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Effectiveness of electroacupuncture on anxiety: a systematic review and meta-analysis of randomized controlled trials

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This systematic review and meta-analysis aimed to comprehensively evaluate the effectiveness of electroacupuncture (EA) for patients with anxiety. Randomized controlled trials (RCTs) on the treatment of anxiety by EA up to November 2022 were searched and collected from nine databases. Hamilton Anxiety Rating Scale (HAMA), self-rating anxiety scale (SAS), and adverse reactions were used as outcome indicators. The quality of relevant articles was evaluated using the Cochrane Collaboration's risk of bias tool. The quality of evidence for each outcome was classified as "low risk," "unclear risk," or "high risk." RevMan 5.0 was used for data analysis. A total of 633 articles were identified from nine electronic databases; 37 RCTs were included, which measured anxiety changes by using EA alone compared to the control group. For the main outcome, EA significantly reduced the HAMA score [Mean difference (MD):-1.13 (95% CI:-2.55-0.29), $|^{2}:80\%|$, and the guality of evidence was moderate. EA significantly reduced the SAS score (MD:-3.47 (95% CI,-6.57--0.36), I²:88%), and the quality of evidence was moderate. Our meta-analysis shows that EA reduces HAMA and SAS. This study suggests that EA can relieve anxiety. For various uses, additional research is needed on its effect when combined with other treatments.

Systematic review registration: https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=345658, identifier (CRD42022345658).

KEYWORDS

electroacupuncture, anxiety, systematic review, meta-analysis, randomized controlled trials

1 Introduction

Anxiety ranks among the top five conditions individuals treat with medical marijuana in Canada and the United States (Reinarman et al., 2011). Anxiety is a detrimental mental disturbance that includes persistent feelings of apprehension, tension, despair, and distress. These disturbances induce physical symptoms such as tachycardia, nervousness, and inability to relax. It is also frequently associated with complications and disability. Anxiety is different from anxiety disorder. Anxiety disorders are one of the most common mental health conditions (Remes et al., 2016; Amorim et al., 2018). The terminology "Anxiety disorders" comprises several conditions, such as panic disorder, social anxiety disorders, anxiety associated with a medical condition, anxiety induced by substance use, and generalized

anxiety disorder. They differ from developmentally normative or stress-induced transient anxiety in persistence and impairment of daily functioning (Craske and Stein, 2016). We targeted anxiety, which is a broader category than anxiety disorders, in order to include more studies.

Anxiety is an emotional response to stimuli that humans perceive as threatening. Anxiety implies responses that affect the psychological and emotional sphere and have physiological and functional consequences (Stamenkovic et al., 2018). Pharmacotherapy and psychotherapy are the conventional treatments for anxiety. Regarding pharmacotherapy, anxiolytics, antidepressants, or monoamine oxidase inhibitors are used, with benzo-diazepines being the most used pharmacological resource as anxiolytics (Remes et al., 2016). However, these pharmacological resources can lead to habituation and cause side effects like chronicity, the need for long-term treatment, and high relapse rates. Due to the seriousness of these effects and the drawbacks of pharmacotherapy, finding an effective treatment with fewer undesirable side effects is a crucial task for modern medicine.

Electroacupuncture (EA), based on traditional Chinese medicine acupuncture, uses an electrical device connected to a needle to send electrical currents to the acupoint, thereby stimulating it (Han et al., 2021). The effect of EA is mediated by beta-endorphin (Ulett et al., 1998). High levels of plasma beta-endorphin may be associated with anxiety (Darko et al., 1992). EA, an improvement of traditional acupuncture, is commonly used to treat chronic pain (Vickers and Linde, 2014; Xiang et al., 2019) because of its safety, efficacy, and fewer side effects. Moreover, EA can also relieve anxiety (Pilkington, 2010), though this evidence is from animal experiments. Numerous studies have shown that EA is well tolerated by patients and is as effective as routine care. EA has displayed anxiety-relief effects in many clinical studies (Han et al., 2021).

The purpose of this study is to describe and critically evaluate the effectiveness of EA in treating anxiety. We provide a review of metaanalyses of research concerning the effectiveness of EA in treating anxiety to complement our study of the randomized clinical trials (RCTs) that have been conducted targeting participants with elevated anxiety levels. Although the previous study (Amorim et al., 2018) provided significant evidence regarding the treatment of anxiety by EA, we searched for RCTs concerning such a treatment to reinforce the research conducted in 2018 (Gao et al., 2020). Additionally, we expanded the scope of the target to anxiety and reinforced the databases or search strategy to collect and analyze more RCTs.

2 Materials and methods

2.1 Criteria for inclusion and exclusion

2.1.1 Study types

RCTs were included. We excluded crossover studies to reduce the risk of potential bias. There were no limitations regarding the publication language of the study.

2.1.2 Participant types

Participants in all groups included people with disease, menopause, addiction, and the healthy. There were no limitations regarding the sex, race, and nationality of the participants. Additionally, we included anxiety but excluded anxiety disorders.

2.1.3 Intervention types and controls

For treatment interventions, studies using EA therapies were included. However, studies that combined EA with other treatments or did not clearly specify anxiety measures were excluded. Control interventions included no treatment or sham acupuncture or other therapies, such as psychosocial interventions, pharmacological interventions, and other conventional interventions.

