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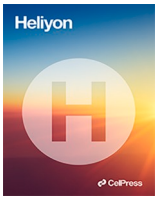

Research article

Electrical acupoint stimulation for the treatment of chemotherapy-induced nausea and vomiting: A systematic review and meta-analysis

Yi Ying [a,*], Hui Wu [b,c,**], Xuyong Chen [a], Ji Zhou [a], Yang Sun [a], Luecheng Fang [a]

[a] Department of Traditional Chinese Medicine, XianJu People's Hospital, Hangzhou Medical College, 317399, Xianju, Zhejiang, China
[b] Department of Endocrinology, Zhejiang Provincial People's Hospital, Hangzhou Medical College, 310014, Hangzhou, Zhejiang, China
[c] Key Laboratory of Endocrine Gland Diseases of Zhejiang Province, 310014, Hangzhou, Zhejiang, China

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ABSTRACT

Background: Chemotherapy-induced nausea and vomiting (CINV) is the most common adverse effect of chemotherapy and affects the continuation of chemotherapy in cancer patients. Electrical acupoint stimulation (EAS), which includes electroacupuncture and transcutaneous electrical stimulation (TES), has been used to treat CINV. This meta-analysis aimed to evaluate the efficacy of EAS in the treatment of CINV.

Methods: Randomized controlled trials (RCTs) of EAS for CINV retrieved form five key databases. Two researchers independently performed article screening, data extraction and data integration. The Cochrane Collaboration's tool for assessing risk of bias was used to assesse the methodological quality according to Cochrane Handbook for Systematic Reviews of Interventions. RevMan 5.4 was used to perform analyses.

Results: 10 RCTs with a total of 950 participants were included. The results showed that there was no significant difference between EAS compared to sham EAS in terms of increasing the rate of complete control of CINV and decreasing the overall incidence of CINV [RR = 1.26, 95 % CI (0.96, 1.66), $P = 0.95$; RR = 1.16, 95 % CI (0.97, 1.40), p = 0.71]. In terms of CINV severity, EAS reduced the occurrence of moderate-to-severe CINV [RR = 0.60, 95 % CI (0.38, 0.94), $P = 0.03$; RR = 0.50, 95 % CI (0.33, 0.76), $P = 0.001$].

Conclusion: EAS could improve moderate-to-severe CINV. However, EAS did not show a significant difference in reducing overall incidence and improving complete control rates compared with sham EAS. Due to limitations in the quality of the included articles, the available studies are insufficient to have sufficient evidence to confirm the efficacy of EAS for CINV. Validation with rigorously designed, large-sample, high-quality clinical trial studies may also be needed.

* Corresponding author. Department of traditional Chinese Medicine, XianJu People's Hospital, Hangzhou Medical College, 317399, Xianju, Zhejiang, China

** Corresponding author. Department of Endocrinology, Zhejiang Provincial People's Hospital, Hangzhou Medical College, 310014, Hangzhou, Zhejiang, China.

E-mail addresses: yingyi3911@sina.com (Y. Ying), latinboy@163.com (H. Wu).

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1. Introduction

The global incidence of cancer continues to escalate annually, with chemotherapy being a widely implemented and efficacious modality of treatment. However, chemotherapy is frequently associated with adverse reactions, the most prevalent of which is chemotherapy-induced nausea and vomiting (CINV) [1]. This condition can lead to electrolyte imbalances, malnourishment, and other complications [2,3], consequently heightening patients' emotional distress, diminishing treatment compliance, and potentially causing treatment cessation, thus profoundly impacting patient quality of life during treatment [4]. In the absence of prophylactic and therapeutic strategies, it is anticipated that CINV will affect over 90 % of patients undergoing high emetic chemotherapy (HEC) regimens and between 30 % and 90 % of those subjected to moderate emetic chemotherapy (MEC) regimens [5]. As such, proactive prevention and management of CINV are imperative for patient welfare in oncological care.

Risk factors for CINV include patient age, the emetogenic potential of chemotherapeutic agents, and the specifics of chemotherapy regimens such as dosage and treatment cycle [6]. Chemotherapeutic agents are stratified into five emetogenic risk categories: high (HEC, $\geq$90 %), moderate (MEC, 30%–90 %), low (10%–30 %), and very low ($<$10 %) [7]. Additionally, CINV is categorized into five temporal types: acute, delayed, anticipatory, fulminant, and refractory. Tailored prophylactic regimens are formulated based on the anticipated emetogenic risk presented by the chemotherapeutic agents in use [8]. Commonly administered medications for CINV management include 5-HT3 receptor antagonists, neurokinin-1 receptor antagonists, steroids, olanzapine, dopamine receptor antagonists, and benzodiazepines [9]. Despite these measures, a significant patient cohort continues to experience CINV [10], with concerns over drug costs and adverse effects such as hypotension, diarrhea, fatigue, and headache constraining the utilization of these antiemetic treatments.

