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GENERAL GYNECOLOGY

Acupuncture for clinical improvement of endometriosis-related pain: a systematic review and meta-analysis

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Abstract

Background Endometriosis is a common chronic gynecological condition characterized by the presence of endometrial tissue outside the uterine cavity, leading to chronic inflammation, pelvic nodules and masses, pelvic pain, and infertility. Acupuncture has been shown to improve pain associated with endometriosis by modulating abnormal levels of prostaglandins, β-endorphins, dynorphins, electrolytes, and substance P. This review aims to evaluate the clinical efficacy of acupuncture in treating endometriosis, specifically focusing on its efficacy in relieving pain associated with endometriosis.

Methods A comprehensive search was conducted in eight databases (PubMed, EMBASE, Cochrane, Web of Science, China National Knowledge Infrastructure (CNKI), the China Biology Medicine (CBM), Wanfang, and Weipu database) to identify randomized controlled trials (RCTs) published from database inception to December 16, 2022, which investigated the use of acupuncture for endometriosis-related pain. Two researchers independently screened articles, extracted data, and assessed methodological quality using the Cochrane Collaboration's risk of bias tool. Meta-analysis was performed using Stata statistical software.

Results A total of 1991 articles were identified, and ultimately, 14 studies involving 793 patients (387 in the acupuncture group and 359 in the control group) were included. The control interventions in the included studies included placebo, traditional Chinese medicine (TCM), and Western medicine treatments. Meta-analysis results showed that compared to the control group, acupuncture treatment for pain associated with endometriosis demonstrated significant reductions in pain severity [SMD = − 1.10, 95% CI (− 1.45, − 0.75), $P < 0.001$], improved response rate [RR = 1.25, 95% CI (1.09, 1.44), $P = 0.02$], and decreased serum CA-125 levels [SMD = − 0.62, 95% CI (− 1.15, − 0.08), $P = 0.024$]. Furthermore, subgroup analysis revealed that electroacupuncture and auricular acupuncture were superior to the control group in reducing pain severity, while auricular acupuncture and warm needling showed greater clinical efficacy compared to the control group. However, there were no significant differences between electroacupuncture or fire needling and the control group in terms of pain relief. The findings suggest that acupuncture is effective in improving pain associated with endometriosis.

Conclusions In conclusion, acupuncture is effective in alleviating dysmenorrhea and pelvic pain associated with endometriosis, reducing serum CA-125 levels, decreasing the size of nodules, improving patients' quality of life, and lowering the recurrence rate. However, it should be noted that the current evidence is limited by the design and quality flaws of the original studies, as well as a lack of research specifically focusing on subtypes of acupuncture. Therefore, caution should be exercised when interpreting the results.

Keywords Endometriosis · Endometriosis-related pain · Acupuncture · Meta-analysis

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What does this study add to the clinical work

Existed studies on acupuncture for endometriosis-related pain did not distinguish treatment method between acupuncture and moxibustion. In our study, we only included articles on acupuncture alone as a treatment method, and divided them into subgroups to compare the efficacy of different acupuncture methods.

Introduction

Endometriosis is a prevalent gynecological condition characterized by the presence of endometrial tissue outside the uterus [1]. It results in chronic inflammation, pain, and infertility, significantly affecting the quality of life for women [2]. In addition, individuals with endometriosis have a much higher likelihood of experiencing depression, anxiety disorders, and emotional disturbances compared to the general population [3]. The most widely accepted pathophysiological hypothesis for endometriosis is based on retrograde menstruation, [2] but other potential factors include genetic predisposition, immune dysfunction, estrogen imbalance, and previous surgeries (such as cesarean section or abdominal procedures) [4].

Treatment options for endometriosis primarily include medication, surgery, and antiretroviral therapy. Commonly used medications include non-hormonal treatments (such as analgesics [5] and nonsteroidal anti-inflammatory drugs) and hormonal therapies (such as combined oral contraceptives, progesterone, and gonadotropin-releasing hormone analogues [GnRHa]) [6]. However, the efficacy of drug treatments is limited [7], and hormone therapy does not eradicate the disease and often causes significant side effects. Progestogen-related adverse reactions include punctate and breakthrough bleeding, weight gain, depression, breast tenderness, and fluid retention, [8] resulting in discontinuation rates of 25–50% [9]. A study compiled existing literature and demonstrated that traditional TCM can serve as a first-line conservative option for managing endometriosis-related pain, showing significant efficacy [10]. However, challenges remain concerning the varied treatment responses based on different TCM syndrome patterns.

Acupuncture is an effective, safe, and cost-effective treatment modality that can address various types of acute and chronic pain. There is growing research evidence supporting the efficacy of acupuncture in relieving various types of pain, particularly chronic pain conditions [11]. Extensive studies in humans and animals have shown that acupuncture exerts various biological effects on the peripheral or central nervous system, neuroendocrine factors, neurotransmitters, and other chemical mediators [12]. Acupuncture can improve pain associated with endometriosis by modulating abnormal levels of prostaglandins, β-endorphins, dynorphins, electrolytes, and substance P [13].

Given the lack of clear consensus on the efficacy of acupuncture as a standalone treatment for endometriosis, the purpose of this meta-analysis is to determine the specific effects of acupuncture in improving pain associated with endometriosis.

Materials and methods

Electronic searches

Two researchers independently searched the following databases: PubMed, EMBASE, Cochrane, Web of Science, China National Knowledge Infrastructure (CNKI), China Biology Medicine (CBM), Wanfang, and Weipu for RCTs of acupuncture for pain associated with endometriosis which published from database inception to December 16, 2022. This was done to identify studies suitable for meta-analysis. The specific search strategy and keywords used included "Endometriosis," "Acupuncture," "acupuncture therapy," "Acupuncture, Ear," "electroacupuncture," and "acupuncture points." In addition, manual searches of reference lists in relevant articles and grey literature were performed to identify eligible studies. The search strategy is detailed in the supplementary file 1.

Registration

In accordance with the study method for meta-analysis and following the study procedures, we have registered our study in PROSPERO, with the registration ID CRD42023389719.

Selection criteria

Participants (P): patients with confirmed endometriosis and pelvic pain diagnosed by laparoscopy.

Intervention/comparison (I/C): the experimental group received acupuncture as an intervention (including body acupuncture, ear acupuncture, electroacupuncture, fire needling, and warm needling). The control group received placebo (routine care, sham acupuncture), Western medicine, or TCM.

Outcome measures (O): primary outcome measures: pain scores, overall efficacy rate. Secondary outcome measures: serum CA-125 (CA125), pelvic mass volume, quality of life

questionnaire (Endometriosis Health Profile-30 [EHP-30]), and recurrence rate after 1 year.

Study design (S): RCTs published in Chinese or English.

Exclusion criteria

(1) Article types: non-RCTs, reviews, conference abstracts, guidelines, animal experiments, case reports, treatment experience summaries, and non-Chinese or non-English literature. (2) Article status: articles with unavailable full-text, incomplete data, or no relevant outcome measures. (3) Participant characteristics: uncertain diagnosis, coexistence of other gynecological diseases, postoperative endometriosis, pregnant or lactating women, comorbidities with severe systemic diseases (e.g., liver or kidney dysfunction, metabolic syndrome, psychiatric disorders), etc. (4) Intervention methods: interventions combining acupuncture with medication, moxibustion, thread-embedding at acupoints, or other interventions apart from acupuncture alone.

