

Review

Acupuncture for rheumatoid arthritis: a systematic review

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The aim of this systematic review is to evaluate the available evidence, from randomized clinical trials (RCTs), of acupuncture for treating patients with RA. Systematic searches were conducted on 17 databases up to April 2008 without the language restriction. All RCTs of acupuncture, with or without electrical stimulation or moxibustion, for patients with RA were considered for inclusion. A total of 236 potentially relevant studies were identified and eight RCTs were included. Four RCTs compared the effects of manual or electro-acupuncture with penetrating or non-penetrating sham acupuncture and failed to show specific effects of acupuncture on pain [$n=88$; weighted mean differences (WMD), 10 cm VAS -0.46 ; 95% CI $-1.70, 0.77$; $P=0.46$; heterogeneity: $\tau^2=0.19$; $\chi^2=2.38$; $P=0.30$; $I^2=16\%$] or other outcome measures. One RCT compared manual acupuncture with indomethacin and suggested favourable effects of acupuncture in terms of total response rate. Three RCTs tested acupuncture combined with moxibustion, vs conventional drugs and failed to show that acupuncture plus moxibustion was superior to conventional drugs in terms of response rate ($n=345$; RR 1.12; 95% CI 0.99, 1.28; $P=0.08$; heterogeneity: $\tau^2=0.00$; $\chi^2=1.34$; $P=0.51$; $I^2=0\%$), pain reduction ($n=105$; WMD, 10 cm VAS 1.53; 95% CI $-0.57, 3.63$; $P=0.15$; heterogeneity: $\tau^2=1.18$; $\chi^2=1.81$; $P=0.18$; $I^2=45\%$) or joint swelling index ($n=105$; WMD, 10 cm VAS 0.25; 95% CI $-1.31, 1.82$; $P=0.75$; heterogeneity: $\tau^2=0.18$; $\chi^2=1.14$; $P=0.28$; $I^2=13\%$). In conclusion, penetrating or non-penetrating sham-controlled RCTs failed to show specific effects of acupuncture for pain control in patients with RA. More rigorous research seems to be warranted.

KEY WORDS: Acupuncture, Moxibustion, Rheumatoid arthritis, Pain, Systematic review.

Introduction

The toxicity and limited efficacy of current treatment medication for RA often causes patients to turn towards complementary therapies hoping that such treatment might improve their symptoms [1]. Acupuncture is one of the most frequently used by patients with RA [1–5]. Acupuncture can be defined as the insertion of needles into the skin and underlying tissues at particular sites, known as points, for therapeutic or preventive purposes [6]. The points can also be stimulated with electricity, lasers, pressure, heat or ultrasound waves. Acupuncture is now a widely accepted intervention for the treatment of a variety of conditions [6]. Acupuncture is claimed to be effective in reducing pain as well as improving quality of life of patients with OA [6–8]. Even though acupuncture is often advocated for RA, relatively few rigorous clinical trials have been published [4]. There are three systematic reviews of acupuncture for RA [9–11]. One of them included eight controlled clinical trials and failed to reach firm conclusions [10]. The second review was based on five studies and also did not draw any definitive conclusions [11]. The third review [9], a Cochrane review, assessed the effects of acupuncture for RA including two RCTs and suggested no specific effects of acupuncture on RA-related symptoms including pain, number of swollen joints, etc. This review included only publications published in English and is now out of date. None of these reviews includes all the RCT data currently available. The aim of this systematic review is to evaluate the evidence available from RCTs of acupuncture for treating patients with RA.

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Materials and methods

Data sources

The following electronic databases were searched from inception up to April 2008: Medline, AMED, British Nursing Index, CINAHL, EMBASE, PsycInfo, The Cochrane Library 2008 (Issue 1), six Korean Medical Databases (Korean Studies Information, DBPIA, Korea Institute of Science and Technology Information, Research Information Centre for Health Database, KoreaMed and Korean National Assembly Library) and four Chinese Medical Databases (China Academic Journal, Century Journal Project, China Doctor/Master Dissertation Full Text DB and China Proceedings Conference Full Text DB). The search terms used were ‘acupuncture AND rheumatoid arthritis’ in Korean or Chinese or English. We also manually searched our departmental files and relevant journals, up to March 2008. Further, the references in all located articles were manually searched for additional relevant articles.