Acupuncture therapy, rooted in traditional Chinese medicine, has garnered increasing recognition for its potential to mitigate the severity and duration of nausea and vomiting, enhancing patient quality of life [11–15] [11–15] [11–15]. Notwithstanding the promising anecdotal evidence, there is a conspicuous paucity of rigorous evidence-based medical research corroborating acupuncture's effectiveness in CINV management. The use of electrical acupoint stimulation (EAS) as a modality of acupuncture therapy specifically targets nausea and vomiting. EAS consists of two types of treatment: electroacupuncture (EA) and transcutaneous acupoint electrical stimulation (TAES). Both EA and TAES exert their therapeutic effects by stimulating acupoints with electrical devices. The main difference between the two is that EA requires needles to be inserted into the skin, whereas TEAS is a non-invasive operation by placing electrode pads on the skin. This study seeks to assess the efficacy of EAS in CINV management through systematic evaluation and meta-analysis of clinical studies, aiming to fortify the evidence base for its application in clinical practice and provide a more robust reference for the treatment and research of CINV.

2. Materials and methods

This systematic review and meta-analysis is presented in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [16] (Supplementary Material 1: PRISMA 2020 Checklist), the review protocol was registered in the PROSPERO database prior to initiating the review process (CRD42024513714).

2.1. Search strategy

A comprehensive search was conducted across five databases (PubMed, EMbase, Cochrane Library, Web of Science, and ClinicalTrials.gov) from the inception of the databases to September 11, 2023. The following terms were used: ("Electroacupuncture [Mesh]" OR "Electrical Stimulation Therapy [Mesh]" OR "Transcutaneous Electrical Nerve Stimulation [Mesh]" OR "Electro-acupuncture" OR "Electro-acupuncture" OR "TENS" OR "TEAS" OR "Electro-pain*" OR "Electro*stimulation*") AND ("Drug Therapy" [Mesh]) OR (((((((therapy, drug [title/abstract]) OR (drug therapies [title/abstract]) OR (therapy, drug [title/abstract]) OR (chemotherap * [title/abstract]) OR (drug therapy * [title/abstract]) OR (cancer* [title/abstract])) OR (antineoplastic drugs [title/abstract])) OR (medication* [title/abstract])) and ("nausea*" OR "vomiting*" OR "eructation" OR "eructation*" OR "queas*"). The detailed search strategy is described in S1 Table (Supplementary Material 2).

2.2. Eligibility criteria

Studies meeting the following criteria were included. (1)population: adult patients who meet the diagnostic criteria for CINV with typical clinical symptoms of regurgitation and/or vomiting of gastric contents through the mouth; (2)intervention: EAS (including EA and TES); (3)comparison: sham EAS or routine care; (4)outcome: Complete control rate of nausea and vomiting, Severity of nausea and vomiting, and Incidence rate of nausea and vomiting; (5)study design: RCTs published in journals, with or without blinding or allocation concealment. Exclusion criteria were applied to studies lacking clear basic information about the participants, lacking clear diagnostic criteria, without complete data or data that could not be extracted, and duplicate publications.

2.3. Study selection

Two reviewers (XC, and JZ) independently screened the titles and abstracts of all trials and indicated the eligibility based on eligibility criteria. Full text articles and their relevant references were selected for further assessment. Disagreements were settled by discussion between the two reviewers, and a third independent reviewer (SY) was invited to participate if necessary.

2.4. Data extraction

Two reviewers (XC, and JZ) independently read and extracted data with a piloted extraction form. The extracted data included the basic information of the included studies (authors, publication date), the basic characteristics of the study paticipants (sample size, gender, age, duration of disease), the interventions, the elements of risk of bias evaluation, the main outcome indicators, follow-up time, and the adverse events.

2.5. Assessment of bias risk

The Cochrane Collaboration's tool for assessing risk of bias was used to assesse the methodological quality according to Cochrane Handbook for Systematic Reviews of Interventions [17]. The assessment included random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other sources of bias. The quality of the article was evaluated on the basis of each rubric, which was categorized as low risk of bias, high risk of bias and unclear risk. Two reviewers (XC and JZ) evaluated the risk of bias in each study independently and disagreements were settled by discussion with a third independent reviewer (SY).

2.6. Statistical analysis

Data were synthesized and analysed using RevMan 5.4 software. Mean difference (MD) and 95 % confidence intervals (CI) were used for continuous variables, and risk ratio (RR) and 95 % CI were used for categorical variables. Heterogeneity was tested using the I^2 test. Studies with high heterogeneity ($P \leq 0.10$ and/or $I^2 \geq 50$ %) were analysed by the random-effects model, and those with low heterogeneity ($P > 0.10$ and $I^2 < 50$ %) were analysed by the fixed-effects model. $P < 0.05$ was considered statistically significant for the difference. If enough studies (n $\geq$ 10) were included in the meta-analysis, publication bias was assessed by funnel plot analysis using RevMan software.

