Acupuncture treatment for migraine: a system review and meta-analysis

Abstract

Background: Migraine is a common neurological disorder with heavy burden of health economics and causes discomfort in patients' life. Approximately 15% of the migraine population reported ineffectiveness and/or contraindications to migraine medication. Acupuncture has been used as an adjuvant therapy for migraine because of potential efficacy and safety.

Objectives: To investigate the efficacy of acupuncture for migraine as compared with sham acupuncture or/and medication.

Search methods: Three databases including Pubmed, Web of Science and Cochrane library were searched for studies on acupuncture to migraine published up until Nov. 10th, 2019. To put it simple, we used "Acupuncture Therapy"; "Acupunct*"; "Electroacupunct*"; "Headache Disorder"; "Headache"; "Migrain*" as key words and MeSH terms.

S**election criteria:** We included articles published in English which carried out randomized control trials (RCTs) that compared acupuncture therapy with sham acupuncture, medication, or sham acupuncture + medication in migraine patients with sample size $\geqslant$ 15 in each group. The endpoints of the these trials must include changes in headache frequency with days per month (HF, d/m), headache frequency with numbers of attacks per month (HA, n/m), Visual Analogue Scale (VAS) score, Migraine Disability Assessment Scores (MIDAS), or response rate (at least 50% frequency reduction).

Data collection and analysis: Two independent reviewers checked eligibility, extracted information, and assessed risk of bias and quality of the trials. Their disagreements were settled through discussion. We calculated pooled effect size estimates with Stata 12.0 statistical software. The fixed effect model was used if there was no significant heterogeneity between studies, otherwise the random effect model was used.

Results: A total of 2784 patients were included in the 17 RCTs, and 16 RCTs were eligible for our analysis. Combined with our previous study, the meta-analysis was

conducted. Compared with sham acupuncture, true acupuncture group showed lower HF (d/m) (MD = -0.94, 95%CI -1.76 to -0.13; P-value of Z test = 0.024; I^2 =72.5%) and lower VAS score (MD = -0.50, 95%CI -0.82 to -0.18; P-value of the Z test = 0.002, I^2 = 0.0%) after treatment. Significant lower HF (d/m) (MD = -0.94, 95%CI -1.72 to -0.15; P-value of Z test =0.02; I^2 =78.3%) and VAS score (MD = -0.90, 95%CI -1.26 to -0.54; P-value of the Z test < 0.001, I^2 = 6.9%) in the true acupuncture group were remained at follow up. However, response rate did not differ significantly between true acupuncture and sham acupuncture groups after treatment (RR = 1.09, 95%CI 0.91 to 1.29; P-value of the Z test = 0.356, I^2 = 0.0%) and at follow-up time (RR = 1.02, 95%CI 0.75 to 1.39; P-value of the Z test = 0.896, I^2 =56.1%).

Compared with medication, acupuncture was associated with higher response rate both after treatment (RR=1.60, 95%CI 1.34 to 1.92; P-value of the Z test = 0.033, I^2 = 45.6%) and at follow-up period (RR=1.69, 95%CI 1.16 to 2.46; P-value of the Z test = 0.006, I^2 = 73.2%). After treatment, acupuncture group had lower VAS score (MD = -2.17, 95%CI -3.35 to -1.00; P-value of the Z test <0.001, I^2 = 87.7%) and lower MIDAS score (MD = -4.81, 95%CI –8.79 to −0.82; P-value of the Z test = 0.018, I^2 = 96.3%). At follow-up, acupuncture reduced HF (d/m) (MD = -1.46, 95%CI -2.46 to -0.45; P-value of Z test =0.04; I^2 =66.6%) and HA (n/m) (MD = -0.96, 95%CI -1.85 to -0.08; P-value of Z test =0.033; I^2 = 92.1%) significantly greater than medication group.

Compared with “sham acupuncture + medication” control group, 2 trial showed that acupuncture was more effective. After treatment, acupuncture group had lower HF(d/m) (MD = -2.20, 95%CI -3.38 to -1.02; P-value of the Z test< 0.001), lower VAS score (MD = -0.90, 95%CI -1.69 to -0.11; P-value of the Z test = 0.025), lower MIDAS score (MD = -2.90, 95%CI -3.65 to -2.15; P-value of the Z test < 0.001) and higher response rate (RR = 1.71, 95%CI 1.22 to 2.39; P-value of the Z test = 0.002) than “sham acupuncture + medication” control group. At follow-up, the differences was still significantly on MIDAS score (MD = -5.80, 95%CI -6.46 to −5.14; P-value of the Z test < 0.001) and response rate (RR = 1.50, 95%CI 1.04 to 2.17; P-value of the Z test = 0.031).

