Systematic Review and Meta-Analysis

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Acupoint stimulation for alcohol use disorder

A systematic review and meta-analysis

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Abstract

Background: To assess the effect of acupoint stimulation for Alcohol use disorders (AUD).

Methods: AUD is a complex disease that threatens the health of the global population. Acupoint stimulation, a sort of therapy applying stimulation on acupoints to produce a therapeutic effect without side effects, has been widely used in AUD patients, but its efficacy remains controversial. Electronic databases (the Cochrane Library, EMBASE, PubMed, CNKI, VIP, Wan-Fang) were systematically searched for randomized controlled trials (RCTs) on acupoint stimulation for AUD from database inception to September 30, 2022. A meta-analysis was performed using Review Manager 5.4 software. Continuous data (scales) were expressed as mean differences (MDs) or standardized mean difference (SMD) with 95% confidence intervals (95% CI). Study methodological quality was assessed according to the Cochrane risk-of-bias tool for trials. The grading of recommendations assessment, development and evaluation was used to assess the certainty of evidence for outcomes.

Results: A total of 16 RCTs with 1097 participants were included. Compared to psychotherapy or drug therapy alone, the combination of acupoint stimulation and other sorts of therapies presented advantages in alleviating alcohol craving (SMD = –1.09, 95% CI = –1.40 to –0.77, df = 2, $P < .00001$, grading of recommendations assessment, development and evaluation very low certainty), (SMD = –2.25, 95% CI = –3.17 to –1.34, df = 3, $P < .00001$, low certainty) and the severity of alcohol withdrawal symptoms (MD = –1.21, 95% CI = –2.32 to –0.1, df = 2, $P = .03$, low certainty), as well as improving anxiety (MD = –3.41, 95% CI = –4.06 to –2.76, df = 4, $P < .00001$, very low certainty) and depression levels (MD = –3.27, 95% CI = –4.92 to –1.62, df = 4, $P = .0001$, very low certainty) on patients with AUD. In addition, a greater effect was also found with the 4-week treatment courses in reducing craving (SMD = –2.18, 95% CI = –2.61 to –1.75, $P < .00001$, low certainty).

Conclusion: Acupoint stimulation and its combined therapy may better relieve AUD symptoms effectively and the treatment duration should be set at more than 2 weeks. However, due to the low-quality of the included RCTs, high-quality studies are needed to further confirm it in the future.

Abbreviations: 95% CI = 95% confidence intervals, AUD = alcohol use disorders, AWS = alcohol withdraw syndrome, GRADE = the grading of recommendations assessment, development and evaluation, MDs = mean differences, RCTs = randomized clinical trials, SMD = standardized mean difference.

Keywords: acupoint stimulation, acupuncture, alcohol use disorder, meta-analysis, randomized controlled trial, systematic review

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

Supplemental Digital Content is available for this article.

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1. Introduction

Alcohol use disorders (AUD) is a complex disease that threatening the health of the global population. The lastest report released by the WHO, alcohol is associated with more than 200 diseases and injuries,[1,2] 5.3 % deaths of total global. From the perspective of economy and public health, abstain from alcohol and abstinence treatment is increasingly focused by society and medical profession. Up to now, only 3 drugs (Disulfiram, Acamprosate and Naltrexone) are approved by the U.S. Food and Drug Administration (FDA) for the treatment of AUD. However the inferior curative effect,[3] negative reactions[4] and high recurrence rate[5] of drugs may deserve more attention. This may indicate that drug therapy alone is insufficient to cure AUD.

Thus combination therapy has attracted growing attention, especially the combination of drug and non-drug therapy.[6,7] Among them, acupoint stimulation, has been widely used in the treatment of AUD patients.[8] It could produce a benign regulative effect on the body, by performing invasive or noninvasive stimulation on specific acupoints, including hand acupuncture and electric acupuncture. Many randomized controlled trials (RCTs) have shown that acupuncture stimulation with lesser nausea, vomiting, headache and other adverse reactions compared with medicine therapy, could actively reduces alcohol cravings and relapse rates.

There are many forms of acupoint stimulation, nevertheless, in the previous systematic review,[9–12] only a few treatment modalities of acupoint stimulation were included, and the effect of acupoint stimulation was vague and contradictory. Therefore, in this study, we include more treatment modalities, including transcutaneous electrical acupoint stimulation and wrist-ankle acupuncture attempt to elucidate the efficacy and safety of acupoint stimulation in treating AUD symptoms.

2. Methods

The meta-analysis was conducted according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA).[13] This protocol has been registered at PROSPERO under registration number CRD42022311976.

2.1. Eligibility criteria

All relevant studies were considered eligible if they included the following: randomization; adult patients (aged 18+) diagnosed with Alcohol Use Disorder (The diagnostic criteria comprised DSM-III, DSM-IV, DSM-V,[14] ICD-10[15] and CCMD-3[16]; intervention with acupoint stimulation (Treatment of disease by stimulating along specific pathways or meridians, applying needling, heat, moxibustion, acupressure, or electric stimulation, or the conjunction etc, according to Pubmed MeSH "acupuncture therapy"); a corresponding comparison group (Sham acupoint stimulation, oral medication or treatment as usual); as a single intervention or as an auxiliary means of integration; assessment of the change in alcohol craving and the severity of alcohol withdraw syndrome (AWS) (as primary outcomes), the severity of anxiety and depression (secondary outcomes).