Study selection

All articles were included that reported an RCT in which human patients with RA were treated with needle acupuncture with or without electrical stimulation or moxibustion (a traditional Chinese method that uses the heat generated by burning herbal preparations containing *Artemisia vulgaris* (mugwort) to stimulate acupuncture points), laser at precise locations for the purpose of therapy or auricular acupuncture. Trials testing Transcutaneous Electrical Nerve Stimulator (TENS) were excluded. Studies comparing two different forms of acupuncture and those in which no clinical data were reported were also excluded. No language restrictions were imposed. Dissertations and abstracts were included provided they contained sufficient detail.

Data extraction and quality assessment

Hard copies of all articles were obtained and read in full. All articles were read by two independent reviewers (M.S.L., B.-C.S.) and data from the articles were validated and extracted according to the pre-defined criteria. Allocation concealment was assessed using the Cochrane classification. Since it is virtually impossible

for an acupuncturist to be blinded to the treatment, we employed a modified version of the Jadad score [12]. Points were awarded as follows: study described as randomized, 1 point; appropriate randomization method, 1 point; inappropriate randomization method, 1 point deducted; patient blinded to intervention, 1 point; evaluator blinded to intervention, 1 point; and description of withdrawals and dropouts, 1 point. The highest possible score was 5 points. Patient blinding was assumed where the control intervention was indistinguishable from acupuncture, even if the word 'blinding' did not occur in the report. The point for evaluator blinding was only given if specified in the text. Discrepancies were resolved through discussions between two reviewers (M.S.L., B.-C.S.) and if needed, by seeking the opinion of the senior author (E.E.).

The quality of acupuncture was assessed by a reviewer (B.-C.S.) as described previously [13], by answering the question, 'how would you treat the patients included in the study?', on five categories including 'exactly or almost exactly the same way', 'similarly', 'differently', 'complete differently' or 'could not assess' due to insufficient information (on acupuncture or on the patient). The degree of confidence that acupuncture was applied appropriately was assessed on the 100 mm visual analogue scale (with 0% = complete absence of evidence that acupuncture was appropriate, and 100% = total certainty that acupuncture was appropriate).

Data synthesis

To summarize the effects of acupuncture on outcomes (mean change of pain reduction or joint swelling index) compared with baseline, we estimated weighted mean differences (WMD) and 95% CIs from each study using the Cochrane Collaboration's software [Review Manager (RevMan) Version 5.0 for Windows, Copenhagen: The Nordic Cochrane Centre]. Relative risk (RR) and 95% CIs were also calculated. The variance of the change was imputed using a correlation factor of 0.4 as suggested by the Cochrane Collaboration. If appropriate, we then pooled the data across studies using random-effects models (if excessive statistical heterogeneity did not exist). The χ^2 -test, τ^2 and the Higgins I^2 test were used to assess heterogeneity.

Results

Study description

The searches identified 236 potentially relevant articles, of which eight met our inclusion criteria (Fig. 1). The key data are summarized in Table 1 [14–21]. Five trials originated from China [16, 18–21], one trial was conducted in Canada [14], one trial was from Brazil [15] and one trial was from the UK [17]. Manual acupuncture alone was used in four trials [15–18], electro-acupuncture was employed in two trials [14, 16] and manual acupuncture combined with moxibustion was used in three trials [19–21]. Two RCTs employed penetrating sham acupuncture on non-acupoints [14, 15], one RCT used sham acupuncture on acupoints [16], one RCT employed non-penetrating acupuncture on acupoints [17] and conventional pharmacological drugs in four trials [18–21]. Six of the included trials adopted a two-armed parallel-group design [14, 16, 18–21], one a three-armed parallel group design [15] and one was a cross-over trial [17].

Study quality and acupuncture validity

The methodological quality of the trials was variable (from 1 to 5). Four RCTs described the methods of randomization [15–17, 21]. Details of drop-outs and withdrawals were described in three trials [15–17]. Three of them reported details about allocation concealment [15–17]. Two of them employed adequate methods [16, 17], while the other did not [15]. Three RCTs adopted both subject blinding and assessor blinding [15–17]. One trial [14] employed

assessor blinding. Adverse events were mentioned in six studies [15–17, 19–21]. Ethical approval was mentioned in two trials [16, 17].

Regarding the quality of acupuncture, the authors would have treated the patients completely differently in one trial [17], differently in one trial [19], similarly in five trials [14, 15, 18, 20, 21] and exactly or almost exactly the same way in one trial [16]. The degree of confidence that acupuncture was applied appropriately ranged from 20% to 90%. Four [15, 16, 19, 21] of the included RCTs were scored >80%, while two trials were <40% [14, 17].