Data extraction

Two authors independently conducted literature screening by first reading the titles and abstracts to exclude studies that did not meet the inclusion criteria, followed by a full-text review of selected articles to determine final inclusion. Any discrepancies were resolved through discussion between the two reviewers, with the involvement of a third party if necessary. Data extraction was performed by the two researchers using a predefined electronic spreadsheet, and cross-checked for accuracy. In case of discrepancies, a third researcher was consulted. The following data information was extracted and recorded: author, publication year, country, sample size, age, patient diagnosis, intervention measures, control measures, intervention protocols, intervention duration, and follow-up duration.

Quality assessment

Two independent researchers used the Cochrane Collaboration Risk of Bias Tool (CCRBT) to evaluate the quality of the included studies. The Cochrane bias risk assessment tool assessed the risk of bias using seven items designed to address six different domains: (1) selection bias, including random sequence generation and allocation concealment; (2) performance bias, involving blinding of participants and personnel; (3) detection bias, encompassing blinding of outcome assessment for participants and personnel; (4) attrition bias, evaluating incomplete outcome data; (5) reporting bias, examining selective reporting; (6) other bias.

Each domain was rated as "high risk," "low risk," or "unclear" as a result of the bias risk assessment. Following completion of the assessment, the two researchers cross-checked their results, and any disagreements were resolved with the assistance of a third researcher.

Statistical analyses

For dichotomous variables, the relative risk (RR) was used as the effect measure to calculate the response rate and the recurrence rate after 1 year. For continuous variables, the standardized mean difference (SMD) was used as the effect measure to calculate outcomes such as pain scores and pelvic mass volume. Both measures were accompanied by 95% confidence intervals (CI).

For this meta-analysis, Stata 15.0 software was used for data analysis. Heterogeneity was quantified using Cochran's Q test and Higgins I^2. A significance level of $P < 0.05$ indicated significant heterogeneity among the included studies, leading to the utilization of a random-effects model. Otherwise, a fixed-effect model was adopted. In cases where heterogeneity was considerable, sensitivity analysis and subgroup analysis were conducted to explore potential sources of heterogeneity. A funnel plot was employed to visually assess publication bias, and statistical tests for publication bias, such as Egger's and Begg's tests, were performed. The trim-and-fill method was used to analyze the influence of publication bias on the results of the meta-analysis when publication bias was detected. A significance level of $P < 0.05$ was considered statistically significant, indicating that the combination of the included studies yielded significant results.

Results

Study selection

Following the search strategy, a total of 1991 relevant articles were obtained from the databases. After removing duplicates, 1086 articles remained. Initial screening based on titles and abstracts resulted in the exclusion of 998 articles, leaving 88 articles for full-text assessment. After 74 articles were further excluded according to a full-text review, 14 RCTs were finally included in the analysis [14–27]. The flowchart of the literature screening process can be found in Fig. 1.

Characteristics of the included studies

Participants

The 14 included studies involved a total of 793 patients, ranging in age from 13 to 46 years. Among these studies,

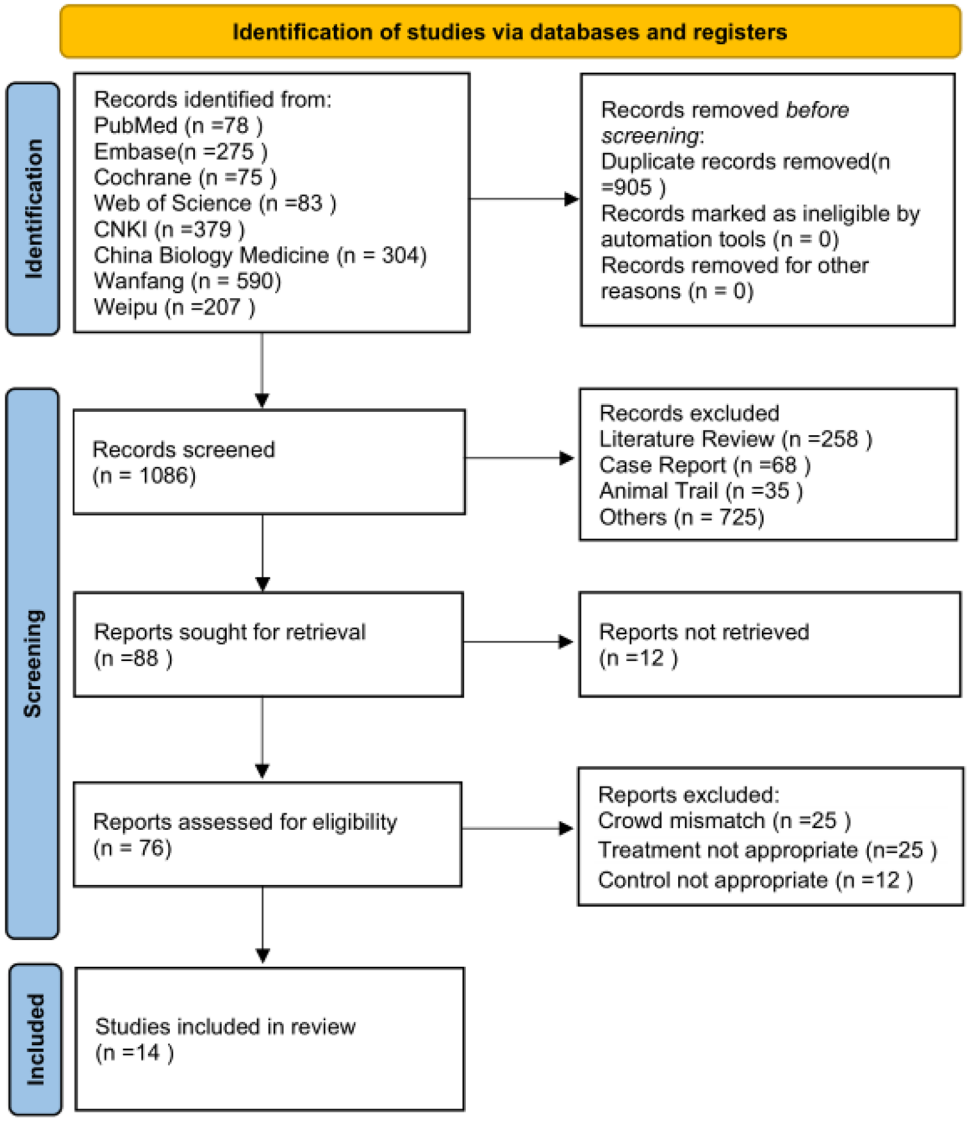

Fig. 1 Flowchart of the trial selection process

eight focused on dysmenorrhea associated with endometriosis, five on pelvic pain related to endometriosis, and one study reported both types of pain. Eleven studies were conducted in China, while 3 were conducted in other regions, namely Australia [14], Brazil [18], and the United States [24].

Interventions

Among the included studies, eight utilized acupuncture, two used warm needling, two employed fire needling, one used electroacupuncture, and one used auricular acupuncture. The treatment duration spanned from 5 weeks to 6 months, while the follow-up period ranged from 2 months to 1 year.

Controls

The primary control methods used in the studies included placebo, TCM, and Western medicine. Three studies [14, 18, 24] utilized placebos (sham acupuncture or routine care), six studies [15–17, 19, 20, 22] used Western medicine, and five studies [21, 22, 25–27] employed TCM. The basic characteristics of included studies are presented in Table 1.

