

Effectiveness comparisons of acupuncture for psoriasis

A Bayesian network meta-analysis protocol

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Abstract

Background: Psoriasis is an immune-mediated polygenic hereditary skin disease quality of the patients' life because of the great trouble it causes to patients. Whereas there is variability when we regard the selection of acupuncture treatments in practice and most choices are made based on personal experience or preference of clinician. This study uses network meta-analysis to compare the effectiveness of different forms of acupuncture for psoriasis and assesses the evidence with the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach.

Methods: We will search for PubMed, Cochrane Library, AMED, EMBASE, WorldSciNet; Nature, Science online and China Journal Full-text Database (CNKI), China Biomedical Literature CD-ROM Database (CBM), and related randomized controlled trials included in the China Resources Database. The time is limited from the construction of the library to April 2019. The quality of the included RCTs will be evaluated by the risk of bias (ROB) tool and the evidence will be evaluated by GRADE. STATA 13.0 and WinBUGS 1.4.3 through the GeMTC package will be used to perform a network meta-analysis to synthesize direct and indirect evidence.

Results: The results of this network meta-analysis (NMA) will be submitted to a peer-reviewed journal for publication.

Trial registration number: PROSPERO CRD42019123437

Abbreviations: CI = confidence interval, CNKI = China National Knowledge Infrastructure, Development and Evaluation, GRADE = Grading of Recommendations Assessment, MD = mean difference, NMA = network meta-analysis, PASI = psoriasis area and severity index, RCT = randomized controlled trial, ROB = risk of bias, SMD = standardized mean difference, TCM = traditional Chinese medicine, VIP = China Science and Technology Journal.

Keywords: a network meta-analysis, acupuncture, protocol, psoriasis

1. Introduction

Psoriasis is an immune-mediated polygenic hereditary skin disease. The typical clinical manifestation of psoriasis is scaly erythema or plaque, which is shown as localized distribution or widespread distribution.^[1,2] Psoriasis is a systemic disease that is often accompanied with injury of joints. Patients who suffer from

moderate to severe psoriasis will have an increased risk of suffering metabolic syndrome and atherosclerotic cardiovascular disease.^[3] This disease can be divided into 4 types of clinical classification, which include vulgaris type, arthropathic type, erythrodermic, and pustular type.^[4] At present, the incidence of psoriasis is yearly increasing, which seriously affects the quality of patients' lives because of the great trouble it causes to patients. According to reports, the incidence of psoriasis accounts for 0.1% to 3% of the worldwide population.^[5] A survey in the United States in recent years has shown that its incidence is 2.6%, which means an account of as many as 6 to 7 million.^[6,7] The cause and mechanism of psoriasis are still being explored. Yet, recently, it has been recognized that psoriasis is controlled by multiple genes and is also affected by factors such as heredity, infection, metabolism, and immune dysfunction. Besides, seasonal changes, long-term wetlands, mental stimulation or trauma, surgery, etc. may induce or exacerbate the disease.^[8,9] Because of its stubbornness and high recurrence rate, curing psoriasis has long been a major mission in the worldwide medicine.

According to the current US Psoriasis Treatment Guide, there are 5 main therapies for this disease: traditional systemic therapy, biologics, topical therapy, phototherapy, and photochemotherapy.^[10] However, there are toxic and side effects if we adopted long-term traditional systemic therapy or biological agents. For example, long-term use of methotrexate can cause liver damage and increase the risk of liver fibrosis in patients.^[11,12]

Z-yX, YZ, and SD contributed equally to the study.

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Cycloheximide has nephrotoxicity and kidney damage would be caused with long-term use. Biological preparations have good clinical effects due to their targeting effects, but some preparations are too broadly targeted or too much inhibited which lead to immunosuppression, infection, or even death. Thus, the use period is short, because the safety of long-term use remains to be verified^[13]; although phototherapy is effective and cost-efficient, its application could not widely promote due to the lack of equipment in some medical institutions.

