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Acupuncture for psoriasis: protocol for a systematic review

Lei Wang,[1,2] Haoyu Yang,[2] Nuo Li,[1] Weiming Wang,[3] Yanping Bai[1]

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[1]Department of Dermatology, China–Japan Friendship Hospital, Beijing, China
[2]School of Graduates, Beijing University of Chinese Medicine, Beijing, China
[3]Department of Acupuncture, Guang'anmen Hospital, China Academy of Chinese Medical Sciences, Beijing, China

Correspondence to
Professor Yanping Bai;
zhi@tsinghua.edu.cn

ABSTRACT

Introduction: The described systematic review aims to assess the effectiveness and safety of acupuncture for psoriasis.

Methods and analysis: We will electronically search for randomised controlled trials in the following databases from inception to 31 March 2015: OVID MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Chinese Biomedical Literature Database, Chinese Medical Current Content, Chinese Scientific Journal Database (VIP database), Wan-Fang Database and China National Knowledge Infrastructure. We will also try to obtain literature by manually searching reference lists, conference proceedings and registers of clinical trials (eg, the Meta Register of Controlled Trials and the Chinese Clinical Trial Registry). Changes in disease status as evaluated by clinical signs or any available tool will be measured as the primary outcome. Global changes as well as changes in participant status (as evaluated by quality of life), safety (as measured by the prevalence and severity of adverse effects or adverse events) and costs (if available) will be measured as secondary outcomes. Two researchers will independently undertake selection of studies, data extraction and assessment of the quality of included studies. Data synthesis and subgroup analyses will be performed using special software (Review Manager). Data will be combined with a random effect model. Results will be presented as risk ratios for dichotomous data and the standardised mean difference for continuous data.

Ethics and dissemination: Ethical approval will not be required as this is a protocol for a systematic review. The systematic review will evaluate the current evidence regarding acupuncture therapy for psoriasis. Findings will be disseminated through peer-reviewed publications and conference presentations.

Trial registration number: PROSPERO CRD 42014013695.

Strengths and limitations of this study

- This will be the first systematic review to assess the effectiveness and safety of acupuncture for psoriasis. It aims to provide a high-quality synthesis of current evidence for patients and dermatologists seeking alternative and effective approaches to psoriasis treatment.
- Study selection, data extraction and assessment of the risk of bias will be conducted independently by two authors.
- It will be difficult to pool data with various acupuncture therapies, so subgroup analyses will be conducted to address this problem.

classified as plaque, guttate, pustular or erythrodermic.[2] Psoriasis affects males and females equally, and usually occurs in the second-to-fourth decade of life.[3] It affects approximately 1–3% of individuals worldwide.[4] The prevalence has been estimated to be 1.5% in the UK,[5] and it affects 7.5 million patients in the USA.[6] Recent data have shown that the prevalence of psoriasis in China has increased from 0.35% in 1984[7] to 0.47% in 2012.[8]

Psoriasis causes considerable psychosocial disability and has a major impact on the quality of life of sufferers.[9] Patients with a diagnosis of psoriasis may also have an increased risk of psoriatic arthritis, obesity, dyslipidemia, hypertension, diabetes mellitus and cardiovascular disease (eg, myocardial infarction, stroke).[10] Thus, the cost of psoriasis to patients and healthcare systems is high.[11]

Psoriasis is regarded as an immune-mediated disease in which genetic and environmental factors have significant roles.[5] Psoriasis is most often chronic or can recur intermittently, so long-term therapy is required.[1] Conventional systemic therapy (eg, methotrexate, cyclosporine, acitretin, photochemotherapy) and biological agents (eg, efalizumab, etanercept, infliximab, adalimumab)[12] can result in only temporary remission of the physical symptoms of psoriasis. Moreover, most patients are dissatisfied with treatment because of the side effects and potential cumulative toxicity of these

INTRODUCTION

Psoriasis is a chronic, recurrent inflammatory skin disease that presents as discrete bright red macules, papules or patches covered with lamellated silvery scales.[1] Psoriasis can be

drugs, as well as the comorbidities associated with the disease (eg, dyslipidemia);[13] hence, there is a demand for more effective therapies.[14]

Acupuncture is an important component of Traditional Chinese Medicine. In recent years, it has been used widely for psoriasis in clinical trials.[15] A recent study showed that acupuncture can alleviate erythema, scales and the local thickening of maculae in some patients.[16] In pre-retrieval of eight electronic databases, we found more than 17 randomised controlled trials (RCTs) of acupuncture for treating psoriasis. However, the effectiveness and safety of acupuncture for psoriasis have not been reviewed systematically.