2.1.4 Outcomes measures

All studies had to use an established rating scale or other effective measures to access the degree of anxiety. The primary outcomes are SAS (Dunstan and Scott, 2020), HAMA (Thompson, 2015). The SAS is a 20-item self-report assessment device built to measure anxiety levels. The total raw scores range from 20 to 80 (20–44: Normal Range, 45–59: Mild to Moderate Anxiety Levels, 60–74: Marked to Severe Anxiety Levels, 75 and above: Extreme Anxiety Levels). HAMA is a psychological questionnaire used by clinicians to rate the se-verity of a patient's anxiety. The secondary outcomes are (1) state–trait anxiety inventory (STAI), (2)Beck Anxiety Inventories (BAI), (3) Symptom Checklist-90-Revised (SCL-90), (4) Hospital Anxiety and Depression Scale (HADS), (5) Generalized Anxiety Disorder questionnaire of 7 items (GAD-7), (6) VAS (anxiety scores), (7) HRSD (Hamilton Rating Scale for Depression), (8) CAS, (9) PAC-QOL (Patient assessment of constipation quality of life).

2.2 Literature searches

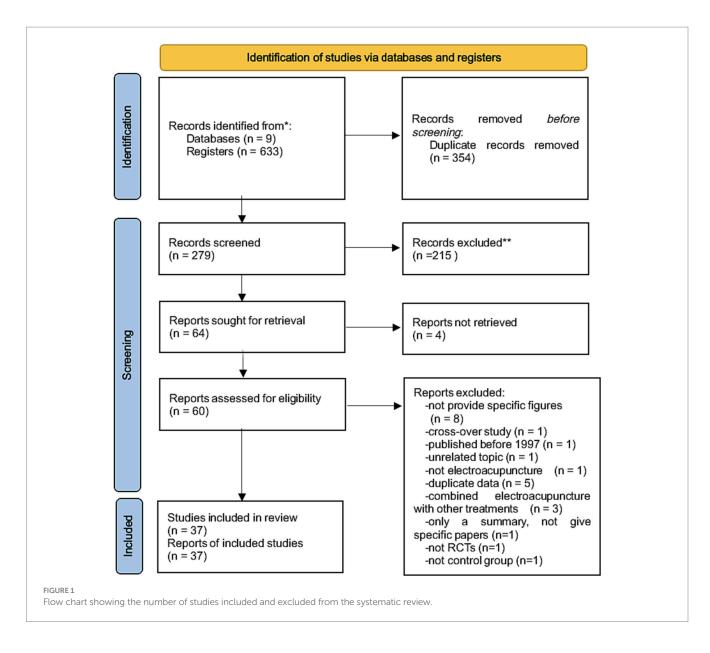
We comprehensively searched the following English, Korean and Chinese electronic databases from their inception date to 11 July 2022: Medline (via PubMed), EMBASE (via Elsevier), Cochrane Central Register of Controlled Trials, Science ON, Korean Studies Information Service System, Research Information Sharing Service, Oriental Medicine Advanced Searching Integrated System, China National Knowledge Infrastructure and American Psychological Association PsycArticles. We additionally reviewed the reference lists of the relevant studies to include any potentially relevant studies. We included both the broad term "anxiety [all fields]" AND "Electroacupuncture [all fields]" AND "Randomized Controlled Trials" [all fields]. The detailed search strategies for each database and search results are presented in Supplementary Table. Results were limited to "human" studies. Searches were performed without restriction by year.

2.3 Data selection

After removing duplicates, the titles and abstracts of the articles were reviewed for first inclusion. For the studies included after the initial screening, the full texts were retrieved and reviewed for final inclusion.

2.4 Data extraction

For the studies finally included, we extracted the following information using a standardized, pilot-tested Excel form: first author's name, publication year, sample size, details of participants,



intervention (acupoints, frequency, duration), control, outcomes, results.

Study selection and data extraction were independently conducted by three researchers (WK, YJ, and YR), and any disagreement was resolved by discussions with the other researchers (HI). If the data were ambiguous or insufficient, we contacted the authors of the included studies via e-mail if possible.

2.5 Quality/risk of bias assessment of included studies

We evaluated the methodological quality of the included studies using the Cochrane Collaboration's risk of bias tool including items of random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, completeness of outcome data, selective reporting, other potential threats to validity. Three researchers (WK, YJ, and YR) independently conducted the risk of bias assessment, and a consensus was reached through discussions with other researcher (HI) if there were disagreements. We classified each item as "low risk," "unclear risk," or "high risk."

2.6 Data analysis

If sufficient studies were selected, a meta-analysis was conducted using the mean difference (MD) for continuous variables as effect estimates. The data was analyzed using the Cochrane Review Manager software (RevMan 5.0). Statistical heterogeneity of the RCTs was evaluated using I² statistics and its 95% CI, where I²>50% or p < 0.05indicated significant heterogeneity. Subgroup analyses were performed for anxiety symptoms to explore potential factors that contributed to the heterogeneity.

3 Results

A total of 633 articles were initially identified from 9 electronic databases. After removing 354 duplicate records, we screened 279

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TABLE 1 Summary of the studies included in the review.