Outcomes

Acupuncture vs penetrating or non-penetrating sham acupuncture. Three RCTs compared the effects of manual or electro-acupuncture on pain with penetrating sham acupuncture on non-acupoints [14, 15] or acupoints [16], and one RCT tested manual acupuncture with non-penetrating sham acupuncture on acupoints [17]. The meta-analysis failed to show superior effects of acupuncture for pain reduction compared with penetrating sham acupuncture ($n=88$; WMD, 10 cm VAS -0.46 ; 95% CI $-1.70, 0.77$; $P=0.46$; heterogeneity: $\tau^2=0.19$; $\chi^2=2.38$; $P=0.30$; $I^2=16\%$; Fig. 2A). Subgroup analyses also failed to show beneficial effects of manual acupuncture compared with penetrating sham acupuncture on pain reduction ($n=64$; WMD, 10 cm VAS -0.19 ; 95% CI $-2.03, 1.65$; $P=0.84$; heterogeneity: $\tau^2=0.84$; $\chi^2=1.91$; $P=0.17$; $I^2=48\%$, Fig. 2B). There was no difference between the random-effects model and the fixed-effects model.

Two RCTs [15, 16] assessed the effects of acupuncture on ACR20 and HAQ, and showed no improvement compared with penetrating sham acupuncture. Three RCTs [15–17] compared acupuncture with penetrating sham acupuncture and failed to suggest effects of acupuncture for disease assessment scale (DAS) index. Four RCTs [14–17] tested acupuncture for improvement of swollen and tender joints, and showed no favourable effects of acupuncture compared with sham acupuncture with or without penetration.

Acupuncture or acupuncture plus moxibustion vs conventional drugs. Three RCTs [19–21] tested acupuncture plus moxibustion vs conventional drugs including indomethacin, diclofenac sodium or MTX, and one RCT [18] compared manual acupuncture with indomethacin. Two RCTs found acupuncture with [21] or without [18] moxibustion to be superior for total effective rate, while two other RCTs [19, 20] found no difference between acupuncture with moxibustion and conventional drug therapy. Considering that moxibustion is one type of acupuncture treatment, the pooling of these RCTs together was considered sufficiently homogeneous to undertake a meta-analysis. However, the result shows that the acupuncture-type treatments on response rate were not statistically significantly superior to conventional drug therapy ($n=454$; RR 1.25; 95% CI 0.97, 1.6; $P=0.08$) although marked heterogeneity was observed in this model ($\chi^2=12.2$; $P=0.007$; $I^2=75\%$). Subgroup analyses also failed to suggest acupuncture plus moxibustion to be superior to conventional drug therapy ($n=345$; RR 1.12; 95% CI 0.99, 1.28; $P=0.08$; heterogeneity: $\tau^2=0.00$; $\chi^2=1.34$; $P=0.51$; $I^2=0\%$; Fig. 2C).

There were also no favourable effects of acupuncture plus moxibustion on pain reduction compared with control ($n=105$; WMD, 10 cm VAS 1.53; 95% CI $-0.57, 3.63$; $P=0.15$; heterogeneity: $\tau^2=1.18$; $\chi^2=1.81$; $P=0.18$; $I^2=45\%$, Fig. 2D) and joint swelling index ($n=105$; WMD, 10 cm VAS 0.25; 95% CI $-1.31, 1.82$; $P=0.75$; heterogeneity: $\tau^2=0.18$; $\chi^2=1.14$; $P=0.28$; $I^2=13\%$; Fig. 2E).