Thus, the aim of this systematic review is to assess the effectiveness and safety of acupuncture for psoriasis patients. The proposed systematic review will answer the aforementioned questions through the following comparisons:

1. Acupuncture alone versus no treatment (if available), placebo or sham treatment;
2. Acupuncture adjunctive to drug therapy versus the same drug therapy alone;
3. Acupuncture adjunctive to other treatment versus placebo or sham treatment adjunctive to other treatment.

METHODS
Types of studies
We will include RCTs that evaluated the effectiveness and safety of acupuncture for psoriasis. Randomised crossover studies and quasi-RCTs will be excluded. Dissertation and abstracts will be included if these studies contain sufficient details for critical evaluation.

Types of participants
Regardless of the subtype of psoriasis, all participants who have been diagnosed as having psoriasis will be focused on. There will be no restrictions on age, sex, ethnicity, education or economic status.

Types of interventions
Studies evaluating any type of acupuncture therapy (body acupuncture, auricular acupuncture, electroacupuncture, fire needling, warm needling, catgut embedding, pricking-cupping, slide-cupping) will be included in the review, regardless of the duration and frequency of treatment.

Control interventions could be 'no treatment', 'placebo acupuncture' (where a needle is attached to the skin surface, does not penetrate the skin, but is placed at the same acupoints as for actual acupuncture treatment), 'sham acupuncture' (non-point acupuncture, ie, 'minimal acupuncture') or 'drug therapy'.

Studies with the following comparisons will be included: (1) acupuncture alone versus no treatment (if available), placebo or sham treatment; (2) acupuncture adjunctive to drug therapy versus the same drug therapy alone; (3) acupuncture adjunctive to other treatment versus placebo or sham treatment adjunctive to other treatment.

We will exclude trials comparing only different forms of acupuncture, and those comparing acupuncture with drug therapy, as these studies cannot be used to detail the net effect of acupuncture or show if acupuncture is efficacious.

Types of outcome assessments
Primary outcomes
Changes in disease status as evaluated by signs (eg, the Psoriasis Area and Severity Index[17]) or any available tool will be measured as the primary outcome.

Secondary outcomes
We will look at four main secondary outcomes: (1) global changes (eg, proportion of participants whose symptoms improved after treatment); (2) changes in participant status as evaluated by quality of life (eg, Dermatology Life Quality Index[18]); (3) safety as measured by the prevalence and severity of adverse effects or adverse events and (4) cost (if available).

Search methods for identification of studies
Electronic searches
We will search the following electronic databases from inception to 31 March 2015 regardless of publication status: OVID MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Chinese Biomedical Literature Database, Chinese Medical Current Content, Chinese Scientific Journal Database (VIP database), Wan-Fang Database and China National Knowledge Infrastructure.

The search strategy has been decided on after a discussion among all reviewers according to the guidance provided by the Cochrane Handbook.[19] We will search the title, abstract and keywords using 'psoriasis', 'psora' or 'psoriasis vulgaris', and 'acupuncture', 'body acupuncture', 'auricular acupuncture', 'electroacupuncture', 'fire needling', 'warm needling', 'catgut embedding', 'pricking-cupping' or 'slide-cupping'. Chinese translations of these search terms will be used to search in Chinese databases. The search strategy for OVID MEDLINE is shown in table 1.

Other sources
We will examine the reference lists of reviews related to acupuncture and psoriasis to identify potentially eligible studies. We will also search conference proceedings in relation to acupuncture and psoriasis. Registers of clinical trials such as ClinicalTrials.gov (http://www.clinicaltrials.gov), the Meta Register of Controlled Trials (http://www.controlled-trials.com) and the Chinese Clinical Trial Registry (http://www.chictr.org/cn/) will also be searched.