2.2. Information sources and search strategy

The following English and Chinese language databases were searched from their inception to September 30: the Cochrane Library, EMBASE, PubMed and CNKI, VIP and Wan-Fang. Searches terms included alcoholism, AUD, alcohol addiction, and alcohol use disorder, and acupoint stimulation, acupuncture, acupressure, auricular acupuncture, electroacupuncture, etc, as either key terms or keywords, with publication types including randomized controlled trial, controlled clinical trial, randomized, etc, (Supplemenntary Digital Content 1, Supplemental Digital Content, http://links.lww.com/MD/I284, which illustrates the retrieval strategy) for the retrieval strategy.

2.3. Study selection, data extraction and data items

The study selection and data extraction process was applied blindly. Two reviewers (Huishan Chen and Peiming Zhang) independently searched the databases, exported references and deleted duplications using Note Express software. Titles and abstracts were independently scanned to assess the suitability of articles for inclusion.

Data extraction was conducted according to predefined criteria using standard data extraction forms. The following information from each study was extracted separately by 2 investigators (Jiaxin Feng and Li Chen): first author, publication year, country, population, mean age, the number of cases and controls, treatment methods for each group (for acupoint stimulation: type, acupoints, manipulation), adverse effects, the sample size for the last intervention and results of outcomes (mean and SD).

2.4. Effect measures

In this study change in alcohol craving and improvement in the severity of AWS were discussed as the primary outcomes, while the severity of the anxiety and the depression as the secondary outcomes. Change in alcohol craving was measured using scores on a visual analogue scale, obsessive compulsive drinking scale (OCDS),[17] Pennsylvania alcohol craving scale (PACS) or self-made evaluation scale. Improvement in the severity of AWS assessed using the clinical institute withdrawal assessment for alcohol scale,[18] which measures 10 parameters of physical and psychiatric symptoms of withdrawal. The degree of anxiety and depression were measured by the Hamilton rating scale for anxiety [19] or state-trait anxiety inventory and Hamilton rating scale for depression (HAMD) or beck depression inventory respectively. Higher scores on all scales above indicate a higher level of craving, AWS, anxiety or depression. Questions about trials or missing data were referred to the first author of the respective publication via email. If there was no response, we omitted the trial from data synthesis. Any uncertainty or disagreement was referred to Jiarong Huang for discussion and resolution.

2.5. Study risk of bias assessment

The Cochrane risk-of-bias tool for trials was assessed using Cochrane risk of bias table by 2 authors (Jiaxin Feng and Li Chen), respectively. A grade of "high risk," "unclear risk," or "low risk" was given for each item. Any disagreement was resolved by discussion with a third investigator (Huishan Chen).

2.6. Synthesis methods

The statistical analysis was conducted using Review Manager 5.4 software (https://training.cochrane.org/online-learning/core-software-cochrane-reviews/revman/revman-5-download/download-and-installation). The meta-analyses were performed to compare mean differences (MDs) with 95% confidence intervals (95% CI) of change in alcohol craving, standardized mean difference (SMD) with 95% CI of improvement in the severity of AWS, degree of anxiety and depression. For data reported before and after treatment, we estimated changes according to methods recommended by the Cochrane Collaboration Handbook (chapter 16.1.3.2, Imputing standard deviations for changes from baseline). Dichotomous variables were expressed as risk ratio (RR) with 95% CI. Heterogeneity was assessed using I^2 text. When $P < .10$ was considered to indicate statistical significance according to the Cochrane hand book. A fixed effects model was adopted to perform meta-analysis when $I^2 \leq 50\%$. When $I^2 > 50\%$ indicated there is a significant heterogeneity, a random effects model was applied. And the source of heterogeneity needed to be further explored via subgroup analysis or sensitivity analysis.

Clinical heterogeneity was assessed by noting the difference in the distribution of participants' gender or age characteristics,

and intervention modalities (combination or simple and duration) among trials. We performed a subgroup analysis to reduce the heterogeneity of the combinations. Clinical heterogeneity was present in each meta-analysis owing to differences in the acupoint stimulation techniques used in the experimental interventions.

Methodological heterogeneity was assessed by some trial design factors including differences in the application of blinding, distribution concealment, and outcomes' evaluation scales.

2.7. Evidence certainty

The certainty of evidence was assessed online with the grading of recommendations assessment, development and evaluation (GRADE), the GRADEpro (https://gradepro.org/).

2.8. Ethics statement

This study is a systematic review and meta-analysis, which was a secondary data processing of previously published studies. All contents were not related to human and animal experiments, so no ethical approval was required.

3. Results

3.1. Study selection and characteristics

Detailed steps of the literature search and study selection are summarized in Figure 1. There were 1530 relative articles identified through databases searching and 8 additional records identified through reading the published reviews. Of these, 273 duplications were omitted by the Note Express software. By scanning titles and abstracts, we first ruled out studies that were non-RCTs, review articles, animal experiments and mechanistic studies, studies that addressed mixed substance abuse, studies on irrelevant topics, and not English or Chinese. Of 24 potentially eligible studies, 6 studies were absence of statistics for effect size and 2 studies' subjects lost more than 20%. To sum up, 16 studies met the inclusion criteria were included in this meta-analysis.