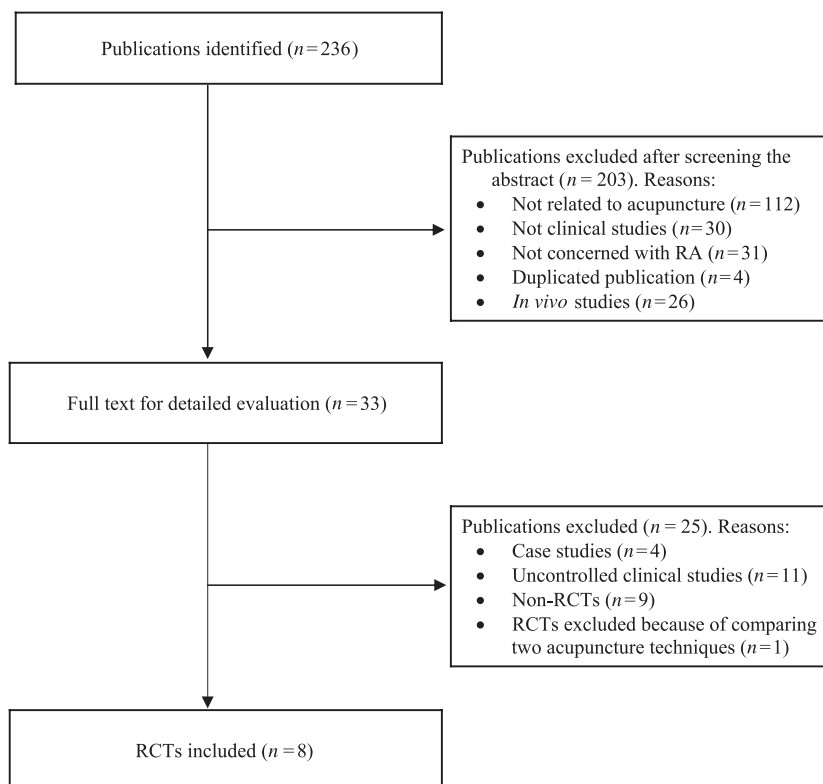


FIG. 1. Flow chart of trial selection process.

Analysis by country

All of the five RCTs originating from China, three (60%) demonstrated positive analgesic effects. Of the three RCTs originating from outside China, only one (33%) was positive. There was no significant difference between the two categories by Fisher's exact tests.

Discussion

Few RCTs have tested the effects of acupuncture for RA. The results for pain reduction failed to show specific effects of acupuncture. For acupuncture combined with moxibustion, the data also failed to demonstrate the effects of acupuncture for pain reduction or joint swelling index compared with conventional drugs. Overall, our findings provide no convincing evidence that acupuncture with or without moxibustion is beneficial for treating RA.

We assessed the methodological quality of the primary studies using a modified Jadad scale. It allocates one point for subject blinding and assessor blinding separately. Of the eight RCTs, only three trials were both patient blinded and assessor blinded [15–17], and one trial was assessor blinded [14]. The other five trials failed to do so and were therefore open to detection bias. The concealment of treatment allocation was reported in three trials [15–17]. Trials with inadequate blinding and inadequate allocation concealment may be subject to selection bias and are likely to generate exaggerated treatment effects. Details of drop-outs and withdrawals were described in only three trials [15–17]. This may lead to exclusion or attrition bias. A power calculation was performed in none of the RCTs.

The duration of the interventions was short in most studies (<3 months) except for one trial [21]. Arguably, longer treatment periods are required for acupuncture to have a chance to show clinical effects. Future trials should therefore have sufficiently large samples, treatment periods and follow-up periods.

Although the three placebo-controlled trials [15–17] were more rigorous than the rest of the studies, none were flawless. All of these RCTs have a small sample size; their results are therefore prone to a type II error. No RCT reported checks on the success of blinding. Unblinding is, therefore, a possibility with the potential for the overestimation of treatment effects, i.e. performance bias. In one cross-over RCT [17] only one acupoint was needed with short treatment times.

Several placebo or sham acupuncture methods have been proposed for trials of acupuncture. They range from penetrating needle non-acupoints [14, 15], superficially puncturing the skin [16] on acupoints to non-penetration on acupoints [17]. In the present systematic review, no evidence of the superiority of real acupuncture was found compared with sham acupuncture regardless of the acupuncture technique employed. Non-penetrating sham acupuncture was reported to be superior to placebo tablets for subjective pain outcomes [22]. This may suggest that the effects of needle acupuncture with or without electric stimulation are non-specific by nature. One trial [14] suggested positive effects of acupuncture on pain reduction of RA. However, this study was too small to generate reliable findings.

One problem with clinical trials of acupuncture is finding a suitable placebo control. Acupuncture placebos include minimal or, superficial needling, penetrating sham or non-penetrating sham acupuncture [23]. However, there is no universally accepted placebo. Therefore, a range of methods have been used some of which may not be adequate.

