REGISTRED REPORT PROTOCOL

Efficacy and safety of Chinese herbal footbaths for the treatment of dysmenorrhea: Protocol for a systematic review and meta-analysis

Min Xiao1*, Lizhou Liu2*, Steve Tumilty2*, Dan Liu3, Yanyan You3, Yunhui Chen1*, Songqi Tang4*, Wei Huang1, George David Baxter2*

1 College of Clinical Medicine/College of Basic Medicine, Chengdu University of Traditional Chinese Medicine, Chengdu, Sichuan, China, 2 Centre for Health, Activity, and Rehabilitation Research, School of Physiotherapy, University of Otago, Dunedin, Otago, New Zealand, 3 West China Hospital, Sichuan University, South Renmin Road, Wu Hou District, Chengdu, Sichuan, China, 4 College of Traditional Chinese Medicine, Hainan Medical University, Haikou, Hainan, China

☯ These authors contributed equally to this work.
* chenyunhui@cdutcm.edu.cn (YC); tangsongqi@hainmc.edu.cn (ST); david.baxter@otago.ac.nz (GDB)

Abstract

Background

Chinese herbal footbaths are an external therapy of traditional Chinese medicine that has been widely used to treat dysmenorrhea. This review aims to systematically evaluate its efficacy and safety for the treatment of dysmenorrhea.

Methods

Databases of PubMed, EMBASE, Cochrane Library, CIHAHL, Web of Science, Chinese National Knowledge Infrastructure(CNKI), Chinese Scientific Journals Database (VIP), Wanfang Database, China Biomedical Literature Database(CBM), and Chinese Biomedical Literature Service System (SinoMed) will be searched from the inception to September 30, 2020. The eligible randomized controlled trials (RCTs) will be identified and included. The primary outcomes include pain intensity measured by validated scales of visual analog scale, numeric rating scale, and response rate of symptom reduction. The secondary outcomes are scores on validated pain questionnaires, quality of life measured by SF-36 or other validated scales, and adverse events. Study selection, data extraction, and assessment of bias risk will be conducted by two reviewers independently. RevMan software (V.5.3.5) will be utilized to perform data synthesis. Subgroup and sensitivity analysis will be performed when necessary. The strength of the evidence will be evaluated with the Grading of Recommendations Assessment, Development and Evaluation System.

Results

A high-quality synthesis of current evidence of Chinese herbal footbaths for patients with dysmenorrhea will be provided in this study.
Conclusion
This systematic review will provide evidence of whether Chinese herbal footbaths are an effective and safe intervention for the treatment of dysmenorrhea.

Systematic review registration
PROSPERO CRD42020188256.

Background
Dysmenorrhea refers to the throbbing or cramping pain in the lower abdomen occurring just before and during menstruation [1]. It is one of the most common gynecologic disorders and classified as primary or secondary dysmenorrhea based on pathophysiology. Primary dysmenorrhea is defined as menstrual pain without pelvic pathology, and secondary dysmenorrhea is usually due to identifiable organic pathologies, such as adenomyosis, endometriosis, and pelvic inflammatory diseases [2]. The prevalence of dysmenorrhea varies between 16% and 91% among women of childbearing age, while the prevalence reaches 80% in adolescents [3, 4]. It is frequently accompanied by nausea, bloating, vomiting, fatigue, diarrhea, headache, lower backache, and dizziness [5]. This ailment negatively influences women’s daily activities, impairs sleep quality, associates with anxiety and depression, represents a risk factor for fibromyalgia, lowers academic performance in adolescents, and decreases effectiveness in women’s daily tasks [6–9]. In severe cases, approximately 3 to 33% of women are absent from work or school for 1 to 3 days each cycle [10, 11]. In the United States alone, dysmenorrhea causes the loss of 600 million working hours and two billion dollars per year [12]. Hence, dysmenorrhea has been considered a public health matter with socio-economic impacts and calls for an increased need for medical care [13].

