The efficacy and safety of acupuncture in women with primary dysmenorrhea
A systematic review and meta-analysis

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Abstract
Background: This systematic review aimed to evaluate the current evidence regarding the efficacy and safety of acupuncture on primary dysmenorrhea.

Methods: Ten electronic databases were searched for relevant articles published before December 2017. This study included randomized controlled trials (RCTs) of women with primary dysmenorrhea; these RCTs compared acupuncture to no treatment, placebo, or medications, and measured menstrual pain intensity and its associated symptoms. Three independent reviewers participated in data extraction and assessment. The risk of bias in each article was assessed, and a meta-analysis was conducted according to the types of acupuncture. The results were expressed as mean difference (MD) or standardized mean difference (SMD) with 95% confidence intervals (CIs).

Results: This review included 60 RCTs; the meta-analysis included 49 RCTs. Most studies showed a low or unclear risk of bias. We found that compared to no treatment, manual acupuncture (MA) (SMD = −1.59, 95% CI [−2.12, −1.06]) and electro-acupuncture (EA) was more effective at reducing menstrual pain, and compared to nonsteroidal anti-inflammatory drugs (NSAIDs), MA (SMD = −0.63, 95% CI [−0.88, −0.37]) and warm acupuncture (WA) (SMD = −1.12, 95% CI [−1.81, −0.43]) were more effective at reducing menstrual pain. Some studies showed that the efficacy of acupuncture was maintained after a short-term follow-up.

Conclusion: The results of this study suggest that acupuncture might reduce menstrual pain and associated symptoms more effectively compared to no treatment or NSAIDs, and the efficacy could be maintained during a short-term follow-up period. Despite limitations due to the low quality and methodological restrictions of the included studies, acupuncture might be used as an effective and safe treatment for females with primary dysmenorrhea.

Abbreviations: AA = auricular acupuncture, AE = adverse event, CET = catgut embedding therapy, CI = confidence interval, CMSS = Cox menstrual symptom scale, EA = electroacupuncture, MA = manual acupuncture, MD = mean difference, MSS = menstrual symptom score, NRS = numeric rating score, NSAID = nonsteroidal anti-inflammatory drug, OC = oral contraceptive, PRISMA = Preferred Reporting Items for Systematic reviews and Meta-Analyses, RCT = randomized controlled trial, RR = risk ratio, RSS = Cox retrospective symptom scale, SD = standard deviations, SF-36 = 36-item short form health survey, SMD = standardized mean difference, SR = systematic review, STRICTA = STandards for Reporting Interventions in Clinical Trials of Acupuncture, TER = total effective rate, VAS = visual analog scale, VRS = seven-point verbal rating scale, WA = warm acupuncture.

Keywords: acupuncture, dysmenorrhea, meta-analysis, primary dysmenorrhea, systematic review

1. Introduction
Primary dysmenorrhea is defined as cramping pain during menstruation without any identifiable pelvic pathology, and it affects most women throughout the menstrual years. Many studies have reported that the prevalence of primary dysmenorrhea varied from approximately 50% to 90%, and 13% to 51% had to limit daily activities, such as school or work absenteeism. In the consensus guidelines of primary dysmenorrhea, nonsteroidal...
anti-inflammatory drugs (NSAIDs) and oral contraceptives (OCs) are recommended as first-line treatments. However, some patients did not experience pain reduction with NSAIDs and did experience side effects such as nausea, dyspepsia, headache, or drowsiness.[10,11] In addition, OCs may not be suitable for patients attempting to become pregnant, and might cause adverse effects such as nausea, vomiting, weight gain, or vaginal bleeding.[12,13]

Acupuncture, derived from China, is a therapeutic modality using the insertion of fine needles with the concepts of Yin and Yang and the circulation of qi. Acupuncture acts primarily by stimulating the nervous system, by local effects due to local antidromic axon reflexes, and by releasing opioid peptides and serotonin. Today, acupuncture is regarded as part of conventional medicine. It is no longer only “alternative medicine,” and it is used in Western medicine.[12] In particular, acupuncture has been widely used to alleviate diverse pains[13] including menstrual pain.

Many clinical trials had been conducted to show efficacy of acupuncture on menstrual pain, and 6 systematic reviews (SRs) have been previously conducted to evaluate the efficacy of acupuncture on primary dysmenorrhea.[14–19] However, the previous SRs included acupressure, the stimulation of acupoints without skin penetration,[14–19] which made the evaluation of acupuncture difficult. Some studies analyzed all types of acupuncture together,[14–17] which increased the heterogeneity. One latest study[19] included all the types of acupuncture except acupressure and analyzed the results separately, but it did not include newly published studies in 2017. Thus, we found it necessary to conduct a study with rigorous criteria that excluded acupressure and included all other types of acupuncture that penetrate the skin, such as embedding therapy, and to synthesize the data according to the type of acupuncture to reduce heterogeneity.

We conducted this study with these criteria to determine the efficacy and safety of acupuncture on primary dysmenorrhea.

2. Methods

2.1. Study registration

The protocol for this study was registered in PROSPERO: CRD42017069258.

2.2. Eligibility criteria

2.2.1. Types of studies. We included all randomized controlled trials (RCTs) that measured pain intensity and related outcomes to evaluate the efficacy of acupuncture in women with primary dysmenorrhea. Case studies, case series, noncontrolled trials, review articles, letters, conference papers, abstracts, and poster presentations were excluded. Studies not written in English, Chinese, or Korean were also excluded.

2.2.2. Types of participants. We included female patients of reproductive age suffering from primary dysmenorrhea. The definition of primary dysmenorrhea was based on cyclic pelvic pain during menstruation without any gynecological pathology such as endometriosis, adenomyosis, or uterine myoma. Patients with secondary dysmenorrhea or serious medical conditions were excluded.

2.2.3. Types of interventions. Manual acupuncture (MA), electroacupuncture (EA), auricular acupuncture (AA), and any other type of acupuncture using needle insertion were included in our study. Pharmacupuncture and acupressure were excluded. Other types of acupuncture that are rarely used in Korean clinical practice, such as eye acupuncture and floating acupuncture were also excluded. Types of control interventions included in our studies were no treatment, placebo acupuncture, and oral medications such as NSAIDs and OCs. Herbal medicines or other traditional medicine treatments used in the control group were excluded from our study.

2.2.4. Outcomes. The primary outcome was pain intensity after the intervention period as measured by any validated scale, such as the visual analog scale (VAS) or numeric rating score (NRS). The secondary outcomes were pain relief measured by total effective rate (TER) or improvement rate; related symptoms measured by the seven-point verbal rating scale (VRS), Cox menstrual symptom scale (CMSS), Cox retrospective symptom scale (RSS), or menstrual symptom score (MSS); quality of life as measured by the 36-item Short Form health survey (SF-36); pain intensity after a follow-up period; and adverse events (AEs).

2.3. Data sources

The following databases were searched for articles published from the database’s inception to December 2017: MEDLINE, Embase, Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library), Allied and Complementary Medicine Database (AMED), Citation Information by NII (CiNii), China National Knowledge Infrastructure (CNKI), Chinese Science and Technology Periodical Database (VIP), Wanfang, Oriental Medicine Advanced Searching Integrated System (OASIS), and the Korean Traditional Knowledge Portal (Korean TK). There was no language restriction. We used Medical Subject Heading (MeSH) terms and their synonyms, and modified the terms according to the strategy of each database. The search terms used are shown in Supplemental Search Terms List, http://links.lww.com/MD/C282.

2.4. Study selection

All studies found based on the search results were saved into EndNote; duplicated studies were excluded. After deleting the duplicates, 3 reviewers, WHL, HSJ, and LHJ, selected the relevant studies independently by title and abstract, and finally selected the included studies using the full text. Any disagreements were resolved by discussion among the 3 reviewers and an arbiter, PKS.

2.5. Data extraction

Three authors, WHL, HSJ, and LHJ, extracted data from the included studies according to the predetermined data forms. The following items were extracted: baseline demographics (journal, author, and year of publication); participants (sample size, sex, and age); intervention (type of acupuncture, periods, and frequency of treatment, and follow-up period); control; and outcome.