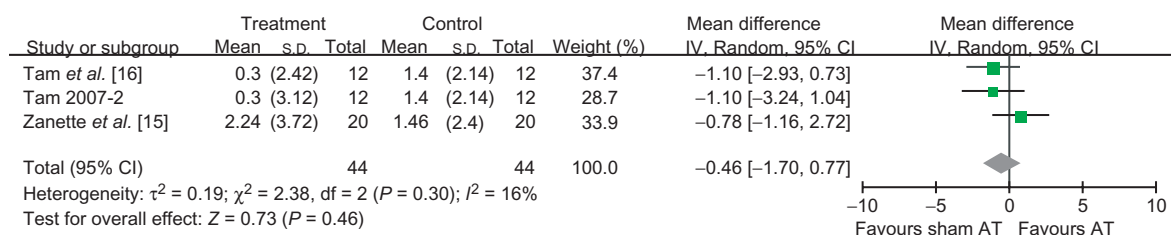
The rationale for the acupuncture point selection was stated in seven RCTs. The authors quoted traditional Chinese theory [16, 18–21] or pilot studies used [14] or the procedure recommended from text books [15] to justify their point selection. Needle stimulation causing a typical needle sensation has been claimed to be important for reaching maximum effects on pain [24, 25]. This needle sensation (De Qi) was considered in three RCTs [15, 16, 20], while five trials did not report such details [14, 17–19, 21]. Three RCTs reported the stimulation and manipulation