3.2. Study characteristics

Sixteen studies (from China, Germany, USA and Sweden) with a total of 1097 participants were included in this summary. All studies[20–35] were designed as RCTs. One of them[11] is muti-center clinical trial.

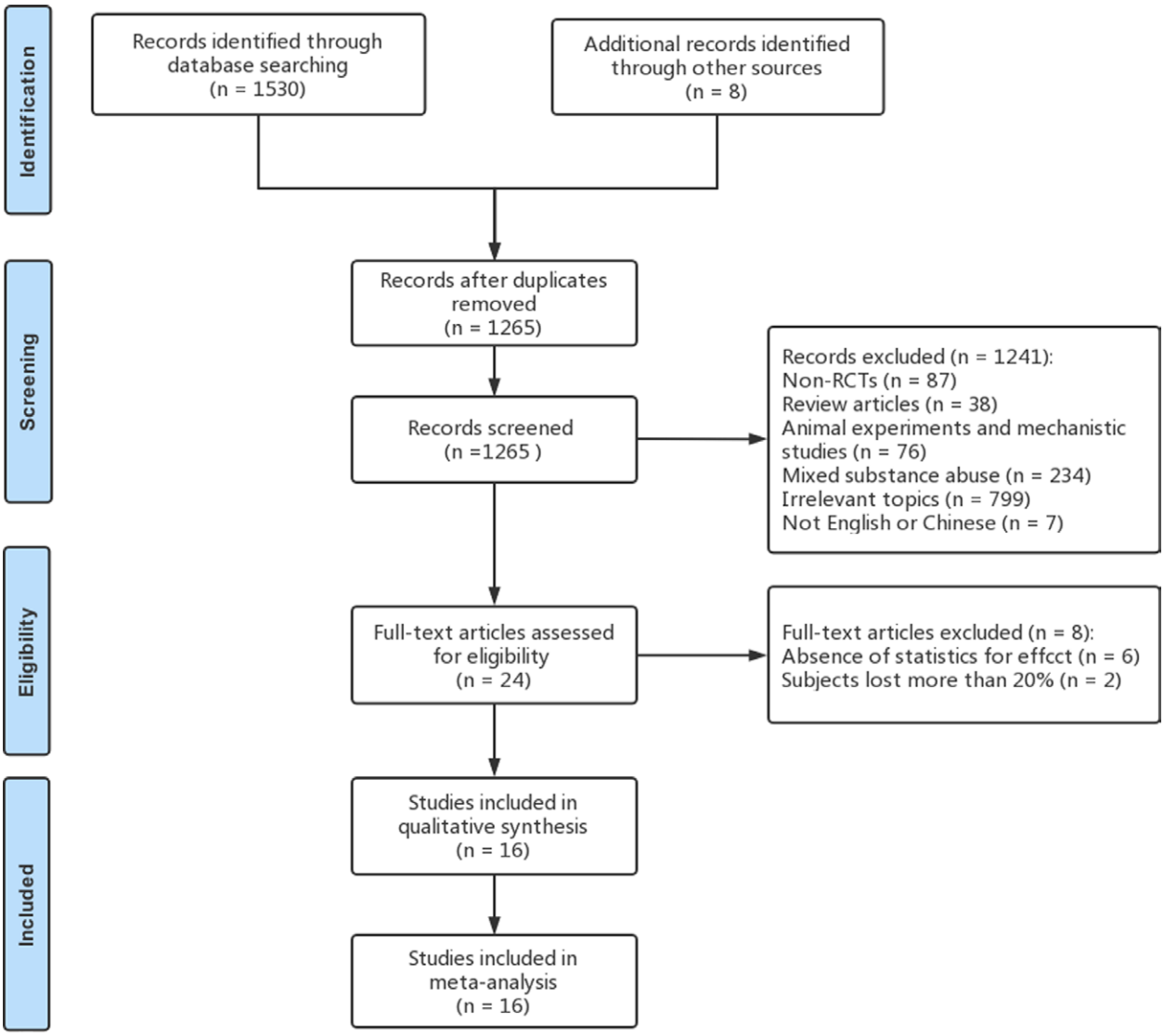

Figure 1. Flow diagram of the study selection process.

Interventions included individual acupuncture or auricular acupuncture or transcutaneous electrical acupoint stimulation, and acupuncture plus drug or psychotherapy or wrist-ankle acupuncture. There are 14[20–28,30–32,34,35] included trials that use craving for alcohol as the outcome, measured using scores on a visual analogue scale, obsessive compulsive drinking scale, Pennsylvania alcohol craving scale or self-made evaluation scale. Three[20,21,28] choose clinical institute withdrawal assessment for alcohol scale as AWS assessment. Eight literatures[23–25,27,29,30,33,35] assess anxiety by Hamilton rating scale for anxiety or state-trait anxiety inventory, and 7[22–25,32,33,35] report depression with Hamilton rating scale for depression or beck depression inventory. However, 2 studies[24,34] did not mention the gender composition of participants. Of all studies, only 6[20,21,23,24,34,35] of them reported adverse effects during the trial. The specific characteristics of the included studies are shown in Table 1.