Data collection and analyses
Selection of studies
This systematic review is scheduled to be completed between 30 November 2014 and 1 July 2015. Before

Table 1 Search strategy used in the OVID MEDLINE database

Number	Search terms
1	randomized controlled trial.pt.
2	controlled clinical trial.pt.
3	randomized.ab.
4	randomized.ab.
5	placebo.ab.
6	randomly.ab.
7	trial.ab.
8	groups.ab.
9	or 1–8
10	exp psoriasis/
11	psoriasis vulgaris. ti, ab. {Including Related Terms}
12	psora. ti, ab. {Including Related Terms}
13	or 10–12
14	exp acupuncture therapy, or acupuncture
15	acupuncture. ti, ab. {Including Related Terms}
16	body acupuncture. ti, ab. {Including Related Terms}
17	auricular acupuncture. ti, ab. {Including Related Terms}
18	electroacupuncture. ti, ab. {Including Related Terms}
19	fire needling. ti, ab. {Including Related Terms}
20	warm needling, ti, ab. {Including Related Terms}
21	catgut embedding, ti, ab. {Including Related Terms}
22	pricking-cupping, ti, ab. {Including Related Terms}
23	slide-cupping, ti, ab. {Including Related Terms}
24	or 14–23
25	9 and 13 and 24

This search strategy will be modified as required for other electronic databases.

selection of studies, a consensus on screening and subsequent procedures will be developed by discussion among all reviewers. Two reviewers (LW and HY) will independently check titles and abstracts retrieved from the search and select all potentially relevant studies. Records will then be moved to and managed by a database set up by EndNote version X6. The two reviewers will read the titles, abstracts and full texts (if required) to choose studies meeting the inclusion criteria. We will also contact the authors of the included studies for clarification (if necessary). None of the reviewers will be blinded to the names of the authors, institutions or journal of publication. Disagreements will be discussed by all reviewers and judged by an arbiter (YB). Details of the selection procedure for studies are shown in a PRISMA flow chart (figure 1).

Extraction and management of data
Two independent reviewers (LW and HY) will extract data using a piloted data extraction form that will be discussed and developed by all reviewers. Disagreements

will be discussed by all reviewers and judged by an arbiter (YB). The following data will be extracted:
1. General information: reference identification, the first author of the article, time of publication and the source/journal.
2. Study methods: design (eg, parallel design), randomisation method, method of allocation concealment, incomplete data, blinding, selective reporting and other sources of bias.
3. Participants: inclusion/exclusion criteria, number (total/per group), age and sex distribution and duration of psoriasis.
4. Interventions and controls: type of acupuncture/control and details of treatment/control regimen, including duration of treatment.
5. Outcome measurement: as described above in the type of outcome measures section.

Assessment of risk of bias in included studies
Two reviewers (LW and HY) will independently assess the risk of bias of the included studies using the tool for assessment of the risk of bias detailed in the Cochrane Collaboration.[19] Disagreements will be discussed by all reviewers and judged by an arbiter (YB). Six domains of each trial will be assessed: generation of random sequences, allocation concealment, blinding, incomplete outcome data, selective reporting and other sources of bias. Studies will be categorised into three levels of bias: low risk, high risk and unclear risk.

Measure of treatment effect
For dichotomous outcomes, data will be expressed as the relative risk (RR) with 95% CIs. For continuous outcomes, the standard mean difference (SMD) with 95% CI will be used. Analyses will involve all participants in the treatment groups to which they were allocated (if such data are available).

Unit of analysis issues
The primary unit of analysis will be every randomised individual. If there are two different control groups in a parallel-group trial, we will separately report a pairwise comparison. If two or more different intervention groups exist in the studies, pairwise comparison results will be presented through different subgroups of intervention in a particular comparison, and their results will not be combined into a single summary measure.