3. Results

3.1. Literature search results

Based on the search strategy, a total of 305 articles were identified, of which 211 duplicate records were removed. After screening titles and abstracts, we excluded 71 articles and selected 23 papers for full-text double review. Out of the 23 articles, 13 were excluded for various reasons, as shown in Fig. 1. Finally, 10 studies were included in the meta-analysis [18–27] [18–27] [18–27].

3.2. Publication characteristics

A total of 950 patients were included in the 10 RCTs analysed after screening, with publication years from 2012 to 2021, sample sizes ranging from 32 to 142, cancer types including breast, gastric, liver, lung, colorectal, ovarian, cervical, and endometrial cancers,

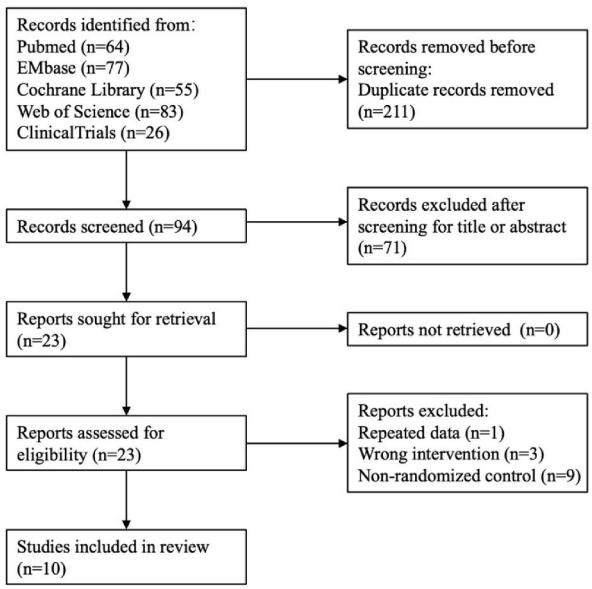

Fig. 1. Flow diagram of the study selection process.

Table 1
Characteristics of included studies.

Study	Chemotherapy agents	Participant		Intervention		Treatment duration	Outcomes	Follow-up
		Number	Age	Treatment	Comparison			
Jane M. Beith et al. 2012 [24]	Adriamycin, Cyclophosphamide, Epirubicin, Fluorouracil	T:15 C:17	T: 52 (9.5) C: 52 (8.4)	EA	sham electrical stimulation	42 days	①②	21 days
Wen-cheng Guo et al. 2018 [20]	Cisplatin	T:62 C:62	T: 62.1 (12.3) C: 60.7 (11.9)	TEA	sham electrical stimulation	7 days	③④⑤⑥	NR
Qi-Wei Li et al. 2020 [23]	Cisplatin, Anthracycline, Taxane	T:62 C:58	T: 60 (56.84–60.48) C: 58 (54.99–60.04)	EA	sham acupoint	5 days	①⑦⑧⑨	16 days
Mao Ting et al. 2021 [19]	Cisplatin	T: 61 C:61	T: 50.66 ± 9.621 C: 50.48 ± 10.748	TEA	routine care	14 days	⑩⑪	14 days
Chris McKeon et al. 2015 [18]	NR	T: 21 C:20	T: 58 (10) C: 62 (15)	EA	routine care	3 days	⑫⑬	4 days
Yehua Shen et al. 2015 [26]	Cisplatin ， Oxaliplatin	T: 51 C: 52	53.4 (20–73)	TEA + tropisetron	sham acupoint + tropisetron	6 days	③⑤⑩⑭	NR
Yang Xiao et al. 2014 [25]	Adriamycin, Cisplatin, Epirubicine,	T: 60 C: 60	NR	TEA + hydrochloride palonosetron	hydrochloride palonosetron	NR	①	NR
Jing Xie et al. 2017 [21]	Cisplatin	T: 72 C: 70	T: 55.4 (41–77) C: 57.5 (30–75)	TEA	sham electrical stimulation	6 days	③④⑤⑩	NR
Xing Zhang et al. 2014 [22]	NR	T: 38 C: 34	NR	TEA + granisetron	sham acupoint + granisetron	3 days	①⑮	NR
Ying Zhu et al. 2020 [27]	Cisplatin	T: 37 C: 37	T: 63.4 (1.7) C: 63.4 (1.5)	TEA	sham acupoint	3 days	⑩⑯⑰	NR

Outcomes : ①Complete control rate of nausea and vomiting; ②WCC and neutrophil count; ③Severity of nausea and vomiting; ④Anorexia scale; ⑤MDASI score; ⑥Karnofsky score; ⑦ECOG score; ⑧SNAQ; ⑨HADS; ⑩Incidence rate of nausea and vomiting; ⑪GI symptom score; ⑫FLIE score; ⑬NRS score of nausea and vomiting; ⑭EuroQoL; ⑮Levels of 5-HT and dopamine; ⑯gastric slow waves; ⑰autonomic functions.

and chemotherapeutic agents including cyclophosphamide, cisplatin, anthracyclines, and paclitaxel.