			Int	tervention					Outcome (p	re \rightarrow pro, $\chi \pm$ s)	
Study	Participants	Sample size (EA/ CT)	Acupoint(s)	Frequency (Hz)	Туре	Duration (min, times/ week, total)	Control	Outcomes	Intervention	Control	Result (O/ <u>∕</u>)
Tong et al. (2022) ①	Conservative breast surgery	36/34	HT7,PC6, EX-HN3, DU20	2	L	pre-op, 30 min, 3 t/w, 8 weeks	NA	SAS	$47.92 \pm 4.05 \rightarrow 41.14 \pm 4.77$	$46.06 \pm 5.08 \rightarrow 49.91 \pm 5.27$	0
Tong et al. (2022)	_	36/34				pre-op and intra-op, 30 min, 3 t/w, 8 weeks	-		47.78±4.92→41.97±4.10		0
Yin et al. (2022)	Insomnia	83/83	GV20, GV29	2	L	30 min, 3 t/w, 8 weeks	SA	SAS	2.9*	0.14*	0
Xu et al. (2022) ①	Functional dyspepsia	24/19	ST25, BL25	2	L	30 min, 3–5 t/w, 4 weeks	Medication (loperamide hydrochloride	SAS	31.63 → 25.41	32.47 → 32.87	0
Xu et al. (2022) ②		25/19	ST25, BL25	50	М	30 min, 3–5 t/w, 4 weeks	capsule 2 mg)		31.85 → 28.9	32.47 → 32.87	0
Bakacak et al. (2020)	HSG	36/37	H7, Du20, Liv-3, P-6, HT7, PC6, LI4, LI10, SP6, LR3, ST36, GB26, CP15, ST28 and Ren-4 points	1-20	L-M	before HSG 20 min	NA	STAI-S	43 → 32	$44 \rightarrow 41$	0
Xing et al. (2020)	Insomnia	30/30	DU20, EX-HN1, EX-HN22, SP6, HT7, PC6, BL62, KI6	2, 100	L-H	30 min, 3 t/w, 4 weeks	CBT	HAMA	$11.42 \pm 4.23 \rightarrow 9.52 \pm 4.02$	$11.81 \pm 5.10 \rightarrow 9.41 \pm 4.73$	Δ
Liu et al. (2020)	PSAD	35/32	GV20, GV16. BL15, HT7	20	М	20 min, e.o.d, 3 t/w, 4 weeks	Medication (Paroxetine, 10–20 mg)	HAMA	$22.20 \pm 4.50 \rightarrow 10.77 \pm 3.45$	21.91±3.83→11.94±2.85	0
Wang et al. (2019)	PCOS	23/20	CV3, CV6, ST29, SP6, SP9, LI4, GV20. The second points: ST25, ST29, CV3, CV6, LR3, PC6, GV20	2	L	30 min, 2 t/w, 16 weeks	SA	SAS	38 → 35	42 → 43	0
Yinjie et al. (2018)	Spinal cord injury	25/25	GV points, back-shu points	5	L	20 min, 1 t/ day, 2 month	Conventional needling	НАМА	$19.16 \pm 6.55 \rightarrow 13.98 \pm 5.64$	$20.52 \pm 7.86 \rightarrow 16.65 \pm 8.70$	0

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			In	tervention					Outcome (p	re \rightarrow pro, $\chi \pm$ s)	
Study	Participants	Sample size (EA/ CT)	Acupoint(s)	Frequency (Hz)	Туре	Duration (min, times/ week, total)	Control	Outcomes	Intervention	Control	Result (O/ <u></u>
Zeng et al. (2018)	MA addiction	31/33	T5, L2, PC6, HT7, ST36, SP6	2	L	3 t/w, 4 weeks	SA	НАМА	$23.32 \pm 5.06 \rightarrow 5.77 \pm 2.53$	$24.61 \pm 5.17 \rightarrow 8.79 \pm 4.46$	0
Teoh et al. (2018)	Diagnostic EUS	64/64	LI4, PC6, ST36	2	L	45 min, before op, during op	SA	VAS	4.4→1.7	4.3 → 5.1	0
Hui et al. (2017)	IAD	39/36	GV20 EX-HN1, LI4, PC6, LR3, SP6	10-100	L-H	30 min, e.o.d for 10 turns, 2 course	PI	SCL-90	$1.5 \pm 0.8 \rightarrow 1.1 \pm 0.9$	$1.5 \pm 0.9 \rightarrow 1.1 \pm 0.8$	0
Jin et al. (2016)	PCOS	35/33	BL18, CV17, LR14, CV4, ST25, CV4, EX-CA1, SP6, ST36, LR3	20	М	30 min, 10 weeks, total 30 ~ 40 times	Medication (dyne-35,1 tablet)	SCL-90	1.52±0.44→1.62±0.46	$1.31 \pm 0.29 \rightarrow 1.56 \pm 0.42$	Δ
Zhao et al. (2015)	D-IBS	32/30	ST25, ST37	2	L	30 min, qd, 6 t/w, 4 weeks	Moxibustion	HAMA	-	***	Δ
Dalamagka et al. (2015) ①	Inguinal hernia	18/18	SP6, ST36, LI4, PC6, BL60, KI3, auricular points Thalamus 26a, Shen-Men55, Lung101	1-2	L	Pre- op 40 min, during surgery, post- op 60 min	SA	STAI	-	***	0
Dalamagka et al. (2015)	-					Pre- op 40 min, post- op 60 min	-			**	0
Xiong et al. (2014) ①	Functional constipation	33/34	LI11, ST37	2	L	30 min, 16 times,	Medication (mosapride	SAS	$39.78 \pm 8.10 \rightarrow 37.90 \pm 8.22$	$39.83 \pm 10.35 \rightarrow 40.17 \pm 13.01$	0
Xiong et al. (2014)②		37/34	LI11, ST37	50	М	4 weeks	citrate, 5 mg)		$40.02 \pm 8.01 \rightarrow 34.49 \pm 7.36$		0
Dias et al. (2014)	Medical students	30/34	ST36, PC6, GB14, GV20, EX- HN1	2	L	20 min, 6–8 weeks	NA	BAI	$15.6 \pm 12.7 \rightarrow 7.9 \pm 6.9$	$12.3 \pm 9.1 \rightarrow 10.8 \pm 9.3$	0