Psoriasis belongs to the category of “Baibi” in traditional Chinese medicine. Traditional Chinese medicine refers to this disease as “Baibi” and “pine bark lichen.”^[14,15] It is named because of the rash-like, white, and itchy skin that could easily pick up. Wind, heat, humidity, poison, phlegm, and phlegm are important factors of the disease. Among them, “poisonous evil” is the key of the disease. “Blood fever” is the main pathological basis of this disease. Yin and Yang disorders of Zang and Fu organs are the basic pathogenesis of this disease.^[16,17] Acupuncture, 1 characteristic treatment of traditional Chinese medicine provides therapy through the acupuncture stimulation, which makes the blood of the meridian Yu points dredged. Therefore, the yin and yang of the 5 internal organs tend to balance. Acupuncture has long history, significant clinical effects, and numerous relative clinical reports.^[18] However, the experimental design and quality of these studies are mixed with good and evil. To some degree, it affects the reliability of the research conclusions which makes the research results difficult to be recognized by the medical community. This study conducted a meta-analysis of published literature based on current research status and we expect to use a network meta-analysis to evaluate the efficacy and safety of acupuncture in the treatment of psoriasis to provide clues for clinical application and research.

2. Methods

This is a systematic review and ethical approval is not necessary.

2.1. Study registration

This systematic review protocol has been registered on PROSPERO as CRD42019123437. (https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=123437)

2.2. Eligibility criteria

2.2.1. Type of study. Randomized controlled trials of acupuncture (electroacupuncture, fire needle, plum blossom needle, acupuncture, embedding) or acupuncture combined with other effective interventions (drugs or other) as treatment methods, and the control group (effective methods other than acupuncture) must exist. The language is limited to Chinese and English. Nonrandomized controlled trials, quasi-randomized controlled trials, case series, case reports, crossover studies will be excluded.

2.2.2. Participants. The patient must be at least 18 years of age and less than or equal to 65 years of age. Gender is not restricted. The stage or severity of the disease is not limited. Psoriasis must be diagnosed according to at least 1 internationally or nationally authorized diagnostic criterion. The international standard refers to the diagnostic criteria for psoriasis in the “Cecil Textbook of Medicine.” Domestic standard refers to the diagnostic criteria for psoriasis in “Skins and Venereology,” “Clinical Dermatology,” or “Integrated Chinese and Western Medicine Skin Dermatology.” The groups were well balanced when they were enrolled.

2.2.3. Types of interventions

2.2.3.1. Experimental interventions. The acupuncture in treating psoriasis will be regarded as experimental interventions, which includes the use of acupuncture, electro-acupuncture, fire acupuncture, plum needle, the massage on the related acupoints. Besides, acupuncture combined with other effective interventions to treat psoriasis will also be included. Considering that the theory of pharmaco-acupuncture and point injection belongs to another part of TCM, which means that they will be considered for exclusion.

2.2.3.2. Control interventions. As for the control interventions, who accepted virtual acupuncture treatment can be used as a placebo-controlled or did not get any treatment or other conventional treatments as a blank control would be adopted. However, once they had accepted acupuncture combined medication or other therapy of TCM, the trials will be rejected.

2.2.4. Outcomes. The primary outcome measurement is based on the psoriasis area and severity index (PASI) scoring criteria. Healing: The rate of decline in PASI score after treatment was >90%. Markedly effective: the rate of decline in PASI score after treatment is 60% to 89%. Effective: The decline rate of PASI score is 20% to 59%. Invalid: The decline rate of PASI score is <20%. PASI score decline rate = (pretreatment PASI score – post-treatment PASI score) / pretreatment PASI score × 100%. Total effective rate = (number of recovery cases + number of effective cases) / total number of cases 100%.

