

BMJ Open Acupuncture for treating alopecia areata: a protocol of systematic review of randomised clinical trials

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ABSTRACT

Introduction: Acupuncture is frequently used in dermatology for treating a number of skin disorders. There is no critically appraised evidence of the potential benefits and harm of acupuncture for alopecia areata (AA). This review aims to systematically evaluate the efficacy of acupuncture for the management of AA in randomised clinical trials (RCTs).

Methods and analysis: 13 databases will be searched from their inception. These include PubMed, AMED, EMBASE, the Cochrane Library, 6 Korean medical databases (Koreanstudies Information Service System, DBPIA, The Town Society of Science Technology, Research Information Sharing Service, KoreaMed and the Korean National Assembly Library), 3 Chinese Databases (China National Knowledge Infrastructure Database (CNKI), the Chongqing VIP Chinese Science and Technology Periodical Database (VIP) and the Wanfang Database). Only randomised clinical trials (RCTs) using any type of acupuncture for AA will be considered. The selection of the studies, data abstraction and validation will be performed independently by two researchers. Methodological quality will be assessed with Cochrane risk of bias.

Dissemination: The systematic review will be published in a peer-reviewed journal. The review will also be disseminated electronically and in print. Updates of the review will be conducted to inform and guide the healthcare practice and policy.

Trial registration number: PROSPERO 2015: CRD42015020397.

INTRODUCTION

Description of the condition

Alopecia areata (AA) is a type of alopecia characterised by no scarring hair loss. The condition is found in 0.1–0.2% of the general population.^{1–3} The cause of AA appears to be related to the disturbance of autoimmune functioning, physical stress, genetic factors and microcirculation.^{1 2} AA could cause significant psychological problems, result in reduced self-esteem and negatively affect the quality of life.^{1 2} The

Strengths and limitations of this study

- The strength of this systematic review is its extensive, unbiased search of various databases without a language restriction.
- The trial screening, data extraction and assessing risk of bias will be conducted independently by two of the authors.
- Our systematic review may pertain to the potential incompleteness of the evidence reviewed, including publication and location bias, poor quality of the primary data and poor reporting of results.

first-line treatments are topical immunotherapy for extensive disease and intralesional corticosteroids for localised hair loss in patches.^{1 2}

Description of the intervention

Acupuncture is one of the most frequently used forms of complementary medicine.⁴ Acupuncture involves the insertion of needles into the skin and underlying tissues at acupuncture points for a therapeutic purpose. Acupuncture points (body, ear, head or tongue) could be stimulated with several types of acupuncture needles, electricity, laser, pressure or heat. The procedure is frequently used in dermatology for treating a number of skin disorders.^{5 6} The most frequently used acupuncture technique is plum-blossom acupuncture (PBA), in which the skin should appear flushed, with bleeding.^{7 8}

How the intervention might work

Acupuncture might help to reduce hair loss by reducing TI attacks on the hair bulb. Additionally, it might stimulate the hair follicles, warm the local collaterals and activate blood circulation.⁸ A recent study shows that electroacupuncture reduces degranulation of the mast cells in the dermis⁹ that is reported to be a possible cause of pathological

changes causing AA. The reliable evidence is unclear.

Why it is important to this review

Acupuncture is frequently used in dermatology for treating a number of skin disorders, including AA.^{5 6} There is no critically appraised evidence such as a systematic review or meta-analysis of the potential benefits and harm of acupuncture for AA.

Objectives

This review aims to systematically evaluate the efficacy of acupuncture for the management of AA reported in randomised clinical trials (RCTs).

METHODS

Study registration

The protocol of this systematic review has been registered on PROSPERO 2015 (registration number: CRD42015020397). This systematic review protocol will be conducted and reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines. We will document the important protocol amendments in the full review.

Criteria for considering studies for this review

Type of studies

RCTs and quasi-RCTs will be included. Cluster RCTs, non-randomised clinical studies, observational studies and case studies will be excluded. Dissertations and abstracts will be included, and no restriction on publications will be imposed. For duplicate publications with different outcome measures originating from one trial and published as separate papers, the original publication will be given priority and the other publications will be excluded.