For the interventions, electroacupuncture or transcutaneous electrical stimulation was the main intervention in the treatment group, with electroacupuncture in 3 studies [18,23,24], transcutaneous electrical stimulation in 4 studies [19–21,27], and transcutaneous electrical stimulation combined with antiemetics in 3 studies [22,25,26]. In the control group, the intervention was sham electrical stimulation in 3 studies [20,21,24], sham acupoints in 2 studies [23,27], sham acupoints combined with antiemetic in 2 studies [22,26], routine care in 2 studies [18,19], and antiemetic alone in 1 study [25]. In addition, there were differences in the duration of treatment between the studies' interventions, ranging from a minimum of 3 days to a maximum of 42 days. Detailed study characteristics are presented in Table 1.

3.3. Risk of bias

Assess the risk of bias for the included RCTs using the RoB 2.0 bias risk assessment criteria in the Cochrane Handbook for Systematic Reviews of Interventions [17]. In the randomization process module, 8 studies [18,20] [18,20–24,26,27] [24,26,27] were judged as low risk; 2 studies [19,25] were judged as high risk. In the deviation from intended interventions module, 7 studies [19,20,22–24,26,27] were judged as low risk, 3 studies [18,21,25] were judged as having some risk. In the missing outcome data module, all studies were judged as low risk. In the measurement of the outcome module, 7 studies [18,20,21,23,24,26,27] were judged as low risk, 1 study [22] was judged as having some risk, and 2 studies [19,25] were judged as high risk. In the selection of the reported result module, all studies were judged as low risk. Based on the bias assessment of each included study, risk of bias graphs were plotted (Figs. 2 and 3).

3.4. Results of meta-analysis

3.4.1. RR of complete control rate

4 studies compared complete control rate of nausea and vomiting after treatment. Subgroup analyses were performed according to the intervention modality, with low inter-study heterogeneity ($P = 0.75$, $I^2 = 0$ %), using the fixed-effects model. Meta-analysis showed that there was no statistically significant difference in the complete control rate of chemotherapy-induced nausea in the EA group compared with the sham EA group [RR = 1.25, 95 % CI (0.84, 1.85), $P = 0.27$]. The difference was not statistically significant in the TES combined with antiemetic group compared with the sham TES combined with antiemetic group [RR = 1.27, 95 % CI (0.87, 1.86), $P = 0.21$] (Fig. 4). In terms of the complete control rate of chemotherapy-induced vomiting, there was no statistically significant difference between the EA group compared with the sham EA group [RR = 1.13, 95 % CI (0.93, 1.37), $P = 0.27$], and the difference between the TES combined with antiemetic group compared with the sham TES combined with antiemetic group [RR = 1.22, 95 % CI (0.85, 1.74), $P = 0.67$] (Fig. 5).

3.4.2. RR of incidence rate

2 studies compared the incidence of nausea and vomiting after treatment. Inter-study heterogeneity was high ($P = 0.11$, $I^2 = 61$ %), so the random-effects model was used. Meta-analysis showed that in terms of the incidence of nausea after chemotherapy, there was no statistically significant difference between the TES group compared with the sham TEA group [RR = 0.43, 95 % CI (0.05, 3.91), $P = 0.45$] (Fig. 6). In terms of the incidence of vomiting after chemotherapy, there was no statistically significant difference between the TES group compared to the sham TES group [RR = 0.75, 95 % CI (0.35, 1.59), $P = 0.45$] (Fig. 7).

Fig. 2. Risk of bias Summary.

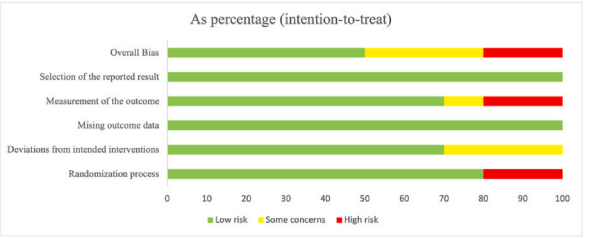

Fig. 3. Risk of bias evaluation chart.