The second outcome measure is based on TCM syndrome evaluation criteria. Healing: The clinical symptoms and signs of TCM disappear or almost disappear, and the syndrome score is reduced by ≥90%. Significant effect: The clinical symptoms and signs of TCM are obviously improved, and the syndrome score is reduced by ≥60%. Effective: Chinese medicine Clinical symptoms and signs have improved, syndrome scores decreased by <60%, but ≥30%. Invalid: The clinical symptoms and signs of TCM were not improved, even worse, and the syndrome score was reduced by <30%. Integral variation formula (Nimodipine method): [(pretreatment score – post-treatment score) ÷ pretreatment score] × 100%.

2.2.5. Data source. Database Search: PubMed, Cochrane Library, AMED, EMBASE, WorldSciNet, Nature, Science online, and China National Knowledge Infrastructure (CNKI), China Biomedical Studies CD-ROM Database (CBM), China Resources Database. A studies review of clinical studies on acupuncture (or acupuncture) for the treatment of psoriasis published in domestic and foreign biomedical journals from the establishment of the library to April 2019. Based on the standards of the Cochrane Collaboration Workbook of the International Evidence-Based Medicine Center, a combination of manual searching and computer-based retrieval will be used to search relevant studies. Search terms include: acupuncture, electroacupuncture, fire needle, plum blossom needle, skin needle, psoriasis, baibi, pine bark lichen. Manual searching would point to the titles and abstracts of the relevant researches in “The Chinese Journal of Dermatovenereology,” “Chinese Acupuncture,” and “Moxibustion,” and “Acupuncture Research.” The complete PubMed search strategy is summarized in Table 1.

2.2.6. Study selection. Applying the EndnoteX7 software to manage the included references. Two qualified evaluators

Table 1**Search strategy used in PubMed database.**

Number	Search terms
1	acupuncture or acupuncture therapy
2	acupoints. ti, ab
3	acupuncture. ti, ab.
4	body acupuncture. ti, ab.
5	manual acupuncture. ti, ab.
6	electro-acupuncture. ti, ab.
7	Electro-acupuncture. ti, ab.
8	dermal needle. ti, ab.
9	skin acupuncture. ti, ab
10	ear acupuncture. ti. ab.
11	auricular acupuncture. ti, ab
12	scalp acupuncture. ti, ab.
13	ocular acupuncture. ti, ab
14	fire needling. ti, ab
15	warm needling. ti, ab.
16	plum blossom needle. ti, ab.
17	or 1-16
18	psoriasis.,ti,ab/
19	pine bark lichen.ti,ab.
20	Baibi.ti,ab
21	or 18-20
22	randomized controlled trial. pt.
23	controlled clinical trial. pt.
24	randomized. ab.
25	placebo. ab.
26	randomly. ab.
27	trial. ab.
28	or 22-27
29	exp animals/ not humans. sh.
30	28 not 29
31	17 and 21 and 30

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

independently screened the titles and abstracts of the selected studies, excluding duplicates and documents that did not significantly conform to the study. After a preliminary evaluation, the selected documents will be read one by one. Exclusions were based on inclusion criteria for uncontrolled studies, no randomization, inconsistent assessment criteria, and similar data. If there were different opinions, the third reviewer should be consulted. Studies information and data extraction were carried out on the final included studies, including the experimental methods of the study, the basic information of the included cases, the observation period, the intervention methods, observation indicators, and test results of the treatment group and the control group (Fig. 1).

2.2.7. Risk of bias. The quality of the studies will be assessed by using the Cochrane Handbook 5.1.0 (Cochrane Handbook 5.1.0). The assessment will include random sequence generation, randomization correctness, allocation scheme hiding, blinding of patients and implementers, accuracy of data results, and other risk of bias. The risk of low bias is expressed as “low risk” and the risk of high bias is expressed as “high risk.” The information provided in the studies is inaccurate or does not provide sufficient information for the bias assessment to be expressed as “unclear risk.” The above content evaluation was independently evaluated by 2 researchers, and any differences will be resolved through discussions with the third reviewer.