3.3. Risk of bias in studies

Details of the the Cochrane risk-of-bias tool for trials of included studies were shown in Table 1. Most studies emphasized randomization and published expected outcomes. Randomization was performed in 16 studies, but only 8 studies[20,21,23–25,28,34,35] reported the details of random sequence generation while the others lacked evidence. Only 3 studies[24,25,35] reported the information of allocation concealment, which were assessed as low risk of bias. Blinding of participants and acupuncturists was not possible by design in 7 studies[20,22,27,28,32,35] comparing acupoint stimulation plus drug or psychotherapy versus drug or psychotherapy, and 1 study[34] comparing acupoint stimulation versus drug; accordingly, these trials were considered to be at high risk of performance bias. There were 8 studies[21,23–26,29,31,33] reported blindness, among which 2[21,25] were double-blind and 5[23,24,26,29,31] were single-blind, which we believe could be rated as low risk, and 1[33] was rated as unclear. And only 2[21,25] do the blinding of outcome assessment, as the researcher who was blind to the type of acupoint stimulation given responded for assessments. There were 4[21,23–25,29,31,33,34] included studies that were assessed as having high risks cause because they did not report complete outcome datas. And there was 1 trial[26] conducted selective reporting with a high risk of bias. No trial reported other kinds of bias. In general, the overall risk of bias in included studies is high.

3.4. Synthesis of results

3.4.1. Alcohol craving. Twelve RCTs (n = 812 participants) were pooled for the general comparison between interventions involving acupoint stimulation and the control groups on the improvement of alcohol craving. There was evidence of a statistically significant effect of acupoint stimulation on alcohol craving compared to all control groups (SMD = –1.17, 95% CI = –1.82 to –0.52, df = 11, P = .0004), but heterogeneity was significant (I^2 = 94%), which should be treated with caution (see Figure S1, Supplemental Digital Content, http://links.lww.com/MD/I285, which shows acupoint stimulation vs all control groups on the improvement). This study, thus, divided the studies according to intervening measure, treatment period and gender, to evaluate the cause of heterogeneity.

Subgroup analysis showed that acupoint stimulation combined with psychotherapy was associated with a better effect than psychotherapy alone in reducing alcohol cravings (SMD = –1.09, 95% CI = –1.40 to –0.77, df = 2, P < .00001; Fig. 2), with the heterogeneity absent, I^2 = 0%.

Acupoint stimulation treatment combined with drugs versus drugs suggested that alcohol craving could be improved (SMD = –2.25, 95% CI = –3.17 to –1.34, df = 3, P < .00001; Fig. 3), but heterogeneity was significant, I^2 = 87%.

Sensitivity analysis with the exclusion of 1 study[20] demonstrated that acupoint stimulation treatment combined with drugs was associated with a better effect than drugs in reducing alcohol cravings (SMD = –2.64, 95% CI = –3.46 to –1.82, df = 2, P < .00001; I^2 = 73%) (Figure S12, Supplemental Digital Content, http://links.lww.com/MD/I286, which show acupoint stimulation plus drug vs drug excluded Liu YJ, 2016 on the improvement of alcohol craving). After reading the whole studies, we found that Liu YJ, 2016[20] used wrist and ankle acupuncture therapy, while the others used body acupuncture. Therefore, it is not considered to be the main source of heterogeneity.

Pooling 3 RCTs that treatment for 2 weeks (n = 294 participants), acupoint stimulation significantly reduced alcohol craving compared to all control groups (SMD = –0.58, 95% CI = –0.81 to –0.35, df = 2, P < .00001), with the moderate heterogeneity, I^2 = 45% (Figure S3, Supplemental Digital Content, http://links.lww.com/MD/I287, which shows treatment for 2 weeks on the improvement of alcohol craving).

Pooling 2 RCTs that treatment for 4 weeks (n = 139 participants), acupoint stimulation combined with drugs significantly reduced alcohol craving compared to drugs alone (SMD = –2.18, 95% CI = –2.61 to –1.75, df = 1, P < .00001, Fig. 4), with the moderate heterogeneity, I^2 = 41%.

Pooling 2 RCTs that treatment for 3 months (n = 120 participants), acupoint stimulation significantly reduced alcohol craving (SMD = –1.97, 95% CI = –3.62 to –0.33, df = 1, P = .02), but heterogeneity was significant, I^2 = 92% (Figure S4, Supplemental Digital Content, http://links.lww.com/MD/I288, which shows treatment for 3 months on the improvement of alcohol craving).

Among the RCTs with desire as an outcome indicator, 6 studies (n = 431 participants) targeted male-only. Data were pooled to show that acupoint stimulation improved alcohol craving (SMD = –1.59, 95% CI = –2.42 to –0.76, df = 5, P = .0002), and the heterogeneity was significant, I^2 = 93%, which should be treated with caution (Figure S5, Supplemental Digital Content, http://links.lww.com/MD/I289, which shows male-only randomized controlled trials).

When sham acupoint stimulation was involved in the control intervention, including the combined effect size of acupuncture plus drug versus sham acupuncture plus drug (SMD = –1.41, 95% CI = –3.56 to –0.74, df = 1, P = .20, and I^2 = 97%) (Figure S6, Supplemental Digital Content, http://links.lww.com/MD/I290, which shows acupoint stimulation plus drug vs sham acupoint stimulation plus drug on the improvement of alcohol craving), acupuncture versus sham acupuncture (SMD = –0.29, 95% CI = –1.12 to –0.54, df = 1, P = .49, and I^2 = 82%) (Figure S7, Supplemental Digital Content, http://links.lww.com/MD/I291, which shows acupoint stimulation vs sham acupoint stimulation on the improvement of alcohol craving), there was no difference in the reduction of craving for alcohol, and heterogeneity was significant. The same is true for the 7-day treatment course (SMD = –2.19, 95% CI = –4.39 to 0.00, df = 1, P = .05, and I^2 = 93%) (Figure S8, Supplemental Digital Content, http://links.lww.com/MD/I292, which shows treatment for 7 days on the improvement of alcohol craving).

