15
#17 5 and 16

A modification of this strategy was used to search the other databases. No restrictions of language were made. In addition, reference sections of original articles, systematic reviews [15–17] and evidence-based guidelines on the management of FMS [11–13] were screened manually and independently by two authors.

Data extraction and management

Two authors screened the titles and abstracts of potentially eligible studies identified by the search strategy (P.K., W.H.). The full-text articles were then examined independently by two authors in order to determine whether they met the inclusion criteria (D.I., W.H.). For the preparation of the meta-analysis, two authors independently extracted the data detailed above using standard extraction forms (P.K., W.H.). Discrepancies were rechecked and consensus achieved by discussion. If necessary, a third author reviewed the data to reach consensus (F.M.).

Assessment of risk of bias in included studies

External validity. In order to estimate the representativeness of study samples for the FMS population in clinical practice, the settings of the studies, the ways of referral to the randomized controlled trials (RCTs), the inclusion and exclusion criteria and the socio-demographic data of the study samples were assessed.

Internal validity. The methodological quality was assessed by the van Tulder score using 11 items [20]. If no detailed information was given to answer the questions of the items, 0 was coded. We arbitrarily classified quality as high (score: 8–11), moderate (score: 5–7) or low (score: 1–4). The modified Cochrane Collaboration tool for assessing risk of bias [18] was utilized: (i) was the allocation sequence adequately generated? (ii) Was allocation adequately concealed? (iii) Was knowledge of the allocated intervention adequately prevented for participants and outcome assessors during the study? (Note: a blinding of the therapists is nearly impossible in non-pharmacological trials.) (iv) Were incomplete outcome data adequately addressed? (v) Were reports of the study free of suggestion of selective outcome reporting?

Measures of treatment effect

Standardized mean differences (SMDs) were calculated by means and S.D.s or change scores for the outcomes of pain, fatigue, sleep disturbances and physical function for both verum and sham acupuncture conditions. For the calculation of SMDs the data of at least two studies were required.

Unit of analysis issues

If studies had two or more control arms, sham acupuncture was the preferred control arm.

Dealing with missing data

Where means or S.D.s were missing, attempts were made to obtain these data through contacting trial authors. When S.D. data were not available from trial authors, they were calculated from *t*-values, CIs or S.E.S, if reported in articles [18]. If these data were not available, we searched the data in meta-analyses of acupuncture in chronic pain [17, 21].

Data analysis and synthesis

Non-parametric tests (Mann–Whitney U-test) were used for the comparison of continuous variables and χ^2-tests for the comparison of categorical variables. Data are presented as median (range). A two-sided $P \leqslant 0.05$ was considered significant.

Meta-analyses were conducted using RevMan Analyses software (RevMan 5.0.17) of the Cochrane Collaboration [22]. In case of different directions of scales, the mean from one set of studies was subtracted from the maximum score of the scale [18]. Examination of the combined results was performed by a random-effects model, because this model is more conservative than the fixed-effects model and incorporates both within-study and between-study variance [23]. SMD used in Cochrane reviews is the effect size known as Hedges (adjusted) *g*. Cohen's categories were used to evaluate the magnitude of the effect size, calculated by SMD, with $g \leqslant 0.2$ = not substantial; $g > 0.2$–0.5 = small effect size; $g > 0.5$–0.8 = medium effect size; and $g > 0.8$ = large effect size [24].

We applied the van Tulder recommendations regarding the levels of evidence as follows. (i) Strong: consistent findings among at least two high-quality (HQ) RCTs; (ii) moderate: consistent findings among at least two moderate-quality (MQ) RCTs and/or one HQ RCT; (iii) limited: one MQ RCT or at least two low-quality (LQ) studies; (iv) conflicting: inconsistent findings among multiple trials; and (v) no evidence: no RCTs available [20].

Assessment of heterogeneity

Heterogeneity was tested using the I^2-statistic with values $> 50\%$ indicating strong heterogeneity. τ^2 was used to determine how much heterogeneity was explained by subgroup differences [18].