2.6. Risk of bias assessment

WHL, HSJ, and LHJ independently assessed the risk of bias for each included study using the following criteria from the Cochrane Handbook for Systematic Reviews of Interventions: random sequence generation; allocation concealment; blinding of participants and personnel; blinding of outcome assessment; incomplete outcome data; and selective reporting. We assessed these 6 criteria using “Low” (“L”), “Unclear” (“U”), and “High” (“H”) as a key for judgements. “Low” indicated a low risk of bias, “Unclear” indicated that the risk of bias was uncertain, and “High” indicated a high risk of bias. Disagreements were resolved by discussion among the 3 reviewers and an arbiter, Park KS.
2.7. Data synthesis

In our review, for studies using the same type of acupuncture, comparator, and outcome measures, the meta-analysis was performed using Review Manager software (RevMan v. 5.3). To assess the effect of acupuncture on primary dysmenorrhea, dichotomous data were analyzed using a risk ratio (RR) with 95% confidence intervals (CIs), and continuous data were analyzed using mean differences (MD) and 95% CIs or standardized mean differences (SMD) with 95% CIs if different scales were used. The chi-square and $I^2$ tests were used to assess statistical heterogeneity.[20] If $I^2 > 50\%$ or $P < .1$, we considered that there was substantial heterogeneity among the trials, and if $I^2 > 75\%$, we considered that there was serious heterogeneity. When serious heterogeneity was indicated, we found sources of heterogeneity by subgroup or sensitivity analysis. Subgroup analysis was conducted according to the treatment periods, and sensitivity analysis was done by excluding each heterogeneous trial. In case of substantial heterogeneity, a random effects model was used; otherwise, a fixed effects model was used to synthesize the data. However, if there were few studies for pooling, a fixed effects model was implemented because it is difficult to obtain a precise estimate of the between-studies variance.[21] If the number of the appropriate studies was only 1, or data were unsuitable for quantitative synthesis, descriptive synthesis of the findings was performed. If the number of studies for pooling was more than 10, publication bias was assessed using a funnel plot.[22]

3. Results

3.1. Study selection

A total of 4244 articles were screened, and 3962 were retrieved. The full texts of 282 studies were reviewed; 222 did not meet our inclusion criteria. Finally, 60 RCTs meeting our criteria were included. All studies were published between January 1987[23] and November 2017[24]. Forty-four studies were published in Chinese,[24-67] 15 in English,[11,23,68-80] and 1 in Korean.[81] Figure 1 shows a Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow of the study selection process.[82]

3.2. Study characteristics

3.2.1. Patients. A total of 3171 patients were treated with MA, EA, warm acupuncture (WA), AA, or catgut embedding therapy (CET); 2730 control patients received no treatment, placebo acupuncture, or oral medications. Of 60 trials, 55 were conducted in China (5653 patients),[24-71,73-79] and 1 each was conducted in America (22 patients),[23] Turkey (35 patients),[72] Australia (92 patients),[80] Thailand (52 patients),[11] and South Korea (47 patients),[81] respectively. The age range of the participants was 10 to 43 years. Table 1 summarizes the characteristics of the included studies.

3.2.2. Acupuncture interventions. Of 60 trials, 35 used MA,[11,23-27,28,29,31,33,37,41,43,44,49-52,57-64,66-70,73,77,80,81] 11
| Study | Country           | Mean age or age range, years | Experimental intervention (n) | Control intervention (n) | Treatment/Follow-up periods | Outcomes   | Meta-analysis |
|-------|-------------------|-----------------------------|-----------------------------|-------------------------|---------------------------|------------|--------------|
|       |                   |                             | Manual acupuncture versus no treatment |                         |                           |            |              |
| An et al[25] | China             | EG: 23 ±3, CG: 23 ±3         | MA (34)                     | No treatment (20)        | 3 cycles/None              | OMSS       | Not done     |
| Bu et al[68] | China             | EG: 19.7, CG: 19.7           | MA (36)                     | No treatment (40)        | 3 cycles/3 months          | OMSS       | Done         |
| Bu et al[27] | China             | EG: 19.65, CG: 19.68         | MA (35)                     | No treatment (40)        | 3 cycles/3 months          | OMSS       | Done         |
| Bu et al[28] | China             | EG: 19.6, CG: 19.6           | MA (36)                     | No treatment (20)        | 3 cycles/None              | OMSS       | Done         |
| Du et al[37] | China             | EG: 18–27, CG: 18–26         | MA (19)                     | No treatment (20)        | 3 cycles/None              | OMSS       | Done         |
| Guo[33]     | China             | EG: 22.10 ±2.86, CG: 22.10 ±2.5 | MA (60)                     | No treatment (30)        | 1 day/180 minutes          | OMSS       | Done         |
| Li et al[37] | China             | EG: 22.34 ±2.92, CG: 22.29 ±3.00 | MA (190)                   | No treatment (186)       | 3 cycles/None              | VAS        | Done         |
| Ma et al[41] | China             | EG: 22.88, CG: 23.10         | MA (34)                     | No treatment (20)        | 3 cycles/3 months          | CMSS       | Done         |
| Ma et al[77] | China             | 16–35                        | MA (344)                    | No treatment (173)       | 3 cycles/None              | CMSS       | Done         |
| Sun et al[49] | China             | EG: 22 ±2.5, CG: 22 ±3       | MA (40)                     | No treatment (20)        | 1 day/180 minutes          | CMSS       | Done         |
| Wang et al[52] | China          | EG: 22.10 ±2.83, CG: 22.11 ±2.50 | MA (25)                     | No treatment (20)        | 1 day/180 minutes          | CMSS       | Done         |
| Xu et al[58] | China             | EG: 22 ±2.5, CG: 22 ±1        | MA (48)                     | No treatment (48)        | 4 cycles/3 months          | CMSS       | Done         |
| Xu et al[59] | China             | EG: 23 ±1, CG: 23 ±1         | MA (48)                     | No treatment (48)        | 5 cycles/3 months          | CMSS       | Done         |
| Yu et al[60] | China             | EG: 23 ±1, CG: 23 ±1         | MA (48)                     | No treatment (48)        | 3 cycles/9 months          | Monthly pain score, Improvement rate | Not done     |
| Manual acupuncture versus placebo acupuncture |                   |                             |                           |                         |                           |            |              |
| Helms[23]   | USA               | 28                           | MA (11)                     | PA (11)                  | 3 cycles/9 months          | Monthly pain score, Improvement rate | Not done     |
| Smith et al[80] | Australia    | 19.2                         | MA (46)                     | PA (46)                  | 3 cycles/6months           | VAS, SF-36, AEs | Not done     |
| Youn et al[81] | Korea          | 18–40                        | MA (25)                     | PA (22)                  | 3 cycles/None              | VAS, AEs   | Not done     |
| Manual acupuncture versus oral medications |                   |                             |                           |                         |                           |            |              |
| Chen and Tu[69] | China            | 14–43                        | MA (52)                     | NSAIDs (40)              | 3 cycles/None              | NSAIDs     | Done         |
| Chen and Ju[70] | China            | EG: 14–35, CG: 13–30         | MA (30)                     | NSAIDs (30)              | 3 cycles/None              | NSAIDs     | Done         |
| Fu[71]      | China             | 13–35                        | MA (50)                     | NSAIDs (50)              | 3 cycles/None              | NSAIDs     | Done         |
| Jiang[72]   | China             | EG: 19.35 ±4.33, CG: 20.55 ±4.51 | MA (34)                   | NSAIDs (34)              | 3 cycles/None              | NSAIDs     | Done         |
| Kiran et al[27] | Turkey         | 15–40                        | MA (11)                     | NSAIDs (24)              | 1 cycle/None               | NSAIDs     | Done         |
| Li et al[28] | China             | EG: 21.05 ±3.86, CG: 22.65 ±3.92 | MA (20)                    | NSAIDs (20)              | 3 cycles/3 months          | NSAIDs     | Done         |
| Ning[73]    | China             | EG: 16–37, CG: 17–35         | MA (45)                     | NSAIDs (45)              | 3 cycles/None              | NSAIDs     | Done         |
| Qiao et al[74] | China            | 16–30                        | MA (20)                     | NSAIDs (20)              | 3 cycles/None              | NSAIDs     | Done         |
| Sriprasert et al[75] | Thailand    | 18–35                        | MA (27)                     | OCS (29)                 | 3 cycles/None              | OCS        | Done         |
| Wang[29]    | China             | EG: 18–21, CG: 18–23         | MA (40)                     | NSAIDs (33)              | 3 cycles/None              | NSAIDs     | Done         |
| Wang et al[31] | China           | EG: 21 ±2, CG: 21 ±2         | MA (30)                     | NSAIDs (30)              | 3 cycles/None              | NSAIDs     | Done         |
| Xie[32]     | China             | 29.6 ±4.8                    | MA (30)                     | NSAIDs (30)              | 3 cycles/3 months          | NSAIDs     | Done         |
| Zhang and Hang[33] | China    | EG: 18.7 ±5.27, CG: 20.1 ±6.39 | MA (45)                   | NSAIDs (45)              | 3 cycles/None              | NSAIDs     | Done         |
| Zhang[34]   | China             | 22.5 ±3.5                    | MA (60)                     | NSAIDs (60)              | 3 cycles/3 months          | NSAIDs     | Done         |
| Zhao[35]    | China             | EG: 22.6 ±2.4, CG: 24 ±8     | MA (40)                     | NSAIDs (40)              | 3 cycles/None              | NSAIDs     | Done         |
| Zhong and Xian[36] | China     | EG: 22.4, CG: 23.2           | MA (40)                     | NSAIDs (40)              | 3 cycles/None              | NSAIDs     | Done         |
| Zhou[37]    | China             | 16.73                        | MA (37)                     | NSAIDs (19)              | 3 cycles/None              | NSAIDs     | Done         |
| Zhou et al[38] | China            | EG: 22.9, CG: 22.6           | MA (42)                     | NSAIDs (42)              | 3 cycles/None              | NSAIDs     | Done         |
| Electroacupuncture versus no treatment |                   |                             |                           |                         |                           |            |              |
| Liu et al[39] | China            | 21.94 ±2.51                  | MA (49)                     | No treatment (48)        | 1 cycle/1 cycle            | VAS, VRS, RSS, AEs | Not done     |
| Mei et al[40] | China            | 15–30                        | MA (13)                     | No treatment (13)        | 1 cycle/1 cycle            | VAS, VRS, AEs | Not done     |
| Shi et al[41] | China            | 15–30                        | MA (10)                     | No treatment (11)        | 1 cycle/1 cycle            | VAS, AEs   | Done         |
| Song et al[42] | China           | EG: 22.1 ±2.2, CG: 22.8 ±2.7 | MA (49)                     | No treatment (48)        | 1 cycle/1 cycle            | VAS, RSS, AEs | Not done     |
| Electroacupuncture versus placebo acupuncture |                   |                             |                           |                         |                           |            |              |
| Study                  | Country | Mean age or age range, years | Experimental intervention (n) | Control intervention (n) | Treatment/Follow-up periods | Outcomes | Meta-analysis |
|------------------------|---------|------------------------------|-----------------------------|--------------------------|-----------------------------|----------|---------------|
| Liu et al[73]          | China   | 21.94 ± 2.51                | EA (49)                     | PA (48)                  | 1 cycle/1 cycle             | VAS, VRS, RSS, AEs           | Done        |
| Liu et al[83]          | China   | 15–30                       | EA (320)                    | PA (48)                  | 1 day/None                  | VAS, VRS, AEs               | Not done    |
| Ma et al[75]           | China   | 22.4 ± 2.8                  | EA (160)                    | PA (48)                  | 1 cycle/1 cycle             | VAS, VRS, AEs               | Done        |
| Lu et al[40]           | China   | NR                          | EA (14)                     | PA (11)                  | 1 cycle/None                | VAS                   | Done         |
| Song et al[76]         | China   | 15-30                       | EA (14)                     | PA (12)                  | 1 day/None                  | VAS, VRS, AEs               | Done        |
| Ma et al[78]           | China   | 22.4 ± 2.8                  | EA (23)                     | PA (11)                  | 1 cycle/None                | VAS, RSS, AEs               | Not done    |
| Song et al[47]         | China   | 22.1 ± 2.2, RG: 22.5 ± 2.4  | EA (163)                    | PA (164)                 | 1 cycle/1 cycle             | VAS, RSS, AEs               | Not done    |