Conclusions: The available evidence suggests that acupuncture is more effective than sham acupuncture and medication in patients with migraine.

Keywords

Acupuncture; Migraine; Treatment; Meta-analysis

Introduction

Migraine is a common neurological disorder with moderate to severe headache lasting from 4 to 72 hours. It has broad effects and a significant social and economic burden,[1] and has become the third prevalent disease and caused serious discomfort in most people's life.[2-4] Some patients can remit from acute migraine headaches by treating with acute therapy,[5] but the others need prophylactic interventions, because their headache are frequent or not easily controlled.[6] Migraines are commonly treated by various drugs, such as metoprolol, propranolol, flunarizine, topiramate and valproic acid.[7-9] But those drugs have limited efficacy.

Acupuncture, a traditional Chinese medical treatment, has become a popular therapy in many countries.[10, 11] Nowadays, acupuncture has been widely used for the prevention of migraine.[12-14] Several studies reported that acupuncture is of equally or even better efficiency, compared with medication, in reducing the migraine attacks.[8, 9, 15] Therefore, with its good curative effect and safety,[16] acupuncture is expected to be an important method for the prevention and treatment of migraine.

However, the efficacy of acupuncture treatment for migraine needs more clinical evidences. The conception of acupoint is also breezing, and how it works remains to be unclear.[17-19] Several clinical studies also found that there was little or no difference on the treatment effect between true acupuncture and sham acupuncture.[20-23] This may come from the stabbing of the needle to the skin, but not the specificity of the acupoints. Several questions need to be answered and more evidence need to be found.

Therefore, the purpose of this meta-analysis is to evaluate the efficacy of acupuncture treatment and discuss the true placebo response in the treatment and prophylaxis of migraine.

Methods

Search Strategy

We searched the following three databases from inception to Nov. 10th, 2019: Pubmed, Web of Science, Cochrane Library. Details of the search strategies in each database

are available in the supplementary files. Put it simple, we used the following key words and MeSH terms: “Acupuncture Therapy”; “Acupunct*”; “Electroacupunct*”; “Headache Disorder”; “Headache”; “Migrain*”; and etc. We also read the references and related systematic reviews to identify further studies that met our selecting criteria.

Inclusion Criteria

Studies included if they meet the following criteria:

(1) Randomized control trials (RCTs) published in English magazines;

(2) RCTs with the participants of migraine;

(3) RCTs with the intervention group treatment of acupuncture by professional or electron;

(4) RCTs with the control group treatment of sham acupuncture or/and medication in detail.

Exclusion Criteria

Studies meet any of the following criteria were excluded:

(1) Not published in English;

(2) Confused migraine with other diseases and had no data of migraine patients alone in detail;

(3) Without the outcome measures we interested (headache frequency, response, VAS or MIDAS scores);

(4) Without the standard diversion or 95% confidence interval (95% CI) of outcome measures;

(5) With the samples <15 in either group;

(6) Acute experiments with only one session of acupuncture treatment;

(7) Trails compared acupuncture to food, herbal drugs, and trials that only compared different forms of acupunctures.

(8) Trails used other methods of acupuncture without needle insertion, for instance, acupressure, laser stimulation or transcutaneous electrical stimulation;

(9) Trials that injected fluids at acupuncture;

(10) Trials that focused on the outcomes of imaging examinations.

Study selection

Two independently reviewers (Ran and Yang) screened the titles and abstracts of all studies for relevance and excluded irrelevant studies after retrieving articles from the 3 databases. And then, the reference management software Endnote was used to remove the duplicate records. Full-text articles were obtained for assessing eligibility according to the inclusion and exclusion criteria, and literatures were excluded if full-text articles were unavailable. Disagreements were resolved by discussion.