Subgroup analysis and investigation of heterogeneity

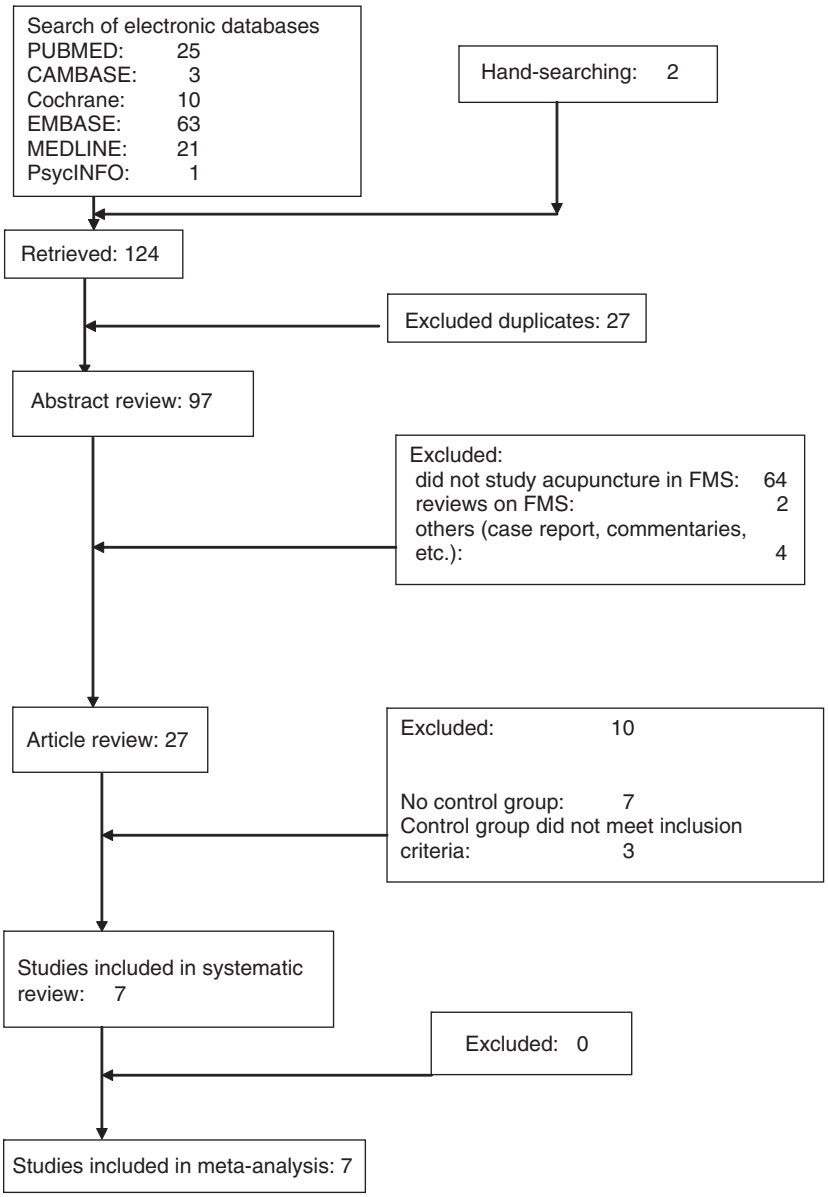
In the case that at least two studies were available, subgroup analyses were performed for type of acupuncture (Chinese *vs* Western *vs* Japanese; needling of standardized *vs* individually adapted acupuncture points), type of stimulation (manual *vs* electric), intensity of acupuncture and type of control acupuncture (sham *vs* simulated acupuncture). These subgroup analyses were also used to examine potential sources of clinical heterogeneity.

Sensitivity analyses

Where at least two studies were available, sensitivity analyses were calculated in order to test the robustness of significant findings obtained. The analyses were performed by comparing studies based on the following internal validity criteria:

(i) inadequate or unclear *vs* adequate sequence generation;
(ii) inadequate or unclear allocation *vs* adequate concealment;
(iii) inadequate or unclear blinding of the patient and the outcome assessor *vs* adequate blinding; and

Fig. 1 Study flow diagram.



(iv) studies with low, moderate and high van Tulder scores.

These sensitivity analyses were also used to examine potential sources of methodological heterogeneity.