(Continued)

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			Int	tervention					Outcome (p	re \rightarrow pro, $\chi \pm$ s)	
Study	Participants	Sample size (EA/ CT)	Acupoint(s)	Frequency (Hz)	Туре	Duration (min, times/ week, total)	Control	Outcomes	Intervention	Control	Result (O/△)
Mao et al. (2014)	WBC	19/19	at least 4 local points around the joint, at least 4 distant points	2	L	30 min, 10 times, 8 weeks	SA	HADS	$-3.5 \rightarrow -0.7$	$-1.0 \rightarrow 0.5$	0
Chen and Fan (2013)	GAD	32/31	GV20,EX- HN1,PC6,HT5,KI6,ST36,SP6,LR3	2-15	L-M	30 min, qd, 5 t/w, 6 weeks	Medication (Celite, 10 ~ 20 mg)	НАМА	21.81±3.93 → 11.28±5.72	$21.45 \pm 4.06 \rightarrow 10.58 \pm 4.84$	Δ
Wang et al. (2012)	E-PTSD	63/64	Ex-HN1, GV20, GV24, GB20	100	Н	30 min, e.o.d, 12 weeks	Medication (paroxetine, 20 mg)	НАМА	11.6±5.11→2.95±2.85	11.7±5.85→3.86±3.15	0
Dias et al. (2012)	Medical students	12/13	ST36, PC6, GB14, GV20, EX- HN1	2	L	20 min, 1 t/w, 8 weeks	NA	BAI	$10.2 \pm 8.7 \rightarrow 5.7 \pm 2.9$	$13.3 \pm 11.4 \rightarrow 14.0 \pm 13.6$	0
Chung et al. (2012)	postpartum depression	5/9	DU20, EX-HN3, EX-HN1, GB15, EX-HN1, GB15, GB8, EX-HN5, ST8, SP6, LR3, HE7, PC6	2	L	30 min, 2 sessions weekly, 4 weeks	SA	HADS	11.0±2.3→8.6±3.7	10.3±2.9→8.7±4.2	0
Zhu et al. (2011)	IAD	39/36	GV20, EX-HN1, LI4, PC6, LR3, SP6	10-100	L-H	e.o.d, total 20 times	the cognition and behavior therapy	SAS	54.1±10.93→44.18±8.85	55.83±9.02→47.31±11.56	0
Ping and	PSAN	34/33	GV20, GV24, EX-HN3, GV26,	a frequency of		30 min, 15	Medication	HAMA	$22.31 \pm 3.14 \rightarrow 15.38 \pm 3.20$	$22.27 \pm 3.22 \rightarrow 14.15 \pm 3.46$	Δ
Songhai (2008)			LI4, LR3, HT7, PC6	80-100/min		times, OD, 2 courses	(Alprazolam, 0.4–0.8 mg)	SAS	$62.42 \pm 7.28 \rightarrow 51.66 \pm 6.57$	$63.75 \pm 6.07 \rightarrow 48.83 \pm 7.13$	\triangle
Peng et al. (2008)	Functional dyspepsia	20/20	PC6, ST36	40	М	30 min, qd, 2 weeks	Medication (Cisapride, 10 mg)	SAS	-	***	0
Gejervall	IVF	78/80	KI11, ST29, LI10, LI4, ST36,	2-80	L-H	From	Medication	VAS	$28.6 \pm 19.8 \rightarrow 6.5 \pm 8.7$	$30.4 \pm 21.2 \rightarrow 7.2 \pm 11.1$	Δ
et al. (2005)			GV20			surgery to recovery	(flunitrazepam 0.5 mg, rectal paracetamol 1 g, alfentanil 0.5 mg)	STAI	34.8±8.4→26.8±5.6	34.3±8.5→28.6±7.8	Δ

(Continued)

TABLE 1 (Continued)