Data Extraction

Two independently reviewers (Ran and Yang) extracted the data. We collected the following information: time of publication, country, sample size, age, time of treatment and follow up, the treatment type of each group, headache frequency of days per month (HF, d/m), headache frequency of numbers of attacks per month (HA, n/m), Visual analogue scale (VAS) score, Migraine Disability Assessment Score (MIDAS), and response rate. Our disagreement was settled by discussion.

We unified the unit of treatment and follow up time by weeks. The treatment of control groups was separated to “sham”, “medication” and “sham + medication”. The headache frequency was sorted by the unit of days per month (d/m) and numbers of attacks per month (n/m). The response rate meant at least 50% frequency reduction. We defined the outcome of treatment as the outcome at the time completing the treatment. If the studies had more than one result of follow up, we chose the result of the longest time within one year.

Risk of Bias Assessment

Two independently researchers (Ran and Yang) evaluated all the studies (except the study of us), using a collaboration tool recommended by the Cochrane Collaboration (Higgins and Green, 2011). Seven points were evaluated: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and “other”. Our disagreement was settled by discussion.

Statistical Analysis

All data analyses were performed with Stata 12.0 statistical software. We analyzed the

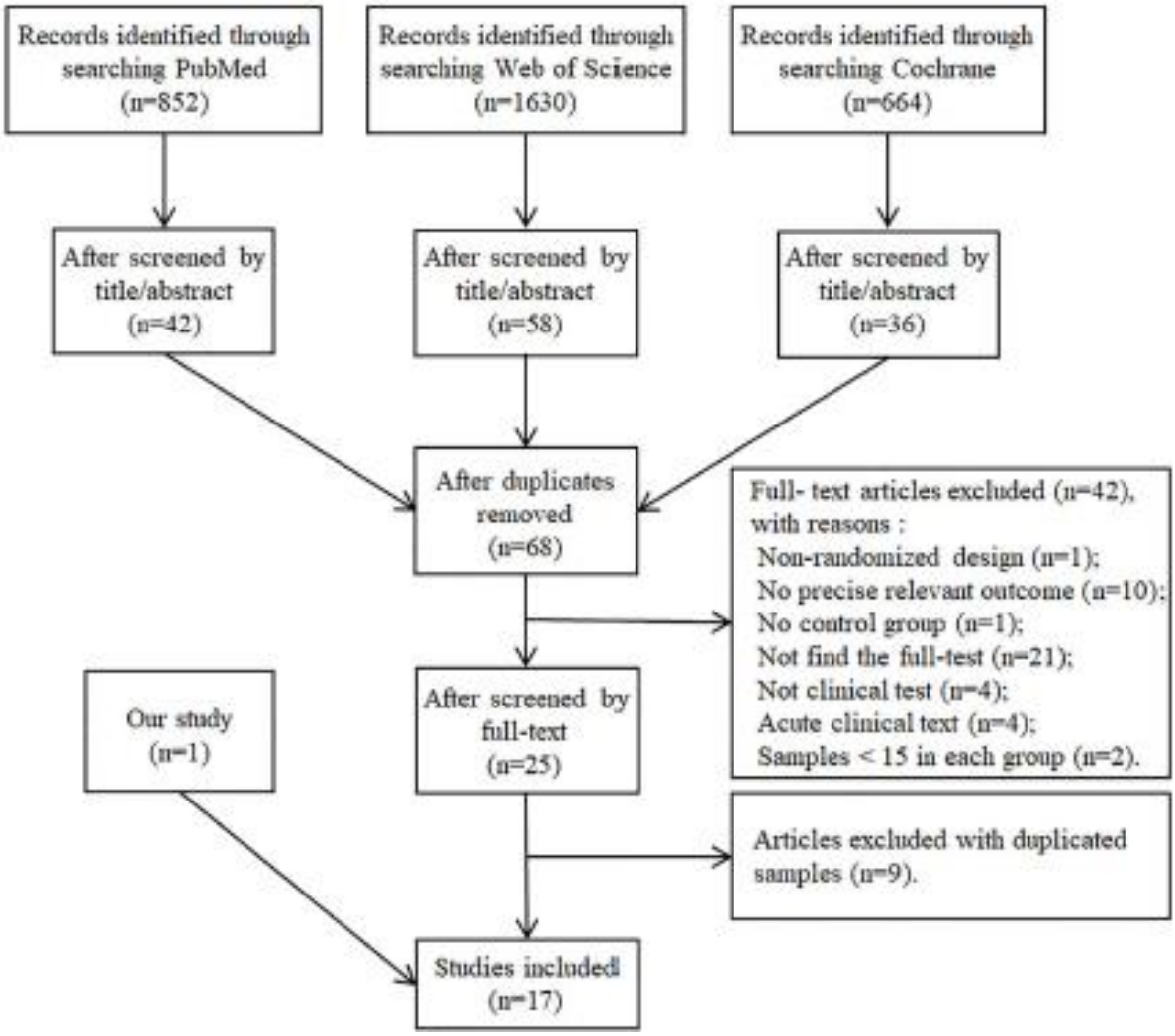
following outcomes of the included studies independently: Headache frequency (days/month), Headache frequency (numbers of attacks/month), VAS, MIDAS score and response rate. We evaluated the heterogeneity by using $\chi 2$ and I-squired statistics. I-squired < 50% means that heterogeneity is not statistically significant. I-squired $\geqslant$ 50% means the existence of heterogeneity. The fixed effect model was used if there was no significant heterogeneity between studies, otherwise the random effect model was used.