Publication bias

Where appropriate, publication bias was assessed using funnel plots generated by means of Revman Analyses Software (at least 10 studies available) [18].

Results

Study selection

The literature search produced 124 citations involving FMS and acupuncture, and clinical trials. Of these, 97 were excluded: 64 did not evaluate acupuncture in FMS, 27 were double hits of controlled studies (study found in at least two data sources) and two were reviews (Fig. 1). After a review of these 27 initially selected articles, a further 20 papers were excluded either because they had no control arm or because acupuncture as add-on to medical therapy was compared with medical therapy (two studies) [25, 26]. One study, comparing acupuncture with pharmacological therapy, was also excluded [27]. Finally, seven RCTs were included in the qualitative and quantitative synthesis [28–34].

Study characteristics

Setting, referral and exclusion criteria (external validity). Four studies were conducted in North America [28, 30, 31,

33] and three in middle Europe [29, 32, 34]. Patients were recruited by registers of hospitals, referral (general practitioner, rheumatologist, hospital departments), local self-help groups and newspaper advertisement. Six studies were conducted within the setting of a university, one within private acupuncture offices [28]. All but one study [28] were single centre based. FMS was diagnosed in six studies by the criteria of the ACR [35] and in one study by the criteria of generalized tendomyopathia [36]. Two studies did not report the exclusion criteria [32, 34]. Five studies excluded patients with previous acupuncture and bleeding disorder [28–31, 33]. Three studies excluded patients with somatic diseases, including inflammatory or rheumatic disease [29–31], FMS-related litigation, respectively [3, 28, 30] and one study due to severe mental disorder [31] (Table 1).

Participants. The median of the mean age of the participants was 47 (range 44–55) years. The median of the percentage of women was 95% (range 90–100%). The median of the percentage of Caucasians was 96% (90–100%).

Interventions. Three studies reported the number of persons screened and randomized with a median of 18% (range 16–95%) [28, 30, 33]. The median of the patients with verum acupuncture in the studies was 21 (range 10–28) and of controls 21 (range 10–58). About 133/151 (87%) patients with verum acupuncture and 206/234 (88%) in the control groups completed therapy ($z = -0.06$; $P = 0.9$). The median of completing patients in the verum acupuncture group was 92% (range 76–100%), and in the control groups 92% (range 80–100%).

The length of the interventions, excluding follow-up, ranged from 2 to 15 weeks with a median of 8 weeks. The median duration of acupuncture treatment was 9 sessions (range 6–25). Four studies performed follow-up, two of which presented outcomes suitable for meta-analysis with a median of the latest follow-up with 26 (range 24–42) weeks.

All studies used traditional Chinese acupuncture points, with two studies utilizing standardized points [28, 33] and five studies utilizing an individualized paradigm [29–32, 34]. Two trials performed electroacupuncture [29, 33], five trials performed manual acupuncture [28, 30–32, 34]. One study used two control arms with different types of sham acupuncture [30], one study used three control arms with two different types of sham and one simulated acupuncture [28], one study compared with simulated acupuncture and no treatment [34]. The remaining studies had one control arm, three of these studies compared verum with simulated acupuncture [31, 33, 34] and one with sham acupuncture [29]. Five studies gave details on co-therapies [28–31, 34], and three of these ensured constancy co-therapies throughout the trial [28, 30, 31] (supplementary table 1, available as supplementary data at *Rheumatology* Online).

Internal validity. Three studies had a high [28, 30, 31], two studies had a medium [29, 33] and two a low van Tulder score [32, 34]. For risks of biases in individual studies, please see supplementary table 2, available as supplementary data at *Rheumatology* Online.

Effects of interventions

Data are reported as follows: SMD (95% CI); *P*-value of test for overall effect. We found strong evidence for the reduction of pain [SMD −0.25 (95% CI −0.49, −0.02); $P = 0.04$] at post-treatment (see supplementary figure 2, available as supplementary data at *Rheumatology* Online). We found no evidence for reduction of fatigue [SMD 0.04 (95% CI − 0.32, 0.39); $P = 0.84$] and sleep disturbances [SMD 0.05 (95% CI − 0.79, 0.83); $P = 0.91$] or improvement of physical function [SMD − 0.15 (95% CI − 0.61, 0.91); $P = 0.52$] at post-treatment. We found no evidence for reduction of pain [SMD − 0.11 (95% CI − 0.72, 0.49); $P = 0.71$] or improvement of physical function [SMD − 0.05 (95% CI − 0.47, 0.37); $P = 0.83$] at latest follow-up (Table 2).