Quality assessment

The risk of bias assessment for the included RCTs was conducted following the Cochrane Handbook for Systematic Reviews of Interventions. Two studies [16, 19] did not specify the method of sequence generation and were rated as having "unclear" risk. The remaining studies used random number tables or computer-generated random sequences and

Table 1 Characteristics of the 14 trials identified in the literature search

Studies	Nation	Study type	Sample size	Age	Clinical diagnose (pain type)※	Intervention		Course of treatment	Follow-up Visit
				T/C		T	C		
Mike A et al. (2021) [14]	Australia	Monocentric	14/15	33.4 ± 7.3	Pelvic pain	Acupuncture	Usual care	2 months	–
Fan HL et al. (2019) [15]	China	Monocentric	31/31	34.5 ± 1.9/35.5 ± 1.5	Menstrual pain	Warm needling	Western medicine	–	–
Shen Q et al. (2017) [16]	China	Monocentric	25/25	36 ± 3/34 ± 4	Menstrual pain Pelvic pain	Warm needling	Western medicine	6 months	12 months
Teng H et al. (2016) [17]	China	Monocentric	43/37	39 ± 4/38 ± 3	Menstrual pain	Fire needling	Western medicine	3 months	–
Tatiane R et al. (2016) [18]	Brazil	Monocentric	20/22	30.45 ± 5.89/31.14 ± 6.92	Pelvic pain	Acupuncture	Simulated therapy	5 weeks	2 months
Zhang X et al. (2015) [19]	China	Monocentric	36/36	33 ± 6/35 ± 7	Menstrual pain	Electroacupuncture	Western medicine	6 months	12 months
Liu QL et al. (2014) [20]	China	Monocentric	30/28	22–48	Menstrual pain	Fire needling	Western medicine	3 months	6–12 months
Xiang DF et al. (2011) [21]	China	Monocentric	30/28	34.6 ± 5.9/34.6 ± 4.9	Pelvic pain	Acupuncture	Traditional Chinese medicine	3 months	–
Lin Y et al. (2010) [22]	China	Monocentric	30/26	29.6	Menstrual pain	Acupuncture	Traditional Chinese medicine	3 months	3 months
Chen LN et al. (2010) [23]	China	Monocentric	35/26	29.6	Menstrual pain	Acupuncture	Western medicine	3 months	3 months
Wayne P et al. (2008) [24]	America	Monocentric	10/8	17.8/17.0	Pelvic pain	Acupuncture	Sham acupuncture	8 weeks	6 months
Xiang DF et al. (2001) [25]	China	Monocentric	37/30	22–45/24–47	Menstrual pain	Auriculoacupuncture	Traditional Chinese medicine	3 months	–
Cai J et al (2015) [26]	China	Monocentric	40/40	33.4 ± 5.7	Pelvic pain	Acupuncture	Traditional Chinese medicine	3 months	–
Zhu ZQ et al. (2010) [27]	China	Monocentric	30/30	15–46	Menstrual pain	Acupuncture	Traditional Chinese medicine	3 months	–

※Menstrual pain and pelvic pain both refer to pain associated with endometriosis

were considered to have a "low" risk of bias. Two studies [16, 19] categorized participants according to their outpatient clinic visits, resulting in a "high" risk of bias. Five studies [14, 15, 17, 18, 21] reported details of the random allocation concealment and were rated as having a "low" risk of bias. The remaining studies did not provide sufficient information, resulting in an "unclear" risk rating. Two studies [18, 24] used sham acupuncture or simulated acupuncture as control interventions, indicating a "low" risk of bias. The other studies used TCM, Western medicine, or routine care as controls, resulting in a "high" risk of bias. Two studies [14, 24] reported blinding of outcome assessors, leading to a "low" risk of bias. The remaining studies did not mention blinding, resulting in an "unclear" risk rating. One study [26] had incomplete outcome data, leading to a "high" risk of bias. The other studies did not have missing outcome data and were considered to have a "low" risk of bias. Two studies [20, 22] did not report all prespecified primary outcome measures, indicating a "high" risk of bias. The remaining studies reported complete outcomes and were assessed as having a "low" risk of bias. It was unclear whether the 14 included studies had other biases, and therefore, they were assessed as "unclear". The risk of bias assessment for the included studies is shown in Fig. 2A and B.

Clinical outcomes of meta-analysis

Variation in pain level

Eight studies (including one reporting two types of pain) compared the difference in pain levels between the acupuncture group and the control group. The pooled results showed significant heterogeneity ($I^2 = 65.7\%$); thus, a random-effects model was employed for analysis. The overall results