TABLE 1. Summary of randomized clinical studies of acupuncture for RA

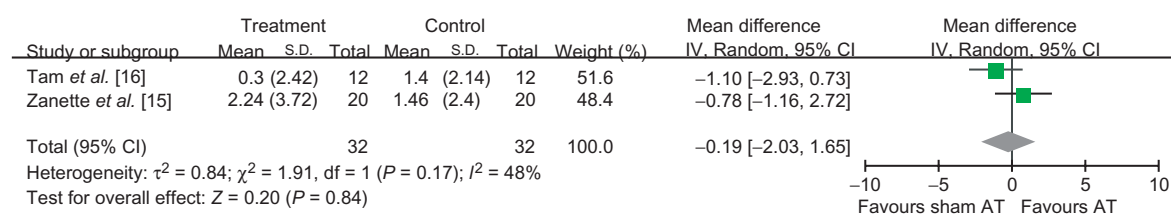
Reference	Design, quality score, ^a allocation concealment, sample size (randomized/analysed), acupuncture validity score [OA, ^b DC ^c]	Time since diagnosis, gender (M/F)	Experimental intervention	Control intervention	Main outcome measures	Intergroup differences	Adverse events (group: number)	Acupuncture points
Man and Baragar [14]	Parallel, AB, 2, unclear [3, 20%]	≥ 5 yrs (14/6)	(A) EA (15 min, 5 mA, once, n = 10), one knee treated with EA and steroid injection in other knee, plus analgesia (B) Penetrating sham EA (non-acupoints, 5 mA, once, 15 min, n = 10), one knee treated with placebo EA and steroid injection in other knee, plus analgesia	(B) Penetrating sham EA (non-acupoints, 5 mA, once, 15 min, n = 10), one knee treated with placebo EA and steroid injection in other knee, plus analgesia	Pain reduction scale (4-point Likert scale)	<i>P</i> < 0.01	Not reported (-)	GB34, SP9, ST43 n.r. n.r.
Zanette <i>et al.</i> [15]	Parallel, DB, 5, not adequate 40/40 [3, 85%]	≥ 6 months (3/37)	(A) AT (20 min, 2 times weekly, for 5 weeks, n = 20) plus analgesia (B) Penetrating sham EA (acupoints, superficial puncture and quickly withdrawn, no-current, 40 min, 2 times weekly for 10 weeks, n = 12)	(B) Penetrating sham EA (acupoints, superficial puncture and quickly withdrawn, no-current, 40 min, 2 times weekly for 10 weeks, n = 12)	(1) ACR20 (2) Pain (VAS) (3) DAS index (4) HAQ (5) PGADA (6) ESR, CRP	(1-4) NS (5) <i>P</i> < 0.001 (6), (7) NS	None reported (+)	EX1, EX27, CV6, CV12, LI4, GV4, GV14, LR3, PC6, SP6, ST36, BL11, BL20, BL22, BL23, BL60 n.r. (stimulation of De Qi) Considered
Tam <i>et al.</i> [16]	Parallel, DB, 5, adequate 36/36 [4, 90%]	9.3 yrs (7/29)	(A) AT (40 min, 2 times weekly for 10 weeks, n = 12) plus analgesia (B) EA (40 min, dense 4 Hz, disperse 20 Hz, 2 times weekly for 10 weeks, n = 12)	(C) Penetrating sham EA (acupoints, superficial puncture and quickly withdrawn, no-current, 40 min, 2 times weekly for 10 weeks, n = 12)	(1) Pain (VAS) (2) ACR 20 (3) DAS index (4) HAQ (5) ESR, CRP	(1-6) NS	AT: tingle sensation, herpes zoster, dyspepsia (last two events were not related with AT)	LI11, TE5, ST36, GB34, GB36, GB39 n.r. (stimulation of De Qi) Considered
David <i>et al.</i> [17]	Cross-over, DB9 5, adequate 64/66 [1, 40%] Parallel, open, 1, n.r. 109/109 [3, 70%]	(A) 8 yrs (B) 12 yrs (median) 45 days to 1 yr (26/83)	(A) AT (4 min, 5 times, n = 56), plus analgesia (B) Non-penetrating sham AT (acupoints, 4 min, 5 times, n = 56), plus analgesia (C) Indomethacin (50 mg × 3/day, n = 48) plus triptolide (<i>Tripterygium wilfordii</i> , 20 mg × 3/day)	(B) Non-penetrating sham AT (acupoints, 4 min, 5 times, n = 56), plus analgesia (C) Indomethacin (50 mg × 3/day, n = 48) plus triptolide (<i>Tripterygium wilfordii</i> , 20 mg × 3/day)	(1) Pain (VAS) (2) DAS index (3) GHQ (4) ESR, CRP (1) Total effective rate	(1-5) NS	None reported (+)	LI3 Manual manipulation n.r.
Wang [18]	Parallel, open, 1, n.r. 109/109 [3, 70%]	(A) 3 yrs (B) 3 yrs (8/37)	(A) AT (40 min, 1 time biweekly, for 4 weeks, n = 30) plus warm needle on AT (twice), plus moxibustion on back Su points, no analgesia	(B) Indomethacin (25 mg × 3/day, n = 15)	(1) Total effective rate (2) Pain reduction (3) Swelling index (4) ESR	(1) <i>P</i> < 0.01	Not reported (-)	Bafeng, SP5, GB40, ST41, BL60, SP3 through KI1, Baxie, LI5, TE4, SI5, TE5, LI3 through PC8 n.r. n.r.
Zhou and Zhu [19]	Parallel, open, 1, n.r. 45/45 [2, 85%]	(A) 3 yrs (B) 3 yrs (8/37)	(A) AT (40 min, 1 time biweekly, for 4 weeks, n = 30) plus warm needle on AT (twice), plus moxibustion on back Su points, no analgesia	(B) Indomethacin (25 mg × 3/day, n = 15)	(1) Total effective rate (2) Pain reduction (3) Swelling index (4) ESR	(1) NS (2) NS (3) NS	AT (none) Control: headache (1), gastric disorders (2)	BL18, BL20, BL23, GV4, LI11, ST36, KI3 plus local points Reinforce and reducing by twirling and lifting and thrusting technique n.r.
Xiang <i>et al.</i> [20]	Parallel, open, 1, n.r. 60/60 [3, 60%]	< 1 yrs (15/45)	(A) AT [one session (40 min, once daily, for 15 days), 1-2 day rest, total 3 session, n = 30] plus electronic moxibustion (3-5 local points, 10-20 min), no analgesia	(B) NSAID (diclofenac sodium 1 tablet × 2/day for 7 weeks, n = 30)	(1) Total efficacy rate (2) Pain reduction (3) Swelling index (4) ESR	(1) NS (2) <i>P</i> < 0.05 (3), (4) NS	AT: needle fainting (1), Control: headache (1), dizziness (1), nausea (2), gastric pain (4)	GB20, LI11, TE5, ST36, SP10, GV14, GV4 n.r. (stimulation of De Qi) Considered
Liu <i>et al.</i> [21]	Parallel, open, 2, n.r. 240/240 [3, 80%]	0.5-10 (42/198)	(A) AT (20 min, twice daily for 3 months, n = 120), plus moxibustion on ST36 (10 min), no analgesia	(B) MTX (intramuscular injection, once weekly, 1st week: 5 mg, 2nd week: 10 mg, from 3rd week: 15 mg, for 3 months, n = 120), plus diclofenac sodium (25 mg × 3/d)	(1) Total effective rate (2) Number of swollen joints (3) ESR	(1) <i>P</i> < 0.05 (2) <i>P</i> < 0.05 (3) NS	AT: no adverse event Control: Gastro-intestinal troubles (14), aminotransferase elevation (3), dizziness (2), urine blood positive (1), exanthema (1)	GB20, SP6, SI4, LI4, PC6 through TE5, ST35, ST36, GB34 through SP9 Twirling technique n.r.