The dichotomic variables suggested that the experimental group was better than the control group, but there was no statistical significance (P = .10), which should be treated with caution.

3.4.2. Severity of AWS. Three RCTs assessed AWS. From these RCTs (n = 225 participants), there was evidence of a significant effect of acupoint stimulation compared to all controls for alcohol withdrawal symptoms (MD = –1.21, 95% CI = –2.32 to –0.1, df = 2, P = .03; Fig. 5), with the moderate heterogeneity, I^2 = 46%.

Table 1

Characteristics of included RCTs and risk of bias summary.

Reference	Intervention/control		Gender (male/female)	Diagnosis	Treatment protocol		Acupoints	Outcomes	Adverse effects	Risk of bias summary ① ② ③ ④ ⑤ ⑥ ⑦
	N	Mean age (yr)			Intervention	Control				
Yun Song[21] 2020, China	62/63	45.51 ± 9.75/44.54 ± 8.32	125/0	DSM-IV	TEAS + Drug	Sham TEAS + Drug	LI4, PC8, PC6, SJ5	①: VAS ②: CIWA-Ar	Acceptable adverse reactions: 15 in intervention, 19 in control	
Florian Krause[24] 2020, Germany	24/24	43.7 ± 9.2	NR	DSM-V	AA	Sham AA	NR	①: OCDS ③: STAI ④: BDI	No adverse events	
Feiyi Zhao[23] 2020, China	31/31	41.88 ± 6.72/42.56 ± 6.31	62/0	DSM-IV	EA + Drug	Sham EA + Drug	GV20, GV26, HT7, LI4, PC6	①: PACS ③: HAMA ④: HAMD	Thirst and bitter taste for Both groups, Control:1 nausea	
Ji Tian[32] 2018, Chian	43/42	48.4 ± 4.2/48.8 ± 4.7	62/22	ICD-10	A + psycho-therapy	psychother-apy	GV20, PC6, ST36	①: VAS ④: HAMD	NR	
Ping Cui[35] 2017, China	40/40	40.23 ± 10.87/42.05 ± 11.55	80/0	ICD-10	EA + Drug	Drug	GV29, LI4, PC6, HT7	①: PACS ③: HAMA ④: HAMD	6 mild headache, nausea after EA; 1 drop-out for severe headache	
Xin Tong[22] 2016, China	30/30	40–65	38/22	CCMD-3	A + psycho-therapy	psychother-apy	GV20, PC6, ST36	①: VAS ④: HAMD	NR	
Yanjiang Liu[20] 2016, China	30/30	45.23 ± 7.34/46.01 ± 8.02	60/0	ICD-10	WAA + Drug	Drug	Upper area 1	①: VAS ②: CIWA-Ar	Intervention:1 mild subcutaneous hemorrhage	
Mengmeng Miao[34] 2015, China	35/33	18–24	NR	DSM-V CCMD-3	A	Drug	GV24, GB13	①: VAS	2 fainting after A; Drug group: 2 thirst and bitter taste, 8 nause, 1 face red	
Qinfeng Zhang[30] 2014, China	30/30	40.51 ± 8.14/41.26 ± 7.84	60/0	ICD-10	EA + Drug	Drug	LI4, ST36	①: PACS ③: HAMA	NR	
Hongqiang Sun[31] 2012, China	45/47	47.10 ± 10.06/45.40 ± 10.05	92/0	ICD-10	TEAS	Sham TEAS	LI4, PC8, PC6, TE5	①: VAS	NR	
Weijie Jin[29] 2011, China	45/47	47.10 ± 10.06/45.40 ± 10.05	92/0	ICD-10	TEAS	Sham TEAS	LI4, PC8, PC6, TE5	③: HAMA	NR	
Wei Wang[28] 2010, China	20/20	43.89 ± 8.38/45.05 ± 7.08	40/0	ICD-10	TEAS + Drug	Drug	LI4, PC8, PC6, TE5	①: VAS ②: CIWA-Ar	NR	
Yahong Zhang[33] 2010, China	32/32	40 ± 4	64/0	CCMD-3	EA + Drug	Sham EA + Drug	GV20, GV29	③: HAMA ④: HAMD	NR	
Min Jin[27] 2006, China	20/15	41.4 ± 8.2	35/0	CCMD-3	EA + psycho-therapy	psychother-apy	NR	①: Self ③: HAMA	NR	
Sapir-Weise R[25] 1999, Sweden	36/36	45 ± 9	51/21	DSM-III (SCID)	AA + Drug	Sham AA + Drug	Ear Lung, Shenmen, Sympathetic	①: 5 grade very strong - none ③④: 5 grade much better - much worse	NR	
Bullock ML[26] 1987, USA	27/27	42	54/0	Self	A + AA	Sham A + Sham AA	3 ear point: Shenmen, and Lung plus Liver/Kidney/Occiput; 2 wrist point: LI4, SJ5 (TE5)	①: answer 2 question with Lickert-Scaled Options	NR	

Low risk of bias, unclear risk of bias, high risk of bias.