Result

Study selection

Figure 1 showed a flow chart of the study selection process according to PRISMA guideline. 852, 1630, 664 records (3146 in total) were retrieved respectively from Pubmed, Web of Science, and Cochrane Library initially. And 42, 58, 36 records (136 in total) were remained after screened by title and abstract respectively, of which 58 were remained after duplicates removed. After reviewing the full text, 51 records were excluded (1 non-RCT, 10 without precise outcome, 1 without control group, 21 full-test unavailable, 4 were not clinical tests, 4 acute clinical tests, 2 with sample size < 15 in each group, 9 article were excluded with duplicated samples). Finally, 16 studies from the 3 databases were eligible for our analysis. And we included one of our studies in this meta-analysis. In total, 17 trials were included for the final analysis.

Figure 1. The flow chart of the study selection process



Study characteristics

Table 1 summarized the characteristics of the included studies. A total of 2784 patients were included in the 17 trials. Five trials recruited participants from China, 4 from Germany, 3 from Italy, and the others from Turkey, Australia, Spain, Czech, America. The trials comprised 9 comparisons of acupuncture group and medication control, 8 comparisons of acupuncture group and sham acupuncture control, 2 comparisons of acupuncture group and sham acupuncture + medication control. All

trials were performed on adults of average ages ranging from 32.5 to 47.9 years old. In the trials, the treatment period was up to 4 / 24 weeks, and mostly was 12 weeks (8 trials). Three trials only assessed the effects of acupuncture immediately after treatment, while other trials assessed the effects of acupuncture after treatment and at followed-up for 12 to 48 weeks.

Table 1. Characteristics of the included studies.

Studies (n=17)	Country	Average age	Patients (T vs C)	Control group	Duration of treatment	Follow up time	Headache measures
Yang (2011)	China	47.9	33 vs 33	Medication	12 weeks	0	HF (d/m), Response, MIDAS
Tastan (2018)	Turkey	33.0	30 vs 30	Medication	12 weeks	0	VAS, MIDAS
Alecrim (2008)	Spain	35.0	19 vs 17	Sham	12 weeks	24 weeks	Response
Allais (2002)	Italy	32.5	77 vs 73	Medication	24 weeks	0	HA (n/m)
Diener (2006)	Germany	37.5	290 vs 317 290 vs 187	Sham Medication	6 weeks	20 weeks	HF (d/m), Response
Facco (2013)	Italy	37.0	41 vs 41	Medication	12 weeks	12 weeks	HF (d/m), MIDAS
Facco (2008)	Italy	35.6	32 vs 30 32 vs 34	Sham + Medication Medication	12 weeks	12 weeks	MIDAS
Li (2012)	China	36.9	121 vs	Sham	4 weeks	12	HF (d/m), HA