Previous studies indicate that the overproduced prostaglandins (PGs) may contribute to the pathomechanisms of dysmenorrhea. PGs are synthesized from arachidonic acid through the cyclooxygenase (COX) pathway. Increased PGs cause hypercontractility and hypoxia of uterine smooth muscle with decreased uterine blood flow and elevated sensitivity of peripheral nerves to pain [14]. Multiple factors such as vasopressin, oxytocin, calcium, oxidative stress, inflammation, and nitric oxide have also been implicated in the mechanism [15–17]. Currently, non-steroidal anti-inflammatory drugs (NSAIDs) are considered the first-line treatment for dysmenorrhea; however, they are ineffective for or intolerable by approximately 15% of patients and may cause gastrointestinal and neurological adverse effects and a higher risk of severe cardiovascular disease with long-term usage [18, 19]. Other options including oral, intravaginal, and intrauterine hormonal contraceptives are generally applicable only to the patients with the desire of contraception [20]. Hence, in recent years, there has been growing interest in integrative medicine, and more and more patients turn to traditional Chinese medicine (TCM) for help [21, 22]. Chinese herbal footbaths are an external therapy of TCM and have been developed and utilized in China to treat various diseases for over 3,000 years [23].

In the therapy of Chinese herbal footbaths, patients with dysmenorrhea are required to soak the feet and legs in a hot herbal infusion for 20 to 30 minutes. It is not just for relaxation, but more importantly, a comprehensive approach that integrates reflection effects, thermal effects, and pharmacological actions of Chinese herbs. In the theoretical system of TCM, the feet have channels and acupuncture points that correspond to viscera and different parts of the
body, and Chinese herbs absorbed through the skin and mucosa can act on the channels, acupuncture points, and viscera to relieve pain [24]. Chinese herbal formulas such as Shaofu Zhuyu Tang (Foeniculi Fructus, Zingiberis Rhizoma, Corydalis Rhizoma, Myrrha, Rhizoma Chuanxiong, Angelicae Sinensis Radix, Radix Paeoniae Rubra, Cortex Cinnamomi, Typhae Pollen, and Trogopteri Feces), Siwu Tang (Radix Rehmanniae Praeparata, Radix Angelicae Sinensis, Rhizoma Ligustici Chuanxiong, and Radix Paeoniae Alba), and Danggui Shaoyao San (Paeoniae Radix Alba, Angelica Sinensis Radix, Atractylodis Macrocephalae Rhizoma, Chuanxiong Rhizoma, Alismatis Rhizoma, and Poria) are commonly used to treat dysmenorrhea effectively based on pattern differentiation. Their pharmacologic effects on analgesia, spasmolysis, microcirculation, anti-inflammation, vasodilatation, and neuroprotection have been well-documented. Experiments have shown these herbal formulas can modulate PGE$_2$ and PGE$_{2\alpha}$ production, block calcium channel and COX-2, increase the expression of nitric oxide and its synthetase, downregulate the contents of oxytocin, vasopressin, endothelin-1, and malondialdehyde, reverse the increased superoxide, and decrease the levels of interleukin-6, tumor necrosis factor-2α, whole blood viscosity, and plasma viscosity [25–30]. Further, footbaths can also improve microcirculation and increase skin permeability to enhance the absorption of TCM herbal formulas and their active compounds [31, 32].

In recent years, a growing body of clinical trials has been conducted to assess the outcomes of Chinese herbal footbaths for the treatment of dysmenorrhea, and the results have suggested it might be an effective and safe therapeutic approach. However, currently no systematic review and meta-analysis have been reported for this specific malady. In this study, eligible randomized clinical trials (RCTs) will be included and systematically synthesized without language and publication restrictions. To the best of our knowledge, this meta-analysis is the first attempt to assess the available evidence of Chinese herbal footbaths for the treatment of dysmenorrhea. Hopefully, the findings of this study may provide helpful evidence for the patients, physicians, and investigators concerned.

Methods
Study registration
This systematic review protocol has been registered on PROSPERO (www.crd.york.ac.uk/prospero/) with number PROSPERO CRD42020188256. It will be performed in accordance with the reporting guidelines and criteria set in the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement checklist (S1 Checklist) [33].