A = acupuncture, AA = auricular acupuncture, BDI = beck's depressions inventory, CIWA-Ar = clinical institute withdrawal assessment for alcohol scale, EA = electroacupuncture, HAMA = hamilton rating scale for anxiety, HAMD = hamilton rating scale for depression, NR = not reported, OCDS = obsessive compulsive drinking scale, PACS = pennsylvania alcohol craving scale, STAI = state-trait anxiety Inventory, TEAS = transcutaneous electrical acupoint stimulation, VAS = visual analogue scale, WAA = wrist-ankle acupuncture.

① Craving, ② Severity of AWS symptoms, ③ Anxiety, ④ Depression.

3.4.3. Anxiety. Seven RCTs assessed alcohol with an anxiety scale. From these RCTs (n = 438 participants), there was evidence of a significant effect of acupoint stimulation compared to all controls for anxiety scale (MD = –3.83, 95% CI = –5.14 to –2.53, df = 6, $P < .00001$), with the significant heterogeneity, I^2 = 78%) (Figure S9, Supplemental Digital Content, http://links.lww.com/MD/I293, which shows acupoint stimulation compared to all controls for anxiety).

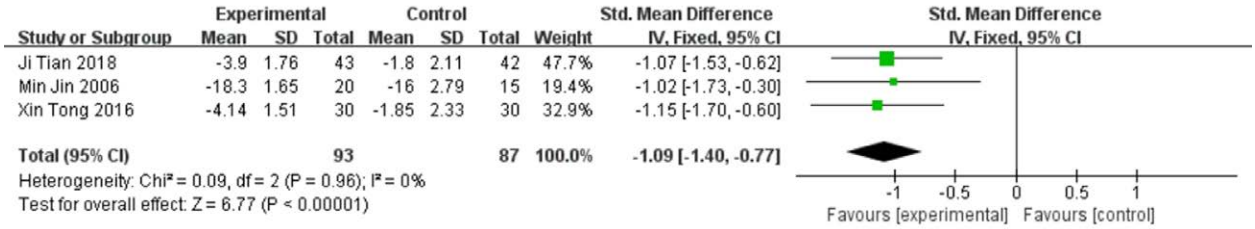

Figure 2. Acupoint stimulation plus psychotherapy versus psychotherapy on the improvement of alcohol craving.

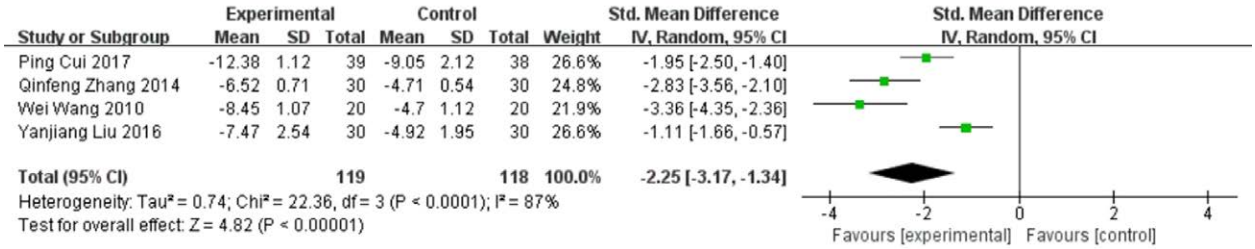

Figure 3. Acupoint stimulation plus drugs versus drugs on the improvement of alcohol craving.

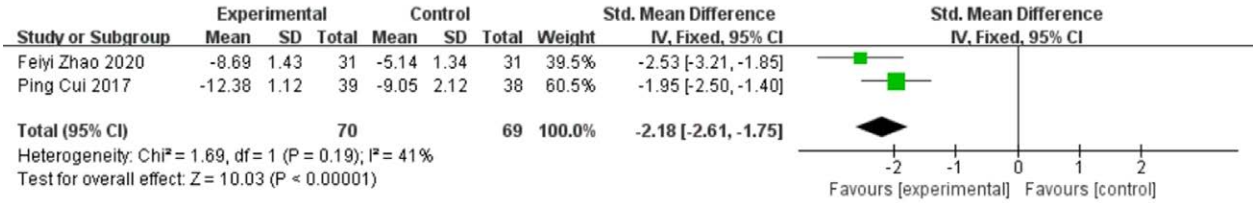

Figure 4. Treatment for 4 weeks on the improvement of alcohol craving.

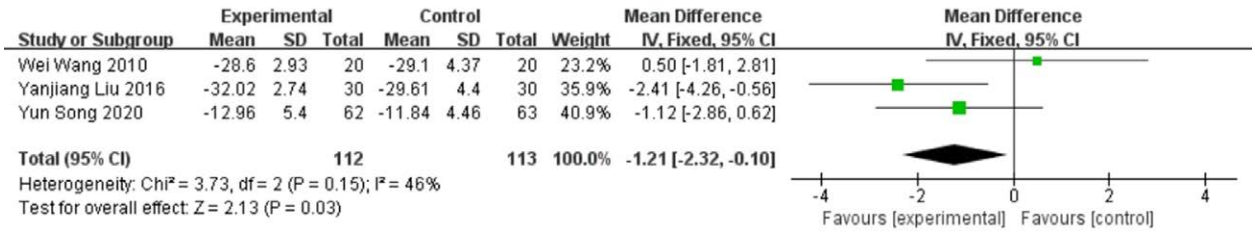

Figure 5. Acupoint stimulation plus drugs versus drugs for alcohol withdrawal symptoms.