Three studies reported on side effects such as discomfort at side of needle sensation, nausea, soreness and worsening of FMS symptoms [28, 29, 33]. The frequency of the side effects reported ranged from 3 to 70% for all types of acupuncture. One study reported a drop out due to side effects in the verum group of 17% and in the sham control group of 15% [29].

Risk of bias and additional analyses

There was significant heterogeneity in the outcomes of sleep and physical function at post-treatment and in pain at latest follow-up (Table 2). Because of the limited number of studies, potential sources of heterogeneity could not be assessed. Subgroup analyses yielded the following results (Table 3): trials with individual selection of acupuncture points, with electrostimulation and less than 10 sessions had significant effects on pain at post-treatment, but not studies with standardized selection of acupuncture points, manual stimulation and more than 10 sessions. Visual inspection of the forest plots revealed that only one study was in favour for the outcome pain (see supplementary figure 2, available as supplementary data at *Rheumatology* Online) with both types of control acupuncture.

Sensitivity analyses demonstrated a significant effect on pain at post-treatment in studies with risks of bias whereas the effect on pain at post-treatment in studies without risks of bias was not significant. The effect on pain at post-treatment was not significant in studies with low and high, but with medium methodological quality (see supplementary table 3, available as supplementary data at *Rheumatology* Online).

Publication bias

Because less than 10 studies were analysed, we did not perform visual inspection of funnel plots for indicators of publication bias.

Table 1 Main study characteristics

			Study population			Treatment group		Control group	Both groups	
Ref.; setting; referral	Mean age; women, *n* (%); race, *n* (%)	Exclusion criteria	Inclusion criteria; comorbidities assessed and reported	No. screened/ randomized, *n* (%)	No. completing, *n* (%)	No. completing, *n* (%)	Kind of treatment; duration of treatment	Kind of treatment; duration of treatment; no./completing, *n* (%)	Co-medication allowed; other co-therapies reported; side effects	Outcome measures used for meta-analysis; follow-up; methodological quality (van Tulder score)
Assefi *et al*. [28]; US private acupuncture offices; advertisment, local self-help groups and doctors	47 years; most women; most White	Other pain syndromes; bleeding disorder; needle phobia; use of narcotics; litigation due to FMS; previous acupuncture	ACR diagnosis; >18 years; pain ≥4/11 VAS; NR	604/100 (16.6)	96/86 (89.6)	25/23 (92.0)	Traditional Chinese manual acupuncture (standardized); 24 sessions (12 weeks)	Sham acupuncture; 24 sessions (12 weeks); 24/22 (91.6); simulated acupuncture; 24 sessions; 23/19 (82.6); acupuncture for unrelated condition (irregular menses); 24 sessions; 25/21 (84.0) not used for comparison	Pharmacological and non-pharmacological therapies constant through study; no further details given; direct acupuncture: 61% (discomfort at side of needle insertion, bruising, nausea); simulated acupuncture: 29%; sham needling: 64%; acupuncture for unrelated condition: 70%	Pain VAS 0–10[a]; fatigue VAS 0–10[a]; sleep VAS 0–10[a]; depressed mood function SF-36 physical summary score; 12 and 24 weeks; 8
Deluze *et al*. [29]; Switzerland University Hospital, Division of Physical Therapy; NR	NR; NR; NR	Severe concomitant disease, neuropathy, bleeding disorder; treatment with morphine-like drugs or anti-coagulants; previous acupuncture	ACR diagnosis; NR	NR	70/55 (64.9)	36/28 (77.8)	Chinese electro-acupuncture; (individually adapted); six sessions (2 weeks)	Sham acupuncture; six sessions (3 weeks)	Physiotherapy; non-steroidal agents, tricyclic anti-depressants; direct acupuncture: drop-out due to side effects (increase in symptoms 2/36, unpleasantness of needle insertion 3/36, ankle oedema 1/36); sham acupuncture: drop-out due to side effects (increase in symptoms 4/34, unpleasantness of needle insertion 1/34)	Pain VAS 0–100; fatigue NA; sleep VAS 0–100; depressed mood NA; physical function NA; No; 7
Harris *et al*. [30]; USA, University Rheumatology Department; newspaper advertisement	47 years; 95% women; 95% White	Bleeding diathesis; inflammatory or autoimmune disorder; regular use of narcotics; history of substance abuse; disability payment or litigation related to FMS	ACR diagnosis for at least 1 year; yes	640/114 (17.8)	114/78 (68.4)	27/15 (55.6)	Traditional Chinese manual acupuncture; (individually adapted); 18 sessions (13 weeks)	Sham acupunctures; traditional needle location without manual stimulation; not used for comparison; 30/19 (63.3); non-traditional needle location with manual stimulation; not used for comparison; 28/20 (71.4); non-traditional needle location without stimulation;	Continuation, but not change of normal treatment regimens, including anti-depressants allowed; acetaminophen or ibuprofen for rescue	Pain VAS 0–10; fatigue MFI; sleep NA; depressed mood NA; function SF-36 Physical Summary Score; no; 9