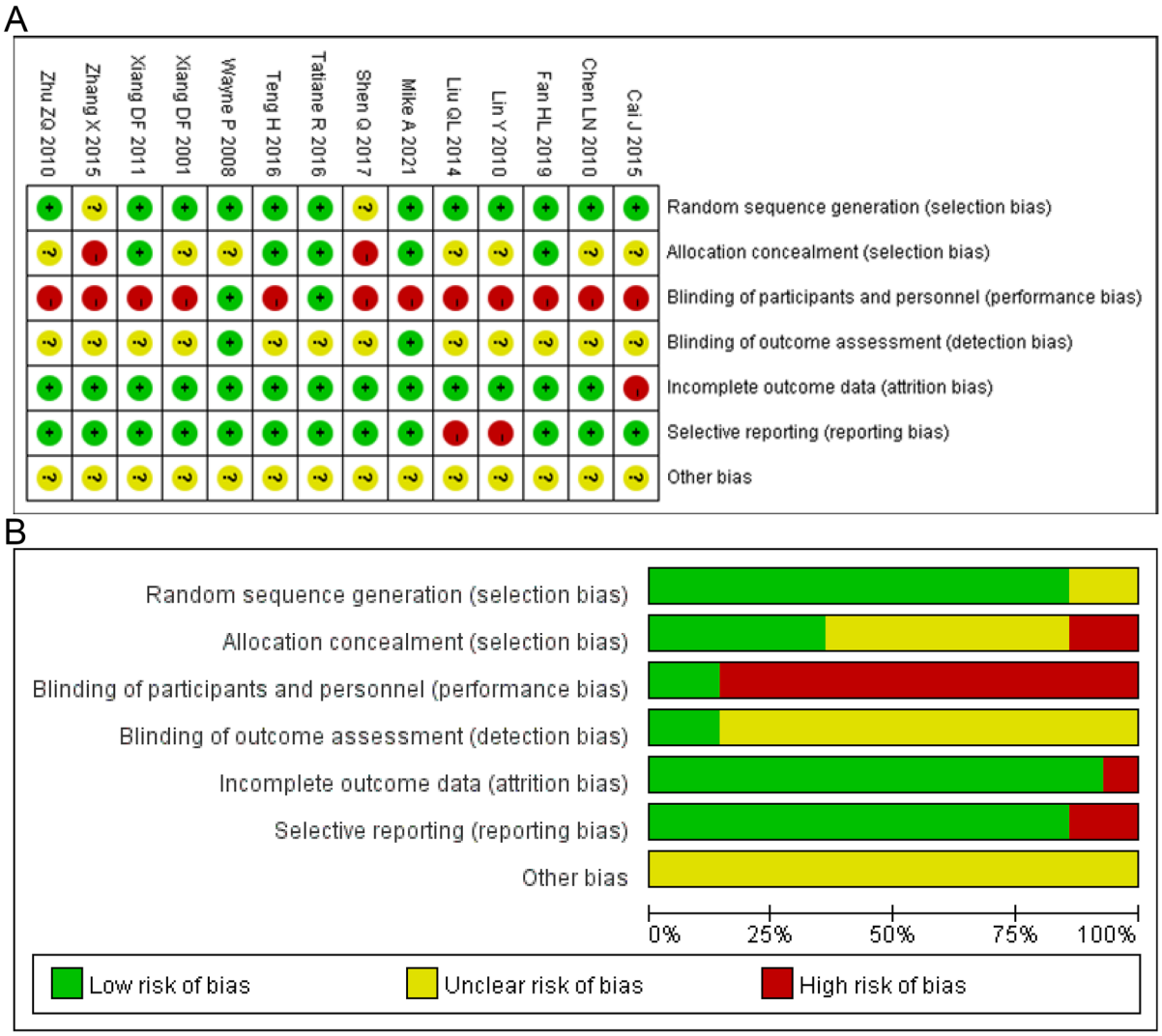

Fig. 2 **A** Risk of bias assessment by individual trials; **B** overall risk of bias assessment using the Cochrane tool

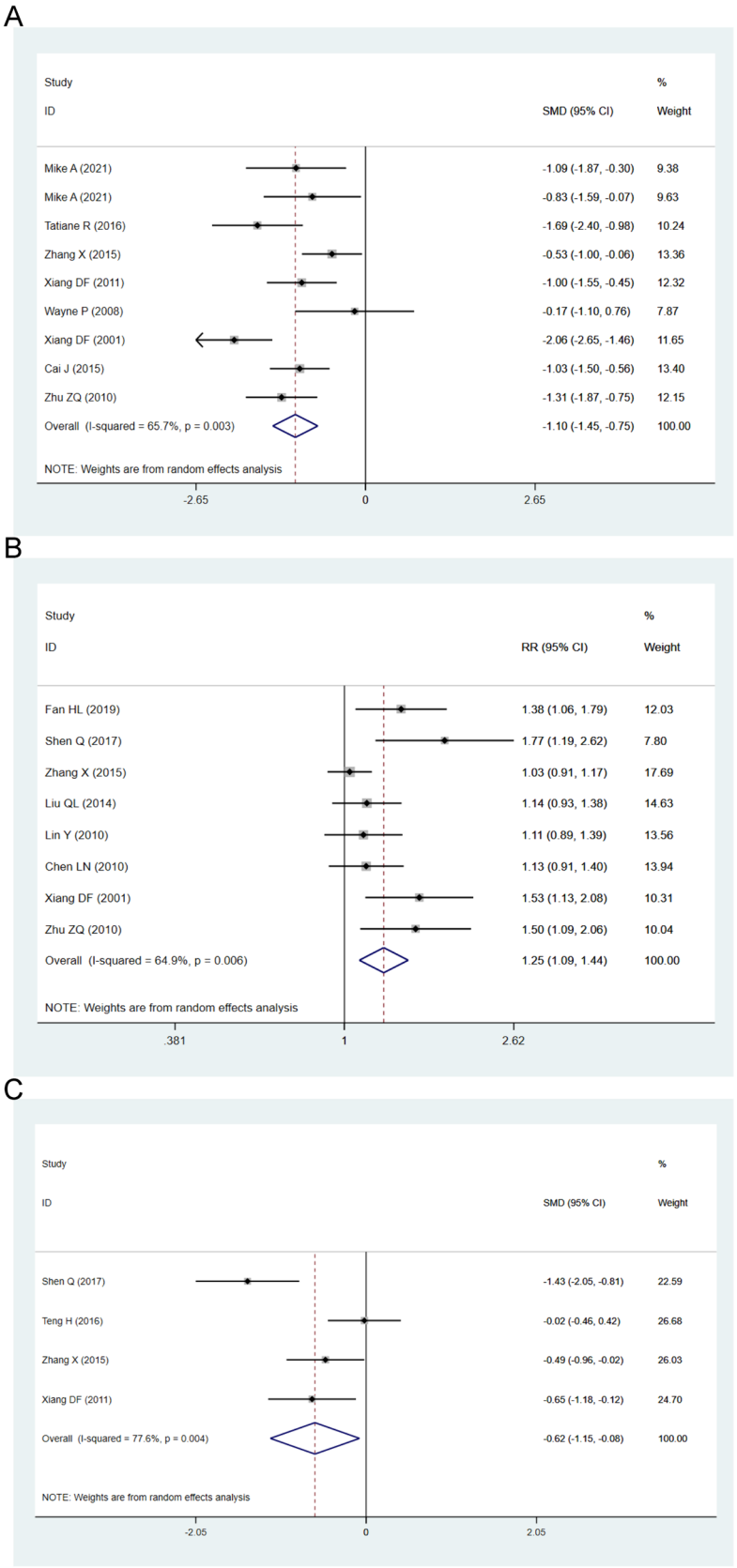

Fig. 3 Forest plot of outcomes of **A** the variation in pain level. **B** Clinical effective rate. **C** Variation in peripheral blood CA-125 level

indicated that acupuncture demonstrated a more significant improvement in pain levels compared to the control group, suggesting a positive effect on alleviating pain associated with endometriosis (SMD = − 1.10, 95% CI − 1.45, − 0.75, $P < 0.001$) (Fig. 3A).

Response rate

Eight studies compared the response rates between the acupuncture group and the control group. The pooled results showed significant heterogeneity ($I^2 = 64.9\%$); thus, a random-effects model was employed for analysis. The overall results indicated that acupuncture had a positive impact on the response rate in patients with endometriosis-related pain when compared to the control group (RR = 1.25, 95% CI 1.09, 1.44, $P = 0.02$) (Fig. 3B).

Variation in serum CA-125 levels

Four studies compared the changes in serum CA-125 levels in peripheral blood between the two groups. The pooled results showed significant heterogeneity ($I^2 = 77.6\%$); thus, a random-effects model was employed for analysis. The summary results indicated that acupuncture had a positive impact on reducing serum CA-125 levels in peripheral blood compared to the control group (SMD = − 0.62, 95% CI − 1.15, − 0.08, $P = 0.02$) (Fig. 3C).

Other outcome measures

Two studies reported pelvic mass volume, three studies reported the EHP-30-item questionnaire (one study [18] reported the total score, one [24] reported both the total score and the scores of the subscales, and one [14] reported only the scores of the subscales. To compare the effect of acupuncture on the quality of life of patients with endometriosis, we standardized the criteria across three studies, all using the total score of the EHP-30), and two studies reported the recurrence rate after one year. Statistical analysis results are presented in the table. Overall, acupuncture showed positive effects in reducing pelvic mass volume, improving the quality of life in patients with endometriosis, and reducing the recurrence rate after 1 year compared to the control group (Table 2).

Subgroup analysis

Subgroup analyses were conducted based on acupuncture method, pain type, and control treatment type for pain level and response rate. In addition, subgroup analysis was conducted according to the scales used for pain scoring. The results indicated that acupuncture significantly reduced pain regardless of the acupuncture method, pain type, or control treatment type (Table 3).

Sensitivity analysis

Sensitivity analyses were performed for pain level (Fig. 4A) and response rate (Fig. 4B) by sequentially excluding each study. The newly pooled effect sizes remained within the range of the original overall effect sizes, indicating that the meta-analysis results were stable and reliable.