Dealing with missing data
If required data are missing, not sufficient or have not been reported in the included studies, we will attempt to contact the first author or corresponding author of the studies by telephone, email or post to obtain the requisite information. If this strategy does not elicit the required information, we will analyse only available data.
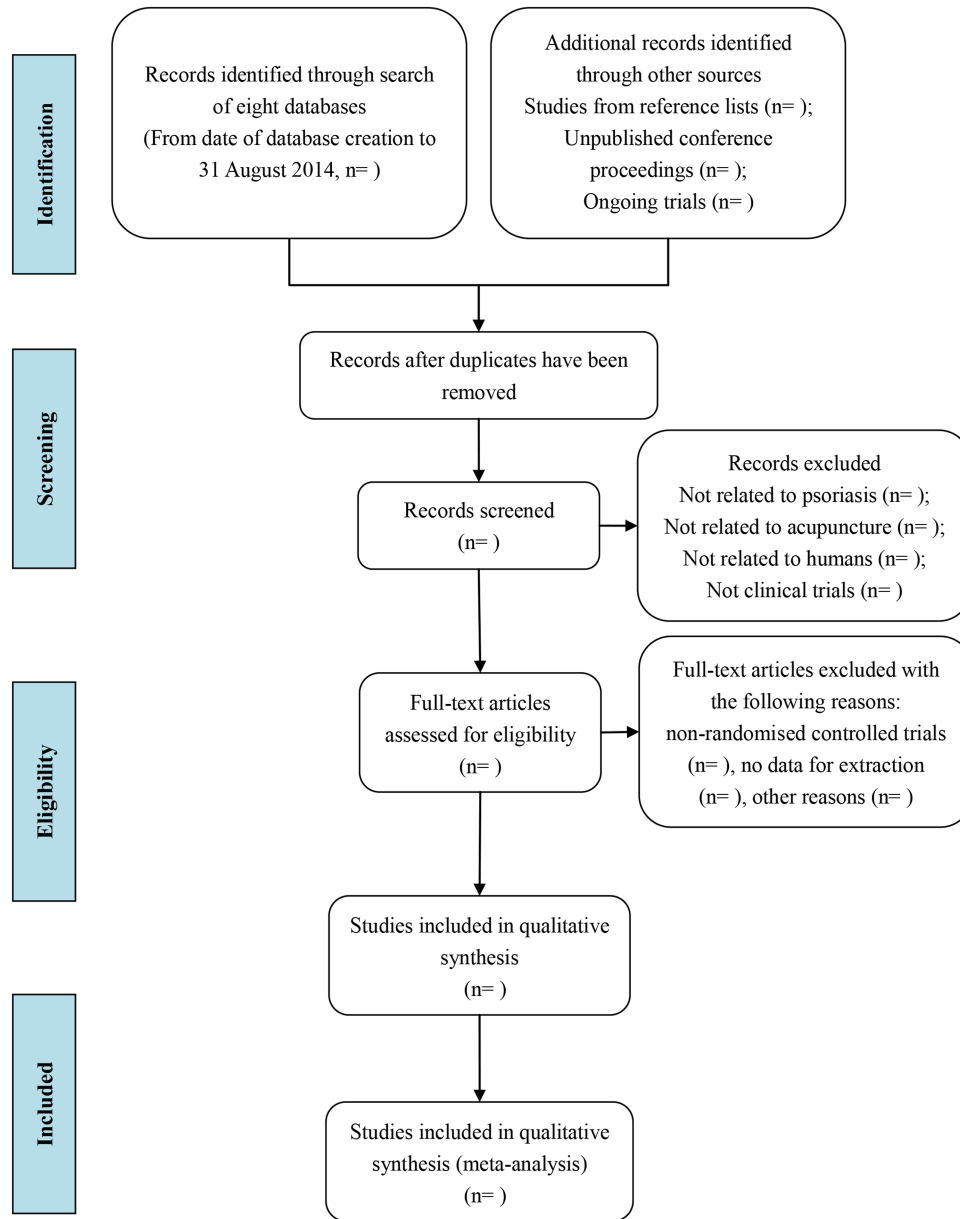
Figure 1 Selection process of studies.