2.2.8. Statistical analysis

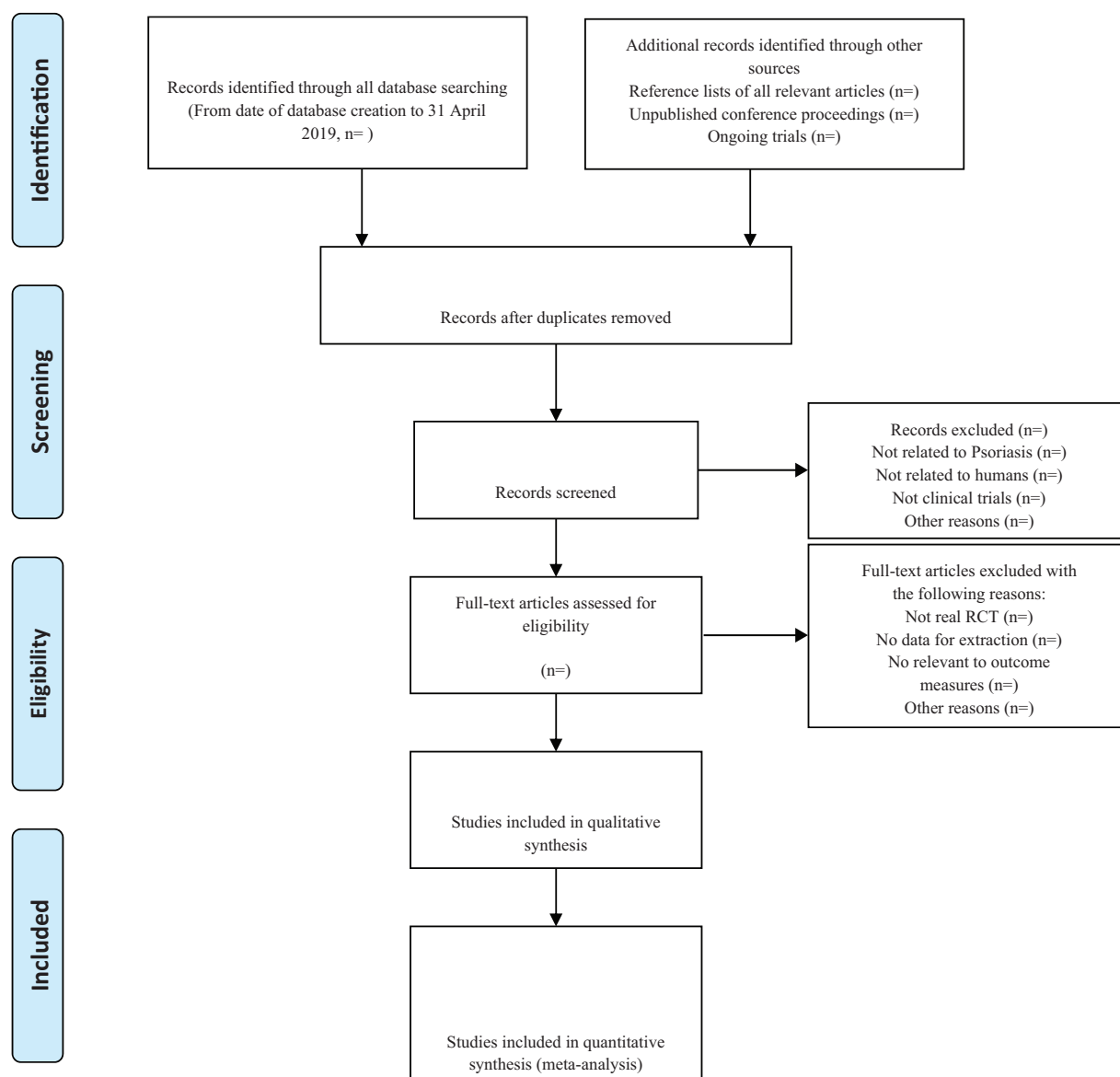
2.2.8.1. Pairwise meta-analysis. The numerical variable will be expressed as the standardized mean difference (SMD) with a confidence interval (CI) of 95%. The heterogeneity of each pairwise comparison will be tested by χ^2 test (test level $\alpha=0.1$). If there were no heterogeneity, a fixed effect model would be used. If there were significant heterogeneity between a group of studies, we would explore the reasons for the existence of heterogeneity from various aspects such as the characteristics of the subjects and the degree of variation of the interventions. Sensitivity analysis or meta-regression and subgroup analysis to explore possible sources of heterogeneity if it is necessary. We will use qualitative analysis of the funnel plot and graph symmetry to assess publication bias. Quantitative methods such as Begg testing and Egger testing will be used to help assess publication bias in the application.