Eligibility criteria
Types of studies. Randomized controlled trials (RCTs) that evaluated the effectiveness and safety of Chinese herbal footbaths for dysmenorrhea will be included. No restrictions will be made on publication status, language, or year of publication. Non-RCTs, reviews, animal-based research, conference proceedings, and literature review will be excluded.

Participants. Patients diagnosed with dysmenorrhea using any recognized diagnostic criteria will be included regardless of age, the source of cases, and the duration and severity of the disease.

Types of interventions. Dysmenorrhea patients are treated with Chinese herbal footbaths, either alone or in any combination with conventional treatments and other administrative forms of Chinese herbal medicine, will be included. There is no restriction regarding the conventional regimen.

Types of comparisons. Dysmenorrhea patients treated with conventional (the same conventional regimen as intervention group in the same original study), a different administrative
form of herbal medicine (such as decoction and pills), placebo, or no treatment will be included.

**Types of outcomes.** The primary outcomes include pain intensity measured by validated scales of visual analog scale [34], numeric rating scale [35], and response rate of symptom reduction. The secondary outcomes are scores on validated pain questionnaires [36], quality of life measured by SF-36 or other validated scales [37], and adverse events.

**Information source and search strategy**

Ten databases including the PubMed, EMBASE, Cochrane Library, CIHAHL, Web of Science, Chinese National Knowledge Infrastructure(CNKI), Chinese Scientific Journals Database (VIP), Wanfang database, China Biomedical Literature Database(CBM), and Chinese Biomedical Literature Service System (SinoMed) will be searched from the inception to September 30, 2020. Two reviewers will search the literature independently. The following terms will be used in a combination for the electronic search: dysmenorrhea, menstrual pain, painful menstruation, period pain, painful period, menstrual cramps, menstrual disorder, pelvic pain, menstrual cramps, painful menstrual periods, Chinese herbal footbaths, bath, hydrotherapy, herbal bathing, lavipeditum, randomized controlled trial, randomized, randomly, trials, and RCT. Any inconsistency will be solved by a third reviewer. Manual searches will be performed for relevant studies found in the reference lists of included studies. The search strategy for PubMed is presented in Table 1 and will be modified upon the requirement of other databases.

**Data collection and analysis**

**Study selection.** Tasks of screening, study selection, and data extraction will be performed independently by two reviewers. The literature will be input into the EndnoteX9 to screen the title and abstract, and the duplications and ineligible studies will be excluded. The final eligible studies will be included after reading the full text of the remaining studies. The corresponding author will be contacted if the full text is not available. Disagreements will be resolved by a third reviewer. The entire process of study selection is presented in a PRISMA flow chart (Fig 1).

**Data extraction and management.** The data extraction will be conducted by two reviews independently in a standard excel spreadsheet, including characteristics of reference ID, author information, year of publication, study type, study design, setting of study, sample size, participant characteristics (age, duration and severity of dysmenorrhea, etc.), Chinese herbal footbaths intervention group and control group (details of Chinese herbal footbaths formulation, randomization, blinding, allocation, intervention approach and duration), and primary and secondary outcome measurements. Studies with less than 30 participants will also be included. Disagreements will be solved by discussion. If the data provided in the research is unclear, missing, or difficult to be extracted reliably, the corresponding author will be contacted by email for clarification. All data will be cross-checked and transferred to RevMan software (V.5.3).

**Assessment of risk of bias.** Two reviewers will independently use the Cochrane risk-of-bias assessment tool to grade the risks of bias as high, unclear, or low risk of bias in terms of the following domains: randomization sequence generation, randomization allocation concealment, blinding of participants, blinding of personnel, blinding of outcome assessors, incomplete outcome data, selective reporting, and other bias. A third reviewer will be consulted for inconsistency. Funnel plots will be conducted to assess publication bias when the included studies are more than 10. If feasible, Egger regression and Begg correlation test will be conducted to identify the funnel plot asymmetry.
Measures of treatment effect. Two reviewers will use RevMan 5.3, independently to synthesize and statistically analyze the efficacy data. A risk ratio (RR) or odds ratio with 95% CIs will be employed for the dichotomous data, while a mean difference (MD) or standard mean difference (SMD) with 95% CIs will be utilized for the continuous data. SMD will be adopted if different assessment tools are used.