Assessment of heterogeneity

We will assess the heterogeneity of the studies before conducting the meta-analysis. Clinical and methodological heterogeneity will be evaluated by noting differences in the distribution of important participant factors between trials and different factors in the trial design. Assessment of statistical heterogeneity will be done using the χ^2 test (significance level: 0.1) and I^2 statistic (an I^2 value of 0% to 50% will be taken to indicate that heterogeneity may not be important, while I^2 values of 50–100% may represent substantial heterogeneity). If there is a low level of heterogeneity among the studies ($I^2 < 50\%$ or $p \geq 0.1$), we will conduct a meta-analysis. If $I^2 \geq 50\%$ or $p < 0.1$, we will consider that significant heterogeneity exists among included trials and a systematic narrative synthesis will be done instead.[20]

Assessment of reporting biases

Funnel plots will be generated to assess reporting biases if sufficient studies (more than 10) are found for the same outcome. Asymmetric funnel plots could occur because of publication biases. A language bias will occur because the study search will focus on Chinese and English medical databases.

Data synthesis

Data synthesis will be conducted using a software program from the Cochrane Collaboration (Review Manager [RevMan] V.5.3 for Windows). For dichotomous data, we will combine the RRs of each study and calculate values for 95% CI using a fixed-effect model if heterogeneity is not detected; we will apply a random effect model if significant heterogeneity is detected.

For continuous data, we will combine the SMD of each study and calculate the 95% CI according to the outcome measurement.

Subgroup analyses

Subgroup analyses will be carried out if sufficient RCTs can be identified according to different interventions, controls and outcome measures. Duration of treatment and combination of treatment (acupuncture or acupuncture adjunctive to another therapy) will also be considered.

Sensitivity analyses

To ensure the robustness of our results, sensitivity analyses will be conducted to remove the impact of lower quality studies, provided that significant heterogeneity still exists after subgroup analyses and verification of inputted data. The meta-analysis will be carried out again after lower quality studies have been removed. We will compare the results of these two meta-analyses, and then make a decision on whether the lower quality studies will be excluded on the basis of sample size, strength of evidence and influence on pooled effective size. However, if all included studies have a high risk of bias, we will not carry out sensitivity analyses.

Grading the quality of evidence

We will judge the quality of evidence for all outcomes using the Grading of Recommendations Assessment, Development, and Evaluation working group methodology.[21] We will assess the quality of evidence through the domains of risk of bias, consistency, precision, publication bias and other domains where appropriate. Quality will be rated as high (further research is very unlikely to change our confidence in the estimate of effect), moderate (further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate), low (further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate) or very low (very uncertain about the estimate of effect).

Ethics and dissemination

This systematic review will not require formal ethical approval because all data used will be anonymous with no concerns regarding privacy. Results will provide a general overview and evidence of the effectiveness and safety of acupuncture therapy for psoriasis. Findings will be disseminated through peer-reviewed publications and conference presentations.

DISCUSSION

Use of complementary and alternative medicines is common among people with skin diseases, especially those with psoriasis.[22] Acupuncture has been used for psoriasis treatment in China[23] and the developed countries.[24] Some studies have suggested that acupuncture is an effective therapy for psoriasis. However, one RCT concluded that classical acupuncture was not superior to sham (placebo) minimal acupuncture for the treatment of psoriasis.[24] A systematic review assessing the effectiveness and safety of acupuncture for psoriasis has not been conducted. We presented a protocol for a systematic review of acupuncture for psoriasis. This review may offer evidence-based information for patients and dermatologists about acupuncture in psoriasis treatment.

The strengths of our review may be twofold. First, our search strategy is comprehensive and includes searching reference lists, conference proceedings and trial registries related to acupuncture and psoriasis. Second, the study selection, data extraction and assessment of the risk of bias will be conducted independently by two authors.

Nevertheless, this systematic review will be limited by methodological challenges inherent in the included trials. Acupuncture therapy can be subdivided into types according to the type of manipulation and needling instrument. Acupuncture therapy may vary greatly in the included studies. Subgroup analyses may resolve this problem and ensure the consistency of interventions, but it will reduce the comparability of included studies and increase the difficulty of meta-analysis. As a result, the systematic review may draw an inaccurate conclusion.

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