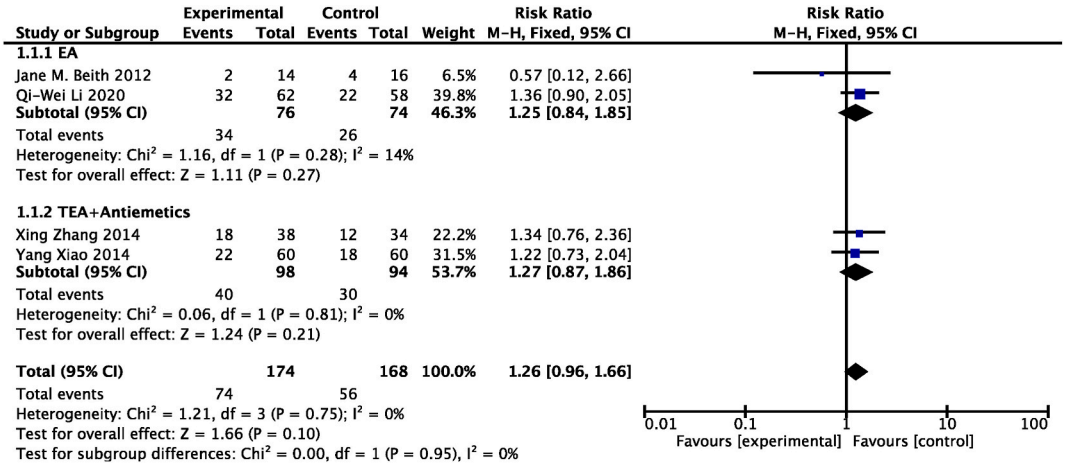

Fig. 4. Forest plot and meta-analysis of the complete control rate of nausea.

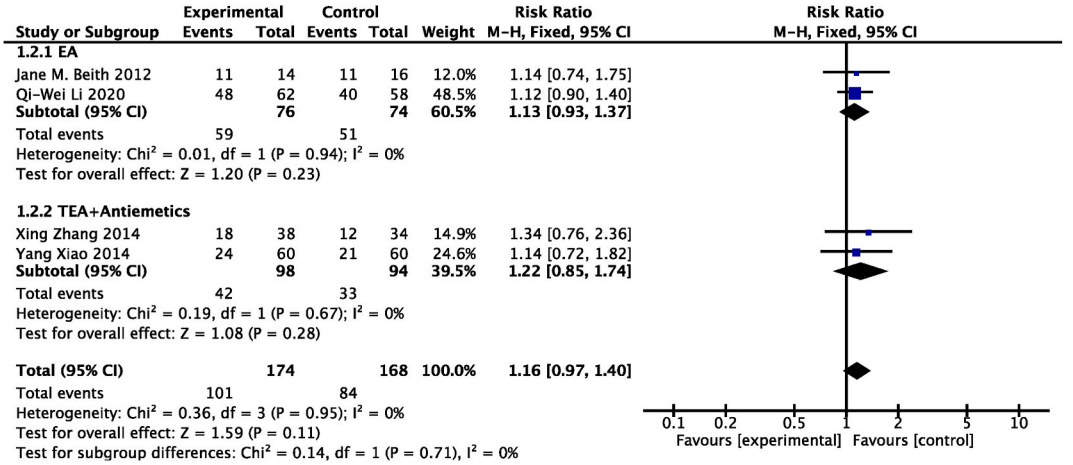

Fig. 5. Forest plot and meta-analysis of the complete control rate of nausea.

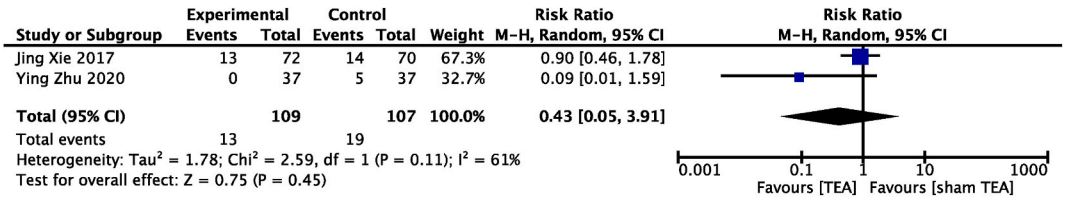

Fig. 6. Forest plot and meta-analysis of the incidence of nausea.

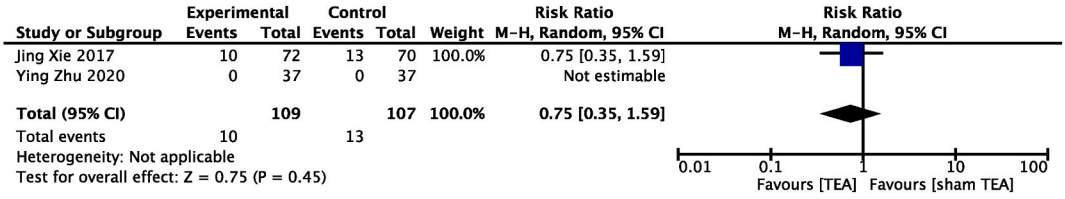

Fig. 7. Forest plot and meta-analysis of the incidence of vomiting.

3.4.3. RR of severity of nausea and vomiting

2 studies compared the severity of chemotherapy-induced nausea. Inter-study heterogeneity was low ($P = 0.45$, $I^2 = 0$ %), and a fixed-effects model was used. Meta-analysis showed that for moderate-to-severe nausea, there was a statistically significant difference between the TES group compared with the sham TES group [RR = 0.60, 95 % CI (0.38, 0.94), $P = 0.03$] (Fig. 8).