			118				weeks	(n/m), VAS
Linde K (2005)	Germany	42.6	145 81	vs	Sham	8 weeks	16 weeks	HF (d/m), HA (n/m), Response
Musil (2018)	Czech	46.1	42 44	vs	Medication	12 weeks	24 weeks	HF (d/m), HA (n/m),VAS, Response, MIDAS
Streng (2006)	Germany	40.1	59 54	vs	Medication	12 weeks	12 weeks	HF (d/m), HA (n/m), Response
Vickers (2004)	America	46.3	161 140	vs	Medication	12 weeks	36 weeks	HF (d/m), Response
Wallasch (2012)	Germany	38.2	18 17	vs	Sham	8 weeks	12 weeks	HF (d/m)
Wang (2011)	America	39.6	70 70	vs	Sham + Medication	4 weeks	12 weeks	HF (d/m), VAS, Response
Wang (2015)	Australia	42.7	26 24	vs	Sham	20 weeks	48 weeks	HF (d/m), VAS
Zhao (2017)	China	37.7	83 80	vs	Sham	4 weeks	20 weeks	HF (d/m), HA (n/m), VAS
Wang(2020)*	China	36.3	58 60 58 29	vs	Sham Medication	4 weeks	12 weeks	HF (d/m), HA (n/m)

T vs C: treatment group vs control group; HF (d/m): headache frequency (days/month); Response: at least 50% frequency reduction; MIDAS: migraine disability assessment scale; VAS: visual analog scale; HA (n/m): headache frequency (times/month); Sham: Sham acupuncture; NA: not reported.

*Our study.

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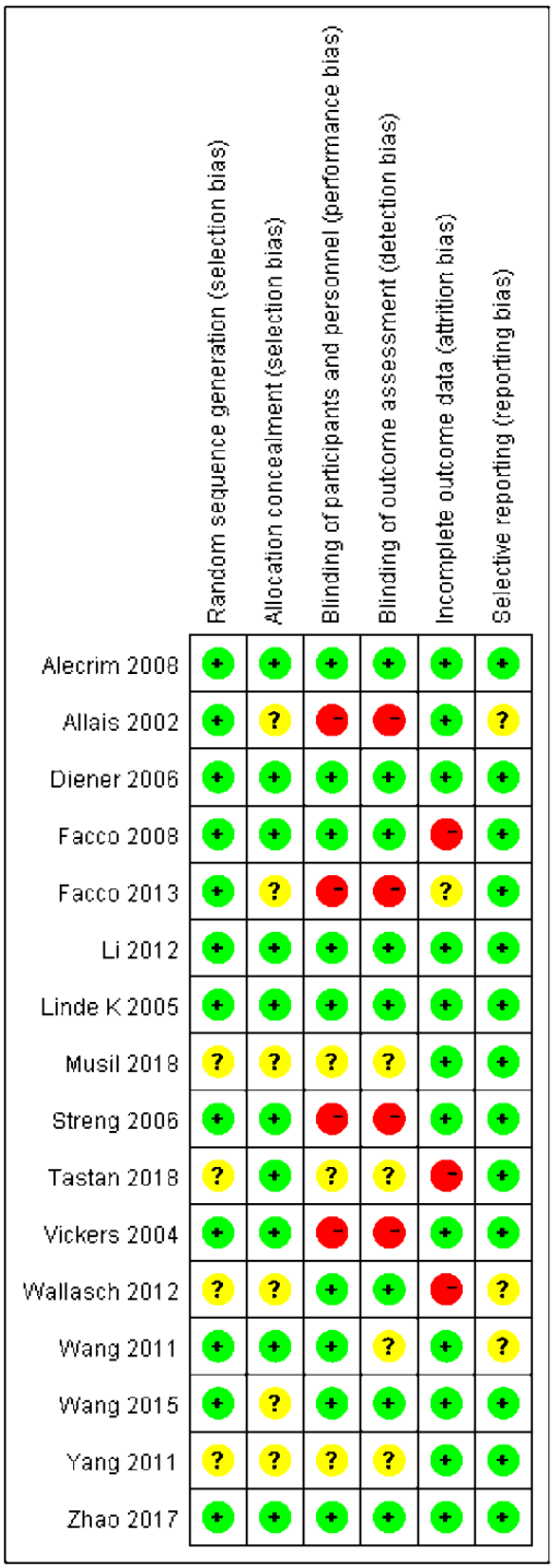
Risk of bias within studies

As presented in Figure 2, most of the included studies were evaluated as having a low risk of bias based on the Cochrane risk of bias tool. For high risk of bias, there were only 0, 0, 4, 4, 3, 0 studies at a high risk of bias respectively in random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, and selective reporting.


Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias)
Blinding of outcome assessment (detection bias)
Incomplete outcome data (attrition bias)
Selective reporting (reporting bias)
Alecrim 2008
Allais 2002
Diener 2006
Facco 2008
Facco 2013
Li 2012
Linde K 2005
Musil 2018
Streng 2006
Tastan 2018
Vickers 2004
Wallasch 2012
Wang 2011
Wang 2015
Yang 2011
Zhao 2017

Effects of treatment

We compared the treatment effects of acupuncture versus medication/sham acupuncture/ acupuncture + medication after treatment and follow up. The effect indicators included headache frequency of days per month (HF, d/m) and headache frequency of numbers of attacks per month (HA, n/m), VAS, MIDAS scores and response rate.

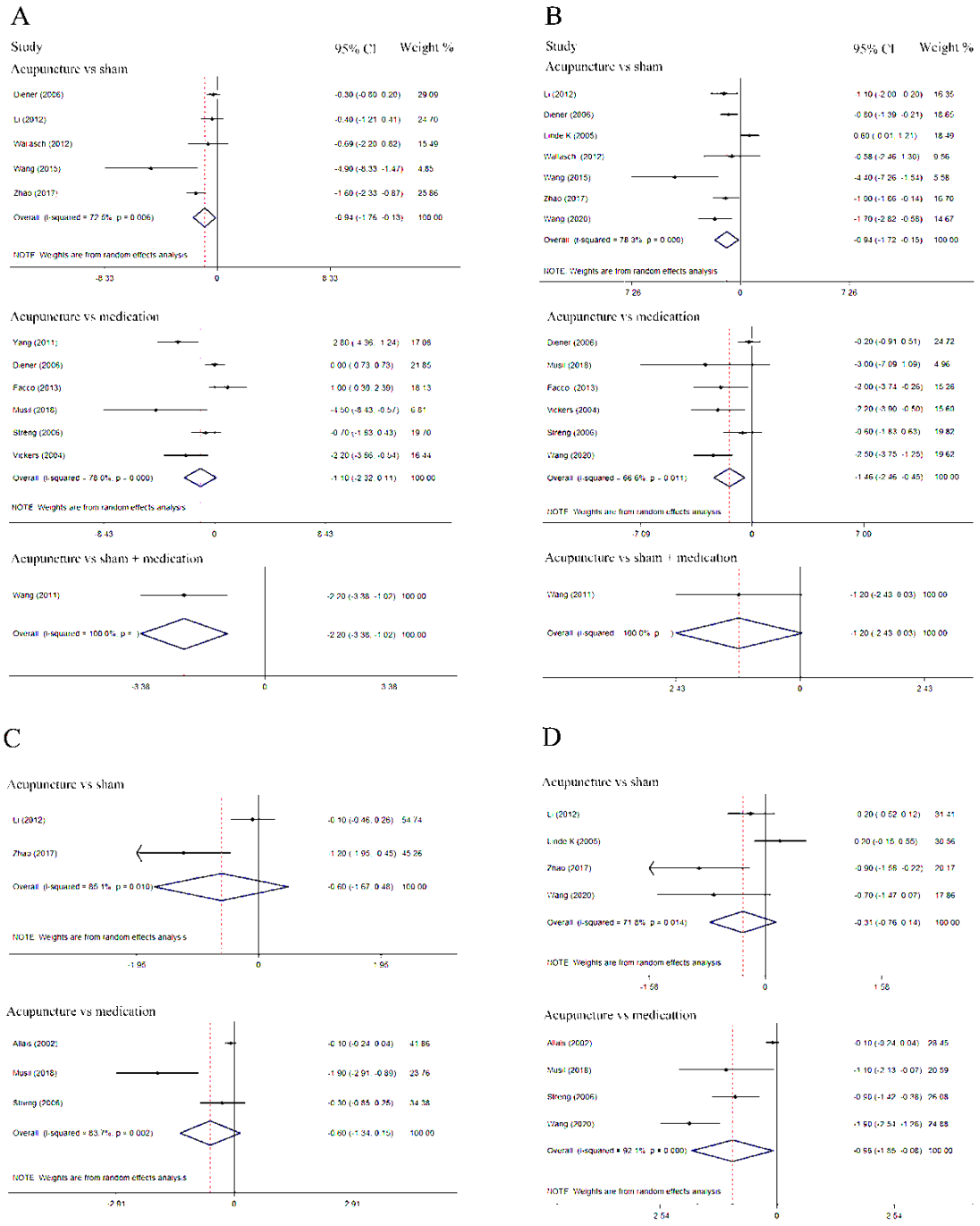
Acupuncture compared to sham acupuncture controls

