INPLASY PROTOCOL

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None declared.

A Protocol for Effectiveness of Acupoint Application of Traditional Chinese Medicine in Treating Primary Dysmenorrhea : Meta-analysis and Data Mining

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Review question / Objective: **Acupoint application of traditional Chinese medicine has a certain therapeutic effect on primary dysmenorrhea, and the systematic evaluation of treatment results and prescriptions is helpful to better explain and apply this technique. In this study, we will explore the existing evidence related to the efficacy and safety of acupoint traditional Chinese medicine application in the treatment of functional constipation to help clinicians better use it in clinical practice.**
Information sources: **An electronic search will be conducted. We will confirm the relevant research from its establishment to July 15, 2020 from Cochrane Central controlled Trials Registry, PubMed, Embase, Science Network, China Biomedical Literature Database (CBM), China Science Journal Database (CSJD), Wanfang Database (Wanfang) and China National knowledge Infrastructure (CNKI). The following three trial registries will also be searched for ongoing studies: current controlled trials: http://www.controlled-trials.com; clinical trials: http://www.ClinicalTrials.gov; China Clinical trial Registry: http://www.chictr.org.cn/index.aspx.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 04 March 2021 and was last updated on 04 March 2021 (registration number INPLASY202130011).

INTRODUCTION

Review question / Objective: **Acupoint application of traditional Chinese medicine has a certain therapeutic effect on primary dysmenorrhea, and the systematic evaluation of treatment results and prescriptions is helpful to better explain and apply this technique. In this study, we will explore the existing evidence related to**

the efficacy and safety of acupoint traditional Chinese medicine application in the treatment of functional constipation to help clinicians better use it in clinical practice.

Condition being studied: Primary dysmenorrhea (PD) refers to periodic pain that occurs before and after menstruation without obvious organic lesions, mainly persistent and spasmodic dull pain, mainly concentrated in the abdomen, can be radiated to the waist and legs, head, etc., can be accompanied by diarrhea, nausea, vomiting, fatigue, dizziness, headache, occasional syncope and fever, so as to affect work and life. About 45% of women in the world suffer from primary dysmenorrhea, with an incidence of about 53% in China. Western medicine is mainly treated with oral non-steroidal anti-inflammatory drugs such as ibuprofen and cyclooxygenase-2 inhibitors, but due to cardiovascular risks, it is easy to cause adverse reactions in the gastrointestinal tract and central nervous system, so it is not easy to be accepted by patients. and found that the commonly used drugs are 25% ineffective. Surgical treatment can relieve pain by cutting off the nerve pathway (uterine nerve or presacral nerve), but it is traumatic and the curative effect is uncertain due to individual differences. Acupoint application is one of the external treatment methods of traditional Chinese medicine, which has the characteristics of definite curative effect, simple use and little side effects. it is widely suitable for common clinical diseases.

METHODS

Search strategy: An electronic search will be conducted. We will identify relevant studies from the Cochrane Central Register of Controlled Trials, PubMed, Embase, the Web of Science, the Chinese Biomedical Literature Database(CBM), the Chinese Scientific Journal Database(CSJD), the Wan-Fang Database(Wanfang) and the China National Knowledge Infrastructure (CNKI) from their inception to January 20, 2020. The search term will consist of 3 parts: intervention method, disease, and study type: ("acupoint appliaction" or " acupoint sticker" or "crude herb moxibustion" or "medicinal vesiculation" or "herbal patch" or "herbal plaster" or "acupoint patch" or "Sanfu" or "acupoint sticking" or "point application therapy" or "drug acupoint application" or "winter diseases treated with acupoint stimulation in summer" or "drugs and points for point application in summer to treat the diseases with attacks in winter" or "acupuncture point application therapies" or "plaster therapy" or "external application therapy" or "acupoint herbal patching") and ("primary dysmenorrhea "or"primary dysmenorrheal" or"primary painful menstruation " or"blood stasis primary painful menstruation" or"primay dysmenorrhea" or "primary pain" or"primary menstruation ache" or "idiopathic dysmenorrhea") and ("randomized controlled trial" or "randomized" or "case control studies" or "observational studies" or "case series" or "trial") and ("blind"). The details of the PubMed and Wan-Fang Database search strategies are provided in Tables 1 and 2. The similar but adaptive search strategies will be applied to other electronic databases. Language will be restricted to English and Chinese. Reference lists of relevant original studies will be screened to identify additional potentially citations. In addition, the following 3 trial registries will be searched for ongoing studies: Current Controlled Trials: http://www.controlled-trials.com; Clinical Trials: http://www.ClinicalTrials.gov; and Chinese Clinical Trial Registry: http://www.chictr.org.cn/index.aspx.