4 studies compared the severity of chemotherapy-induced vomiting. Subgroup analyses were performed according to intervention modality, with low inter-study heterogeneity ($P = 0.39$, $I^2 = 0$ %), using a fixed-effects mode. Meta-analysis showed that both TES and TES combined with antiemetic agents reduced the incidence of moderate-to-severe vomiting, with a statistically significant difference [RR = 0.56, 95 % CI (0.34, 0.92), $P = 0.02$; RR = 0.37, 95 % CI (0.16, 0.85), $P = 0.02$] (Fig. 9).

3.4.4. Adverse event

Adverse events were mentioned and described in 5 artucles.1study [20] reported adverse reactions of constipation, headache, vertigo, and insomnia during the trial in both TES and control group patients, but none of the differences were statistically significant when compared between the control group.1 study [21] reported adverse reactions of constipation, headache, and two cases of redness, swelling, and itching on the local contact surface in both EA and sham EA group pa, and in the electroacupuncture group, but none of the differences were statistically significant when compared between the groups. However, none of the differences were statistically significant when comparing between groups.3 studies [22,24,26] reported no adverse reaction responses occurred during the trial. The remaining studies did not mention and report whether any adverse events occurred.

4. Discussion

Recent advancements in the domain of CINV management have witnessed the introduction of novel antiemetic agents, yet approximately 40 % of oncology patients undergoing chemotherapy continue to experience these distressing symptoms [28]. CINV remains a formidable obstacle in chemotherapy, with nausea and vomiting significantly hindering patient well-being and treatment adherence. A specific investigation into breast cancer patients undergoing anthracycline and cyclophosphamide regimens indicated a mere 32 % efficacy in controlling nausea, despite adherence to guideline-recommended antiemetic protocols [29]. Vomiting is defined as a reflex action by which the stomach contents are expelled through the mouth, while nausea is characterized as a condition marked by a feeling of revulsion and (or) an urgent need to vomit. Nausea and vomiting often occur concurrently; however, many of the currently available antiemetic medications have a very limited therapeutic effect in alleviating nausea induced by chemotherapy [30]. Vomiting typically occurs when a stimulus exceeds a certain threshold and can be readily controlled once neuronal signaling is reduced below this threshold. In contrast, nausea represents a response with a dynamic threshold that is influenced by the interaction of intrinsic factors and psychological elements within an individual [31]. Consequently, nausea is more challenging to manage and assess compared to vomiting [32,33].

EAS is a therapy that implements electrical stimulation on acupoints, including EA and TAES, to alleviate symptoms and promote recovery. Previous meta-analyses in the literature on CINV have primarily focused on pharmacological treatments or acupuncture combined therapies [34–39] [34–39] [34–39]. This study represents the first systematic evaluation and meta-analysis of AES for the treatment of CINV. It included ten RCTs, and the meta-analysis results indicated that neither electroacupuncture nor transcutaneous electrical nerve stimulation (TENS) combined with antiemetic drugs significantly increased the complete control of nausea and vomiting. Transcutaneous electrical nerve stimulation alone did not reduce the incidence of CINV, suggesting that the overall control effect of AES is not significant compared to sham stimulation. This is similar to previous meta-analysis results of acupuncture interventions for CINV [35]. Regarding severity, there are various standards for grading nausea and vomiting; clinically, the NCI-CTCAE version 4.03 is commonly used. According to this, nausea is graded as follows: Grade 1: appetite loss without changes in eating habits;

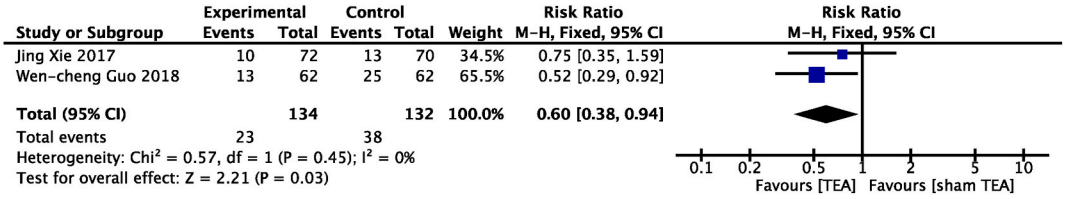

Fig. 8. Forest plot and meta-analysis of chemotherapy-induced moderate to severe nausea.

