INPLASY

Efficacy of acupuncture for chronic urticaria: a systematic review and meta-analysis of randomized controlled trials

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 September 2025 and was last updated on 18 September 2025.

INTRODUCTION

Review question / Objective To evaluate the efficacy and safety of acupuncture for chronic urticaria (CU) compared with antihistamines alone, and to determine whether adding acupuncture to antihistamines provides additional clinical benefit.
PICOS framework:
1. Population (P): Patients with CU of any age, sex, or disease duration, using diagnostic definitions consistent with national or international guidelines.
2. Intervention (I): Interventions were acupuncture given alone or with standard antihistamines, including manual acupuncture (MA), electroacupuncture (EA), auricular acupuncture, acupoint catgut embedding (ACE), and bloodletting therapy (with or without cupping). Trials using other traditional Chinese medicine methods (moxibustion, herbal medicine, additional pharmacologic agents beyond antihistamines) or non-needle techniques (laser acupuncture, acupressure) were excluded.
3. Comparator (C): Comparators were limited to antihistamine therapy alone.
4. Outcomes (O): Effective rate; Urticaria Activity Score over 7 days (UAS7); Dermatology Life Quality Index (DLQI); Serum total immunoglobulin E (IgE); Interleukin 4 (IL-4); Interferon gamma (IFN-γ).
5. Study design (S): Randomized controlled trials (parallel-group), with no language restrictions.

Rationale CU presents with recurrent wheals or angioedema for at least 6 weeks and can markedly affect quality of life. Second-generation oral antihistamines are the recommended first-line therapy, but many patients have incomplete control or require dose escalation. Access to advanced agents may be limited, which sustains interest in adjunctive or alternative options such as acupuncture. Randomized trials have examined acupuncture for CU, either as monotherapy or combined with antihistamines, yet results are variable. Earlier reviews often mixed needle and non-needle procedures, used inconsistent

outcome definitions, and incompletely captured Chinese-language studies, which lowers clinical interpretability. Comparisons were not always anchored to a single control, so it remains uncertain whether acupuncture alone or acupuncture plus antihistamines provides benefit over antihistamines alone. Safety reporting has also been inconsistent. This review will focus strictly on needle-based acupuncture and two prespecified contrasts: 1) acupuncture versus antihistamines alone; and 2) acupuncture plus antihistamines versus antihistamines alone. We will assess UAS7 and trial-defined clinical response, quality of life (DLQI), selected biomarkers including total IgE, IL-4, and IFN-γ, and treatment-emergent adverse events. Planned subgroup analyses by acupuncture modality and antihistamine class, together with sensitivity analyses and a formal risk-of-bias assessment, aim to address heterogeneity and the certainty of the evidence.

Condition being studied CU is a relapsing inflammatory skin disorder defined by recurrent wheals, pruritus, and sometimes angioedema that persist for at least 6 weeks. It includes chronic spontaneous urticaria, where no specific external trigger is identified, and chronic inducible urticarias, which are provoked by stimuli such as pressure, cold, or heat. Lesions are transient, typically resolving within 24 hours, yet the disease can fluctuate for months to years and substantially impairs sleep, work productivity, and quality of life. Pathophysiology centers on mast cell activation with release of histamine and other mediators. Proposed mechanisms include type I autoimmunity related to IgE, type IIb autoimmunity with IgG autoantibodies to FcεRI or IgE, neuroimmune interactions, and contributions from infections or medications in selected patients. Disease activity often follows an unpredictable course with periods of remission and relapse. Guideline-based management recommends second-generation oral H1 antihistamines as first-line therapy, with dose escalation for inadequate control. Patients who remain symptomatic may receive add-on agents such as leukotriene receptor antagonists, omalizumab, or ciclosporin, although access and tolerability can vary. Clinical assessment commonly uses the UAS7 to quantify symptoms and the DLQI to capture patient-reported impact. Biomarkers such as total IgE and selected cytokines are sometimes reported in trials, and recurrence after treatment discontinuation is a clinical concern. This review focuses on this disease context.