**Electro-acupuncture versus NSAIDs**

| Study                  | Country | Mean age or age range, years | Experimental intervention (n) | Control intervention (n) | Treatment/Follow-up periods | Outcomes | Meta-analysis |
|------------------------|---------|------------------------------|-----------------------------|--------------------------|-----------------------------|----------|---------------|
| Fang et al[30]         | China   | 22 ± 2.7, RG: 22 ± 2.6       | EA (31)                     | NSAIDs (25)              | 3 cycles/None               | TER      | Done          |
| Wei[55]                | China   | 14.0 ± 1.8, RG: 13.0 ± 2.3   | EA (30)                     | NSAIDs (30)              | 3 cycles/None               | VAS, TER | Done          |

**Auricular acupuncture versus NSAIDs**

| Study                  | Country | Mean age or age range, years | Experimental intervention (n) | Control intervention (n) | Treatment/Follow-up periods | Outcomes | Meta-analysis |
|------------------------|---------|------------------------------|-----------------------------|--------------------------|-----------------------------|----------|---------------|
| Li et al[38]           | China   | 19.0 ± 0.5                   | AA (35)                     | NSAIDs (35)              | 3 cycles/None               | VAS      | Not done      |

**Warm acupuncture versus NSAIDs**

| Study                  | Country | Mean age or age range, years | Experimental intervention (n) | Control intervention (n) | Treatment/Follow-up periods | Outcomes | Meta-analysis |
|------------------------|---------|------------------------------|-----------------------------|--------------------------|-----------------------------|----------|---------------|
| Gu[32]                 | China   | 21.5 ± 1.0, RG: 21.3 ± 1.1   | WA (25)                     | NSAIDs (30)              | 3 cycles/None               | VAS, CMSS, TER | Done        |
| Li[56]                 | China   | 18–38                        | WA (100)                    | NSAIDs (30)              | 3 cycles/3 months           | TER      | Done          |
| Ma[42]                 | China   | 22 ± 5.3                     | WA (40)                     | NSAIDs (40)              | 3 cycles/2 months           | TER      | Done          |
| Shi and Guo[46]        | China   | 24.2 ± 2.20, RG: 24.6 ± 1.94 | WA (22)                    | NSAIDs (22)              | 3 cycles/None               | VAS, TER | Done          |
| Wang[42]               | China   | 13–35                        | WA (50)                     | NSAIDs (50)              | 3 cycles/None               | TER      | Done          |
| Wang and Gao[46]       | China   | 23.72 ± 2.09, RG: 23.00 ± 2.20 | WA (25)                   | NSAIDs (25)              | 3 cycles/3 months           | TER, AEs | Done          |
| Wu et al[46]           | China   | 21.5 ± 2.3                   | WA (30)                     | NSAIDs (30)              | 3 cycles/None               | TER      | Done          |
| Zhong and Wei[46]      | China   | 22.24 ± 3.12, RG: 20.36 ± 3.44 | WA (33)                   | NSAIDs (31)              | 3 cycles/None               | VAS, AEs | Done          |

**Warm acupuncture with NSAIDs versus NSAIDs**

| Study                  | Country | Mean age or age range, years | Experimental intervention (n) | Control intervention (n) | Treatment/Follow-up periods | Outcomes | Meta-analysis |
|------------------------|---------|------------------------------|-----------------------------|--------------------------|-----------------------------|----------|---------------|
| Kong[38]               | China   | 17–25, RG: 18–25             | WA+NSAIDs (60)              | NSAIDs (40)              | 3 cycles/None               | TER      | Done          |
| Li[54]                 | China   | 15–32                        | WA+NSAIDS (30)              | NSAIDs (30)              | 3 cycles/None               | TER      | Done          |

**Catgut embedding therapy versus NSAIDs**

| Study                  | Country | Mean age or age range, years | Experimental intervention (n) | Control intervention (n) | Treatment/Follow-up periods | Outcomes | Meta-analysis |
|------------------------|---------|------------------------------|-----------------------------|--------------------------|-----------------------------|----------|---------------|
| Bi et al[39]           | China   | 25.3 ± 3                     | CET (33)                    | Analgesics (35)          | 3 cycles/3 months           | VAS, TER, MSS, SF-36 | Done        |
| Chen et al[40]         | China   | 19.85 ± 2.12, RG: 19.79 ± 2.19 | NSAIDs (43)                | NSAIDs (43)              | 3 cycles/None               | TER, AEs | Done          |

AA = auricular acupuncture, AE = adverse event, CET = catgut embedding therapy, OG = oral group, CMSS = Cox menstrual symptom scale, EA = electroacupuncture, EG = experimental group, MA = manual acupuncture, MSS = menstrual symptom score, NR = not reported, NRS = numeric rating score, NSAIDs = nonsteroidal anti-inflammatory drug, OCs = oral contraceptives, PA = placebo acupuncture, RSS = Cox retrospective symptom scale, SF-36 = 36-item Short Form health survey, TER = total effective rate, VAS = visual analog scale, VRS = seven-point verbal rating scale, WA = warm acupuncture.