Type of participants

Trials involving participants with AA regardless of sex, age and cause will be included.

Type of interventions and controls

Trials in which any type of acupuncture was used as an adjunct to conventional treatment, usual care or standard or other types of complementary therapies will also be included if the control group received the same concomitant treatments as the acupuncture group. The studies that compared two types of acupuncture will be excluded.

Type of outcome measures

Primary outcomes:

- ▶ Hair regrowth
- ▶ Response rate
- ▶ Rate of hair loss

Secondary outcomes:

- ▶ Quality of life

- ▶ Satisfaction with the appearance of hair
- ▶ Adverse events

Search methods for identifying the studies

Electronic searches

The following electronic databases will be searched from inception: PubMed, AMED, EMBASE, the Cochrane Central Register of Controlled Trials and the Cochrane Database of Systematic Review, DARE, six Korean Medical Databases (Koreanstudies Information Sharing Service, DBPIA, The Town Society of Science Technology Research Information Sharing Service, KoreaMed and the Korean National Assembly Library) and three Chinese Medical Databases (CNKI, VIP and Wangfang).

Searches of other resources

Additionally, we will manually search our departmental files and relevant journals (Focus on Alternative and Complementary Therapies and Forschende Komplementärmedizin und Klassische Naturheilkunde). The references in all the located articles will be manually searched for further relevant articles. Dissertations and abstracts will be included.

Study strategies

Our search strategy will include main keywords ‘acupuncture’ and ‘alopecia areata’ (see online supplement 1).

Data collection and analysis

Study selection

Two of the authors (HWL and JHJ) of the review independently will screen the titles and abstracts of the searched studies, perform the study selection and recorded their decisions on a standard eligibility form. The arbitrator (MSL) will decide on the study selection when a consensus cannot be reached. The details of the selection process will be shown in the PRISMA flow diagram (figure 1).

Data extraction and management

All of the included articles will be read in full. Three independent reviewers (HWL, JHJ and JAL) will extract the data, including the methods (eg, design, blinding, duration of follow-up), sample (eg, population size, conditions, age, duration of disease), intervention and control treatment, and outcome measures, according to the predetermined criteria. The extracted data will be tabulated for further analysis. Details regarding the acupuncture and control interventions will be extracted on the basis of the revised Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA). Any disagreement among the authors will be resolved by discussion with all of the authors. When the reported data are insufficient or ambiguous, one author (MSL) will contact the corresponding authors of the included studies by e-mail or telephone to request additional information or clarification.