Publication bias

Publication bias in pain improvement (Fig. 5) and response rates (Fig. 6) was visually displayed using a funnel plot. Begg's and Egger's tests were employed to assess the bias. The results indicated that, for the pain improvement measure, the Begg's test yielded a P value of 1.000, and the Egger's test yielded a P value of 0.928. For the response rate measure, the Begg's test yielded a P value of 0.009, and the Egger's test yielded a P value of 0.000. These findings suggest the possibility of publication bias in the response rate. Therefore, we further employed a trim-and-fill method to address the bias. The trim-and-fill analysis, after adding two studies, yielded an adjusted result of RR = 1.193, 95% CI 1.031, 1.355, which showed minimal change compared to the original result. This indicates that even if publication bias exists, it does not significantly affect the overall results (Fig. 7).

Discussion

Meta-analysis of clinical effect

This study systematically evaluated 14 RCTs comparing the clinical efficacy of acupuncture as monotherapy versus other treatments (sham acupuncture, Western medicine, or TCM)

Table 2 Meta-analysis of the secondary outcome measures

Variable	Number of studies	Effect value	95% CI	I^2 for heterogeneity	P value
Pelvic mass volume	2	− 1.81	− 2.25, − 1.37	0.0%	$P < 0.001$
EHP-30	3	− 1.29	− 2.28, − 0.30	76.50%	0.01
Recurrence rate after 1 year	2	0.55	0.29, 1.05	0.0%	0.07

Table 3 Subgroup analyses of the pain level and clinical effective rate

Variable	Subgroup		Number of studies	Effect value	95% CI	I^2 for heterogeneity	*P* value
Pain level	Acupuncture type	Acupuncture	7	− 1.07	− 1.35, − 0.80	22.2%	*P* < 0.001
		Electroacupuncture	1	− 0.53	− 1.00, − 0.06	–	0.029
		Auriculoacupuncture	1	− 2.06	− 2.65, − 1.46	–	*P* < 0.001
	Pain type	Menstrual pain	4	− 1.18	− 1.87, − 0.49	81.9%	*P* < 0.001
		Pelvic pain	5	− 1.05	− 1.42, − 0.67	39.5%	0.001
	Control type	Usual care	4	− 0.99	− 1.59, − 0.39	56.4%	0.001
		Western medicine	1	− 0.53	− 1.00, − 0.06	–	0.029
		Traditional Chinese medicine	4	− 1.33	− 1.79, − 0.87	65.1%	P < 0.001
Clinical effective rate	Acupuncture type	Acupuncture	3	1.20	1.01, 1.42	29.60%	0.034
		Warm needling	3	1.55	1.28, 1.87	–	*P* < 0.001
		Auriculoacupuncture	1	1.53	1.13, 2.08	–	0.007
		Electroacupuncture	1	1.03	0.91, 1.17	–	0.643
		Fire needling	1	1.14	0.93, 1.38	–	0.205
	Pain type	Menstrual pain	8	1.25	1.09, 1.44	64.90%	0.002
		Pelvic pain	1	1.29	1.12, 1.49	-	0.005
	Control type	Western medicine	6	1.27	1.06, 1.54	74.00%	0.011
		Traditional Chinese medicine	3	1.34	1.06, 1.69	68.80%	0.013
Scale type	Pain score	VAS	7	− 1.131	− 1.56, − 0.70	73.70%	*P* < 0.001
		NRS	1	− 0.957	− 1.50, − 0.41	–	0.001

for endometriosis-related pain. The comparison was made in terms of pain level, efficacy rate, serum CA-125, pelvic mass volume, EHP-30 score, and recurrence rate after 1 year. The results indicated that acupuncture had superior efficacy compared to the control group in all six aspects mentioned above.

Furthermore, based on the significant heterogeneity observed in the results and the differences in study characteristics, we performed subgroup comparisons for pain level improvement and response rate based on acupuncture method, pain type, and control treatment type. In terms of acupuncture method, we compared the pain level improvement by acupuncture, electroacupuncture, and auricular acupuncture with that in the control group, as well as the response rate achieved by acupuncture, electroacupuncture, auricular acupuncture, fire needling, and warm needling with that in the control group. The results showed that acupuncture, electroacupuncture, and auricular acupuncture were superior to the control group in reducing pain levels. Acupuncture, auricular acupuncture, and warm needling achieved higher response rates compared to the control group, while electroacupuncture and fire needling did not show statistically significant differences in improving response rates compared to the control group. Regarding pain type, we differentiated the improvement in pain level and response rate achieved by acupuncture in dysmenorrhea and pelvic pain associated with endometriosis. The analysis indicated that acupuncture had significant benefits in improving pain and increasing response rates for both symptoms. For control treatment type, we compared the pain level improvement and response rate achieved by acupuncture with those obtained with TCM, Western medicine, and conventional care. The results showed that acupuncture had advantages over TCM, Western medicine, and conventional care in reducing pain levels. Acupuncture also had advantages over TCM and Western medicine in improving response rates. The above results suggest that acupuncture methods may contribute to the observed heterogeneity. However, caution should be exercised in interpreting the results due to the limited number of studies available for different acupuncture types.

Thirteen studies reported the selection of acupoints, with one study reporting the use of auricular acupoints. The most commonly chosen meridians were the Ren Meridian (12 studies) [14–23, 26, 27] and the Spleen Meridian (8 studies) [14–20, 27]. The Ren Meridian originates from the uterus and is referred to as the "Sea of Yin Channels" in TCM, while the Spleen Meridian governs blood circulation. Both meridians pass through the abdomen, making them suitable for regulating menstruation and treating reproductive system diseases. The most frequently selected acupoints were Zhongji (RN3), Guanyuan (RN4), Qihai (RN6) (all on the