(continued)

Table 1 Continued

Ref.; setting; referral	Mean age; women, *n* (%); race, *n* (%)	Exclusion criteria	Study population			Treatment group		Control group	Both groups	
			Inclusion criteria; comorbidities assessed and reported	No. screened/ randomized, *n* (%)	No. completing, *n* (%)	No. completing, *n* (%)	Kind of treatment; duration of treatment	Kind of treatment; duration of treatment; no./completing, *n* (%)	Co-medication allowed; other co-therapies reported; side effects	Outcome measures used for meta-analysis; follow-up; methodological quality (van Tulder score)
								27/15 (55.5) used for comparison		
Harris *et al.* [31]; USA, Rheumatology Department; NR	44 years; 100% women; NR	Previous experience with acupuncture; bleeding diathesis; current use or history of opioid or narcotic analgesics; or autoimmune disorder; pregnancy or nursing; severe psychiatric disorder, including major depression	ACR diagnosis; 18–75 years	NR	20/20 (100)	10/10 (100)	Traditional Chinese manual acupuncture (individually adapted); nine sessions (8 weeks)	Simulated acupuncture: non-skin-penetrating pricking sensation at non-acupuncture points;10/10 (100)	Continuation, but not change of normal treatment regimens including anti-depressants allowed; acetaminophen or ibuprofen for rescue; NR	Pain MPQ Total[a]; fatigue NA; sleep NA; depressed mood NA; HRQOL NA; no; 8
Lautenschläger *et al.* [32]; Switzerland University, Rheumatology Department; NR	50 years; 95% women; NR	NR	Generalized tendomyopathia	NR	37/34 (91.9)	17/15 (88.2)	Traditional Chinese manual acupuncture (individually adapted: 8–10 of 25 pre-defined points could be chosen); six sessions (2 weeks)	Simulated acupuncture: non-skin penetrating; disconnected laser with skin contact on acupuncture points on the back; 20/19 (95)	NR; NR	Pain VAS 0–10; fatigue NA; sleep NA; depressed mood NA; HRQOL NA; 12 weeks, no details suited for meta-analysis presented; 4
Martin *et al*. [33]; USA, University Pain Department; Physicians	49 years; 95% women; 96% White	Bleeding disorder; previous acupuncture	ACR; NR	60/50 (83.3)	50/49 (98.0)	25/25 (100)	Traditional Chinese electro-acupuncture; (standardized); 25 sessions (6–12 weeks)	Sham acupuncture; six sessions (2–4 weeks); 25/24 (96.0)	NR; mild bruising and soreness, per cent NR; 2/25 mild vagovasal symptoms	Pain VAS 0–10; fatigue VAS 0–10; sleep NA; depressed mood VAS 0–10; function FIQ Physical Impairment; 4 and 28 weeks; 7
Sprott [34]; Germany, University Internal department; NR	55 years; NR; NR	NR	NR; NR	NR	30/NR	10/NR	Traditional Chinese manual acupuncture (individually adapted); six sessions (2 weeks)	Simulated acupuncture; non-skin penetrating; disconnected laser with skin contact on acupuncture points; six sessions (2–4 weeks; 10/NR; no treatment: not used for comparison; 10/NR	Active and passive physiotherapy, local applications of cold or heat; electrotherapy: acetaminophen for rescue medication; NR	Pain VAS 0–10[b]; fatigue NA; sleep NA; depressed mood; HRQOL NA; 8 weeks[b]; 3