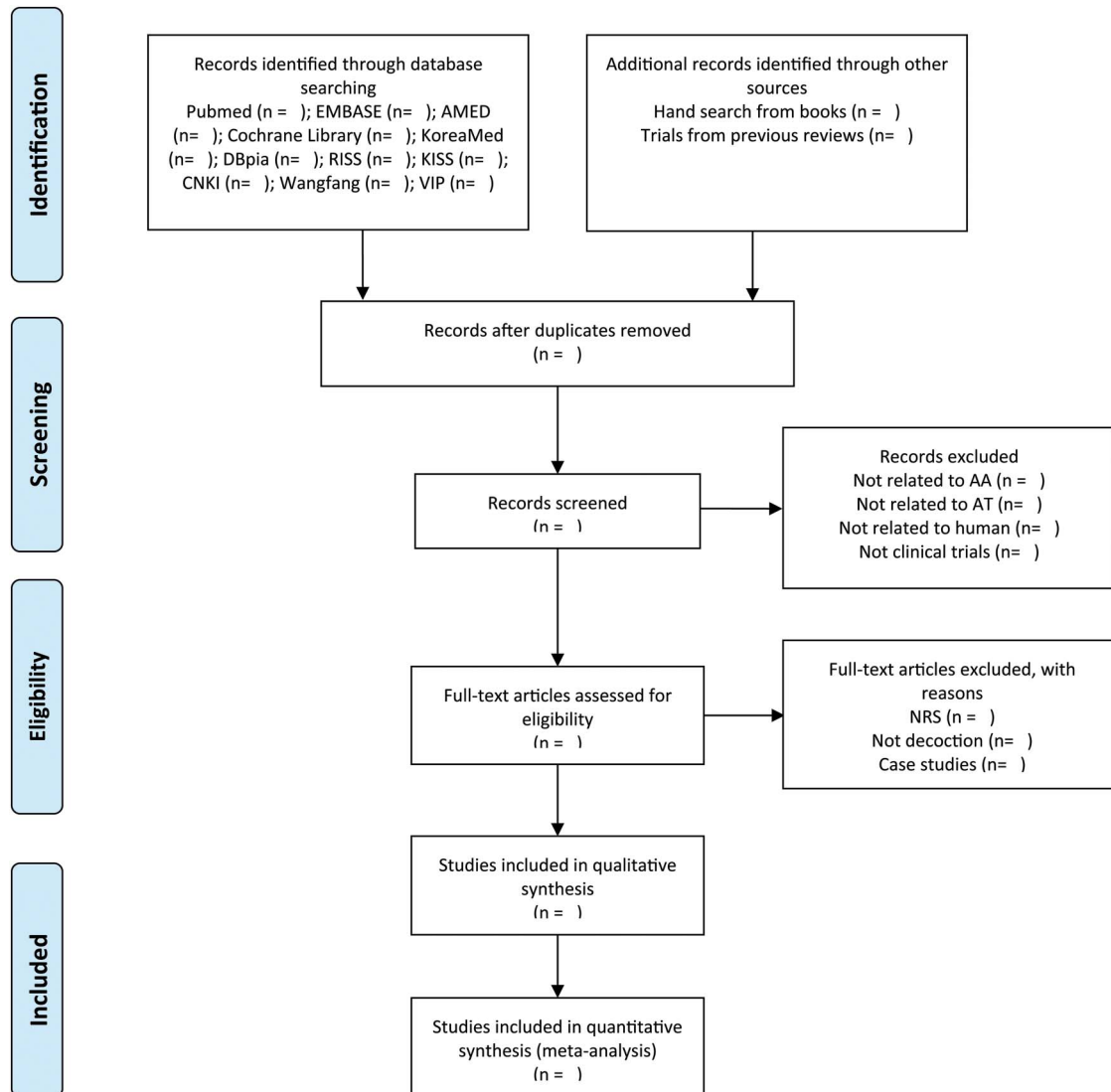


Figure 1 Flow diagram of the trial selection process. AA, alopecia areata; AT, acupuncture; NRS, non-randomised studies.

Assessment of risk of bias in included studies

According to the guidelines of the Cochrane Handbook of Systematic Reviews of Interventions, the risk of bias will be assessed to evaluate the methodological quality of the included studies.¹⁰ The following domains will be evaluated for methodological quality: sequence generation, allocation concealment, blinding of participants and outcome assessors, incomplete outcome data and selective outcome reporting. Blinding of practitioner is not possible because of the nature of acupuncture; therefore, only the blinding of participants and outcome assessors will be evaluated. The evaluated domains will be judged as ‘Low,’ ‘High’ or ‘Uncertain’ according to the criteria of the Cochrane guidelines.

Assessment of the quality of acupuncture

Acupuncture is a complex intervention with many possible variations in its delivery. We will assess the quality of the acupuncture by the reviewer (JAL and JHJ) as described previously reported;¹¹ the reviewer’s answer to the question, “how would you treat the patients included

in the study?” will be in five categories, including ‘exactly or almost exactly the same way’, ‘similarly’, ‘differently’, ‘complete differently’ or ‘could not assess’ due to insufficient information (on acupuncture or on the patient). The degree of confidence that acupuncture will be applied appropriately was assessed on the 100 mm visual analogue scale (with 0%=complete absence of evidence that acupuncture was appropriate, and 100%=total certainty that acupuncture was appropriate). Discrepancies will be resolved through discussions between the two reviewers.

