INPLASY PROTOCOL

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Conflicts of interest:
None.

Chinese patent herbal medicine for Henoch-Schonlein purpura nephritis in children: a systematic review of randomized controlled trials

Xue, X[1]; Liu, XH[2]; Lu, CL[3]; Jin, XY[4]; Liu, Q[5]; Wang, XQ[6]; Liu, JP[7].

Review question / Objective: **Types of participants: All participants are children under 14 years old with HSPN. No restriction is applied on sex or race of participants. Types of intervention: In addition to basic treatment (including: diet management, avoidance of allergens, anti-infection, anti-platelet aggregation, anti-allergy, angiotensin-converting enzyme inhibitors / angiotensin receptor blockers and other symptomatic treatments.), experimental groups take "HQH" or "HQH combined with glucocorticoid(GC)" or "HQH combined with GC and immunosuppressant(IS)"treatments. While control groups are administered "GC" or "GC combined with IS" on the basis of basic treatment (BT). Types of outcome measures: Primary outcome measures: (1)clinical curative rate; (2)total effective rate. Secondary outcome measures: (1)24 h urinary protein excretion; (2) urine sediment erythrocyte count; (3)urine β2 micro-globulin(β2-MG); (4)immune cells and inflammatory factors; (5)adverse events.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 31 December 2020 and was last updated on 31 December 2020 (registration number INPLASY2020120148).

INTRODUCTION

Review question / Objective: **Types of participants: All participants are children under 14 years old with HSPN. No restriction is applied on sex or race of participants. Types of intervention: In addition to basic treatment (including: diet management, avoidance of allergens, anti-infection, anti-platelet aggregation, anti-allergy, angiotensin-converting enzyme inhibitors / angiotensin receptor blockers**

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Condition being studied: Henoch-Schönlein purpura nephritis (HSPN) is listed as the most common secondary glomerular diseases among children, approximately 15% to 20% of children eventually could develop chronic renal failure. Chinese patent medicine Huaiqihuang(HQH) has been widely used in children's HSPN clinically. This study aims to evaluate the effectiveness and safety of HQH for HSPN in children, so as to provide evidence for clinical medication.

METHODS

Participant or population: All participants are children under 14 years old with HSPN. No restriction is applied on sex or race of participants.

Intervention: In addition to basic treatment (including: diet management, avoidance of allergens, anti-infection, anti-platelet aggregation, anti-allergy, angiotensin-converting enzyme inhibitors / angiotensin receptor blockers and other symptomatic treatments.), experimental groups take "HQH" or "HQH combined with glucocorticoid(GC)" or "HQH combined with GC and immunosuppressant (IS)"treatments.

Comparator: While control groups are administered "GC" or "GC combined with IS" on the basis of basic treatment (BT).

Study designs to be included: Randomized controlled trials (RCTs) regardless of the blinding method is identified.

Eligibility criteria: (1) All participants are children under 14 years old with HSPN. (2)No restriction is applied on sex or race of participants. (3)Rcts.

Information sources: We will search the following Chinese and English databases from their inception to December 2020. Chinese databases include China National Knowledge Infrastructure (CNKI), Wan Fang, Chinese Science and Technology Journal Database (VIP), and SinoMed Database. English databases include PubMed, EMBASE, the Cochrane Library, and Web of Science. Trial registers including Clinical Trials. gov and the World Health Organization International Clinical Trials Registry Platform are also searched. Additionally, related reviews, conference papers, references lists and gray literatures also are searched manually to minimize the missed detection rate. No language or publication type is imposed. Taking 'PubMed' as an example, the retrieval strategy is as follows: #1: 'Purpura, Schoenlein-Henoch'[Mesh], #2: 'Nephritis'[Mesh], #3: #1 AND #2, #4: 'Henoeh-Sehonlein purpura nephritis', #5: 'purpura nephritis', #6: 'HSPN',#7: 'Immunoglobulin A vasculitis with nephritis', #8: 'IgAVN', #9: #3 OR #4 OR #5 OR #6 OR #7 OR #8, #10: 'child'[Mesh], #11: 'children', #12: #10 OR #11,#13: #9 AND #12, #14:'Huaiqihuang', #15:'HQH', #16: #14 OR #15, #17: #13 AND #16.

Main outcome(s): Primary outcome measures: (1)clinical curative rate; (2)total effective rate.

Additional outcome(s): Secondary outcome measures: (1)24h urinary protein excretion; (2)urine sediment erythrocyte count; (3)urine β2 micro-globulin(β2-MG); (4)immune cells and inflammatory factors; (5)adverse events.

Quality assessment / Risk of bias analysis: 1.Risk of bias in included RCTs: Two authors will assess and validate the quality

of included trials independently according to Cochrane Handbook for Systematic Reviews of Interventions. Seven items including random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other bias (pharmaceutical funding and comparability of baseline data of subjects between groups), are used to be judged as "unclear risk", "low risk", or "high risk". Any disagreements are resolved by discussion with a third author JP Liu. 2.Quality of evidence for main findings: Two reviewers will summarize the quality of evidence for main findings using the "Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach", independently. The quality of evidence for the main findings are graded as GRADE working Group grades of evidence.

Strategy of data synthesis: RevMan 5.3 software will be used for data analysis. For continuous data, we will use mean difference(MD) with 95% confidence intervals(CI) or standardized mean difference(SMD) with 95% CI(When the measurement unit of outcome is different, in order to eliminate the influence of the dimension, SMD is selected). And for dichotomous data, we use relative risk(RR) with 95% CI. We perform meta-analyses for trials if the study design, interventions, control and outcome measures were similar. Other data not suitable for pooling analysis will be synthesized qualitatively. I-square(I2) is used to test the statistical heterogeneity as recommended by the Cochrane Handbook for Systematic Reviews of Interventions. We use random effects model for data pooling with substantial statistical heterogeneity (50%≤I2), otherwise a fixed effect model is applied. And we will finish funnel plots to test for the possibility of publication bias if there are enough studies(generally, more than 10 trials).

Subgroup analysis: To reduce clinical heterogeneity, we will conduct subgroups analyses of different interventions. At present, the treatment mainly includes basic treatment(symptomatic treatment, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers), glucocorticoid (GC) and immunosuppressant (IS). Among them, IS mainly included cyclophosphamide and mycophenolate mofetil. All of subjects both in experimental and control groups are given basic treatment(BT). In case of the data is available, they are divided into the following subgroups: "GC+HQH vs. GC"; "GC+IS+HQH vs. GC+IS" and "HQH vs. BT" respectively.

Sensibility analysis: If the data is available, we will conduct sensitivity analysis to explore the robustness of results.

Country(ies) involved: China.

Keywords: Chinese patent herbal medicine, Huaiqihuang, Henoch-Schonlein purpura nephritis, children, randomized controlled trials, systematic review

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