* These studies had two comparison arms, that is, no treatment group and placebo acupuncture group.
used EA,[30,40,47,48,55,73–76,78,79] 11 used WA,[32,35,36,39,42,45,46,53,54,65] 1 used AA,[81] and 2 used CET.[26,71] The number of acupuncture used varied from 1 to 21. The most frequently used point was Sanyinjiao (SP6), followed by Guanyuan (CV4), Diji (SP8), Cialiao (BL32), Zusanli (ST36), Xuehai (SP10), Taichong (LR3), Zhongji (CV3), Shiqizhui (EX-B8), and Shenshu (BL23). The only point used in 9 trials that used EA was Sanyinjiao (SP6). Twenty-one trials used different acupoints or added acupoints based on traditional Chinese medicine patterns.[26,31,33,36,50,53,54,57,60] Treatment duration ranged from one day to 3 menstrual cycles; 25 trials included follow-ups.[23,24,26–28,33,36,42,45,47,49,50,52,54,57,60,62,66,67,70,71,80] which varied from 180 minutes to one year. The time of intervention started before menstruation started in 31 trials,[27–29,32,34,42,45,51,53–60,62,63,65,66,68,69,72] when menstruation started in 4 trials,[46,73,75,78] when pain occurred in 10 trials,[24,33,40,41,47–49,52,74] and continuous treatment except for menstrual periods in 6 trials.[11,23,26,39,71,75] De-qi sensation was performed in most trials, but 4 studies did not mention about De-qi sensation.[26,38,40,50] Additional interventions to acupuncture were included in 15 trials,[11,33,35,40,47,48,59,60,73–76,78,80] Table 2 shows the acupuncture points and treatment methods of the included studies based on STandards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) recommendations.[4] 3.2.3. Control interventions. Of the 35 trials that used MA, 14 compared MA to no treatment,[25,27–29,32,37,41,49,52,58–60,68,71] 3 compared MA to placebo acupuncture,[25,28,81] and 18 compared MA to oral medications.[11,23,24,34,43,44,45,51,57,61–64,66,67,69,70,72] Most of the medications were NSAIDs, and only 1 was an OC.[11] Of the 11 trials that used EA, 4 compared EA to nonacupoint EA (placebo EA), or no treatment,[47,73,75,78] 5 compared EA to nonacupoint EA,[40,48,74,75,79] and 2 compared EA to NSAIDs.[50,55] Of 11 trials that used WA,[32,35,36,39,42,45,46,53,54,65] 2 trials compared WA plus NSAIDs to NSAIDs,[35,39] and 9 trials compared WA to NSAIDs.[32,35,36,39,42,45,53,54,65] One trial compared AA to NSAIDs.[38] Two trials compared CET to NSAIDs.[26,71] All of the placebo controls used nonacupoint acupuncture, not sham acupuncture.

3.2.4. Outcome measures. Twenty-seven trials measured pain intensity using VAS,[25,27–29,32,37,41,49,52,58–60,68,71] 5 used VRS,[40,47,48,58,60,73,75,76] and 8 used RSS.[40,47,48,58,60,73,75,76] Thirty trials measured pain relief[23,24,26,30–32,34,36–39,42–46,50,51,53–56,61–64,66,67,69–71] Six trials measured overall menstruation symptoms using MSS.[24,26,44,55,71] Three trials measured the quality of life using SF-36.[11,26,80] Twelve trials reported AEs.[11,47,54,62,65,71,73,75,76,78,80,81] Finally, of 25 trials conducting follow-ups, 10 trials reported the pain intensity after an follow-up period,[23,26,33,45,52,57,59,73,80] which varied from 180 minutes to 9 months by study. Most studies reported various outcomes measuring dysmenorrhea and related symptoms.

3.3. Risk of bias

All 60 studies mentioned randomization. Twenty trials used random number tables,[23,24,26,33,38,43,44,49,51,52,54,57–61,65,67,71,80] 10 used a computer-generated sequence,[11,48,73–80] 5 used central random method,[26,29,37,40,41] and 1 used the draw method.[12] Three trials used the order of joining the study,[34,69,72] and the other 8 studies did not report the details of randomization. Sixteen studies reported appropriate allocation concealment[11,23,28,30,37,40,41,47,48,73–77,79,81] using computer programs, central telephone controls, sealed envelopes, or independent individual controls. It is difficult to achieve blinding to both participants and practitioners for the characteristics of study design in acupuncture intervention, but 14 studies mentioned efforts to minimize performance bias,[23,28,40,47,48,73–81] so we assessed the risk of bias as low. Twelve trials reported assessor blinding,[23,28,40,48,73–80] but most of the others did not report the details.

Most of the studies had no missing data, performed intention-to-treat (ITT) analysis, or had similar numbers and reasons of drop-outs. However, the details of drop-outs and withdrawals were not reported in 6 studies,[27,30,36,66,71,81] considered to be a high risk in reporting bias. Forty-nine studies reported all outcomes clearly as mentioned in protocol studies or methods,[11,23,25,27–28,37,39,41–46,48,49,56,62,72–74,78–80] and were assessed as a low risk of bias in selective reporting. Six studies reported the outcomes unclearly[46,67,68,76,83] and were assessed as an unclear risk of bias, and 5 studies did not report all outcomes as planned,[11,35,38,60,76,77] and were assessed as a high risk of bias. There was a low risk of other sources of bias based on lack of clear evidence. As shown in Figures 2 and 3, most of the studies included in this meta-analysis achieved a low or unclear risk of bias of the quality assessment items.

3.4. Data synthesis

3.4.1. Manual acupuncture

3.4.1.1. MA versus no treatment. VAS. Five studies,[11,34,49,52,58,59] were included in the meta-analysis to synthesize VAS data. As shown in Figure 4A, the pooled results showed serious heterogeneity ($I^2 = 98\%$). We conducted a subgroup analysis, and the pooled results showed that after treatment of 1 day, MA more effectively reduced primary dysmenorrhea than no treatment ($n = 210$, MD = $-1.59$; 95% CI $[-2.12, -1.06]$; P < 0.001, $I^2 = 60\%$).

VRS. One study[68] reported that after the treatment of 3 menstrual cycles, MA more effectively reduced primary dysmenorrhea than no treatment ($n = 96$, MD = $-2.04$; 95% CI $[-2.11, -1.97]$; P < 0.001).

CMSS for pain intensity. Six studies[27–29,41,68,77] were included in the meta-analysis to synthesize CMSS for pain intensity data. As shown in Figure 4B, after treatment of 3 menstrual cycles, MA more effectively reduced pain than no treatment ($n = 838$, MD = $-7.08$, 95% CI $[-8.53, -5.63]$, $P < 0.001$, $I^2 = 50\%$). Two studies[25,37] reported the subscales of CMSS for pain intensity; 1 study[25] reported the MA significantly reduced abdominal pain, and the other[37] reported that the MA significantly reduced extra bed time.

RSS. Two studies[58,60] were included for meta-analysis to synthesize RSS data. As shown in Figure 4C, after treatment of 3 menstrual cycles, MA more effectively reduced pain than no treatment ($n = 141$, MD = $-10.47$, 95% CI $[-10.74, -10.20]$, P < 0.001, $I^2 = 93\%$).