Both after treatment (5 trials) and at follow-up (7 trials), true acupuncture was associated with a statistically significant reduction over sham on HF (d/m). The MD was -0.94 (95%CI -1.76 to -0.13; P-value of Z test = 0.024; I^2 =72.5%) after treatment (Figure 3.A) and -0.94 (95%CI -1.72 to -0.15; P-value of Z test =0.02; I^2 =78.3%) at follow-up (Figure 3.B). However, no significant difference was detected between the two groups on HA(n/m) after treatment (2 trials) (MD = -0.60, 95%CI -1.67 to 0.48; P-value of Z test =0.275; I^2 =85,1%) (Figure 3.C) and at follow-up (4 trials) (MD = -0.31, 95%CI -0.76 to 0.14; P-value of Z test =0.179; I^2 =71.8%)(Figure 3.D).

Three trials compared true acupuncture with sham acupuncture on VAS score both after treatment and at follow-up. The VAS score was statistically significant lower in the true acupuncture group than in the sham acupuncture group. The MD was -0.50 (95%CI -0.82 to -0.18; P-value of the Z test = 0.002, I^2 = 0.0%) after treatment and -0.90 (95%CI -1.26 to -0.54; P-value of the Z test < 0.001, I^2 = 6.9%) at follow-up.

Three trials compared true acupuncture with sham acupuncture on response rate after treatment (2 trials) and at follow-up (3 trials). Response rate did not differ significantly between true acupuncture and sham acupuncture groups after treatment (RR = 1.09, 95%CI 0.91 to 1.29; P-value of the Z test = 0.356, I^2 = 0.0%) and at follow-up (RR = 1.02, 95%CI 0.75 to 1.39; P-value of the Z test = 0.896, I^2 =56.1%).

Figure 3. Comparison of headache frequency



Acupuncture compared to medication controls

A total of 7 trials compared HF (d/m) between acupuncture and medication, and 4 trials compared HA (n/m). Acupuncture reduced HF (d/m) (MD = -1.46, 95%CI -2.46 to -0.45; P-value of Z test =0.04; I^2 =66.6%) and HA (n/m) (MD = -0.96, 95%CI -1.85 to -0.08; P-value of Z test =0.033; I^2 = 92.1%) significantly more than medication at

follow-up, but no significant difference was detected on HF (d/m) (MD = -1.10, 95%CI -2.32 to 0.11; P-value of Z test =0.075; I^2 =78.0%) and HA (n/m) (MD = -0.60, 95%CI -1.34 to 0.15; P-value of Z test =0.115; I^2 =83.7%) at the end of treatment.

The score of VAS was significant lower in the acupuncture group than in the medication group after treatment (MD = -2.17, 95%CI -3.35 to -1.00; P-value of the Z test <0.001, I^2 = 87.7%; 2 trials), but the significance was not maintained at follow-up (MD =0.05, 95%CI –0.56 to 0.66, P-value of the Z test = 0.872; one trail).

The score of MIDAS was significant lower in the acupuncture group than in the medication group after treatment (MD = -4.81, 95%CI -8.79 to -0.82; P-value of the Z test = 0.018, I^2 = 96.3%; 5 trials), but the significance was not maintained at follow-up (MD = -4.43, 95%CI -9.03 to 0.18; P-value of the Z test = 0.018, I^2 = 93.7%; 2 trials).

The proportion of patients got at least 50% reduction in migraine frequency was significant higher in the acupuncture group than in the medication group after treatment (RR=1.60, 95%CI 1.34 to 1.92; P-value of the Z test = 0.033, I^2 = 45.6%; 5 trials), but the significance was not maintained at follow-up (RR=1.69, 95%CI 1.16 to 2.46; P-value of the Z test = 0.006, I^2 = 73.2%; 4 trials).