Dealing with missing data. If required data is elusive or missing, the reviewer will contact the corresponding author of the RCT reported by email. If data remains unobtainable, the reviewer will exclude the study. The potential impact of missing data will be assessed with a sensitivity analysis.

Assessment of heterogeneity. Heterogeneity will be assessed using Q-test and $I^2$ statistic. The fixed-effects model will be adopted if the heterogeneity deems low ($I^2<50\%$), the random-effects model will be applied for moderate heterogeneity (50% $< I^2 < 75\%$), and subgroup analysis or narrative analysis will be provided when the heterogeneity is high ($I^2>75\%$).

Data synthesis. In accordance with the Cochrane guideline, the fixed-effects model will be applied for the pooled data when the heterogeneity is low, the random-effect model will be utilized when heterogeneity is moderate, and a subgroup analysis or meta-regression will be conducted to investigate the potential sources if heterogeneity is considerably high. A $p$-value less than 0.05 is deemed as statistically significant. A narrative description will be provided when the meta-analysis is not feasible.

Table 1. Search strategy for the PubMed.

| No. | Search terms |
|-----|--------------|
| #1  | dysmenorrhea |
| #2  | menstrual pain |
| #3  | painful menstruation |
| #4  | period pain |
| #5  | painful period |
| #6  | cramps |
| #7  | menstrual disorder |
| #8  | pelvic pain |
| #9  | menstrual cramps |
| #10 | painful menstrual periods |
| #11 | #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 |
| #12 | Chinese herbal footbaths |
| #13 | bath* |
| #14 | hydrotherapy |
| #15 | herbal bathing |
| #16 | lavipeditum |
| #17 | #12 OR #13 OR #14 OR #15 OR #16 |
| #18 | #11 AND #17 |
| #19 | randomized controlled trial |
| #20 | randomized* |
| #21 | randomly* |
| #22 | trials |
| #23 | RCT |
| #24 | #19 OR #20 OR #21 OR #22 OR #23 |
| #25 | #11 AND #18 AND #24 |

*Represents one or more characters of all characters.

https://doi.org/10.1371/journal.pone.0250685.t001
Subgroup analysis. If the necessary data are available, subgroup analyses will be conducted for the subtype of dysmenorrhea (primary/secondary), severity and duration of dysmenorrhea, footbaths alone versus control group, footbaths in combination with other treatments versus control group, and primary outcome measurements.

Sensitivity analysis. Sensitivity analysis will be carried out if feasible, and the robustness of the pooled results of the included RCTs will be assessed from such perspectives as the methodological quality, sample size, missing data, or high risk of bias.

Grading the quality of evidence. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) will be applied to assess the strength of the evidence as high, moderate, low, or very low [38].

Ethics and dissemination plan. Ethical approval is unnecessary since this protocol is for systematic review and does not involve privacy data. Final reports of this study will be disseminated in peer-reviewed journals, the PROSPERO website, and relevant academic conferences. All data collected in the study, upon completion, will be made available with the publication of reports.

Discussion

Dysmenorrhea is one of the most common gynecological complaints that impair women’s quality of life and effectiveness of day-to-day activities. Conventional treatment for dysmenorrhea such as NSAIDs may induce severe adverse events, and therefore an increasing number of patients worldwide are using TCM to relieve the ailment. Chinese herbal footbaths are a unique external therapy of TCM and have attracted increasing attention due to their effectiveness, fewer side effects, and favorable adherence [23, 39, 40]. It has been considered an ideal combination of heat therapy, reflex therapy, and Chinese herbal therapy. In recent years,
several clinical trials have demonstrated the effectiveness and safety of Chinese herbal footbaths on the treatment of dysmenorrhea, indicating it may hold considerable promise for relieving dysmenorrhea. Herein, a critical evaluation and comprehensive synthesis of the available evidence will be performed in this systematic review to assess the efficacy and safety of Chinese herbal footbaths for the treatment of patients with dysmenorrhea. Hopefully, conclusions drawn from this study may benefit patients, physicians, and investigators concerned. The process of conducting this systematic review will include identification, study inclusion, data extraction, and data synthesis. If amendments were necessary, the date and statement of changes with corresponding reasons would be provided.