VAS after follow-up. Five studies[13,49,52,58,59] were included for meta-analysis to synthesize VAS after follow-up data. As shown in Figure 4D, the pooled results showed serious heterogeneity ($I^2 = 98\%$). We conducted a subgroup analysis, and after a 180-minute follow-up, MA was significantly more effective than no treatment ($n = 210$, MD = $-1.22$, 95% CI $[-1.53, -0.91]$, P < 0.001, $I^2 = 0\%$).
### Table 2

Acupuncture interventions of the included studies based on STRICTA recommendations.

| Study                  | Names of points (n) | Depth of insertion | De-qi response or needle stimulation | Number of treatment sessions | Frequency and duration sessions | Needle retention time | Additional interventions |
|------------------------|--------------------|--------------------|-------------------------------------|-----------------------------|---------------------------------|----------------------|--------------------------|
| An et al[25]           | SP6, BL32, SP8, EX-B8 (7) | NR                 | De-qi                              | 15 or 9                     | Once per day 3–7 days before menstruation started, or once per day for 3 days after menstrual pain appeared, 3 cycles. | 30 min               | None                     |
| Bu et al[68]           | SP6, BL32, SP8, EX-B8 (7) | Depth based on "Science of Channels and Collaterals and Acupoints" | De-qi                             | 3–7                         | Once per day 3–7 days before menstruation started, 3 cycles. | 30 min               | None                     |
| Bu[27]                 | EX-B8 (1)          | 0.5–1 cun           | De-qi                              | 9–21                        | Once per day 3–7 days before menstruation started until menstrual amount maximized, 3 cycles. | 30 min               | None                     |
| Chen and Tu[69]        | SP6, SP8, SP10, LI4 (8) | NR                 | De-qi                              | 15                          | Once per day 1–2 days before menstruation started for 5 days, 3 cycles. | 1 h                  | None                     |
| Chen and Ju[70]        | EX-B8 (1) or SP6, BL32, SP8, EX-B8 (7) | EX-B8: 0.5–1 cun | De-qi                             | 9–21                        | Once per day 3–7 days before menstruation started, 3 cycles. | 30–60 min            | None                     |
| Chen et al[72]         | HT7, KI3, ST36, ST30, CV2, CV4, PC6 | NR                 | De-qi                              | 21                          | Once per day for 7 days from 4 days before menstruation started, 3 cycles | 30 min               | None                     |
| Fu ke[31]              | SP6, ST36, EX-CA1, CV4 + LR3, SP8 (Excess pattern) or SP10, BL17 (Deficiency pattern) | 0.5–1 cun | De-qi                              | 9                           | Once per day when menstrual pain appeared for 3 days, 3 cycles | 30 min               | None                     |
| Guo[33]                | EX-B8 (1)          | 0.5–1 cun           | De-qi                              | 9                           | The day when menstrual pain appeared | 20 or 30 min         | None                     |
| Helms[23]              | SP6, SP8, SP10, LI4 (8) | NR                 | De-qi                              | NR                          | Once per week, 3 cycles except during menstrual periods. | 30–40 min            | None                     |
| Jiang[34]              | BL31, BL32, BL33, LR3, SP6, SP8, CV4, ST36 (15) | NR                 | De-qi                              | 21                          | Once per day for 7 days from 4 days before menstruation started, 3 cycles | 30 min               | None                     |
| Kiran et al[72]        | GT7, PO6, U4, U10, SP6, LR3, ST36, GB32, SP15, EX-CA1, CV4 (21) | NR                 | De-qi                              | 9                           | Once per day when menstrual pain appeared | 45 min               | None                     |
| Li et al[35]           | EX-B8 (1) or SP6, BL32, SP8, EX-B8 (7) | EX-B8: 0.5–1 cun | De-qi                              | 15–21                       | Once per day from the first day when menstrual pain appeared to the third day of menstruation, 3 cycles | 30 min               | None                     |
| Ma et al[77]           | EX-B8 (1) or SP6, BL32, EX-B8 (7) | EX-B8: 0.5–1 cun | De-qi                              | 9                           | Once per day when menstrual pain appeared | 30 min               | None                     |
| Ma et al[78]           | EX-B8 (1) or SP6, BL32, EX-B8 (7) | EX-B8: 0.5–1 cun | De-qi                              | 9                           | Once per day when menstrual pain appeared | 30 min               | None                     |
| Ning[43]               | BL32, SP6, CV4 (5) | 0.5–1 cun           | De-qi                              | NR                          | Once per day for 7 days from 4 days before menstruation started, 3 cycles | 15 min               | None                     |
| Qiao et al[44]         | CV4, SP6, SP8, EX-B8 (6) | 0.5–1 cun           | De-qi                              | NR                          | Once per day when menstrual pain appeared | 15 min               | None                     |
| Smith et al[45]        | SP4, ST29, CV3, BL32, SP8, SP10 (7) + LR3, SP6, LI4, CV5, BL32, SP10, CV6, SP8, SP4 (Stagnation of qi and blood) or ST36, CV4, CV6, BL7, SP8, BL20, BL32, (Deficiency of qi and blood) or, BL23, CV3, CV6, SP6, CV4, CV4, LU7, N6, ST36 (Stagnation of coldness) or GB4, LI1, LI2, ST25, BL32, ST40, SP9, ST28, SP6, BL22 (Stagnation of coldness) | 0–2 cm | De-qi                              | 21                          | Once per day for 7 days from 4 days before menstruation started, 3 cycles | 30 min               | None                     |
|                        |                    | 0.5–1 cun           | De-qi                              | NR                          | Once per day when menstrual pain appeared | 30 min               | None                     |
|                        |                    | 0.5–1 cun           | De-qi                              | 9                           | Once per day when menstrual pain appeared | 30 min               | None                     |
|                        |                    | 0.5–1 cun           | De-qi                              | 9                           | Once per day when menstrual pain appeared | 30 min               | None                     |
|                        |                    | 0.5–1 cun           | De-qi                              | 9                           | Administration of OTCs or analgesics per patient's request. | 30–40 min            | None                     |
Table 2 (continued).

| Study                  | Names of points (n)                                                                 | Depth of insertion                                                                 | De-qi response or needle stimulation | Number of treatment sessions | Frequency and duration sessions | Needle retention time | Additional interventions |
|------------------------|-----------------------------------------------------------------------------------|------------------------------------------------------------------------------------|--------------------------------------|------------------------------|-----------------------------|----------------------|--------------------------|
| Sriprasert et al. [11] | CV6, CV3, SP6, SP6 (6)                                                            | De-qi                                                                             | 30 mm                                | 30 min                       | Admit naproxen 250 mg 1 T unless pain alleviated. |
| Sun et al. [49]        | SP6 (2) or SP6, CV4 (3)                                                           | De-qi                                                                             | 9 + α                                | Once per day                 | None                         |
| Wang [50]              | CV6, CV3, CV4, SP10, SP6 (7) + CV12, BL23 (Deficiency or cold pattern) or BL18 | De-qi                                                                             | 30 min                                | None                         |
| Wang et al. [51]       | SP6, CV4 (3)                                                                       | De-qi                                                                             | 21 + α                                | Once per day                 | None                         |
| Xie [57]               | CV4, CV6, ST36, SP6 (7) + SP8, LR3 (Excess pattern) or BL17, ST10 (Deficiency pattern) | De-qi                                                                             | 9 + α                                | Once per day                 | None                         |
| Xu et al. [59]         | CV4, CV6, ST36, SP6 (7) + SP8, LR3 (Excess pattern) or BL17, ST10 (Deficiency pattern) | De-qi                                                                             | 9 + α                                | Once per day                 | None                         |
| Zhang and Yang [60]    | CV4, CV6, ST36, SP6 (7) + SP8, LR3 (Excess pattern) or BL17, ST10 (Deficiency pattern) | De-qi                                                                             | 9 + α                                | Once per day                 | None                         |
| Zhang 2014 [61]        | SP6, CV3, EX-CA1, etc. (5) + ST28, SP6 (Stagnation of coldness and dampness) or BL19 (Stagnation of qi and blood) | De-qi                                                                             | 30 min                                | None                         |
| Zhao [63]              | CV4, CV6, ST36, SP6 (7) + SP8, LR3 (Excess pattern) or BL17, ST10 (Deficiency pattern) | De-qi                                                                             | 15 + α                                | None                         |
| Zhong and Xian [64]    | CV6, BL32, SP10, SP6 (6) + ST29, CV3 (Stagnation of coldness and dampness) or CV4, BL19, ST6, BL23, KI6 | De-qi                                                                             | NR                                  | None                         |