Acupuncture compared to "sham acupuncture + medication" control

Two trials reported compared acupuncture group with sham acupuncture + medication group. Acupuncture reduced HF(d/m) significantly more than "sham acupuncture + medication" control at the end of treatment (MD = -2.20, 95%CI -3.38 to -1.02; P-value of the Z test< 0.001), but the significance was not maintained at follow-up (MD = -1.20, 95%CI -2.43 to 0.03; P-value of the Z test = 0.056).

The score of VAS was significant lower in the acupuncture group than in the "sham acupuncture + medication" control group after treatment (MD = -0.90, 95%CI -1.69 to -0.11; P-value of the Z test = 0.025), but the significance was not maintained at follow-up (MD = -0.80, 95%CI -1.61 to 0.01; P-value of the Z test = 0.054).

The score of MIDAS was significant lower in the acupuncture group than in the "sham acupuncture + medication" control group both after treatment (MD = -2.90, 95%CI -3.65 to -2.15; P-value of the Z test < 0.001) and at follow-up (MD = -5.80, 95%CI -6.46 to -5.14; P-value of the Z test < 0.001).

The response rate was significant higher in the acupuncture group than in the "sham acupuncture + medication" control group after treatment(RR = 1.71, 95%CI 1.22 to 2.39; P-value of the Z test = 0.002) and at follow-up(RR = 1.50, 95%CI 1.04 to 2.17; P-value of the Z test = 0.031).

Discussion

This meta-analysis compared the efficacy of acupuncture treatment for migraine with sham acupuncture group and medication group. We discussed the effect size of acupuncture on HF (d/m), HA (n/m), VAS, MIDAS scores and response rate both after treatment and at follow-up.

True acupuncture, compared with sham acupuncture, resulted in a significant reduction in HF (d/m), VAS, scores both after treatment and at follow up. Although both true and sham acupuncture reduced HA(n/m), but no significant difference was found on HA(n/m) and response rate. These results might support the superior of true acupuncture over sham on migraine.

When compared with medication, acupuncture resulted in a significant lower score in VAS and MIDAS, and a better response rate after treatment. At follow-up, acupuncture was superior to medication in reducing HF (d/m) and HA (n/m), and associated with a better response rate. In other outcomes, no significant difference was found between acupuncture and medication. In total, acupuncture might be more effective than medication in treatment and prevent of migraines. These results could be showed in other clinical studies and reviews of meta-analysis.[6, 24, 25]

Only one trial compared acupuncture to "sham acupuncture + medication". Although acupuncture showed an improvement in HF(d/m), VAS, MIDAS, and response rate after treatment or/and at follow-up, but further study with larger sample still needed to provide high quality of evidence.

Conclusion

The available evidence suggests that true acupuncture might be more effective than sham acupuncture and medication in patients with migraine. This meta-analysis still provided evidence that there is an effect over sham in the majority of endpoints both after treatment and at follow-up. Acupuncture can be considered as a treatment option

for patients willing to undergo this treatment.

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Searching Strategies

Pubmed

#1 (((((Headache Disorders[MeSH Major Topic]) OR Headache[MeSH Major Topic]) OR headache*[Title/Abstract]) OR migrain*[Title/Abstract]) OR cephalgi*[Title/Abstract]) OR cephalalgi*[Title/Abstract]
#2 (((Acupuncture Therapy[MeSH Major Topic]) OR acupunct*[Title/Abstract]) OR electroacupunct*[Title/Abstract]) OR electro- acupunct*[Title/Abstract]
#3 #1 and #2

Web of Science

#1
Topic: (Acupuncture)
#2
Title: (acupunct*) OR Title: (electroacupunct*) OR Title: (electro-acupunct*)
#3
#2 OR #1
#4
Topic: (headache)
#5
Title: (headache*) OR Title: (migrain*) OR Title: (cephalgi*) OR Title: (cephalalgi*)
#6
#5 OR #4
#7
#6 AND #3

Cochrane

#1 MeSH descriptor: [Acupuncture Therapy] explode all trees
#2 (acupunct* or electroacupunct* or electro - acupunct*):ti,ab,kw (Word variations have been searched)
#3 #1 or #2
#4 MeSH descriptor: [Headache Disorders] explode all trees

#5 MeSH descriptor: [Headache] this term only
#6 (headache* or migrain* or cephalgi* or cephalalgi*):ti,ab,kw (Word variations have been searched)
#7 #4 or #5 or #6
#8 #3 and #7