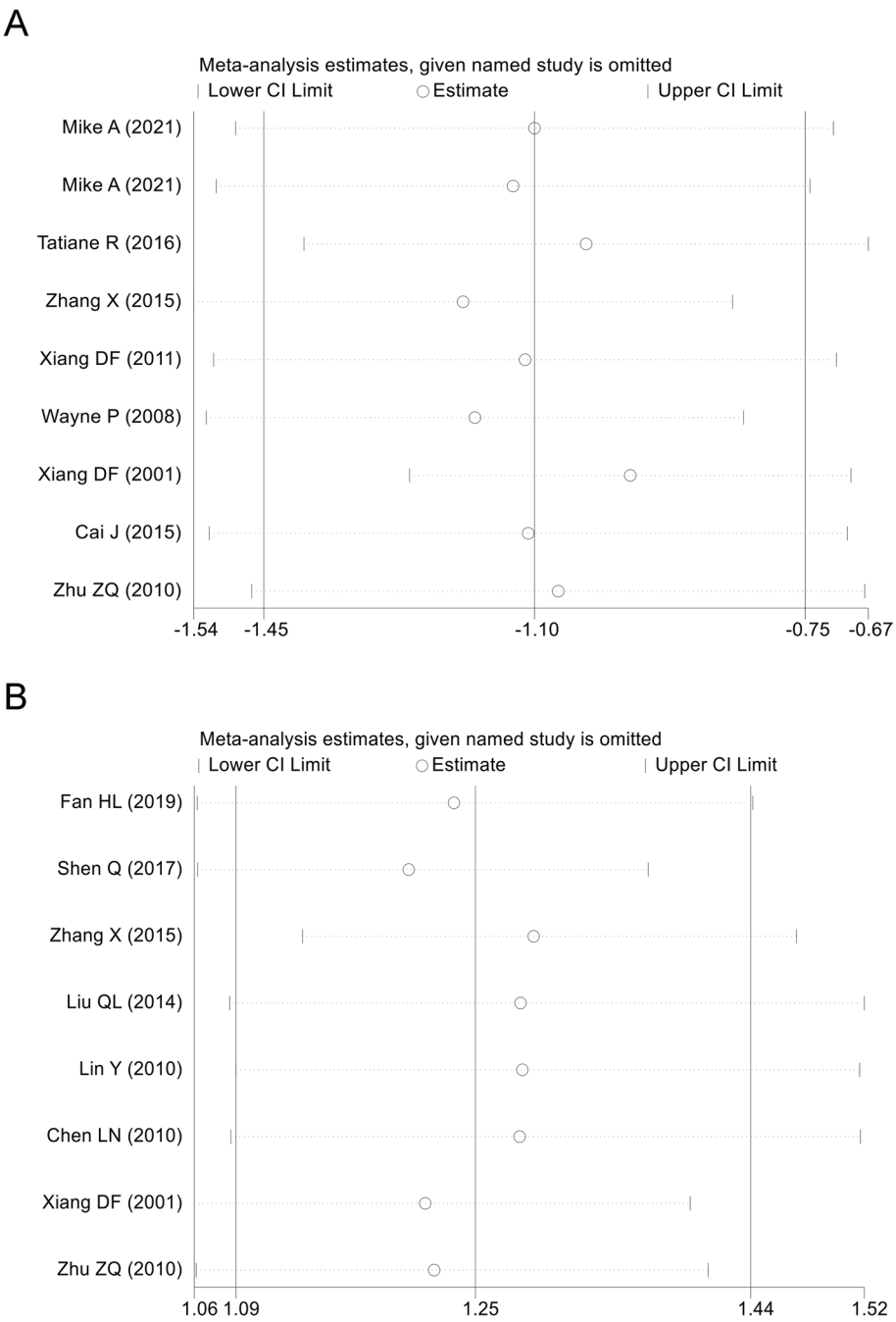

Fig. 4 Sensitivity analysis of **A** pain level. **B** Clinical effective rate

Ren Meridian), and Sanyinjiao (SP6) (on the Spleen Meridian). Zhongji (RN3), Guanyuan (RN4), and Qihai (RN6) are located in the lower abdomen and have a close therapeutic effect, while Sanyinjiao (SP6) is the meeting point of the Foot Taiyin, Foot Shaoyin, and Foot Jueyin meridians, providing the function of regulating menstruation and relieving pain. Regarding the timing of acupuncture, 8 studies [17, 20–23, 25–27] chose to perform acupuncture 5–7 days before menstruation, with each session lasting 20–30 min.

When comparing our study with existing meta-analyses [28, 29] on acupuncture for endometriosis-related pain, both our study and Xu et al.'s [28] study demonstrated the positive effects of acupuncture in reducing pain levels, improving response rates, and lowering serum CA-125 levels. Likewise, Xiao et al. [29] reported positive effects of acupuncture in reducing pain levels and improving response rates. However, the interventions included in the existing meta-analyses were not solely acupuncture but also combinations of acupuncture with TCM, acupoint application, acupoint embedding, and moxibustion. Therefore, they cannot specifically address the effects of acupuncture as a monotherapy for endometriosis-related pain. Our study specifically included RCTs using

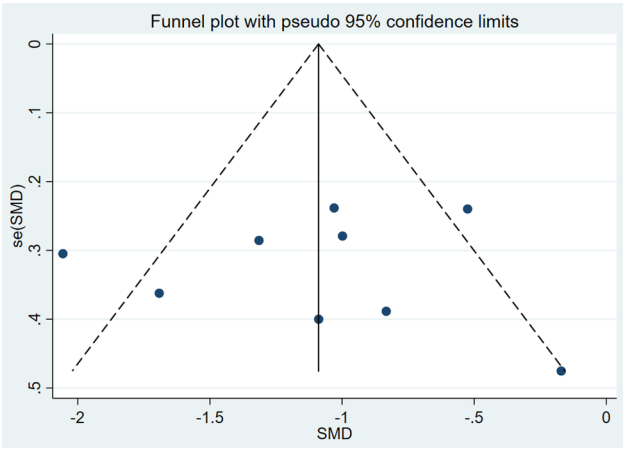

Fig. 5 Funnel plot of pain level

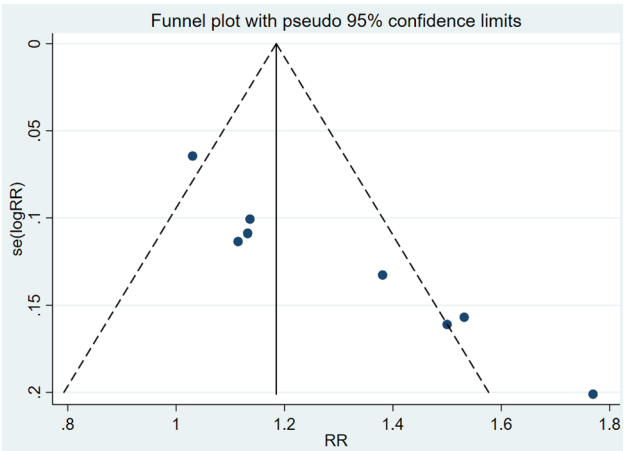

Fig. 6 Funnel plot of clinical effective rate

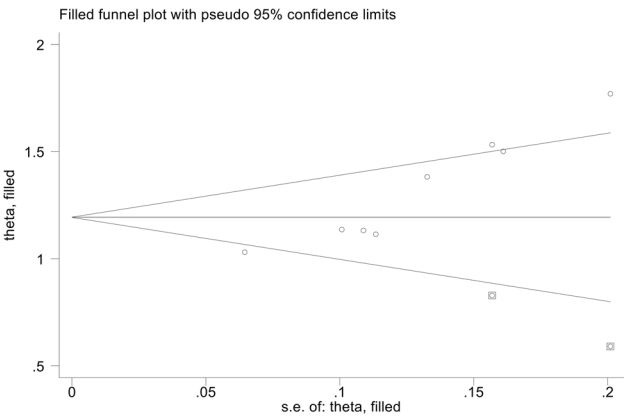

Fig. 7 Filled funnel plot of clinical effective rate

acupuncture as the intervention, allowing us to evaluate the efficacy of acupuncture for endometriosis-related pain. Moreover, Xiao et al. [29] differentiated subgroups based on different control treatment types and compared their efficacy with acupuncture. They found that acupuncture was superior to TCM and Western medicine in terms of overall response rate and improvement in symptom scores. They also compared acupuncture combined with TCM versus TCM alone and found no statistically significant differences in efficacy rates for endometriosis-related pain. Based on the above findings, we observed that there was no significant advantage of acupuncture combined with TCM compared to TCM alone. However, the present study demonstrated that acupuncture alone showed superior clinical efficacy compared to TCM. By comparing the original studies included in the two meta-analyses and analyzing the TCM used in the included literature, it is speculated that differences in TCM may have contributed to these results. Furthermore, to determine whether acupuncture alone is superior to acupuncture combined with TCM, further literature research or the design of clinical trials is necessary. This will also be the direction for our future follow-up studies.