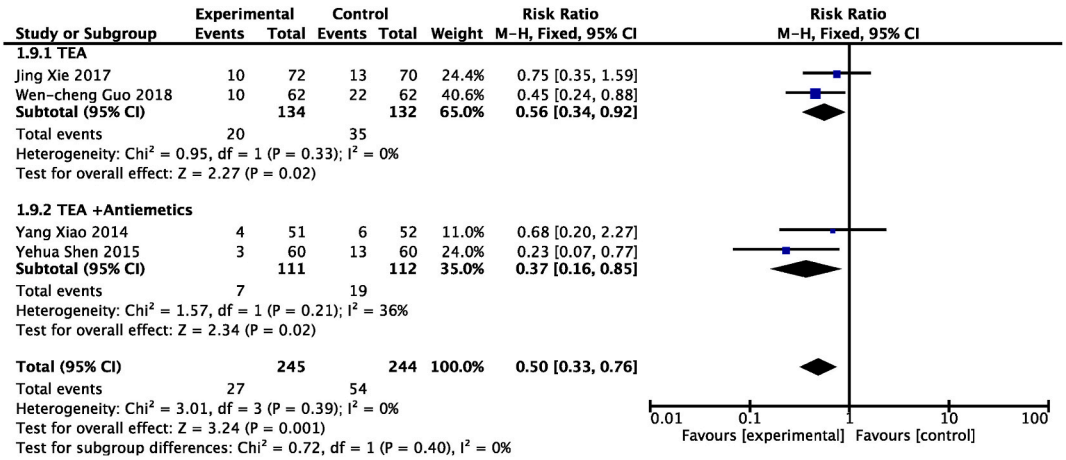

Fig. 9. Forest plot and meta-analysis of chemotherapy-induced moderate-to-severe vomiting.

Grade 2: decreased oral intake without significant weight loss, dehydration, or malnutrition; Grade 3: inadequate oral intake of energy and fluids, requiring nasal feeding, total parenteral nutrition, or hospitalization. The grading for vomiting is: Grade 1: 1–2 times within 24 h at 5-min intervals; Grade 2: 3–5 times within 24 h at 5-min intervals; Grade 3: more than 6 times within 24 h at 5-min intervals, necessitating nasal feeding, total parenteral nutrition, or hospitalization; and Grade 4: life-threatening conditions requiring urgent intervention. Most patients in the included studies had Grade 1–3 nausea and vomiting. Grades 2 and 3 nausea and vomiting were combined as moderately severe. The meta-analysis results showed that transcutaneous electrical stimulation could reduce the occurrence of moderate to severe nausea and vomiting, and when combined with antiemetic drugs, could reduce the occurrence of moderately severe vomiting. In terms of patients' quality of life, one study [26] assessed using the EuroQol score and found that patients in the transcutaneous electrical stimulation combined with antiemetics group had a higher EuroQol score on the fourth day compared to the antiemetic-only group (72.83 vs. 65.94, $P = 0.04$), with no significant difference on other days; cancer-related symptoms were assessed using the MD Anderson Symptom Inventory (MDASI), and no significant difference in MDASI scores was found at any time point. Another study in patients on a cisplatin-based chemotherapy regimen showed no significant difference in MDASI scores between the transcutaneous electrical stimulation group and the sham stimulation group ($P = 0.18$), suggesting that acupoint electrical stimulation does not significantly improve the quality of life in CINV patients [20].

The pathogenesis of CINV is a multifactorial process that involves neurotransmitters and receptors in the central nervous system and gastrointestinal tract [31]. Various neurotransmitters and their receptors participate in the development of CINV, mainly including the neurotransmitter 5-hydroxytryptamine (5-HT3) and its receptors, substance P and NK-1 receptors, dopamine, and D2 receptors, which are the main targets of most current antiemetic treatments [40–42] [40–42] [40–42]. The emetic response to chemotherapy is thought to occur through two different mechanisms: the peripheral pathway and the central pathway. 5-HT3 is an important neurotransmitter involved in acute emesis, which can be activated within 24 h post-chemotherapy, with a variety of 5-HT3 receptors located in vagal afferent fibers, the chemoreceptor trigger zone (CTZ), and the nucleus tractus solitarius [41]. Delayed nausea and vomiting are more commonly associated with substance P [43,44], which is released upon exposure to chemotherapy and binds to NK-1 receptors, signaling directly to the chemoreceptor trigger zone and the vomiting center in the brain, leading to delayed vomiting [45]. Compare with transcutaneous electrical nerve stimulation (TENS), a treatment administering mild electrical currents to the surface of the skin to stimulating peripheral nerves, EAS produces therapeutic effects by stimulating acupoints. From the theory of traditional Chinese medicine, the function of acupoints works by connecting the meridians, regulating the Qi and blood. Modern studies have shown that acupuncture can stimulate the release of natural endogenous opioids (endorphins) and neurotransmitters, which can alter the experience of discomfort such as CINV and pain [12]. Several clinical trials have demonstrated the efficacy and safety of acupuncture treatment for CINV, although the exact mechanisms remain unclear [46,47]. In terms of acupoint selection, the most frequently used acupoints for relieving gastric discomfort such as nausea and vomiting include ST36, CV12, and PC6 [48–50] [48–50] [48–50]. ST36 can enhance the immune system and promote gastrointestinal function [51]. PC6 is the most commonly used acupoint for nausea relief and has been found to reduce the incidence of nausea and vomiting when used in conjunction with antiemetic drugs [52]. CV12 is a crucial acupoint for addressing digestive-related discomfort, and animal experiments suggest that electroacupuncture at CV12 may exert its antiemetic effect by inhibiting the secretion of duodenal 5-HT3 and the activity of the nucleus of the solitary tract [53]. These acupoints may provide a reference for subsequent clinical studies and animal experiments.