(continued)
| Study | Names of points (n) | Depth of insertion | De-qi/response or needle stimulation | Number of treatment sessions | Frequency and duration sessions | Needle retention time | Additional interventions |
|-------|---------------------|--------------------|-------------------------------------|-------------------------------|------------------------------|----------------------|------------------------|
| Zhou et al. | (Deficiency of liver and kidney) or LR2, SP9 (Liver depression and heat-dampiness) BL32 (2) + CV4 (Deficiency pattern) or CV4, BL23 (Coldness pattern) or HT6, K10 (Heat pattern) | 1.5 cun | De-qi | 21 + a | Once per day from 7 days before menstruation started, 3 cycles | 30 min | None |
| Zhou et al. | BL31, BL32, BL33, BL34 (4) | 50–65 mm | De-qi | 1 | Once per day from 7 days before menstruation started, 3 cycles | 30 min | None |
| Fang et al. | CV4, CV3, SP6, ST36 (6) | SP6, CV4, CV3: 0.5–1 cun ST36: 0.8–1 cun | De-qi, Electrical stimulation (frequency at 300–500/min, the highest intensity each participant could tolerate, connecting CV4 with CV3, ST36 with SP6) | 15 | Once per day for 3 days, 3 cycles | 30 min | None |
| Liu et al. | SP6, the points 0.5cm apart from SP6 (4) | NR | De-qi, Electrical stimulation (2/100 Hz AC, the highest intensity each participant could tolerate) | 3 | Once per day 24 hours after menstruation started for 3 days, 1 cycle | 30 min | Administration of aspirin if VAS ≥ 80 mm. |
| Liu et al. | SP6, the points 5mm proximal to SP6 (4) | 25–40 mm | De-qi, Electrical stimulation (2/100 Hz AC, the highest intensity each participant could tolerate) | 1 | The day when menstrual pain appeared ≥ VAS 40 mm | 30 min | Administration of aspirin unless pain alleviates. |
| Liu et al. | SP6, the points 0.5cm apart from SP6 (4) | 10–30 mm | De-qi, Electrical stimulation (2/100 Hz AC, 0.5–1.6mA, the highest intensity each participant could tolerate) | 3 | Once per day when menstruation started for 3 days, 1 cycle | 30 min | Administration of aspirin if VAS ≥ 80 mm. |
| Lu 2014 | SP6, the points 2 mm apart from SP6 (4) | 1–2 cun | De-qi, Electrical (2/100 Hz, the highest intensity each participant could tolerate) | 1 | The day when menstrual pain appeared ≥ VAS 40 mm | 30 min | Administration of aspirin if VAS ≥ 80 mm. |
| Ma et al. | SP6, the points 2 mm upper from SP6 (4) | 25–40 mm | De-qi, Electrical stimulation (2/100 Hz AC, the highest intensity each participant could tolerate) | 3 | Once per day for 3 days, 1 cycle | 10 min for first session, 30 min for second and third sessions | Administration of aspirin if VAS ≥ 80 mm. |
| Shi et al. | SP6, the points 0.5cm proximal to SP6 (4) | 1–1.2 cun | De-qi, Electrical stimulation (2/100 Hz AC, 0.5–1.6mA, the highest intensity each participant could tolerate) | 3 | Once per day for 3 days 24 hours after menstruation started, 1 cycle | 30 min | Administration of aspirin if VAS ≥ 80 mm. |
| Shi et al. | SP6, the points 5mm proximal to SP6 (4) | 25–40 mm | De-qi, Electrical stimulation (2/100 Hz AC, the highest intensity each participant could tolerate) | 1 | The first day when menstrual pain ≥ VAS 40 mm appeared | 30 min | Administration of aspirin unless pain alleviates. |
| Song 2013 | SP6, the points 2–5mm apart from SP6 (4) | 25–30 mm | De-qi, Electrical stimulation (2/100 Hz AC, 0.5–1.6mA, the highest intensity each participant could tolerate) | 3 | Once per day for 3 days from the first day when menstrual pain ≥ VAS 40 mm appeared, 1 cycle | 30 min | Administration of aspirin if VAS ≥ 80 mm. |
| Song et al. | SP6, the points 2–5mm apart from SP6 (4) | 1–1.2 cun | De-qi, Electrical stimulation (2/100 Hz AC, the highest intensity each participant could tolerate) | 3 | Once per day for 3 days from the first day when menstrual pain appeared ≥ VAS 40 mm | 30 min | Administration of aspirin if VAS ≥ 80 mm. |
| Wei et al. | ST25, CV3, CV4, GB25, BL23, BL27, BL28, SP6, etc. (14) + LR3, LI, SP10 (Stagnation of qi and blood), or SP6, SP9 (Stagnation of coldness and dampness) | NR | De-qi, Electrical stimulation (6 Hz AC, the highest intensity each participant could tolerate) | 30 | Once per day for 10 days from 7 days after menstruation started, 3 cycles | 30 min | None |
| Auricular acupuncture | Internal genitals, Liver, Endocrine, Shenmen, etc. (4) | NR | NR | NR | 7–10 days before menstruation started for 15 days, alternating between the left and right ear every 3 days, 3 cycles | 3 days | None |

(continued)
| Study                  | Names of points (n) | Depth of insertion | De-qi response or needle stimulation | Number of treatment sessions | Frequency and duration sessions | Needle retention time | Additional interventions |
|------------------------|---------------------|--------------------|-------------------------------------|-----------------------------|--------------------------------|-----------------------|-------------------------|
| Gu [32]               | SP6, CV3, CV6, etc. (4) | NR                 | De-qi                              | 36                          | Once per day from 3 days before menstruation started to the third day after menstruation started, 3 cycles | NR                    | None                    |
| Kong [32]             | Stagnation of qi and blood: LR3, CV6, CV3, ST29, SP6, SP10, BL32 (12) Stagnation of coldness and dampness: U11, CV6, SP9, ST29, CV3, BL32 (10) Deficiency of kidney qi: SP6, SP6, CV4, BL23, KI3, BL32 (11) | NR                 | De-qi                              | 15–21                      | Once per day 3 days before menstruation started for 5–7 days, 3 cycles | 20 min                 | Oral administration of ibuprofen 1 T 3 times daily for 3 days before menstruation started. |
| Li [34]               | Stagnation of coldness and dampness: CV4, ST36, SP6 (5) Deficiency of liver and kidney CV4, CV6, SP6, ST36 (6) LR3, SP9 (4) | NR                 | De-qi                              | 12–18                      | Once per day 3–5 days before menstruation started to the second day of menstruation started, 3 cycles | 30 min                 | None                    |
| Liu [34]              | SP6, CV3, ST29, CV6, SP8 (8) | 1.5–2 cun           | De-qi                              | 18                         | Once per day 2–3 before menstruation started for 6 days, 3 cycles | 30 min                 | None                    |
| Qin et al [34]        | EX-CA1, CV4, CV3, CV6, SP6, ST36, U4, LR3, SP10, SP8, SP9 (19) CV6, CV4, SP6 (4) | 0.5–1 cun           | De-qi                              | 3                          | Once per day 2 days before menstruation started for 10 days, 3 cycles | 30 min                 | None                    |
| Shi and Gu [34]       | SP6, SP10, ST36, CV4, LR3 (9) | 1 cun               | De-qi                              | 15                         | The first day of menstruation, 3 cycles | 30 min                 | None                    |
| Wang and Gao [34]     | BL32 (2)            | 20–35 mm            | De-qi                              | 15                         | Once per day 5 days before menstruation started for 5 days, 3 cycles | NR                    | None                    |
| Wu et al [34]         | BL32, SP6 (4)       | BL32: 1.5 cun SP6: 1 cun | De-qi                              | 21                         | Once per day 7 days before menstruation started, 3 cycles | NR                    | None                    |
| Zhong and Wei [34]    | CV4, ST29, SP6 (4)  | CVA, ST29: 1–2 cun SP6: 1–1.5 cun | De-qi                              | 21                         | Once per day from 5 days before menstruation started to the second day of menstruation, 3 cycles | NR                    | None                    |
| Catgut embedding therapy | Bl et al [34]      | Before menstruation: CV4, EX-CA1, SP5, BL32 (7) After menstruation: BL23, BL18, BL20 (6) + BL17, ST25 (Stagnation of qi and blood), ST29 (Stagnation of coldness), K14, SP10 (Stagnation of dampness and heat), SP6 (Deficiency of liver and kidney), ST36 (Deficiency of qi and blood) | Deeply into subcutaneous fat layer | Removing needles with swirling to lead needle sensation | 6                          | Twice per cycle (3 days before, 12–14 days after menstruation started), 3 cycles | NR                    | None                    |
| Chen et al [34]       | SP6, BL32, CV6 (6) + BL23 (Stagnation of qi and blood) or BL18 (Stagnation of qi and blood) or ST36 (Deficiency of qi and blood) | Subcutaneous or muscular layer | NR                              | 6                          | Twice per cycle (7 days before menstruation started, 10 days after menstruation finished), 3 cycles | NR                    | None                    |

AC = alternating current, NR = not reported, OC = oral contraceptive, STRICTA = Standards for Reporting Interventions in Clinical Trials of Acupuncture.
3.4.1.2. MA versus placebo acupuncture. Pain intensity. Three studies reported pain scores,[23,80,81] but data were unsuitable for pooling because the score systems of the studies were different from each other. One study[23] reported that MA lowered monthly pain score after treatment of 3 menstrual cycles (n = 22, MD = -70.67, 95% CI [−126.52, −14.82], P = .01) and another study[80] reported that MA lowered the pain score after treatment of 3 menstrual cycles without significant differences (n = 92, MD = -0.9, 95% CI [−1.8, 0.4], P = .21). The other study[81] also reported that there were no significant differences between groups after treatment of 3 menstrual cycles (n = 47).