METHODS

Search strategy

Databases and dates:

– PubMed, Embase, Web of Science Core Collection, Cochrane CENTRAL, and CNKI, from inception to July 2025. No language limits. We will also search ClinicalTrials.gov, WHO ICTRP, and screen reference lists of eligible studies and reviews.

Scope:

– CU and needle-based acupuncture only. Eligible designs are randomized controlled trials. Non-needle traditional procedures such as moxibustion, cupping, bloodletting, acupressure, laser acupuncture, and pharmacopuncture will be excluded during screening.

Search concepts:

– Acupuncture terms: Acupuncture Therapy, acupuncture, manual acupuncture, electroacupuncture, acupoint catgut embedding, auricular acupuncture, scalp acupuncture.
– CU terms: Urticaria, chronic urticaria, chronic spontaneous urticaria, hives, wheal, angioedema.
– Trial filter: randomized, randomised, randomly, randomized controlled trial, placebo, sham.

Example PubMed string:

("Urticaria"[Mesh] OR urticaria OR "chronic urticaria" OR "chronic spontaneous urticaria" OR hives OR wheal* OR angioedema) AND ("Acupuncture Therapy"[Mesh] OR acupuncture OR "manual acupuncture" OR electroacupuncture OR "acupoint catgut embedding" OR "auricular acupuncture" OR "scalp acupuncture") AND (randomized controlled trial[pt] OR randomized[tiab] OR randomised[tiab] OR randomly[tiab] OR placebo[tiab] OR sham[tiab]) NOT (moxibustion[tiab] OR cupping[tiab] OR bloodletting[tiab] OR acupressure[tiab] OR laser[tiab] OR pharmacopuncture[tiab]).

Participant or population People with CU, defined as recurrent wheals with or without angioedema for at least 6 weeks. No restrictions on age, sex, setting, geography, or disease duration. Trials that specifically enroll CSU are eligible. Studies limited to acute urticaria will be excluded.

Intervention Interventions were acupuncture given alone or with standard antihistamines, including MA, EA, auricular acupuncture, ACE, and bloodletting therapy (with or without cupping). Trials using other traditional Chinese medicine methods (moxibustion, herbal medicine, additional pharmacologic agents beyond antihistamines) or

non-needle techniques (laser acupuncture, acupressure) were excluded.

Comparator Oral antihistamines alone as usual care. Any agent or class and dose strategy as defined in the trials. For multi-arm trials, effect estimates will be anchored to the antihistamine-only control.

Study designs to be included Parallel group randomized controlled trials, including two arm and three arm designs. No blinding restrictions. Quasi randomized trials, non randomized studies, crossover trials, single arm studies, and observational designs will be excluded. No language restrictions will be applied.

Eligibility criteria Inclusion:
1. Parallel group randomized controlled trials with at least one eligible contrast: a) acupuncture monotherapy vs oral antihistamines alone, or b) acupuncture plus oral antihistamines vs oral antihistamines alone.
2. Participants diagnosed with CU defined as wheals with or without angioedema for at least 6 weeks. Trials that specifically enroll CSU or mixed CU are eligible.
3. Needle-based acupuncture limited to manual body acupuncture or acupoint catgut embedding.
4. Report at least one prespecified outcome such as UAS7, trial-defined clinical response, DLQI, IgE, IL-4, IFN-γ, recurrence, or adverse events.
5. No language restrictions. Full text available or sufficient data for effect estimation.

Exclusion:
1. Non-randomized, quasi-randomized, crossover, single-arm, or observational designs.
2. Comparators without an antihistamine only control, for example acupuncture vs sham acupuncture without antihistamines.
3. Non-needle traditional procedures such as moxibustion, cupping, bloodletting, acupressure, laser procedures, pharmacopuncture, or auricular-only techniques.
4. Concomitant herbal medicine or other adjuncts beyond antihistamines in either arm.
5. Acute urticaria only, or trials exclusively enrolling chronic inducible urticarias without CSU or general CU.
6. Duplicate publications or overlapping datasets, where the most complete or latest report will be retained.