Measures of treatment effect

Dichotomous data will be presented as a risk ratio (RR) with 95% CIs. For continuous data, the mean difference (MD) will be used with 95% CIs. In cases of outcome variables with different scales, the standard mean difference (SMD) will be used instead of the weighted MD (WMD).

Unit of analysis issues

The meta-analysis will include data from parallel group design studies. In the case of cross-over trials, we will use

the first phase of the data. If there are multiple time point observations, the data will be analysed as either a short-term (within 4 weeks) or long-term (over 4 weeks) follow-up.

Dealing with missing data

If missing data are detected, we will request any missing or incomplete information be given by the original study investigators.

Assessment of heterogeneity

A fixed-effects model and a random-effects model will be simultaneously used for the meta-analysis. Heterogeneity will be tested with the Higgins I^2 test. We will calculate the I^2 statistic, which provides a measure of the inconsistencies among the included studies. We will use a 50% cut-off point for meaningful heterogeneity among the included studies. If heterogeneity is observed, subgroup analysis will be conducted.¹²

Assessment of reporting biases

Funnel plots will be used to detect reporting biases and small-study effects. If more than 10 studies are included in the meta-analysis, the test for funnel plot asymmetry will be conducted using Egger's method.^{13 14}

Data synthesis

If a significant number of studies are identified, a meta-analysis will be conducted with simultaneous use of fixed-effect and random-effect models. All statistical analyses will be performed using RevMan 5.2.7 (the Cochrane Collaboration) software. To summarise the effects of acupuncture on outcomes (response rate), we will abstract the risk estimates (relative risk, RR) and 95% CIs. We will use the mean difference with 95% CIs for continuous outcomes. For studies with insufficient information, we will contact the primary authors to acquire and verify data, where possible. If appropriate, we will then pool the data across studies using random-effect models. The strength of the body of evidence will be assessed with GRADE.

Subgroup analysis and investigation of heterogeneity

To explore differences in effect sizes, subgroup analyses will be conducted on the following topics: the severity of depression, sex, the type of acupuncture, the design of the trial (eg, crossover group or parallel group), the dose of acupuncture and treatment frequency. We will also summarise the standardisation and characteristics of acupuncture from all included studies. In the case of sham controlled trials, we will analyse the results according to the three types of sham acupuncture, including acupuncture without penetration at the acupuncture points, acupuncture with penetration at the acupuncture points in shallow or no stimulation, and acupuncture penetration at non-acupuncture points.

Sensitivity analysis

Sensitivity analysis will be conducted according to the following criteria:

1. Methodological qualities (sequence generation, allocation concealment, or blinding)
2. Sample size (small sample studies, eg, less than 40 participants in each group, or large sample studies, eg, more than 40 participants in each group).

Ethics and dissemination

Ethical approval is not required given that this protocol is for a systematic review. The findings of this review will be disseminated widely through peer-reviewed publications and conference presentations.

DISCUSSION

This systematic review will provide a detailed summary of the current state of evidence on the effectiveness of the acupuncture in treating AA. There are several issues which will be discussed in the full review, including acupuncture as a complex intervention, no inertness of sham acupuncture and practitioner blinding. The review will benefit patients and practitioners in the field of traditional and complementary medicine.

Contributors HWL and MSL conceived the study. The protocol was drafted by HWL, JAL, JHJ, HJL, HSL and MSL. The search strategy was developed and will be run by HWL and JHJ. Copies of studies will be obtained by JHJ and HJL. Selection of the studies to be included will be carried out by HWL and JHJ. MSL will act as an arbiter in the study selection stage. Extraction of data from studies will be conducted by HWL, JHJ, and JAL. Entering data into RevMan will be conducted by HJL and HSL. Carrying out the analysis will be performed by HWL, JHJ and MSL. Interpretation of the analysis will be performed by HWL, JHJ, JAL, HJL, HSL and MSL. The final review will be drafted by HWL, JHJ, JAL, HJL, HSL and MSL. The review will be updated by HWL, JHJ and MSL.

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Competing interests None declared.

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