			In	tervention					Outcome (p	re \rightarrow pro, $\chi \pm$ s)	
Study	Participants	Sample size (EA/ CT)	Acupoint(s)	Frequency (Hz)	Туре	Duration (min, times/ week, total)	Control	Outcomes	Intervention	Control	Result (O/ <u>∕</u>)
Luo et al. (1998)	Depressive	133/108	GV20, EX-HN3	2	L	45 min, 6 t/w, 6 weeks	Medication (amitriptyline, 161 mg)	HRSD	$1.35 \pm 0.05 \rightarrow 0.17 \pm 0.03$	$1.24 \pm 0.06 \rightarrow 0.32 \pm 0.05$	0
Rampes et al. (1997)	AD or -abuse	23/16	НТ7	100	Н	30 min, weekly, 6 weeks	Counseling	CAS	11→4.6	9.2 → 12.0	0
Lee et al. (2020)	Insomnia	49/49	HT7, PC6, BL63, KI4	4	М	30 min, 2–3 t/w, for 4 weeks	SA	HADS	4.59 → 2.63	4.85 → 3.28	0
Yin et al. (2020)	Depressive	27/24	GV20, GV24, GV29, bilateral EX-HN22, HT7, SP6, PC6.	30	М	30 min, e.o.d, 3 t/w, 8 weeks	SA	НАМА	$22.33 \pm 8.76 \rightarrow 10.53 \pm 7.53$	$24.87 \pm 8.42 \rightarrow 20.90 \pm 8.17$	0
Zhao et al. (2018)	C-IBS + healthy (7)	30/30	ST25, ST37 bilaterally	2	L	30 min, OD, 6 t/w, 4 weeks	Moxibustion	НАМА	-	***	0
Xu et al. (2020)	Functional constipation	30/30	LI11, ST37 bilaterally	2/50	L-H	30 min, 3–5 t/w, 4 weeks	Medication (mosapride citrate, 5 mg)	SAS		**	0
Li et al. (2020)	РМІ	42/42	GV20, GV24, GV29, CV6, CV4, bilateral EX-HN22, SP6, HT7, GV4, BL23, KI3, KI7	2.5	L	30 min, 1–3 t/w, 8 weeks	SA	SAS	46.43±4.45→44.98±3.85	47.43±6.66→48.10±6.04	0
Caiyuzhu et al. (2017)	Manopasual	25/25	CV4, EX-CA1, ST25, SP6	10, 50	M-H	30 min, e.o.d, 3 t/w, 8 weeks	SA	SAS	38.72±5.37→32.67±4.46	39.50±6.45→31.89±5.05	
Zhang et al. (2018)	Depressive	30/30	GV20, GV24, PC6, HT7, SP6, LR3	10, 50	M-H	QD, 30 min, 5 days/week, 8 weeks	Music	НАМА	18.07±2.74→10.60±1.94	18.03±3.20 → 9.67±3.33	
Ma et al. (2021)	knee osteoarthritis	38/39	LI10,LI11,TE14,LI14,LU5,TE9	2	L	QD post OP, 20 min, 5 days	Medication (fentanyl, 0.25 µg)	HADS	10.23±3.37→9.00	10.58±2.98→7.00	Δ

(Continued)

			<u>u</u>	Intervention					Outcome (pr	Outcome (pre \rightarrow pro, $\chi \pm$ s)	
Study	Participants	Sample size (EA/ CT)	Acupoint(s)	Frequency (Hz)	Type	Duration (min, times/ week, total)	Control	Outcomes	Intervention	Control	Result (O/△)
Kim et al.	MDD	14/16	GV20, EX-HN3	10	Μ	20 min, 20	SA	STAI (state)	-2.58*	-1.25*	0
(2021)						sessions, 8 weeks		STAI (trait)	-5.42*	1.3*	0
Yeung et al. (2019)	Yeung et al. Long-term b (2019) users	72/72	EX-HNI, EX-HN22, GB8, ST8, EX-HN5, GB15, PC6, HT7, SP6, LV3, EX-HN3, GV24, GV20	4	Ч	30 min	SA	HADS	3.5 → 3.9	3.8 → 4.3	0
EA: electro acu (daily);SA: Shaı Beck Anxiety Iı analoesia: VAS:	puncture; STAI:state-tra m acupuncture; LAIS, HIS nventory; GAD-7: Gener vistial analooue scale: O	ait anxiety inver 5: Low, High int ralized Anxiety PU- ovum nick	EA: electro acupuncture, STAI:state-trait anxiety inventory; PI: psychological intervention; SCL-90: Symptom Checklist-90-Revised;SAS: Self-rating anxiety scale; BAI: the Beck Anxiety Inventories; HADS: Hospital Anxiety and Depression Scale; gd: quaque die (daily);SA: Sham acupuncture; LIS, HIS: Low, High intensity stimulation; Tid: tid ter in die (3 times a day); NI: no intervention; qn: quaque nocte; e.o.d: every other day; ESAS: Edmonton Symptom Assessment System; OD: once a day;SAS: self-rating anxiety scale; BAI: Beck Anxiety Inventory; GAD-7: Generalized Anxiety Disorder questionnaire of 7 items; OASIS: OASIS: OASIS: OA: Scale; GAT: cognitive behavioral therapy; SSRIs: selective serotonin reuptake inhibitors; PCA: patient-controlled sedation and analoue sedered and failor 1: Low, 7.5 Hiers; OASIS: MI: Hou Hon, 200 Hor): LI, Her Fanore overland Li and Hier and System; OT: Anarove with and successing section and second factore action and factore action factore action and factore action action action action action action action for an action for a factore action action action action action action factore action a	L-90: Symptom Chec times a day); NI: no ii IS: Overall Anxiety S 17.) M: Mid (6.49 Hz)	klist-90-Rev itervention; verity and l · H· High (5	vised;SAS: Self-rat qn: quaque nocte; mpairment Scale; 0.100 Hz): T_H-T	ing anxiety scale; BAI e.o.d: every other da CBT: cognitive behav he range overlans I. a	: the Beck Anxiety Inv y; ESAS: Edmonton Sy rioral therapy; SSRIs: s nd H. *Ananoe value-*	entories; HADS: Hospital Anxi mptom Assessment System; Ol elective serotonin reuptake inh et Cranh only no specific foruse	Symptom Checklist-90-Revised;SAS: Self-rating anxiety scale; BAI: the Beck Anxiety Inventories; HADS: Hospital Anxiety and Depression Scale; qd: quaque die a day); NI: no intervention; qn: quaque nocte; e.o.d: every other day; ESAS: Edmonton Symptom Assessment System; OD: once a day;SAS: self-rating anxiety scale eval Anxiety severity and Impairment Scale; GBT: cognitive behavioral therapy; SSRIs: selective serotonin reuptake inhibitors; PCA: patient-controlled sedation a Midi (6.49H2). H Hido (64):100H2). LH: The rance overlans I and H: #-hanoe value. #Scale: Or The J	aaque die nxiety scale; BAI: . sedation and .e: O: The FA