Subgroup analysis showed that acupoint stimulation combined with other treatments (psychotherapy/drugs) was associated with a better effect than other treatments (psychotherapy/drugs) in reducing anxiety (MD = –3.41, 95% CI = –4.06 to –2.76, df = 4, $P < .00001$; Fig. 6), with the moderate heterogeneity, $I^2 = 30\%$.

3.4.4. Depression. Six RCTs assessed depression scale. From the 6 RCTs (n = 396 participants), there was evidence of a significant effect of acupoint stimulation compared to all controls for depression scale (MD = –2.91, 95% CI = –4.51 to –1.31, df = 5, $P = .0004$), but heterogeneity was significant, $I^2 = 90\%$ (Figure S10, Supplemental Digital Content, http://links.lww.com/MD/I294, which shows acupoint stimulation compared to all controls for depression).

Subgroup analysis showed that acupoint stimulation combined with other treatments (psychotherapy/drugs) was associated with a better effect than other treatments (psychotherapy/drugs) in reducing depression (MD = –3.27, 95% CI = –4.92 to –1.62, df = 4, $P = .0001$; Fig. 7), but heterogeneity was significant, $I^2 = 91\%$.

3.5. Evidence quality and efficacy-effectiveness spectrum

The evidence quality of main outcomes ranged from very low to low (Table 2) and the other outcomes ranged from very low to moderate (see Supplementary Digital Content 2, Supplemental Digital Content, http://links.lww.com/MD/I295, table that illustrate evidence certainty).

4. Discussion

4.1. Summary of evidence

This meta-analysis further shed light on the efficacy of acupoint stimulation combined with psychotherapy or drug therapy in reducing specific clinical symptoms, including alcohol

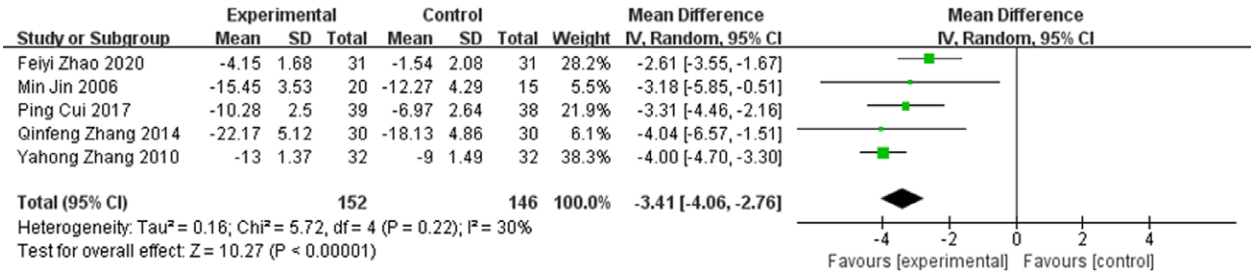

Figure 6. Acupoint stimulation plus psychotherapy/drugs compared to psychotherapy/drugs for anxiety.

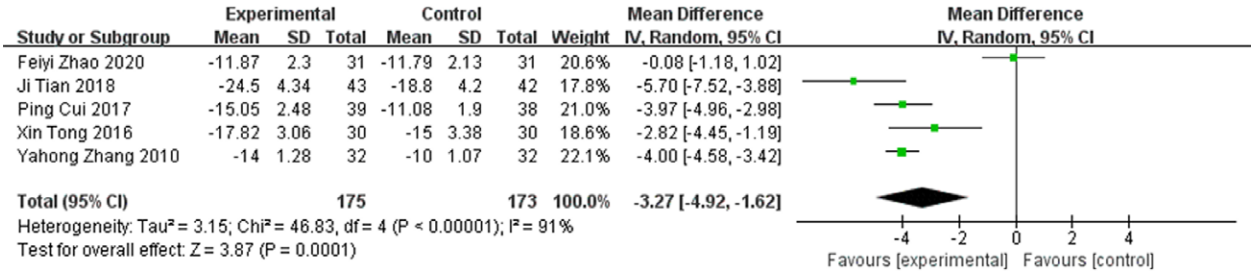

Figure 7. Acupoint stimulation plus psychotherapy/drugs compared to psychotherapy/drugs for depression.

Table 2

Summary of findings: Acupoint stimulation plus psychotherapy/drugs compared to psychotherapy/drugs for AUD.