Supporting information
S1 Checklist. PRISMA 2009 checklist. (DOC)

Author Contributions
Conceptualization: Yunhui Chen, Wei Huang, George David Baxter.
Data curation: Min Xiao, Lizhou Liu, Dan Liu.
Formal analysis: Dan Liu, Yanyan You, Yunhui Chen.
Funding acquisition: Songqi Tang.
Investigation: Dan Liu, Yunhui Chen, Songqi Tang.
Methodology: Lizhou Liu, Steve Tumilty, Yunhui Chen, George David Baxter.
Project administration: Yunhui Chen, Wei Huang.
Supervision: Steve Tumilty, Songqi Tang, George David Baxter.
Validation: Min Xiao, Dan Liu, Yunhui Chen, Songqi Tang, Wei Huang.
Writing – original draft: Steve Tumilty, Yunhui Chen.
Writing – review & editing: Min Xiao, Lizhou Liu, Steve Tumilty, Yunhui Chen, George David Baxter.

References
1. Osayande AS, Mehulic S. Diagnosis and initial management of dysmenorrhea. Am Fam Physician. 2014 Mar; 89(5):341–6. PMID: 24695505
2. Proctor M, Farquhar C. Diagnosis and management of dysmenorrhoea. BMJ. 2006 May; 332(7550):1134–1138. https://doi.org/10.1136/bmj.332.7550.1134 PMID: 16690671
3. Ju H, Jones M, Mishra G. The prevalence and risk factors of dysmenorrhea. Epidemiol Rev. 2014; 36:104–13. https://doi.org/10.1093/epirev/mxt009 PMID: 24284871.
4. Agarwal AK, Agarwal A. A study of dysmenorrhea during menstruation in adolescent girls. Indian J Community Med. 2010 Jan; 35(1):159–164. https://doi.org/10.4103/0970-0218.62586 PMID: 20606943
5. Alsaleem MA. Dysmenorrhea, associated symptoms, and management among students at King Khalid University, Saudi Arabia: An exploratory study. J Family Med Prim Care. 2018 Jul-Aug; 7(4):769–774. https://doi.org/10.4103/jfmpc.jfmpc_113_18 PMID: 30234051
6. Hailermeskel S, Demissie A, Assefa N. Primary dysmenorrhea magnitude, associated risk factors, and its effect on academic performance: evidence from female university students in Ethiopia. Int J Womens Health. 2016 Sep; 8:489–496. https://doi.org/10.2147/IJWH.S112768 PMID: 27695366
7. Chantler I, Mitchell D, Fuller A. Actigraphy quantifies reduced voluntary physical activity in women with primary dysmenorrhea. J Pain. 2009 Jan; 10(1):38–46. https://doi.org/10.1016/j.jpain.2008.07.002 PMID: 18722817
8. Gagua T, Tkeshelashvili B, Gagua D, McHedishvili N. Assessment of anxiety and depression in adolescents with primary dysmenorrhea: a case-control study. J Pediatr Adolesc Gynecol. 2013 Dec; 26 (6):350–4. https://doi.org/10.1016/j.pjag.2013.06.018 PMID: 24075089
9. Iacovides S, Avidon I, Baker FC. What we know about primary dysmenorrhea today: a critical review. Hum Reprod Update. 2015 Nov-Dec; 21(6):762–78. https://doi.org/10.1093/humupd/dmv039 PMID: 26346058
10. Zannoni L, Giorgi M, Spagnolo E, Montanari G, Villa G, Seracchio R. Dysmenorrhea, absenteeism from school, and symptoms suspicious for endometriosis in adolescents. J Pediatr Adolesc Gynecol. 2014 Oct; 27(5):258–65. https://doi.org/10.1016/j.pjag.2013.11.008 PMID: 24746919
11. Bernardi M, Lazzeri L, Perelli F, Reis FM, Petraglia F. Dysmenorrhea and related disorders. F1000Res. 2016; 5:6145. https://doi.org/10.12688/f1000research.11682.1 PMID: 28944048
12. Proctor ML, Hing W, Johnson TC, Murphy PA. Spinal manipulation for primary and secondary dysmenorrhea. Cochrane Database Syst Rev. 2006 Jul; 2006(3):CD002119. https://doi.org/10.1002/14651858.CD002119.pub3 PMID: 16855988
13. Schoep ME, Adang EMM, Maas JWM, De Bie B, Aarts JWM, Nieboer TE. Productivity loss due to menstruation-related symptoms: a nationwide cross-sectional survey among 32 748 women. BMJ Open. 2019 Jun; 9(6):e026186. https://doi.org/10.1136/bmjopen-2018-026186 PMID: 31248919
14. Zhou SF, Wang HY. One review on the latest etiology research progress of primary dysmenorrhea. Reproductive and Developmental Medicine.2018 Dec; 2(3):171–177.