records based on the titles and abstracts, and examined 64 eligible reports further for retrieval. Among these, full-texts were not available for 4 of them. A full-text review was conducted for the remaining 60 articles. After excluding 20 articles for the following reasons: 8 studies did not provide specific figures, 1 study did not use EA, 1 study was a cross-over study, 1 study was not an RCT, 1 study did not include a control group which was inconsistent with our intentions, 1 study only provided a summary but not specific papers, 1 study was unrelated to the topic, 5 studies contained duplicate data, and 4 studies combined EA with other treatments. Finally, a total of 37 studies were included in our analysis (Figure 1).

3.1 Study characteristics

The articles included in the review were published in English, Korean, and Chinese between the start date and 11 July 2022, with a variety of patient conditions represented. The most frequently studied conditions were insomnia (4 studies) and depression (3 studies), followed by functional dyspepsia, polycystic ovary syndrome, irritable bowel syndrome, functional constipation, and healthy participants (2 studies each). Other conditions were studied only once. The EA group utilized a total of 68 acupuncture points, with PC6 used most frequently (19 times), followed by GV20 (18 times) and SP6 (15 times). HT7 was used 12 times, while ST36 and LR3 were used 10 and 9 times, respectively. The electricity frequency categories in the EA group were Low (2-5 Hz) in 19 studies, L-H (the range overlapping L and H) and L-M in 6 studies each. The control group was most commonly treated with SA (sham acupuncture) or drugs, with 12 studies each. Psychological interventions were used in 3 studies, while moxibustion and NA were used in 2 studies each. The most commonly used outcome measures were HAMA and SAS (11 studies each), followed by HADS (5 studies), while other measures were used only once or twice (Table 1).

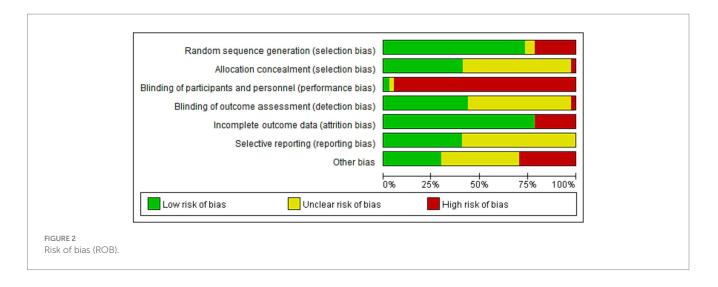
3.2 Quality/risk of bias of included studies

All 27 studies included in the analysis reported their methods for random sequence generation, which included the use of computer programs and random number generators, and were assessed as having a low risk of bias. Among the allocation concealment methods used, 15 studies used sealed envelopes and were assessed as having a low risk of bias, while 21 studies had an uncertain risk due to lack of specific description about blinding of participants and investigators. Thirty-five studies were evaluated as high risk, one was unclear, and only one study was evaluated as having a low risk of blindness. Sixteen RCTs reported detailed outcome assessment of blindness and were rated as having a low risk of bias. Regarding data integrity, all 29 studies provided detailed descriptions, indicating a low risk of bias. All expected outcomes, including adverse events, were reported in the 15 studies, which were assessed as having a low risk of bias. However, the remaining studies either did not document the protocol or did not mention adverse events, leading to high or uncertain risks. There were 11 studies with high-risk sources of bias, 11 with low-risk, and others were unclear. The risk of bias in each trial is presented in Figures 2, 3.

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TABLE 1 (Continued)

group reduced anxiety values more than the control group; Δ : The Control group reduced anxiety values more than the EA group



3.3 Intervention effects

The studies included in the analysis used EA as the intervention for anxiety in patients with various diseases. The patient populations across the studies were diverse, with three studies focusing on patients with depression and insomnia, and two studies each on patients with constipation, functional indigestion, Internet addiction, polycystic ovary syndrome, and general medical students experiencing anxiety. The remaining studies examined the use of EA for anxiety symptoms independent of any particular disease. Acupuncture points, frequency, and outcome scales varied across the studies. HAMA and SAS were the most frequently used outcome measures, with 11 trials using them. HADS was used in five trials. A meta-analysis was performed on studies using HAMA and SAS as outcome measures, while other studies used different outcome measures.

3.3.1 HAMA

A total of 11 RCTs investigated the effect of EA on HAMA scores in our meta-analysis. Meta-analysis of 9 RCTs involving 9 trials with 609 participants were not statistically significant (MD: -1.13 (95% CI -2.55 to 0.29), 1²:80%, Figure 4).

3.3.2 SAS

A total of 11 RCTs investigated the effect of EA on SAS scores in our meta. Meta-analysis of 6 RCTs involving 8 trials with 554 participants revealed significant differences in HAMA score reduction (MD: -3.47 (95% CI -6.57 to -0.36), I²:88%, Figure 5) and no significant publication bias.