Participant or population: This review will include patients of any age diagnosed with primary dysmenorrhea, regardless of gender, race, study area, and educational status. The diagnostic criteria of primary dysmenorrhea refer to the Clinical guidelines for Primary dysmenorrhea issued by the Canadian Association of Obstetrics and Gynecology in 2017. Suprapubic pain that occurs in women before or a few hours after menstruation is most obvious at the peak of menstruation and lasts for 2 to 3 days. Pain is mostly

located in the middle of the lower abdomen, can be shown as colic pain, can also be shown as dull pain, and radiation to both sides of the lower abdomen, waist and thigh. Can be accompanied by diarrhea, nausea, vomiting, fatigue, dizziness, headache, occasional syncope and fever, affecting work and life. The obvious organic lesions of reproductive organs and other gynecological diseases were excluded by B-ultrasound and gynecological examination, such as endometriosis, adenomyosis or uterine leiomyoma.

Intervention: The experimental group was treated with acupoint application of traditional Chinese medicine, regardless of the treatment scheme of traditional Chinese medicine, acupoint selection and application time. There are no restrictions on the age and country of origin of the participants.

Comparator: The experimental group was treated with drug treatment, untreated, placebo, false acupoint catgut embedding or placebo acupoint catgut embedding, acupuncture / electroacupuncture, and other intervention measures in the control group were the same as those in the intervention group.

Study designs to be included: It includes randomized controlled trials, observational studies, case series and case-control studies. The following types of articles were excluded: case series, observational studies (including cohort studies and case-control studies) and retrospective studies, qualitative studies, animal experiments, review articles.

Eligibility criteria: Randomized controlled trial (RCT) compared the efficacy of important acupoint application in the treatment of primary dysmenorrhea with untreated, placebo or conventional drugs. All eligible trials will be included, regardless of language and publication type. There are no restrictions on the region, race, age and sex of the patients.

Information sources: An electronic search will be conducted. We will confirm the relevant research from its establishment to July 15, 2020 from Cochrane Central controlled Trials Registry, PubMed, Embase, Science Network, China Biomedical Literature Database (CBM), China Science Journal Database (CSJD), Wanfang Database (Wanfang) and China National knowledge Infrastructure (CNKI). The following three trial registries will also be searched for ongoing studies: current controlled trials: http://www.controlled-trials.com; clinical trials: http://www.ClinicalTrials.gov; China Clinical trial Registry: http://www.chictr.org.cn/index.aspx.

Main outcome(s): 1. Pain intensity, as a continuous variable, was measured by the visual analogue score ((VAS)), The Cox Menstrual Symptom Scale（CMSS） or other effective score. 2.The duration of pain: the number of hours of pain during the first three days of menstruation. 3. Quality of life is measured by effective scales, such as concise form (SF) 36.

Additional outcome(s): 1. The overall improvement in general menstrual symptoms (such as nausea and fatigue) was measured by changes in indicators of dysmenorrhea symptoms self-reported or observed by the researchers.2. Use of additional drugs (Measured by the percentage of women who need additional drugs).3. The adverse reactions of the treatment were measured by the incidence and type of side effects.

Quality assessment / Risk of bias analysis: Two review authors will independently evaluate each included study and will follow the domain-based evaluation as developed by the Cochrane Handbook for Systematic Reviews of Interventions. They will assess the following domains: (1) selection bias (random sequence generation and allocation concealment), (2) performance bias (blinding of participants and personnel), (3) detection bias (blinding of outcome assessment), (4) attrition bias (incomplete outcome data), (5) reporting

bias (selective reporting), (6) other bias (such as pre-sample size estimation, early stop of trial). Each domain will be divided into three categories: 'low risk', 'high risk', or 'unclear risk'.

Strategy of data synthesis: We will analyze the data with RevMan software (Version 5.3) (Available at: https://community.cochrane.org/help/tools-and-software/revman-5) provided by The Cochrane Collaboration.A meta-analysis using random or fixed effects models will be conducted to summarize the data. Continuous data will be pooled and presented as mean differences or standardized mean difference with their 95% CI. Dichotomous data will be pooled and expressed as risk ratio with their 95% CI. We will interpret it using the following criteria: I^2 values of 25% is considered low levels of heterogeneity, 50% indicated moderate levels, and 75% indicated high levels. Since low or moderate heterogeneity suggests little variability among these studies, the data will be analyzed in a fixed-effects model. When significant heterogeneity occurs among the studies ($P < 0.05$, $I^2 > 50\%$), a random-effect model will be performed to analyze the data.

Subgroup analysis: When substantial heterogeneity was detected, we explored the sources of heterogeneity by performing a subgroup analysis according to the type of intervention (such as catgut embedding, moxibustion, acupuncture, electroacupuncture, etc.) ,control group or syndrome types of TCM. We assessed publication bias by using a funnel plot if 10 or more studies were included. If the data is insufficient, qualitative synthesis will be conducted instead of quantitative synthesis.

Sensitivity analysis: To assess the influence of each individual study, leave-one-out sensitivity analysis was performed iteratively by removing one study at a time to confirm that the findings were not influenced by any single study.

Country(ies) involved: China.

Keywords: acupoint application of traditional Chinese medicine, supplementary and replacement therapy, acupoint application, primary dysmenorrhea, data mining, scheme, systematic review.

Conflicts of interest: We declare that we have no financial and personal relationships with other people or organizations that can inappropriately influence our work, there is no professional or other personal interest of any nature or kind in any product, service and/or company that could be construed as influencing the position presented in, or the review of, the manuscript entitled.

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