Pain relief. One study[23] reported that after treatment of 3 menstrual cycles, MA provided a significant improvement in pain compared to placebo acupuncture (n = 22, RR = 2.50, 95% CI [1.12, 5.38], P < .05).

SF-36. One study[80] reported that after treatment of 3 menstrual cycles, there was no significant difference in all SF-36 subscales or both component scores between the 2 groups (n = 92, bodily pain MD = -6.1, 95% CI [−15.1, 2.8], P = .18; General health MD = 5.1, 95% CI [−3.0, 13.2], P = .22; Vitality MD = 3.2, 95% CI [−5.1, 11.6], P = .44; Social function MD = 1.1, 95% CI [−8.0, 10.3], P = .81; Role emotional MD = 2.2, 95% CI [−12.7, 17.1], P = .77; Mental health MD = 6.0, 95% CI [−1.7, 13.6], P = .13; Overall Physical Component MD = -2.3, 95% CI [−5.9, 1.2], P = .19; Overall Mental Component MD = 3.5, 95% CI [−1.1, 8.1], P = .71).

Pain intensity after follow-up. Two studies[23,80] reported this outcome. One study[23] reported MA maintained pain reduction until 9 months after the completion of treatment (n = 22, MD = -64.90, 95% CI [−122.11, −7.69], P < .03). The other[80] reported there were no significant differences between the groups after 3- and 9-month follow-up periods.

AEs. Two studies[80,81] reported there were no AEs.

3.4.1.3. MA versus oral medications. Pain intensity. Five studies[44,51,57,70,72] comparing MA to NSAIDs reported VAS, and 1 study[11] comparing MA to OCs reported a change in NRS. As shown in Figure 4F, the MA was significantly more effective at reducing pain than NSAIDs (n = 255, SMD = -0.63, 95% CI [−0.88, −0.37], P < .001, I² = 0%). Meanwhile, OCs were more effective than MA after treatment of 3 menstrual cycles (n = 52, MD = 1.58, 95% CI [0.36, 2.80], P < .01).

Pain relief. Fourteen studies[24,31,34,43,44,50,51,61–64,66,69,70] comparing MA to NSAIDs were included for meta-analysis to synthesize TER data. As shown in Figure 4F, MA provided significant pain relief compared to NSAIDs (n = 1,049, RR = 1.17, 95% CI [1.11, 1.22], P < .001, I² = 0%). The funnel plot of those studies did not show asymmetry. One study[67] reported pain relief as percentage using 6-Likert score, and also showed significant pain relief compared to NSAIDs (n = 84, RR = 2.97, 95% CI [1.75, 5.05], P < .01).

MSS. Three studies[24,44,51] comparing MA to NSAIDs reported MSS. As shown in Figure 4G, MA was significantly more effective at improving menstrual symptoms than NSAIDs after treatment of 3 menstrual cycles (n = 190, SMD = -0.53, 95% CI [−0.84, −0.23], P < .001, I² = 2%).

SF-36. One study[11] reported that there was no significance difference between the 2 groups after treatment of 3 menstrual cycles (n = 52, MD = -1.82, 95% CI [−9.36, 5.72], P = .64).

VAS after follow-up. One study[81] reported that after a 3-month follow-up, MA was significantly more effective than NSAIDs (n = 60, MD = -1.39, 95% CI [−2.65, −0.13], P < .05).

AEs. Two studies[11,62] reported AEs. One study[11] reported one case of regional discomfort or hemorrhage, 4 cases of headache or myalgia, and 1 case of fever in the MA group, which were all mild. Meanwhile, in the OCs group[11], 9 cases of abnormal uterine bleeding, 5 cases of headache or myalgia, 3 cases of weight gain, 2 cases of nausea or vomiting, and 1 case of breast bleeding were reported; they were all already known AEs of OCs and were not severe. The other study[62] reported 3 cases of elevated alanine transaminase (ALT), 2 cases of blurred vision, 3 cases of lumbar and leg pain, and 5 cases of others, which were predictable reactions, and soon disappeared.

3.4.2. Electroacupuncture. 3.4.2.1. EA versus no treatment. VAS. Four studies[47,73,76,78] reported that EA was significantly more effective at reducing pain than no treatment (n = 97, MD = -15.36, 95% CI [−22.16, −8.95], P < .001[73]; n = 26, MD = -23.19, 95% CI [−32.06, −14.33], P < .001[76]; n = 20, MD = -22.50, 95% CI [−31.70, −13.30], P < .005[78]; n = 97, P < .001; details of data not shown[47]). Data were unsuitable for pooling for means and SDs were not reported.

VRS. Two studies[73,76] reported that there was no significant difference between the groups. Data were unsuitable for pooling.
because they reported the results only in graphs, which made it hard to extract raw data. AEs. Four studies reported AEs, but one study showed 1 case of dizziness after EA.

3.4.2.2. EA versus placebo acupuncture. VAS. Nine studies were included in the meta-analysis because the other 3 did not provide SDs. As shown in Figure 5A, the VAS of the EA group was significantly lower than placebo group (n = 826, SMD = −0.32, 95% CI [−0.63, −0.01], P = .04, I² = 69%). Of the 3 studies included from meta-analysis, one study reported that EA was significantly more effective in reducing pain than the placebo group in cold-dampness stagnation after one session of treatment (n = 487, MD = −8.2, 95% CI [−13.5, −2.9], P < .005); in other types, there was no significant difference. Another study showed the same result after treatment of 1 menstrual cycle (n = 25, MD = −20.78, 95% CI [−29.82, −11.73], P < .001). The other RCT reported that there was no significant difference between the groups after treatment of 1 menstrual cycle (n = 97, details of data not shown).

VRS. Three studies reported VRS, but only 2 were included in the meta-analysis because the third did not provide SDs. As shown in Figure 5B, after treatment of 1 menstrual cycle, the VRS in the EA group was lower than the placebo group, but there was no significance (n = 347, MD = −0.20, 95% CI [−0.43, 0.03], P = .10, I² = 61%). The other study also reported a change of VRS in the EA group that was lower than the placebo group, but there was no significance (n = 322, reduction from 3.94 to 3.08 vs reduction 3.72 to 3.02).

VAS after follow-up. One study reported that after one-cycle follow-up, there were no significance differences between EA and PA groups (n = 322, MD = −1.40, 95% CI [−2.2, 0.7], P = .28). The other 2 studies also showed no significance in VAS (data not shown).

VAS after follow-up. One study reported that after one-cycle follow-up, there were no significance differences between EA and PA groups (n = 322, MD = −1.40, 95% CI [−2.2, 0.7], P = .28). The other 2 studies also showed no significance in VAS (data not shown).

VAS after follow-up. One study reported that after one-cycle follow-up, there were no significance differences between EA and PA groups (n = 322, MD = −1.40, 95% CI [−2.2, 0.7], P = .28). The other 2 studies also showed no significance in VAS (data not shown).

3.4.2.3. EA versus NSAIDs. VAS. One study reported that after treatment of 3 menstrual cycles, EA was significantly effective at reducing pain than NSAIDs (n = 60, MD = −1.40, 95% CI [−2.2, −0.59], P < .01).

Pain relief. Two studies reported TER, but as shown in Figure 5C, the pooled results showed no significant differences between the 2 groups (n = 140, RR = 1.80, 95% CI [0.99, 1.18], P = .09, I² = 0%).

3.4.3. Auricular acupuncture. AA versus NSAIDs. VAS. One study reported that after treatment of 3 menstrual cycles, there were no significant differences between the 2 groups (n = 70, MD = −0.20, 95% CI [−0.90, −0.50], P = .58).
Figure 4. Meta-analysis of the studies evaluating the effects of MA on primary dysmenorrhea. (A) MA vs no treatment, outcome: VAS. (B) MA vs no treatment, outcome: CMSS for pain intensity. (C) MA vs no treatment, outcome: RSS. (D) MA vs no treatment, outcome: VAS after follow-up. (E) MA vs NSAIDs, outcome: VAS. (F) MA vs NSAIDs, outcome: TER. (G) MA vs NSAIDs, outcome: MSS. CMSS = Cox menstrual symptom scale, MA = manual acupuncture, NSAID = nonsteroidal anti-inflammatory drug, MSS = menstrual symptom score, RSS = Cox retrospective symptom scale, TER = total effective rate, VAS = visual analog scale.