2.2.8.2. Network meta-analysis. STATA 13.0 and WinBUGS1.4.3 through the GeMTC package will be used to perform network meta-analysis (NMA) to synthesize direct and indirect evidence. The NMA will be undertaken primarily in WinBUGS using the Markov chain Monte Carlo method.^[19] Convergence of the simulations will be evaluated with potential scale reduction factor and Gelman-Rubin-Brooks plots.^[20] The selection of the final model will depend on the deviance information criterion (DIC) value. Generally, a model with a smaller DIC value is better.^[21] Numerical variables will be presented as SMD with 95% credible intervals. The rank of treatments for each outcome will be conducted as surface under the cumulative ranking curve. The evidence relationship of included studies will be figured out by STATA. If there is a “closed loop,” the node splitting method will be used to evaluate the inconsistency of each loop.^[22,23]

2.2.8.3. Quality of evidence. The GRADE method will also be used to assess the quality of evidence for key outcomes. This assessment will be conducted through a Guideline Development Tool (GRADEpro GDT, <https://gradepro.org/>).

3. Discussion

Psoriasis is an immunological skin disease characterized by T lymphocyte-mediated hyperproliferation of keratinocytes. Its etiology and pathogenesis have been extensively studied domestic and overseas, yet it is still unclear.^[24,25] Psoriasis has been reported all over the world. Due to the distinction of ethnicity, geographical location, and environment, the prevalence of different populations exists with great difference. The disease is prone to recurrence and has a long course of disease, and it is more likely to invade young adults. The disease has serious impacts on the health and mental state of patients and it is one of the refractory skin diseases.^[26] With the deep understanding of psoriasis and its complications, the trials and clinical reports of Chinese medicine treatment of psoriasis have been gradually increasing. As 1 part of traditional Chinese medicine, acupuncture has the characteristics of small side effects, simple and easy to use, and has long been used to treat immune skin diseases. Acupuncture therapy mainly achieves the therapeutic effect by stimulating the body's righteousness and regulating the balance of qi and blood.^[27] Although many studies have evaluated the effectiveness of acupuncture in the treatment of psoriasis, there is



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Figure 1. The PRISMA flow chart.

still a lack of evaluation and comparison of various treatments. To the best of our knowledge, NMA has not been used in recent years to compare the effectiveness of acupuncture in the treatment of psoriasis. The results of NMA can provide a possible ranking for acupuncture treatment of psoriasis. In addition, we will use the GRADE method to assess the quality of evidence for key outcomes. We hope that the results will provide clinicians with the best options for treating psoriasis and provide them with research directions. Although we will conduct a comprehensive search in this study, languages other than Chinese and English will be limited, which will lead to some bias. In addition, the literature on acupuncture treatment of psoriasis has a small sample size and low overall quality, which may affect the authenticity of this study. Therefore, the author hopes that in the future, there will be more rigorous and reasonable multicenter

randomized controlled trials to explore the clinical efficacy of acupuncture treatment of psoriasis, so that assure the objectivity and rationality of conclusion.

Author contributions

Data curation: Zhi-yin Xie, Yu Zhou, Sheng Deng, Wei Ding.

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Writing – review & editing: Yu Zhou, Xing-wu Duan.

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