Information sources Electronic databases: PubMed, Embase, Web of Science Core Collection, Cochrane CENTRAL, and CNKI, from inception to July 2025, without language restrictions. Trial registries: ClinicalTrials.gov and WHO ICTRP to identify ongoing or completed but unpublished RCTs. Other sources: backward and forward citation tracking of all included studies and relevant reviews, and hand searching of reference lists. When key information is missing, we will contact study authors for clarification or additional aggregate data. Records will be deduplicated before screening. The full search will be rerun before data synthesis to capture newly published studies.

Main outcome(s) Effective rate; Urticaria Activity Score over 7 days (UAS7); Dermatology Life Quality Index (DLQI); Serum total immunoglobulin E (IgE); Interleukin 4 (IL-4); Interferon gamma (IFN-γ).

Data management All retrieved records from database searches will be imported into reference management software (EndNote X9) for deduplication. Title and abstract screening, followed by full-text eligibility assessment, will be performed using Microsoft Excel with predefined inclusion and exclusion criteria. A standardized data extraction form will be used to collect relevant variables, including study characteristics, intervention details, outcome measures, and follow-up duration. Two reviewers will independently extract and verify data. Discrepancies will be resolved through discussion or consultation with a third reviewer. Final datasets will be stored securely on password-protected institutional computers.

Quality assessment / Risk of bias analysis The risk of bias of included randomized controlled trials will be independently assessed by two reviewers using the Cochrane Risk of Bias 2.0 (RoB 2) tool. This tool evaluates five domains: (1) bias arising from the randomization process, (2) bias due to deviations from intended interventions, (3) bias due to missing outcome data, (4) bias in measurement of the outcome, and (5) bias in selection of the reported result. Each domain will be judged as “low risk,” “some concerns,” or “high risk,” and an overall risk-of-bias judgment will be assigned accordingly. Any disagreements will be resolved through discussion or by consulting a third reviewer. Results will be presented in tabular and graphical formats.

Strategy of data synthesis Analyses were performed in Cochrane RevMan (version 9.8.2; The Cochrane Collaboration). Dichotomous outcomes were pooled as risk ratios (RR) with 95% confidence intervals, and continuous outcomes as mean differences or standardized mean differences

with 95% confidence intervals (CI) according to scale consistency. Heterogeneity was assessed with the chi-square test and I^2 statistic. Random-effects models were used when heterogeneity was substantial ($I^2 > 50\%$ or $P < 0.10$); otherwise fixed-effect models were applied. Prespecified subgroup analyses (intervention type, acupuncture modality, treatment duration) explored heterogeneity. Sensitivity analyses excluded studies with high risk of bias, small samples, or extreme values to test robustness.

Subgroup analysis Primary subgrouping will be by antihistamine used in the control and add-on arms. When data allow, we will analyze by specific agent; otherwise we will group by class or generation. If reported, we will further separate standard dose vs up-dosed regimens. Subgroup effects will be tested using a chi-square test for interaction within random effects meta-analyses. Multi-arm trials will be handled by splitting the shared control or by using appropriate methods to avoid double-counting.

Sensitivity analysis Leave-one-out sensitivity analyses will be performed for each meta-analysis by iteratively removing one study at a time. We will examine the stability of the pooled effect size, confidence interval, and heterogeneity. Results will be considered robust if conclusions regarding direction and statistical significance remain unchanged across iterations.

Language restriction No language restrictions.

Country(ies) involved Taiwan.

Keywords Acupuncture; Chronic urticaria; Antihistamines; Systematic review; Meta-analysis.

Contributions of each author

Author 1 - I-Chang Lai - Author 1 conceptualized the review topic, conducted the systematic database search, organized the extracted data, prepared all tables and figures, drafted the initial manuscript, and will oversee the submission process. Author 1 and Author 2 contributed equally to this work and are co-first authors.
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Author 2 - Kuan-Chun Lee - Author 2 conducted risk of bias assessment, synthesized the extracted data, supported the refinement of tables and figures, and participated in the formatting of the final version of the manuscript. Author 1 and Author 2 contributed equally to this work and are co-first authors.
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