INPLASY PROTOCOL

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None declared.

Chinese Herbal Medicine in Incomplete Immune Reconstruction in AIDS Patients Experiencing Antiretroviral Treatment: A Systematic Review and Meta-Analysis of Randomized Trials

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Review question / Objective: **Are Chinese herbal medicines effective and safe for incomplete immune reconstruction in HIV/AIDS patients who experienced antiretroviral therapy?**
Condition being studied: **Incomplete immune reconstruction is a phenomenon for AIDS patients who receive HAART treatment but are still unable to effectively resume immunity. At present, there is still no recognized effective therapy for clinical use. Studies have confirmed the long-term effects of Chinese herbal medicines (CHMs) on maintaining or delaying the decline of HIV/AIDS CD4+ counts, and have achieved lasting effects. Thus, we did a systematic review to evaluate the effectiveness and safety of CHMs for incomplete immune reconstruction in HIV/AIDS patients and to assess the tendency of effect size at different time-point outcomes for immune function.**

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INTRODUCTION

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METHODS

Search strategy: We searched the following electronic databases from their inception to 15th August 2021: Pubmed, the Cochrane Library, EMBASE, Web of Science, China National Knowledge Infrastructure (CNKI), Wanfang database, Chinese Scientific Journal Database (VIP) and Chinese biomedical literature database (CBM). We also hand-searched the reference lists of all full-text papers for additional relevant reports. Searches were limited to randomized controlled trials in all languages. Details of the search strategy are available from the authors on request.

Participant or population: We will include HIV/AIDS participants with the incomplete immune reconstruction of AIDS. Diagnosis criteria for incomplete immune reconstruction of AIDS is that CD4+ cell count <200 cells/μL for patients receiving HAART treatment for more than 1 year and within 2 years, or CD4+ cell count <350 cells/μL for patients receiving HAART for more than 2 years, or after 4~7 years of treatment, the CD4 cell count is ≤ 350 cells/μL or 500 cells/μL, and the level of HIV RNA is below the baseline.

Intervention: The intervention of CHM can be used alone or as adjunctive therapy. We include the dosage form including, but not limited to, traditional Chinese medicine preparation (such as oral liquid, tablet, capsule, pill, powder, medicinal paste or injection) and compound decoction.

Comparator: Eligible control therapy includes one or a combination of a placebo, western medicine and antiretroviral therapy. Western medicine therapy includes symptomatic treatment except for antiretroviral therapy.Eligible control therapy included one or a combination of a placebo, western medicine and antiretroviral therapy. Western medicine therapy includes symptomatic treatment except for antiretroviral therapy.

Study designs to be included: Randomized controlled trials regardless of blinding or publication types.

Eligibility criteria: We will include all randomized controlled trials (RCTs), regardless of blinding or publication types, on CHM for HIV/AIDS participants with the incomplete immune reconstruction of AIDS. Diagnosis criteria for incomplete immune reconstruction of AIDS is that CD4+ cell count <200 cells/μL for patients receiving HAART treatment for more than 1 year and within 2 years, or CD4+ cell count <350 cells/μL for patients receiving HAART for more than 2 years, or after 4~7 years of treatment, the CD4 cell count is ≤ 350 cells/μL or 500 cells/μL, and the level of HIV RNA is below the baseline. The intervention of CHM should be used alone or as adjunctive therapy. We will include the dosage form including, but not limited to, traditional Chinese medicine preparation (such as oral liquid, tablet, capsule, pill, powder, medicinal paste or injection) and compound decoction. Eligible control therapy includes one or a combination of a placebo, western medicine and antiretroviral therapy. Western medicine therapy includes symptomatic treatment except for antiretroviral therapy.Outcomes, as follows, will be included: 1) primary outcomes of immune function (CD4+, CD8+, CD45RA+, CD45RO+ lymphocyte count, etc.) and quality of life score like Karnofsky (KPS) score. 2) Secondary outcome as the effective rate of immune reconstitution. The effective rate can be defined as the increase of CD4+ ≥ 30% or 50 cells/μL after treatment. 3) Safety outcome as the incidence of adverse reaction/events or safety indicators of liver and kidney function.Types of study to be included: Randomized controlled trials regardless of blinding or publication types.

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Information sources: We searched the following electronic databases from their inception to 15th August 2021: Pubmed, the Cochrane Library, EMBASE, Web of Science, China National Knowledge Infrastructure (CNKI), Wanfang database, Chinese Scientific Journal Database (VIP) and Chinese biomedical literature database (CBM). We also hand-searched the reference lists of all full-text papers for additional relevant reports.

Main outcome(s): 1) immune function including CD4+, CD8+, CD45RA+, CD45RO+ lymphocyte count, etc. 2) quality of life score like Karnofsky (KPS) score.

Additional outcome(s): 1) the effective rate of immune reconstitution. The effective rate was defined as the increase of CD4+ ≥ 30% or 50 cells/μL after treatment. 2) Safety outcome as the incidence of adverse reaction/events or safety indicators of liver and kidney function.

Quality assessment / Risk of bias analysis: The Cochrane Risk of Bias (RoB) will be employed to evaluate the methodological quality of included RCTs. The six authors in pairs will independently assess the quality and consensus will be reached by discussion with a third party (Liu JP) in case of discrepancy. Six elements will be assessed: random sequence generation, allocation concealment, blinding of outcome assessors, incomplete outcome data, free of selective reporting, and other bias. Disagreements will be resolved by discussion with a third party (JP Liu).

Strategy of data synthesis: All data will be recorded in RevMan Software (version 5.4.1) (Review Manager, 2020). For dichotomous variables, we will calculate the risk ratio (RR) with 95% confidence intervals (CIs). For continuous variables, we will calculate the mean difference (MD) with 95% CI. We will use the I2 test and $\chi 2$ test for heterogeneity. We will do a meta-analysis in a random-effect model to estimate the effect sizes because it gives similar weights to studies with different sample sizes and substantial heterogeneity would be expected between studies (e.g., for type and duration of interventions and follow-up periods). If the data fails to meet the condition of meta-analysis, we will synthesis the data narratively.

Subgroup analysis: If data permits, we will do a subgroup analysis according to the time-point of outcome measurement post-treatment (as 3 months, 6 months, 12 months, etc.).

Sensitivity analysis: Sensitivity analyses will be performed if there are enough trials for determining the robustness of the conclusions.

Country(ies) involved: China.

Keywords: HIV; AIDS; incomplete immune reconstruction; Chinese herbal medicine; randomized clinical trials; systematic review.

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