The order of the presented studies is arranged according to the year of publication and alphabetic order. [a]Provided on request. [b]Not provided on request; data found in [21]. FIQ: Fibromyalgia Impact Questionnaire; MFI: Multi-dimensional Fatigue Inventory; MPQ: McGill Pain Questionnaire; NR: not reported, SF-36: Short-form health survey; VAS: Visual analogue scale.

Table 2 Effect sizes of verum acupuncture compared with control acupuncture on selected outcome variables

Outcome title	Number of study arms	Number of patients	Effect size SMD (95% CI)	Test for overall effect *P*-value	Heterogeneity I^2 (%); τ^2
Post-treatment					
01 Pain	7	242	−0.25 (−0.49, −0.02)	0.04	1; 0
02 Fatigue	3	147	0.04 (−0.32, 0.39)	0.84	16; 0.84
03 Sleep	2	87	0.05 (−0.79, 0.83)	0.91	76; 0.28
05 Physical function	3	149	−0.15 (−0.61, 0.91)	0.52	51; 0.9
Latest follow-up					
01 Pain	2	87	−0.11 (−0.72, 0.49]	0.71	50; 0.09
02 Physical function	2	87	−0.05 (−0.47, 0.37)	0.83	0; 0

Table 3 Subgroup analysis of the effect size on pain at post-treatment

Outcome title	Number of studies	Number of patients	Effect size SMD (95% CI)	Test for overall effect *P*-value	Heterogeneity; I^2 (%); τ^2
Type of acupuncture					
Individually adapted acupuncture points	5	188	−0.38 (−0.67, −0.09)	0.01	0; 0
Standardized acupuncture points	2	91	−0.04 (−0.54, 0.47)	0.43	33; 0.04
Type of stimulation					
Electro	2	104	−0.43 (−0.81, −0.04)	0.03	0; 0
Manual	5	175	−0.19 (−0.52, 0.14)	0.28	14; 0.02
Type of control acupuncture					
Sham acupuncture[a]	3	179	−0.13 (−0.58, 0.33)	0.58	50; 0.08
Simulated acupuncture[a]	5	179	−0.24 (−0.83, 0.14)	0.22	34; 0.07
Number of sessions					
Less than 10	4	132	−0.54 (−0.89, −0.19)	0.002	0; 0
More than 10	3	147	−0.03 (−0.36, 0.29	0.84	0; 0

[a]Ref. [28] with one control arm each.

Discussion

Summary of main results

We found strong evidence for the reduction of pain at post-treatment while there was no evidence for a positive effect on other main symptoms of FMS. We found moderate evidence that the positive effects could not be maintained at follow-up. Adverse events were inconsistently reported. We conclude from the available data that acupuncture was not associated with serious harmful events. The low drop-out rate indicates a good acceptance of this treatment by the patients.

Applicability of evidence

Studies were conducted in the setting of primary, secondary and tertiary care in USA and middle Europe. Patients were recruited by various ways of referral including all levels of care. The majority of participants were adult female and Caucasians. All studies which reported these criteria excluded patients with previous acupuncture experience and bleeding disorders. The majority of studies excluded patients with severe physical diseases. Patients with mental disorders or FMS-associated litigation were excluded by a minority of studies. Therefore, the results are applicable to the vast majority of patients in clinical practice.

Quality of evidence

There was a great variability of the methodological quality of studies. The positive effect on pain at post-treatment was not robust against potential methodological biases. The inconsistent results were mainly due to one high-quality study in which sham and simulated acupuncture were superior to verum acupuncture [28]. This study differed from its design from the others: acupuncture was delivered by eight acupuncturists in private settings, whereas the other studies used one or two acupuncturists and acupuncture was carried out in hospital departments.