15. Dikensoy E, Balat O, Penc S, Balat A, Cekmen M, Yurekli M. Malondialdehyde, nitric oxide and adrenomedullin levels in patients with primary dysmenorrhea. J Obstet Gynaecol Res. 2008 Dec; 34 (6):1049–53. https://doi.org/10.1111/j.1447-0756.2008.00802.x PMID: 19012707
16. Szmidt MK, Granda D, Sicinska E, Kaluza J. Primary Dysmenorrhea in Relation to Oxidative Stress and Antioxidant Status: A Systematic Review of Case-Control Studies. Antioxidants (Basel). 2020 Oct; 9 (10):1191. https://doi.org/10.3390/antiox9101191 PMID: 33076228
17. Barciowska Z, Rajkowska-Labon E, Grzybowska ME, Hansdorfer-Korzon R, Zorena K. Inflammation Markers in Dysmenorrhea and Therapeutic Options. Int J Environ Res Public Health. 2020 Feb; 17 (4):1191. https://doi.org/10.3390/ijerph17041191 PMID: 32068959
18. Marjoribanks J, Ayeleke RO, Farquhar C, Proctor M. Nonsteroidal anti-inflammatory drugs for dysmenorrhea. Cochrane Database Syst Rev. 2015 Jul; 2015(7):CD001751. https://doi.org/10.1002/14651858.CD001751.pub3 PMID: 26224322
19. Harifuroosh S, Asghar W, Jamali F. Adverse effects of nonsteroidal antiinflammatory drugs: an update. Evid Based Med. 2018 Jul; 23(3):78–81. https://doi.org/10.1136/ebmed-2017-111613 PMID: 30137388
20. Burnett M, Lemyre M. No. 345-Primary Dysmenorrhea Consensus Guideline. J Obstet Gynaecol Can. 2017 Jul; 39(7):585–595. https://doi.org/10.1016/j.jogc.2017.04.017 PMID: 28625286
21. Yu A. Complementary and alternative treatments for primary dysmenorrhea in adolescents. Nurse Pract. 2014 Nov; 39(11):1–12. https://doi.org/10.1097/01.NPR.0000454984.19413.28 PMID: 25325520
22. Mittal R. Role of contemporary therapy in treatment of dysmenorrhea. International Journal of Advance Research, Ideas and Innovations in Technology. 2019 Jan; 5(1), 9–11.
23. Han L, Wei SB. Clinical Application of Chinese Herbal Footbaths for the Treatment of Gynecological Disorders. Hunan Journal of Traditional Chinese Medicine. 2013 Nov; 29(11): 145–146.
24. Chen J, Li Y, Su M. Progress and Prospects on the Development of Liposomes for Dermal and Transdermal Delivery Application in the Field of Traditional Chinese Medicine. Journal of Nanjing University of Traditional Chinese Medicine. 2013 Sep; 35(05):623–630.
25. Huang X, Su S, Duan JA, Sha X, Zhu KY, Guo J, et al. Effects and mechanisms of Shaofu-Zhuyu decoction and its major bioactive component for Cold—Stagnation and Blood—Stasis primary dysmenorrhea rats. J Ethnopharmacol. 2014 Jul; 154(3):696–703. https://doi.org/10.1016/j.jep.2014.04.044 PMID: 24837303
26. Liu P, Li W, Li ZH, Qian DW, Guo JM, Shang EX, et al. Comparisons of pharmacokinetic and tissue distribution profile of four major bioactive components after oral administration of Xiang-Fu-Si-Wu Decoction effective fraction in normal and dysmenorrheal symptom rats. J Ethnopharmacol. 2014 Jul; 154 (3):696–703. https://doi.org/10.1016/j.jep.2014.04.044 PMID: 24837303
27. Lee HW, Jun JH, Ki KJ, Ko BS, Lee CH, Lee MS. Herbal medicine (Danggui Shao-yao San) for treating primary dysmenorrhea: A systematic review and meta-analysis of randomized controlled trials. Maturitas. 2016 Mar; 85:19–26. https://doi.org/10.1016/j.maturitas.2015.11.013 PMID: 26857875
28. Fang Z, Lu B, Liu M, Zhang M, Yi Z, Wen C, et al. Evaluating the pharmacological mechanism of Chinese medicine Si-Wu-Tang through multi-level data integration. PLoS One. 2013 Nov; 8(11):e72334. https://doi.org/10.1371/journal.pone.0072334 PMID: 24223693
29. Park KS, Park KI, Hwang DS, Lee JM, Jang JB, Lee CH. A review of in vitro and in vivo studies on the efficacy of herbal medicines for primary dysmenorrhea. Evid Based Complement Alternat Med. 2014;2014:296860. https://doi.org/10.1155/2014/296860 PMID: 25431607.