Mechanism of acupuncture treatment for endometriosis

The mechanisms underlying pain associated with endometriosis are complex and diverse, and have not been fully elucidated. They can primarily be categorized into three main factors: anatomical structure factors, pelvic microenvironment factors, and sensitization of the nervous system [30]. Acupuncture has been proven to have analgesic effects [31] and is effective in treating pain related to endometriosis. In recent years, many scholars have analyzed the mechanisms of acupuncture in treating endometriosis-related pain through both clinical studies and animal experiments. However, a comprehensive and systematic exploration of its mechanisms remains lacking. Current studies have indicated that acupuncture improves pain associated with endometriosis by enhancing the body's analgesic, endocrine, and immune functions, as well as blood rheology [32].

Analgesic effects of acupuncture. Increased prostaglandin (PG) secretion is one of the mechanisms of pain and is positively correlated with the degree of pain associated with endometriosis. Prostaglandin E (PGE) can cause pain by stimulating uterine contractions, leading to increased intrauterine pressure and reduced blood flow. In a study by Bai et al. [33] on a rat model of endometriosis, acupuncture treatment resulted in a significant increase in blood and endometrial PGE2 levels and a significant decrease in PGF1α levels in rats of the experimental group. The study also found that the levels of serum Ca2+ were low, while the levels of K+, Na+, and Cl− were high in rats of the experimental group. After acupuncture treatment, these levels essentially returned to normal, suggesting that changes in

electrolyte levels in the body are involved in the formation of dysmenorrhea associated with endometriosis, and acupuncture may produce analgesic effects through this pathway.

Acupuncture for regulating endocrine function. Endometriosis is an estrogen-dependent disease in which hormonal changes may affect the ability of endometrial cells to proliferate, attach to mesothelial cells, and/or evade immune-mediated clearance [34]. The action of estrogen is primarily mediated by estrogen receptors (ERs). In endometriosis, the expression level of ectopic endometrial ERα is significantly downregulated, whereas ERβ expression is much higher than that in normal endometrium [35]. Studies [36] have shown that acupuncture in a rat model of endometriosis can regulate the ERα/ERβ ratio, thereby reducing the diameter of ectopic cysts.

Acupuncture for regulating immune function. The development of endometriosis is related to abnormalities in the body's immune regulation. Immune factors wield significant influence in the processes of implantation, localization, adhesion, and growth of endometriosis [37]. Studies [38] on acupuncture in a rat model of endometriosis have found significant reductions in the serum levels of IgA, IgG, and IgM, increased spleen CD3, CD4, and CD4/CD8 ratio, enhanced peritoneal fluid NK cell activity in rats, and reduced serum levels of IL-1 and IL-6. Acupuncture can regulate the disordered immune mechanisms in endometriosis by inhibiting an overly activated humoral immune response and improving cellular immune function.

Scholars have summarized the pathways and mechanisms proven to be involved in acupuncture treatment for pain associated with endometriosis [39]. Acupuncture improves endometriosis-related pain through NF-κB, JAK2/STAT3, MAPK, VEGF/VEGFR, and PGE2 signaling pathways.

Many clinical studies have proven that acupuncture can reduce the serum CA-125 level in patients with endometriosis. Nevertheless, there remains a dearth of investigation into the underlying mechanisms, necessitating further research efforts.

Strengths

This meta-analysis has several strengths. First, it involved a comprehensive search across eight databases, ensuring a more extensive retrieval of relevant studies. Second, all 14 included RCTs exclusively utilized acupuncture as the intervention. Moreover, this study conducted detailed subgroup analyses, further comparing the efficacy of acupuncture for different types of pain. It also analyzed the differences in pain severity improvement among various acupuncture techniques and examined the variations in efficacy between acupuncture and different types of control treatments. Therefore, the conclusions drawn from this study are more comprehensive, providing more meaningful insights for the clinical treatment of endometriosis-related pain.

Limitations

This study has several limitations: (1) the included studies were mostly single-center trials with small sample sizes. (2) In terms of experimental design, most of the literature did not mention the implementation of allocation concealment and blinding, which could introduce potential bias and affect the reliability of the conclusions. (3) The majority of the included studies utilized acupuncture as the intervention, while there were fewer studies investigating other acupuncture techniques such as electroacupuncture, auricular acupuncture, and fire needling. (4) Subjectivity in outcome assessment scores may introduce implementation bias and measurement bias. (5) The included studies lacked long-term follow-up, preventing the confirmation of the long-term effects of acupuncture on endometriosis-related pain.

Perspectives

Given the aforementioned limitations, it is anticipated that future work will incorporate more multi-center, large-sample, and well-designed randomized controlled trials on different types of endometriosis-related pain and various acupuncture techniques.

Conclusions

Acupuncture is effective in relieving dysmenorrhea and pelvic pain associated with endometriosis, reducing serum CA-125 levels, decreasing pelvic mass volume, improving patients' quality of life, and lowering the recurrence rate. Therefore, acupuncture can be considered an effective alternative therapy. However, the current study designs still have some shortcomings, and future large-scale, multicenter RCTs are desired to further confirm the efficacy of acupuncture.

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Data availability The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Conflict of interest The authors declare that they have no competing interests.