Outcomes	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	No. of participants (studies)	Certainty of the evidence (GRADE)	Risk difference with acupuncture (95% CI)
Acupoint stimulation plus psychotherapy compared to psychotherapy for AUD								
Alcohol craving	Seriousa	Not serious	Very seriousb,c	Seriousd	None	180 (3 RCTs)	⨁◯◯◯ Very low	SMD −1.09 (−1.4 to −0.77)
Acupoint stimulation plus drugs compared to drugs for AUD								
Alcohol craving	Not seriouse	Not seriousf,g	Seriousc	Seriousd	None	237 (4 RCTs)	⨁⨁◯◯ Low	SMD −2.25 (−3.17 to −1.34)
Alcohol craving (treatment for 4 w)	Seriouse,h	Not serious	Not serious	Seriousd	None	139 (2 RCTs)	⨁⨁◯◯ Low	SMD −2.18 (−2.61 to −1.75)
AWS	Not seriouse	Not serious	Seriousc	Seriousd	None	225 (3 RCTs)	⨁⨁◯◯ Low	MD −1.21 (−2.32 to −0.1)
Acupoint stimulation plus psychotherapy/drugs compared to psychotherapy/drugs for AUD								
Anxiety	Seriouse,h	Not serious	Very seriousb,c	Seriousd	None	(5 RCTs)	⨁◯◯◯ Very low	MD −3.41 (−4.06 to −2.76)
Depression	Seriouse,h	Very seriousf	Seriousc	Seriousd	None	(5 RCTs)	⨁◯◯◯ Very low	MD −3.27 (−4.92 to 1.62)

95% CI = 95% confidence intervals, AUD = alcohol use disorders, AWS = alcohol withdraw syndrome, CI = confidence interval, GRADE = grading of recommendations assessment, development and evaluation, MD = mean difference, SMD = standardized mean difference.

[a]. Neither selection bias nor blinding was mentioned.

[b] The outcome measures were administered using a home-made scale.

[c] The course of treatment was not uniform.

[d] With small sample size.

[e] Partial selection bias and blinding were not mentioned.

[f] $I^2 > 50\%$, $P < .10$.

[g] Courses of heterogeneity could be explored.

[h] Cases are missing and outcome data were incomplete.

[i] There were no statistical difference between the 2 groups.

craving and withdrawal, as well as in improving anxiety and depression level for AUD. Acupoint stimulation plus drugs showed better effect than it plus psychotherapy with relatively higher evidence quality. When subgroup analysis was conducted by different treatment duration, the results indicated that in reducing alcohol craving, acupoint stimulation showed a better effect with 4 weeks. However, because of the high risk of bias and serious imprecision, the evidence was of low quality. The effect size of acupoint stimulation was smaller in trials with a sham control treatment, and with significant heterogeneity. It may be considerate related to the nonspecific therapeutic effect of acupuncture, which should be treated with caution.

4.2. Comparisons with previous studies

In the past, few systematic reviews have quantitatively presented the abstinence effect of acupoint stimulation therapy on patients with AUD. Compared with previous meta-analysis,[9–12] acupoint stimulation therapy has a wider form and more emphasis on the effect of acupoint, which includes traditional acupuncture, electroacupuncture, ear acupuncture, TEA, etc,. The results of the previous studies were similar to this study, when used as an adjunct therapy, acupuncture stimulation is effective in alleviating alcohol craving and AWS. Meanwhile, Shin NY, 2017[11] and Liu XX, 2018[12] reported acupuncture could improve anxiety, which is consistent with our results. Depression was assessed in our study and not found in the

other reviews. Study shows that acupoint stimulation therapy can reduce the degree of depression and improve the quality of life of patients with AUD. Li[36,37] have confirmed the effect of acupuncture on improving psychological state. At the same time, Several studies published in recent years using more rigorous methods and reporting more cautious conclusions have been included in this study, with a total of 16 RCTs, more than ever before. And GRADE was used to evaluate the quality of evidence, which had not been carried out in previous studies, thus increasing the credibility.

In addition, subgroup analysis was conducted to explore the source of heterogeneity, which was considered in relation to the unreasonable design of sham acupuncture, diversity of acupoint stimulation, insufficient sample size, and different research objects. Such as, the use of nonspecific acupuncture points in the ear as a control intervention in the trial[25] may have led to an overestimation of the effects of placebo acupuncture, thereby reducing the effects of acupuncture. This design issue should be noted when planning future research.

4.3. Strengths and limitations

In terms of the strengths of this review, first, a more detailed and in-depth search has been made, and the current included studies are relatively complete. Second, the GRADE quality evaluation and the heterogeneity are discussed, and subgroup analysis of the relationship between duration and efficacy is conducted, which provides ideas for the follow-up research method of RCT. Regarding the limitations, the completion and conviction of the conclusion may be weakened by the following aspects. Firstly, clinical heterogeneity associated with different acupoint stimulation techniques limits our ability to identify which techniques are more effective in treating alcohol dependence. Secondly, sham acupoint stimulation also varies from randomized controlled trial, which may lead to an underestimation of the effectiveness of acupuncture. Thirdly, there was a lack of rigorous reports on randomization methods and allocation concealment and control of implementation bias. Furthermore, follow-up analysis was not performed in this analysis, long-term effects of acupoint stimulation were not identified.

4.4. Implications for clinical practice and further research

It is a primary care priority as an alternative therapy that helps reduce alcohol cravings, severity of AWS, anxiety and depression in AUD patients, thereby improving quality of life. The combination of acupoint stimulation with psychotherapy or medication is more effective than either therapy alone, and the 4-week duration of treatment was better. However, the quality of evidence is low, which needs to be further rigorously proven, and the stability of their long-term effects on AUD remains to be determined further.

5. Conclusion

In this study, the evidence showed that acupoint stimulation and its combined therapy may be safe and effective in the treatment of AUD symptoms with a treatment duration of more than 2 weeks. However further studies with rigorous methodological quality are needed to support our conclusions.

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Writing – review & editing: Li Chen, Jiarong Huang, Peiming Zhang, Liming Lu, Chunzhi Tang.

Correction

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