^aQuality score: Jadad score. ^bOA: quality of acupuncture: 0, could not assess; 1, complete differently; 2, differently; 3, similarly; 4, exactly or almost exactly the same way. ^cDC: degree of confidence; degree of confidence that acupuncture was applied in an appropriate manner on 100 mm visual scale (with 0% = complete absence of evidence that the acupuncture was appropriate, and 100% = total certainty that the acupuncture was appropriate). DAS: Disease Assessment Scale; AT: acupuncture; EA: electroacupuncture; PGADA: physician's global assessment of disease activity; NS: not significant; VAS: visual analogue scale; n.r.: not reported; (+): mentioned in text; (-): not mentioned in text.

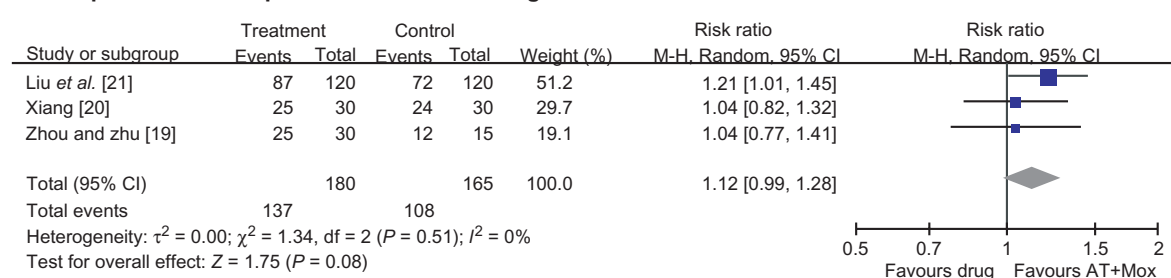
A Pain reduction—ATs vs sham AT



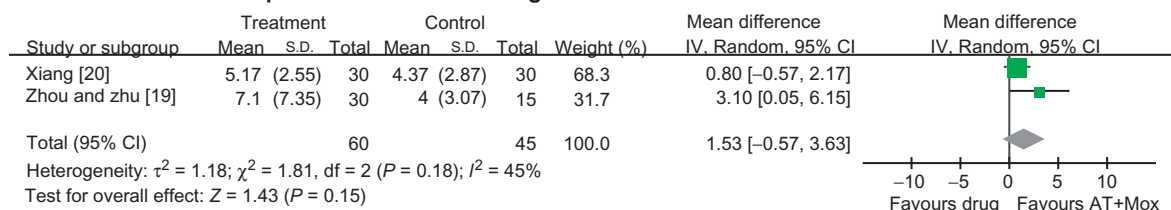
B Pain reduction—ATs vs sham AT



C Response rate—AT plus moxibustion vs drug



D Pain reduction—AT plus moxibustion vs drug



E Joint swelling index—AT plus moxibustion vs drug

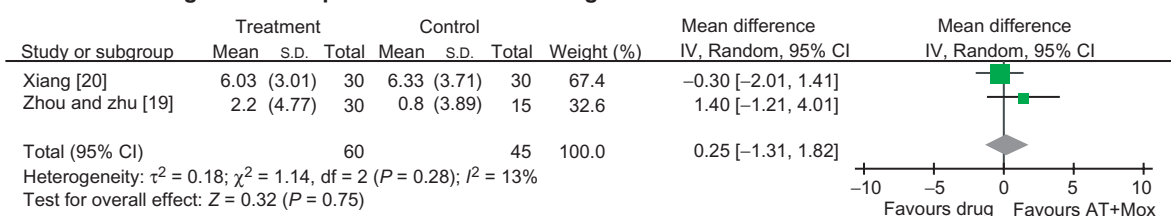


Fig. 2. Forest plot of effects of (A) acupuncture techniques (manual or electro-acupuncture), (B) manual acupuncture for RA on pain reduction compared with sham acupuncture; acupuncture combined with moxibustion for RA on (C) response rate, (D) pain reduction and (E) joint swelling index compared with drug therapy. AT, acupuncture; EA, electro-acupuncture. ^aThis study employed a 3-arms trial.

methods [17, 19, 21]. In the present data set, we found no evidence that the presence or absence of De Qi exerted an important influence on the clinical outcome.