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References

1. Patel BG, Lenk EE, Lebovic DI, Shu Y, Yu J, Taylor RN (2018) Pathogenesis of endometriosis: interaction between endocrine and inflammatory pathways. Best Pract Res Clin Obstet Gynaecol 50:50–60. https://doi.org/10.1016/j.bpobgyn.2018.01.006
2. Chapron C, Marcellin L, Borghese B, Santulli P (2019) Rethinking mechanisms, diagnosis and management of endometriosis. Nat Rev Endocrinol 15(11):666–682. https://doi.org/10.1038/s41574-019-0245-z
3. Farshi N, Hasanpour S, Mirghafourvand M, Esmaeilpour K (2020) Effect of self-care counselling on depression and anxiety in women with endometriosis: a randomized controlled trial. BMC Psychiatry 20(1):391. https://doi.org/10.1186/s12888-020-02795-7
4. Peiris AN, Chaljub E, Medlock D (2018) Endometriosis Jama 320(24):2608. https://doi.org/10.1001/jama.2018.17953
5. Brown J, Crawford TJ, Allen C, Hopewell S, Prentice A (2017) Nonsteroidal anti-inflammatory drugs for pain in women with endometriosis. Cochrane Database Syst Rev. https://doi.org/10.1002/14651858.CD004753.pub4
6. Streuli I, de Ziegler D, Santulli P, Marcellin L, Borghese B, Batteux F, Chapron C (2013) An update on the pharmacological management of endometriosis. Expert Opin Pharmacother 14(3):291–305. https://doi.org/10.1517/14656566.2013.767334
7. Brown J, Crawford TJ, Datta S, Prentice A (2018) Oral contraceptives for pain associated with endometriosis. Cochrane Database Syst Rev. https://doi.org/10.1002/14651858.CD001019.pub3
8. Berlanda N, Somigliana E, Vigano P, Vercellini P (2016) Safety of medical treatments for endometriosis. Expert Opin Drug Saf 15(1):21–30. https://doi.org/10.1517/14740338.2016.1121991
9. Sinaii N, Cleary SD, Younes N, Ballweg ML, Stratton P (2007) Treatment utilization for endometriosis symptoms: a cross-sectional survey study of lifetime experience. Fertil Steril 87(6):1277–1286. https://doi.org/10.1016/j.fertnstert.2006.11.051
10. Ni Z, Cheng W, Sun S, Yu C (2020) Feasibility analysis of traditional Chinese medicine as a first-line option for the conservative management of endometriosis. China Matern Child Health 35(1):178–181
11. Fan AY, Miller DW, Bolash B, Bauer M, McDonald J, Faggert S, He H, Li YM, Matecki A, Camardella L, Koppelman MH, Stone JAM, Meade L, Pang J (2017) Acupuncture's role in solving the opioid epidemic: evidence, cost-effectiveness, and care availability for acupuncture as a primary, non-pharmacologic method for pain relief and management-white paper 2017. J Integr Med 15(6):411–425. https://doi.org/10.1016/S2095-4964(17)60378-9
12. Patil S, Sen S, Bral M, Reddy S, Bradley KK, Cornett EM, Fox CJ, Kaye AD (2016) The role of acupuncture in pain management. Curr Pain Headache Rep 20(4):22. https://doi.org/10.1007/s11916-016-0552-1
13. Xi J, Cao X, Gao Y, Cheng J, Xia Y (2019) Progress in the study of the mechanism of acupuncture in the treatment of endometriosis. Acupunct Res 44(10):5–26
14. Armour M, Cave AE, Schabrun SM, Steiner GZ, Zhu X, Song J, Abbott J, Smith CA (2021) Manual acupuncture plus usual care versus usual care alone in the treatment of endometriosis-related chronic pelvic pain: a randomized controlled feasibility study. J Integr Complement Med 27(10):841–849. https://doi.org/10.1089/acm.2021.0004
15. Fan H (2019) Analysis of the effect of acupuncture in the treatment of endometriosis. Doctor 4 (4)
16. Shen Q, Lu J (2017) Clinical observation on acupuncture treatment of endometriosis. Shanghai Acupunct Moxibustion J 36(06):711–714. https://doi.org/10.13460/j.issn.1005-0957.2017.06.0711
17. Teng H, Wang J, Liu Y, Xiao D (2016) Effect of fire targeting on CA-125 levels and EMAb in patients with endometriosis. Shanghai Acupunct Moxibustion J 35(07):844–846. https://doi.org/10.13460/j.issn.1005-0957.2016.07.0844
18. Sousa TRd, Souza BCd, Zomkowisk K, Rosa PCd, Sperandio FF (2016) The effect of acupuncture on pain, dyspareunia, and quality of life in Brazilian women with endometriosis: a randomized clinical trial. Complement Ther Clin Pract 25:114–121
19. Zhang X, Li W (2015) Efficacy on endometriosis treated with electroacupuncture. Chinese Acupunct Moxibustion 35(4):323–326
20. Liu Q, Teng H, Wang J, Liu Y, Xie Y, Wang S (2014) Clinical observation on fire needle treatment of endometriosis. Shanghai Acupunct Moxibustion J 33(08):734–735. https://doi.org/10.13460/j.issn.1005-0957.2014.08.0734
21. Xiang DF, Sun QZ, Liang XF (2011) Effect of abdominal acupuncture on pain of pelvic cavity in patients with endometriosis. Chinese Acupunct Moxibustion 31(2):113–116
22. Lin Y, Chen L (2010) Abdominal acupuncture for endometriosis. Henan Tradit Chinese Med 30(5):500–501
23. Chen L, Lin Y, Yuan L, Huang H (2010) Abdominal acupuncture in the treatment of endometriosis dysmenorrhea in 35 cases. Hunan J Traditional Chinese Med 26(06):75–76. https://doi.org/10.16808/j.cnki.issn1003-7705.2010.06.043

24. Pm W, Ce K (2008) Japanese-style acupuncture for endometriosis-related pelvic pain in adolescents and young women: results of a randomized sham-controlled trial. J Pediatr Adolesc Gynecol 21(5):247–257. https://doi.org/10.1016/j.jpag.2007.07.008
25. Xiang D, Situ Y, Liang X, Cheng L, Zhang G (2001) Clinical study on 37 cases of endometriosis dysmenorrhea treated by ear-embedded needle method. J Chinese Med. https://doi.org/10.1016/j.jpag.2007.07.008
26. Cai J, Wang S (2015) Observation on the effect of abdominal acupuncture in the treatment of pelvic pain in endometriosis. Health 9(19):117–190
27. Zhu Z, Lv C, Jiang H, Li L (2010) Observation on the efficacy of abdominal acupuncture in the treatment of dysmenorrhea due to endometriosis. Chinese Med Ethnic Minorities 19(13):156. https://doi.org/10.3969/j.issn.1007-8517.2010.13.122
28. Xu Y, Zhao W, Li T, Zhao Y, Bu H, Song S (2017) Effects of acupuncture for the treatment of endometriosis-related pain: A systematic review and meta-analysis. PLoS ONE 12(10):e0186616. https://doi.org/10.1371/journal.pone.0186616
29. Xiao X, Zhou Z, Wang P, Qin K, Wang X (2017) Meta-analysis of acupuncture in the treatment of endometriosis. Jiangxi Tradit Chinese Med. https://doi.org/10.1016/j.jbspin.2017.02.005
30. Coutaux A (2017) Non-pharmacological treatments for pain relief: TENS and acupuncture. Joint Bone Spine 84(6):657–661
31. Fan AY et al (2017) Acupuncture's role in solving the opioid epidemic: evidence, cost-effectiveness, and care availability for acupuncture as a primary, non-pharmacologic method for pain relief and management-white paper 2017. J Integr Med 15(6):411–425
32. Sun KF, He MR, Li N et al (2019) Pain mechanism of ems and analgesic mechanism of acupuncture and moxibustion in treating EMs. J Clin Acupunct Moxibustion 35(11):91–95
33. Bai SF, Li SP, Li L (2003) The effect of the analgesia mechanism of acupuncture therapy on treating endometriosis. Liaoning J Tradit Chinese Med 01:77–78. https://doi.org/10.13192/j.ljtcm.2003.01.78.baishf.056
34. Burney RO, Giudice LC (2019) Reprint of: pathogenesis and pathophysiology of endometriosis. Fertil Steril 112(4):e153–e161
35. Maekawa R et al (2019) Aberrant DNA methylation suppresses expression of estrogen receptor 1 (ESR1) in ovarian endometrioma. J Ovarian Research. https://doi.org/10.1186/s13048-019-0489-1
36. Wu CT, Li MY, Zhang XY et al (2021) Effect of acupuncture and moxibustion with traditional Chinese medicine in regulating endometrial tissue ERα/ERβ in rats with endometriosis. Shanghai J Tradit Chinese Med 55(11):59–65. https://doi.org/10.16305/j.1007-1334.2021.2108116
37. Mou YF, Song CH, Xie LZ et al (2024) Progress in clinical and mechanism research of acupuncture treatment of endometriosis. Inform Tradit Chinese Med 41(01):85–90. https://doi.org/10.19656/j.cnki.1002-2406.20240115
38. Li SP, Liu C, Xue Q et al (2008) Effect of acupuncture therapy on immune function of rats endometriosis. Liaoning J Tradit Chinese Med 04:595–596. https://doi.org/10.13192/j.ljtcm.2008.04.119.lishp.045
39. Feng Z, Gan NM, Huang DJ et al (2023) Progress in pain mechanism of acupuncture treatment of endometriosis through regulating different signal pathways. Jiangsu J Tradit Chinese Med 55(11):77–81. https://doi.org/10.19844/j.cnki.1672-397X.2023.11.022