Figure 5. Meta-analysis of the studies evaluating the effects of EA on primary dysmenorrhea. (A) EA versus PA, outcome: VAS. (B) EA versus PA, outcome: VRS. (C) EA versus NSAIDs, outcome: TER. EA = electroacupuncture, IV = inverse variance, NSAIDs = nonsteroidal inflammatory drugs, NSAID = nonsteroidal anti-inflammatory drug, PA = placebo acupuncture, SD = standard deviations, TER = total effective rate, VAS = visual analog scale, VRS = seven-point verbal rating scale.
### 3.4.4. Warm acupuncture

#### 3.4.4.1. WA versus NSAIDs. VAS.

Three studies\[32,46,65\] were included in the meta-analysis to synthesize VAS data. A meta-analysis of the 3 studies involving 178 participants was implemented, but the results showed serious heterogeneity (\(I^2=94\%\)). We conducted a sensitivity analysis by excluding the trial\[65\] with effect sizes largely different from the others. Statistical heterogeneity was reduced after exclusion. As shown in Figure 6A, with 2 remaining studies, the VAS of the WA group was significantly lower than NSAIDs group (n = 114, SMD = 1.12, 95% CI [1.81, 0.43], \(P = .002, I^2 = 66\%\)).

#### 3.4.4.2. WA plus NSAIDs versus NSAIDs. TER.

Two studies\[35,39\] reported that WA adding on NSAIDs provided significant pain relief compared to only NSAIDs after treatment of 3 menstrual cycles (n = 160, RR = 1.28, 95% CI [1.12, 1.46], \(P < .001, I^2 = 0\%\)).

### 3.4.5. Catgut embedding therapy

#### 3.4.5.1. CET versus NSAIDs. VAS.

One study\[26\] reported that CET was significantly more effective than NSAIDs after treatment of 3 menstrual cycles (n = 70, t = -2.70, \(P < .01\)).

#### 3.4.5.2. CET versus NSAIDs. TER. Two studies\[35,39\] reported that WA adding on NSAIDs provided significant pain relief compared to only NSAIDs after treatment of 3 menstrual cycles (n = 160, RR = 1.28, 95% CI [1.12, 1.46], \(P < .001, I^2 = 0\%\)).

#### 3.4.5.3. CET versus NSAIDs. MSS. Two studies\[26,71\] reported that CET effectively reduced menstrual symptoms compared to NSAIDs after treatment of 3 menstrual cycles with serious heterogeneity as shown in Figure 7B (n = 162, SMD = -1.57, 95% CI [-1.95, -1.19], \(P < .001, I^2 = 98\%\)).

#### AEs. Two studies\[54,65\] reported AEs. One study\[54\] reported 5 cases of nausea, vomiting, and fever in the NSAIDs group, and the other study\[63\] reported there were no AEs.

### Figure 6.

Meta-analysis of the studies evaluating the effects of WA on primary dysmenorrhea. (A) WA vs NSAIDs, outcome: VAS. (B) WA vs NSAIDs, outcome: TER. (C) WA plus NSAIDs vs NSAIDs, outcome: TER. CI = confidence interval, IV = inverse variance, NSAIDs = nonsteroidal anti-inflammatory drugs, SD = standard deviations, TER = total effective rate, VAS = visual analog scale, WA = warm acupuncture.
VAS after follow-up. One study reported[26] that after a 3-month follow-up, CET was significantly more effective than NSAIDs (n = 70, t = 4.72, P < 0.01).

AEs. One study reported 6 cases of gastrointestinal discomforts, headache, dizziness, and insomnia in the NSAIDs group.

4. Discussion

4.1. Summary of the main results

This systematic review was aimed to summarize and evaluate acupuncture treatment to reduce menstrual pain and its associated symptoms. As a result, we suggest that acupuncture might have beneficial effects for improvement of dysmenorrhea and remain efficacious after short-term follow-up.

We conducted comparisons separately according to the characteristics of interventions and controls. MA was significantly more effective than no treatment, and NSAIDs for reduction of menstrual pain and its associated symptoms, and remained effective after a short-term follow-up compared to no treatment and NSAIDs. The MA-induced analgesic effect could be explained by C-fiber involvement during the practitioners' manipulation for the de-qi response.[85] However, no significant difference was observed between MA and placebo acupuncture or between MA and OCs. It was difficult to determine the superior effect of OCs compared to MA because there was only one relevant study.[11]

The results showed that EA was significantly more effective at reducing menstrual pain than no treatment,[47,73,76,78] placebo acupuncture,[40,48,73–76,78,79] but not effective at improving its associated symptoms.[47,73,76] The results comparing with NSAIDs were inconclusive due to the small sample size. The results showed WA might also relieve menstrual pain compared to NSAIDs alone. WA increases the circulation of qi and blood through the needle body during thermal heating. It provides analgesic effects by stimulating nerve transfer and relaxing uterine muscle spasms.[91]

CET might also be effective for primary dysmenorrhea. CET is a therapeutic modality based on acupuncture theory and continuous stimulation of acupoints with embedded thread, and its continuous stimulation prolongs the effects of acupuncture. In addition, the embedded thread gradually liquefies and is absorbed, and stimulates the points physically and chemically.[24] With this mechanism, CET might be considered to demonstrate analgesic effects and maintain the effects for short-term follow-up.

Severe AEs of acupuncture were not observed. Thirteen of the 60 studies reported AEs of acupuncture. Most of the reported AEs were regional pain or discomfort, hematoma, and dizziness. Those mentioned were mild, similar to previously known AEs.[92]

The applicability of acupuncture to primary dysmenorrhea in other settings is unclear. Fifty-seven of the trials were conducted in Asian countries: 55 in China, 1 in Thailand, and 1 in South Korea. The acupuncture practitioners might have different treatment skills according to the nations in which they were trained, and the participants might have different preconceptions and familiarity with acupuncture according their cultures.[89] In addition, the variability of the details of interventions and controls could make applicability unclear.

4.2. Strengths and limitations of this review

Six SRs which evaluate the efficacy of acupuncture on primary dysmenorrhea have previously been conducted,[14–19] and 2 of them were published in 2016[17] and 2019[19], respectively. However, there were some differences between these 2 SRs and
our review. They may arise from the different search strategies, inclusion criteria, and analysis methods. In particular, the Cochrane review analyzed 42 studies, just separating the treatment types into acupuncture and acupressure. Liu et al. review analyzed 23 studies with similar strategies to our review, did not include 10 trials newly published in 2017, and did not include other modalities of acupuncture such as WA or CET, frequently used in clinical fields. Our review included all types of acupuncture that stimulate acupoints by penetrating the skin, including CET, and synthesized data separately according to the characteristics of the interventions and controls.

Our study had some limitations, and those results mentioned above should be interpreted with caution. One was that most of the included trials achieved a low or unclear risk of bias. The unclear judgements appeared mostly in the domains of allocation concealment and blinding of participants/practitioners/outcome assessors, because the details were not described. The blinding of participants is critical for subjective outcomes such as pain, but blinding of both participants and practitioners was difficult due to the characteristics of acupuncture intervention. The other limitation was that there was substantial heterogeneity among the pooled trials. We tried to reduce the heterogeneity by synthesizing the data separately depending on the characteristics of the interventions and controls, subgroup analysis, and sensitivity analysis, but the unresolved heterogeneity in some cases still existed. We considered this heterogeneity derived from the small sample sizes in some outcomes and the methodological variations among the included studies. The methods of interventions varied in the frequency, duration of each session, selection of acupoints, and de-qi methods. The variations of controls also appeared in different components of NSAIDs. These variations could influence the results of the trials, and were considered to cause unresolved heterogeneity.

4.3. Implications of this review for practice and research

To provide convincing evidence of the efficacy of acupuncture for primary dysmenorrhea, future RCTs should adhere to rigorous standards assessing the risk of bias, such as conducting randomization allocation concealment and trying to avoid performance bias. In addition, those trials should be reported as STRICTA guidelines to clear the specific method of each intervention.

5. Conclusions

The results of this study suggest that acupuncture might reduce menstrual pain and associated symptoms more effectively compared with no treatment or NSAIDs, and the efficacy could be maintained during a short-term follow-up period. However, the efficacy of acupuncture compared to a placebo was not convincing. The safety of acupuncture appeared because a few mild AEs were reported. Our suggestions had limitations because the quality of the included RCTs was low, and methodological restriction existed in this study. More rigorously designed trials are required to confirm our findings.

Author contributions

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