The fact that, overall, there is no good evidence leads to three possible interpretations. First, either acupuncture is ineffective or second, it was not administered optimally. For instance, the number of treatment sessions could have been too small to generate a significant effect; stimulation could have been insufficient; or the protocol applied in the acupuncture group might not have been suitable for treating RA. The rationale for

the point selection, as stated in the included RCTs, was that it followed traditional Chinese medicine (TCM) theory. In most trials, the quality of acupuncture was only moderate but four trials scored >80% on the confidence score. The third interpretation is that sham acupuncture is effective, which is supported by two very large RCTs [26, 27]. The observed effects of penetrating sham acupuncture on non-acupoints might be due to a physiological effect of needling or the therapeutic relationship.

One argument for using acupuncture for the management of RA might be that it causes fewer adverse events than drug

treatment. Six RCTs [15–17, 19–21] assessed adverse events of acupuncture treatment and two RCTs did not [14, 18]. Mild adverse effects of acupuncture such as pain and gastro-intestinal symptoms were noted. Relative to those of standard drug treatments, such as NSAIDs, these are mild, infrequent and perhaps even negligible.

Assuming that acupuncture is beneficial for treating RA, possible mechanisms of action may be of interest. These include an anti-inflammation, modulation of autonomic nervous system or analgesic effects of acupuncture in patients suffering from RA. It has been claimed that acupuncture influences specific and non-specific cellular influx, activation of cell proliferation and regulation of subsequently involved cells that will result in a complex mechanism of transport, further breakdown and clearance of all bioactive mediators [28]. Another hypothesis is that the anti-inflammatory actions of acupuncture are mediated via the reflexive central inhibition of the innate immune system [29]. Acupuncture increases autonomic tone and acetylcholine output while decreasing inflammatory molecules including cytokines, CRP and ESR, etc. [29]. However, the findings of several studies suggest that these biomarkers are not involved. [15–17]. Anti-inflammatory effects may also be explained by modulation of autonomic nervous system and changes of the function of the hypothalamic–pituitary–adrenal axis as a response to the needle stimulus [29–31]. For acupuncture combined with moxibustion [19–21], the positive changes of these factors might imply the equivalent effects of acupuncture to those of analgesics. This might correspond with the analgesic theories of acupuncture, which claim to reduce pain through stimulating the serotonergic, noradrenergic and opioid system, for other pain conditions such as OA or back pain [32–34]. Another possibility is the synergetic effects of heat from moxibustion on the stimulation of acupuncture [35]. None of these theories are, however, currently fully established.

Our review has a number of important limitations. Although strong efforts were made to retrieve all RCTs on the subject, we cannot be absolutely certain that we succeeded. Moreover, selective publishing and reporting are other major causes for bias, which have to be considered. It is conceivable that several negative RCTs remain unpublished and thus the overall picture may be distorted [36, 37]. Most of the included RCTs that reported positive results come from China, a country that has been shown to produce no negative acupuncture studies [38]. Further limitations include the paucity and the often suboptimal methodological quality of the primary data. In total, these facts limit the conclusiveness of this systematic review considerably.

One could argue that RCTs of acupuncture could generate false negative results because of the complex characteristics of acupuncture [39, 40]. On the other hand, each randomization may introduce a selection bias which, in turn, would render any results difficult or impossible to interpret. Therefore, we believe that the exclusion of such studies was the correct decision.

In conclusion, the evidence for the effects of acupuncture for treating RA is not convincing. The number, size and quality of the RCTs are too low to draw firm conclusions. Further rigorous RCTs are warranted but need to overcome the many limitations of the current evidence.

Rheumatology key messages

- Acupuncture is frequently used by patients with arthritis and several RCTs reported it to be effective in reducing symptoms of OA.
- Several systematic reviews have assessed the effects of acupuncture in RA but none of these evaluations included all of the available data.
- Based on an assessment of all the included RCTs, we found the data to be insufficient to suggest that acupuncture is an effective treatment for RA. Further rigorous RCTs need to overcome the many limitations of the current evidence.

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