3.4 Subgroup analysis

Since anxiety is a common symptom in many diseases, the primary symptoms of the patients in the studies were not anxiety, but rather other diseases. Therefore, we conducted a meta-analysis using participant status to explore potential differences that may be attributed to variations in patients' diseases. Among the 37 studies, there were 28 unique participant statuses, indicating little overlap and considerable diversity. The most frequent participant status was insomnia and depression, followed by constipation, diarrhea, Internet addiction, polycystic ovarian syndrome, and two studies involving general patients. We categorized the studies into psychiatric disorders and digestive disorders for the meta-analysis.

3.4.1 Mental symptoms

A total of 13 RCTs investigated the effects of EA on participants with psychiatric conditions in the meta-analysis. Insomnia, depression, stress disorder, and methamphetamine addiction were included, but Internet addiction was not included (Grant and Chamberlain, 2016). A meta-analysis of 8 RCTs using HAMA outcome measure found results that can infer the tendency that anxiety is effective compared to previous graph results, but were not statistically significant (Figures 4, 5; MD: -1.01 (95% CI -2.47 to 0.45), I²:82%, Figure 6).

4 Discussion

Anxiety ranks in the top 10 causes of disability worldwide (Remes et al., 2016). Pharmacotherapy and psychotherapy are the conventional treatments for anxiety. However, these pharmacological resources can lead to habituation and cause side effects. Due to its chronicity, high relapse rates, and need for long-term maintenance treatment, there is an urgent need for effective treatment of anxiety with fewer undesirable side effects. Several studies have shown the positive effects of acupuncture on state anxiety (Yang et al., 2021).

This study aimed to update the treatment effect of EA on anxiety by collecting data from RCTs. In this review, we searched several databases to identify comprehensive data sources. The purpose of this review was to provide an overview of previous studies and investigate the effectiveness of EA. Forty-one trials from 37 studies were included in this review, and 20 studies were suitable for metaanalysis. They were mainly conducted in Korea, the United States, and China. The conditions of the patients almost varied without overlapping.

The frequently used acupoint (PC6) was among patients with poststroke onset insomnia and was reported to be effective due to



the reduction in sympathetic hyperactivities after acupuncture (Lee et al., 2009). Reduction of sympathetic hypersensitivity was shown to relieve anxiety in this study. The second most used acupoint was GV20. Acupuncture at this point calms the mind and invigorates the brain (Er-Jun et al., 2020). The third and fourth most frequently used acupoints were SP6 and HT7. EA at SP6 and HT7 reduced serum dopamine levels in patients with anxiety, suggesting that EA at SP6 and HT7 could improve the threshold of awakening and regulate abnormal emotions (Li et al., 2022). For the 13 RCTs in the previous paper (Amorim et al., 2018) related to anxiety and acupuncture, PC6 was used seven times, HT7 five times, GV20 three times, and SP6 two times. All four acupuncture points frequently used in our paper were also frequently used in previous papers. Therefore, the four acupoints are often used to relieve anxiety.

For the electric frequency, 19 out of 37 experiments used a low frequency of 2–5 Hz. Two experiments used 100 Hz high frequency alone. In general, in the case of low frequency, beta-endorphin in the brain and enkephalin and dynorphin in the spinal cord are secreted, and it is known that serotonin is involved in high frequency. Anxiety is associated with beta-endorphin, so lower frequencies were used more frequently (Han and Sun, 1990).

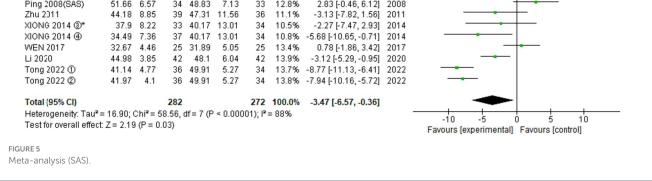
The degree of risk of bias (ROB) in other parts is compliant, but the ROB of performance bias is high. This is because the acupuncturist's blindfold is difficult to implement.

The outcome measures frequently used in this study are divided into two types: using HAMA and SAS to score the acuteness of anxiety level of patients. The results were generally effective, but the heterogeneity was high, so the interpretation should be careful. In previous studies, various outcome indicators were used to measure anxiety. Although a study reported that STAI was the most popular inventory for determining the degree of anxiety during an RCT (Amorim et al., 2018), our analysis confirmed that HAMA and SAS were more frequently used as measures of anxiety to determine the effect of EA.

Previous studies have investigated the relationship between anxiety disorders and acupuncture. We expanded the range of anxiety disorders and checked whether EA was effective on more transient anxiety states. Unlike the existing papers on the relationship be-tween acupuncture and anxiety, we selected studies that only compared the results of the EA and control groups and excluded studies on other treatments. Therefore, the effect of EA on anxiety was observed more clearly.