This study has several limitations, as there was inconsistency in the standards and methods of outcome indicator evaluation, and only a small portion of the data from the 10 studies included could be meta-analysed, leading to uncertainty in the results of this systematic review. The studies incorporated in this paper varied in terms of the acupoints used for electrical stimulation, the frequency and duration of interventions, the specific antiemetic drugs and dosages used, and the emetogenic risks of the chemotherapy regimens among the included patients, which may contribute to differences in study outcomes and thus be a source of heterogeneity. The commonly used means of sham EAS include sham electrical stimulation and sham acupuncture points. In sham electrical stimulation

group, the electrodes were placed on the same acupoints as the treatment group, but no electric stimulation was applied. In sham acupoint group, treatment was applied at points adjacent to the true acupoint, which do not belong to traditional Chinese meridians. However, the current implementation of sham EAS still needs improvement. For sham acupoints, the stimulation points may not be chosen far enough away from the meridian points that it can still be therapeutically effective. In studies using TAES as intervention, the electrode pads have a certain stimulation area, which makes the selection of sham acupoints more difficult. For sham electrostimulation, the antiemetic effect of conventional acupuncture can still be exerted through the acupoint after the needle is inserted even without electrical stimulation, which reduces the difference in efficacy between true EAS and sham EAS. The above factors may have contributed to the result that true EAS and sham EAS did not show significant differences in reducing overall incidence and increasing complete control rates in this study. In terms of outcome evaluation, the assessment of nausea and vomiting is subjective, and commonly used evaluation indices include the incidence of nausea and vomiting, severity grading, the Functional Living Index-Emesis (FLIE), and the MASCC Antiemetic Tool (MAT), which should be employed appropriately to more accurately reflect the effects of CINV treatment. Furthermore, there are greater challenges in the assessment and treatment of delayed CINV of longer duration [54]. To further explore the preventive and moderating effects of acupoint electrical stimulation on CINV, well-designed large-sample RCTs with standardized intervention protocols and accurately measurable outcome indicators are required. Due to the characteristics of acupuncture operations, it is challenging to implement blinding for clinical operators and subjects, but it is necessary to combine practical considerations and implement blinding to the greatest extent possible within the operational range, to provide a more objective and reliable theoretical basis for the application of acupuncture-related techniques in the treatment of CINV. In order to design a more standardized RCT, we give the following recommendations: 1) Optimize the implementation of control groups. It is difficult to achieve double-blind in studies using manual needle and electroacupuncture. For studies using EA, placebo needle is recommended to minimize the interference of conventional needle. In terms of blinding, TAES is more advantageous and can be controlled by placebo electrode for the same selected points. There will be no electrical output from the sham electrode pads after setting up the electrotherapy machine using the same parameters. Only the person in charge of the trial knows whether the electrode is real or placebo, not the operator or the patient, thus making it double-blind. 2) Refine inclusion criteria: EAS may differ in efficacy for different degrees of severity of nausea and vomiting. A rating of the degree of nausea and vomiting should be added to the inclusion criteria, or patients should be enrolled based on the emetogenic risk rating of the chemotherapy regimen. 3) Set the optimal stimulation parameters for EAS. Acupuncture is effective in treating nausea and vomiting in Chinese clinical research and practice, but the studies included in this paper had mostly negative results. Compared with traditional acupuncture, EAS adds electrical stimulation, so the choice of current parameters, such as waveform and current frequency, is crucial to thetreatment. The ideal frequency of electrical stimulation for TAES and EA, as well as the current frequency intensity used for patients with CINV for different degrees of severity, are issues that can be explored in subsequent studies. 4) Find more appropriate evaluation indicators to reduce subjective bias in efficacy evaluation.

5. Conclusions

EAS could improve moderate-to-severe CINV. However, EAS did not show a significant difference in reducing overall incidence and improving complete control rates compared with sham EAS. Due to limitations in the quality of the included articles, the available studies are insufficient to have sufficient evidence to confirm the efficacy of EAS for CINV. Validation with rigorously designed, large-sample, high-quality clinical trial studies may also be needed.

Ethics approval and consent to participate

This study was based on previously published studies; therefore, ethical approval and patient consent are not relevant.

Consent for publication

Not applicable.

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CRediT authorship contribution statement

Yi Ying: Writing – original draft, Funding acquisition. **Hui Wu:** Writing – review & editing, Supervision, Conceptualization. **Xuyong Chen:** Formal analysis, Data curation. **Ji Zhou:** Formal analysis, Data curation. **Sun Yang:** Formal analysis, Data curation. **Luecheng Fang:** Writing – review & editing, Methodology.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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