30. Sosorburam Dorjbat, Wu ZG, Zhang SC, Hu P, Zhang HY, Jiang T, et al. Therapeutic effects of traditional Chinese herbal prescriptions for primary dysmenorrhea. Chinese Herbal Medicines. 2019 Jan; 11(1):10–19.

31. Matsumoto S, Shimodozono M, Etoh S, Shimozono Y, Tanaka N, Kawahira K. Beneficial effects of footbaths in controlling spasticity after stroke. Int J Biometeorol. 2010 Jul; 54(4):465–73. https://doi.org/10.1007/s00484-009-0300-x PMID: 20157740

32. Lee JH, Seo EK, Shim JS, Chung SP. The effects of aroma massage and foot bath on psychophysiological response in stroke patients. J Phys Ther Sci. 2017 Aug; 29(8):1292–1296. https://doi.org/10.1589/jpts.29.1292 PMID: 28878450

33. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009 Jul 21; 6(7):e1000097. https://doi.org/10.1371/journal.pmed.1000097 PMID: 19621072.

34. Reed MD, Van Nostran W. Assessing pain intensity with the visual analog scale: a plea for uniformity. J Clin Pharmacol. 2014 Mar; 54(3):241–4. https://doi.org/10.1002/jcph.250 PMID: 24374753

35. Williamson A, Hoggart B. Pain: a review of three commonly used pain rating scales. J Clin Nurs. 2005 Aug; 14(7):798–804. https://doi.org/10.1111/j.1365-2702.2005.01121.x PMID: 16000093

36. Melzack R. The McGill pain questionnaire: from description to measurement. Anesthesiology. 2005 Jul; 103(1):199–202. https://doi.org/10.1097/00000542-200507000-00028 PMID: 15983473

37. Endicott J, Nee J, Harrison W, Blumenthal R. Quality of Life Enjoyment and Satisfaction Questionnaire: a new measure. Psychopharmacol Bull. 1993; 29(2):321–6. PMID: 8290681.

38. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008 Apr; 336(7650):924–6. https://doi.org/10.1136/bmj.39489.470347.AD PMID: 18436948

39. Zeng HL, Li J. Traditional Chinese Medicine Foot Bath Application Profile. Journal of Practical Traditional Chinese Internal Medicine. 2014 Oct; 28(09):171–172.

40. Zheng HM, Li J. Clinical application of Chinese herbal footbaths: research progress. Jiangsu Journal of Traditional Chinese Medicine. 2013 Dec; 45(12):75–77.