This review had several limitations. First, the diversity of data could not be secured because it was impossible to research other databases, such as the Japanese database. To overcome this shortcoming, multi-regional studies are required to supply solid clinical outcomes and diverse mechanistic techniques (Guo et al., 2020). Second, the EA parameters, including acupoints and times and frequency of EA, were selected without a consolidated standard in the included studies, which could be a potential source of clinical heterogeneity (Gao et al., 2021). Third, this study regarded EA as the only intervention and did not explore the combined use of other treatment methods for better efficacy. Only the efficacy of EA alone was reviewed; hence, the effect of EA combined with other treatments is unknown. Further research is needed in this area (Zhou et al., 2022). Fourth, studies with a high methodological quality were relatively limited, based on the

	-	erimen		-	ontrol			Mean Difference		Mean Difference
Study or Subgroup	Mean			Mean			Weight	IV, Random, 95% CI		IV, Random, 95% CI
Ping 2008(HAMA)	15.38	3.2		14.15		33	12.8%	1.23 [-0.37, 2.83]		-
Wang 2012	4.65	3.44	63	5.59	3.18	64	13.9%	-0.94 [-2.09, 0.21]		
Chen 2013	11.28	5.72	32	10.58	4.84	31	10.1%	0.70 [-1.91, 3.31]	2013	
Cui 2018	13.98	5.64	25	16.65	8.7	25	6.8%	-2.67 [-6.73, 1.39]	2018	
Liang 2018	5.77	2.53	31	8.79	4.46	33	12.4%	-3.02 [-4.78, -1.26]	2018	
Zhang 2018	10.6	1.94	30	9.67	3.33	30	13.4%	0.93 [-0.45, 2.31]	2018	+-
LIU 2020	10.77	3.45	35	11.94	2.85	32	13.1%	-1.17 [-2.68, 0.34]	2020	
Xing 2020	9.52	4.02	30	9.41	4.73	30	11.1%	0.11 [-2.11, 2.33]	2020	
Yin 2020	10.53	7.53	27	20.9	8.17	24	6.3%	-10.37 [-14.70, -6.04]	2020	
Total (95% CI)			307			302	100.0%	-1.13 [-2.55, 0.29]		•
Heterogeneity: Tau ² =	= 3.41; C	hi² = 3	9.78, df	r= 8 (P -	< 0.000	001); I ^z	= 80%			
Test for overall effect:	Z=1.58	6 (P = 0	0.12)							Favours [experimental] Favours [control]
										Favours [experimental] Favours [control]
FIGURE 4										
Meta-analysis (HAMA).										
		erimen			Control			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Tota	Weight	t IV, Random, 95% CI	Year	IV, Random, 95% CI
Ping 2008(SAS)	51.66	6.57	34	48.83	7.13	33	3 12.8%	2.83 [-0.46, 6.12]	2008	



Chudu on Cubaroun		erimen			ontrol		Mainht	Mean Difference	Veen	Mean Difference
Study or Subgroup	Mean			Mean			Weight			IV, Random, 95% CI
Ping 2008(HAMA)	15.38	3.2	34	14.15	3.46	33	13.8%	1.23 [-0.37, 2.83]	2008	
Wang 2012	2.95	2.85	63	3.86	3.15	64	15.2%	-0.91 [-1.95, 0.13]	2012	
Chen 2013	11.28	5.72	32	10.58	4.84	31	10.8%	0.70 [-1.91, 3.31]	2013	
Liang 2018	5.77	2.53	31	8.79	4.46	33	13.3%	-3.02 [-4.78, -1.26]	2018	
Zhang 2018	10.6	1.94	30	9.67	3.33	30	14.4%	0.93 [-0.45, 2.31]	2018	+
LIU 2020	10.77	3.45	35	11.94	2.85	32	14.0%	-1.17 [-2.68, 0.34]	2020	
Xing 2020	9.52	4.02	30	9.41	4.73	30	11.9%	0.11 [-2.11, 2.33]	2020	
Yin 2020	10.53	7.53	27	20.9	8.17	24	6.7%	-10.37 [-14.70, -6.04]	2020	
Total (95% CI)			282			277	100.0%	-1.01 [-2.47, 0.45]		•
Heterogeneity: Tau ² =	= 3.37; CI	hi² = 38	3.79, df	= 7 (P <	< 0.000	001); I ^z :	= 82%			
Test for overall effect	Z=1.35	(P = 0)	.18)							
			,							Favours [experimental] Favours [control]
URE 6										
ta-analysis (Mental :										

Cochrane Collaboration's assessment tool. Critical information related to allocation concealment, blinding methods of participants, and personnel and outcome assessment was missing in most of the included trials (Guo et al., 2020). Due to the active manipulation of EA, most clinical studies could not be completely blinded.

However, unlike previous studies, the scope of the subjects was not limited to anxiety disorders with long-term symptoms; it included many studies by broadening the scope of subject RCTs to include transient anxiety emotions. As EA is effective for anxiety, it is expected to be used as an adjunct therapy in surgery and as a direct anxiety treatment. Since we only targeted RCTs in which electroacupuncture was treated as a single treatment, the relationship between electroacupuncture and anxiety could be identified.

5 Conclusion

The information gathered in this systematic review leads to observation and conclusion that is that different methodologies (different acupoints, frequency type, duration) lead to similar results which are decreased levels of anxiety. Our meta-analysis shows that EA reduces HAMA and SAS. The evidences from this study suggest that EA can help in relieving anxiety.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

WH, YK, and YL: conceptualization, methodology, formal analysis, investigation, data curation, writing—original draft preparation, and visualization. WH: software. HJ: writing—review and editing. HJ, KK, and SK: supervision, project administration. S-G.K: Writing – review & editing, Supervision, Project administration, and Funding acquisition. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyg.2023.1196177/ full#supplementary-material

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