Agreements and disagreements with other systematic reviews

Our conclusions are not in line with the outcome of a previous qualitative systematic review on acupuncture in

FMS, which concluded that there is moderate evidence for the efficacy of manual acupuncture in FMS [15]. On the other hand, the finding of a small but significant reduction of pain in this study is not in line with the conclusions of two other systematic reviews on acupuncture in FMS, indicating that acupuncture is not effective in relieving FMS symptoms [16, 17]. At this point, our results are in line with the conclusions of a systematic review on acupuncture, that the efficacy of acupuncture using classical points when compared with sham or minimal acupuncture is overestimated [37]. A recent systematic review on acupuncture in a variety of chronic pain conditions found a small difference [SMD −0.17 (95% CI − 0.26, −0.08)] between verum and placebo acupuncture [21], which is comparable with the effect we found. The authors also report a tendency for larger effects of verum acupuncture when the comparative placebo procedure was penetrative (compared with simulated acupuncture). However, our results do not confirm this finding.

Strengths and weaknesses

Our review is the first study available, meta-analysing all available outcomes of acupuncture effects on FMS. Furthermore, the data were stratified to different types of verum and placebo acupuncture and the applicability of the results [38] assessed. The review includes several trials of high methodological quality. However, for two of the studies, the means and S.D.s of outcomes required for meta-analysis were not included in the original publication [28, 31] but were provided on request. Furthermore, mean and S.D.s for the outcome pain of another study was not included in the publication, and was also not provided on request [34]. Nonetheless, it was possible to extract this information from the figure of a meta-analysis of acupuncture in chronic pain syndromes [21]. Overall, the techniques of acupuncture and especially the verbal instructions given to the patient were only incompletely reported. No study reported the adherence to treatment. Some of the trials showed methodological weaknesses. However, the main weakness of the meta-analysis presented here is the limited number of studies and patients included. Moreover, the modalities and dosages of verum and sham acupuncture and the assessments used in the trials were heterogeneous.

Unanswered questions and future research

A problem in trials evaluating acupuncture for chronic pain syndromes is that physiologically, point specificity, the crux of sham acupuncture, may not be applicable. Mechanisms like the so-called 'diffuse noxious inhibitory controls' are largely independent of specific points, but most likely relevant for the analgesic effects of acupuncture [39, 40]. Moreover, it is doubtful that penetrating the skin qualifies as a sham condition in FMS. Applying verum acupuncture *vs* 'minimal acupuncture' or 'acupuncture at non-acupuncture points' could simply be a trial comparing different acupuncture conditions [41]. In addition, even a slight touch of the skin can have positive effects on the affective level of pain perception [42]. Therefore, skin-penetrating verum acupuncture and skin-touching simulated acupuncture could simply compare two different sensory stimulating techniques and would thus not represent an inactive control for treatment.

Since acupuncture is popular among FMS patients, further rigorous studies are warranted. Multicentre studies involving a larger number of patients and treatment centres of all levels of care, adequate blinding of patients and observers, as well as comparisons of acupuncture with standard medical care and/or control procedures such as simulated or minimal acupuncture are needed. Moreover, different forms of stimulation (manual *vs* electric acupuncture) and intensities of stimulation should be tested [41] and specific guidelines, namely the Standards for Reporting Interventions in Controlled Trials of Acupuncture recommendations [43], should be followed when acupuncture trials are reported. A recent RCT of acupuncture for another functional somatic syndrome, namely irritable bowel syndrome, suggested that the effects of sham acupuncture can be enhanced by an empathic physician style [44]. Therefore, acupuncturists' verbal instructions and non-verbal communication are required to be standardized in acupuncture trials. In order to assess the patient component of the therapeutic effect of acupuncture, it is also necessary to assess the patients' expectations regarding acupuncture. Finally, the integration of acupuncture into multicomponent therapy (e.g. aerobic exercise and psychological therapy) should be compared with multicomponent therapy without acupuncture.

Rheumatology key messages

- Acupuncture has a small analgesic effect in FMS, which cannot be clearly distinguished from bias.
- Acupuncture cannot be recommended as a single therapy for the management of FMS.

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Supplementary data

Supplementary data are available at *Rheumatology* Online.

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