INPLASY PROTOCOL

To cite: Zheng et al. Does Chinese herbal remedy Tangcao tablet work for the treatment of HIV/AIDS：a systematic review of controlled clinical trials. Inplasy protocol 202260042. doi: 10.37766/inplasy2022.6.0042

Received: 09 June 2022

Published: 09 June 2022

Corresponding author:
Jian-ping Liu

liujp@bucm.edu.cn

Author Affiliation:
Center for Evidence-Based Chinese Medicine, Beijing University of Chinese Medicine, Beijing, China.

Support: **No. 81673828; No. G20190001122.**

Review Stage at time of this submission: **Formal screening of search results against eligibility criteria.**

Conflicts of interest:
None declared.

Does Chinese herbal remedy Tangcao tablet work for the treatment of HIV/AIDS：a systematic review of controlled clinical trials

Zheng, RX[1]; Li, X[2]; Li, J[3]; Liu, ZW[4]; Jiang, F[5]; Robinson, N[6]; Liu, JP[7].

Review question / Objective: **This study aims to evaluate the effectiveness and safety of Tangcao tablet (Tangcao) for treating people with HIV/AIDS.**
Condition being studied: **Acquired immunodeficiency syndrome (AIDS) is a chronic infectious disease characterized by severe immunodeficiency caused by the human immunodeficiency virus (HIV). The infection attacks specifically the white blood cells, CD4+T (CD4) cells, weakening the immunity of individuals against infections such as tuberculosis. Without treatment, patients with AIDS may survive up to 2 years. Pneumocystis pneumonia and infections of the central nervous system are two of the most common causes of death in people with AIDS. AIDS still remains a significant global public health problem, with an estimated 37.7 million people infected with HIV at the end of 2020.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 09 June 2022 and was last updated on 09 June 2022 (registration number INPLASY202260042).

INTRODUCTION

Review question / Objective: **This study aims to evaluate the effectiveness and safety of Tangcao tablet (Tangcao) for treating people with HIV/AIDS.**

Condition being studied: **Acquired immunodeficiency syndrome (AIDS) is a chronic infectious disease characterized by severe immunodeficiency caused by the human immunodeficiency virus (HIV). The infection attacks specifically the white blood cells, CD4+T (CD4) cells, weakening**

the immunity of individuals against infections such as tuberculosis. Without treatment, patients with AIDS may survive up to 2 years. Pneumocystis pneumonia and infections of the central nervous system are two of the most common causes of death in people with AIDS. AIDS still remains a significant global public health problem, with an estimated 37.7 million people infected with HIV at the end of 2020.

METHODS

Search strategy: The main search terms included HIV Infections, HIV, Acquired immunodeficiency Syndrome. The term "Tangcao" were searched in full text, and the word variations have been searched. The example of search strategy of PubMed are as follows:
#1 HIV Infections[MeSH] OR HIV[MeSH] OR hiv[tw] OR hiv-1*[tw] OR hiv-2*[tw] OR hiv1[tw] OR hiv2[tw] OR hiv infect*[tw] OR human immunodeficiency virus[tw] OR human immune deficiency virus[tw] OR human immuno-deficiency virus[tw] OR human immune-deficiency virus[tw] OR ((human immun*) AND (deficiency virus[tw])) OR acquired immunodeficiency syndrome[tw] OR acquired immune deficiency syndrome[tw] OR acquired immuno-deficiency syndrome[tw] OR acquired immune-deficiency syndrome[tw] OR ((acquired immun*) AND (deficiency syndrome[tw])) OR "sexually transmitted diseases, viral"[MESH:NoExp]
#2 (Tang?cao[all]) OR (Tangcao*[all])
#3 #1 AND #2
EndNote 20 will be used to manage retrieved records, and preliminary exclude the duplicates.

Participant or population: Patients with HIV infection or AIDS or both.

Intervention: Tangcao used alone or combined with antiviral therapy (ART) as an intervention in treatment group.

Comparator: Comparators include but not limit to ART or placebo.

Study designs to be included: Controlled trials, such as randomized controlled trial (RCT), controlled clinical trial (CCT).

Eligibility criteria: Controlled trials regarding the Tangcao tablet for patients with HIV infection or AIDS will be included. The interventions can be Tangcao with or without ART. ART or placebo as comparator(s) in the control group will be included. The primary outcomes include CD4 cell count, and severe adverse events that required patients to withdraw from the study. Secondary outcomes are body weight; HIV viral load, CD4/CD8, CD8+T (CD8) cell count, and other adverse events. Any duplications and studies with inadequate or missing data were excluded. Publications in English and Chinese will be included.

Information sources: The following databases will be searched: Chinese databases: China National Knowledge Infrastructure, Wanfang Database, Chongqing Vip, and SinoMed. English databases: PubMed, Web of Science, Embase, and the Cochrane Library. Additionally, Clinical Trials.gov, the Chinese clinical trial registry (http://www.chictr.org.cn/searchproj.aspx), and the World Health Organization (WHO) International Clinical Trials Registry Platform (http://apps.who.int/trialsearch/) were searched. The last search was performed on 9 June 2022.

Main outcome(s): CD4 cell count; severe adverse events that required patients to withdraw from the study.

Additional outcome(s): Body weight; HIV viral load, CD4/CD8, CD8 cell count, adverse events.

Quality assessment / Risk of bias analysis: The Cochrane risk of bias tool (Cochrane Handbook-Table 8.5.d: Criteria for judging risk of bias in the 'Risk of bias' assessment tool) will be used to assess the quality included trials.

Strategy of data synthesis: Information will be collected by data extraction include

aspects as follows: (1) Details of study populations: diagnostic criteria, trial inclusion-exclusion criteria, characteristics of participants; (2) Information on the intervention: course of treatment, doses; (3) Information on the control: placebo or HAART; (4) Outcome measures: CD4 cell count, adverse events, body weight count, efficiency rate, symptom score, index of other laboratory tests (blood routine, liver function, HIV viral load, CD8+ T (CD8) cell, CD4/CD8; (5) measurement time point; (6) Effect data for the relevant outcomes: results of the above outcomes that were reported in trials, effect size of the relative outcome. Authors will be contacted to obtain additional information if needed. According to Cochrane risk of bias tool (Cochrane Handbook-Table 8.5.d: Criteria for judging risk of bias in the "Risk of bias" assessment tool), two authors (RX Zheng and J Li) will perform the assessment independently judging with terms as "Low risk", "Unclear risk", and "High risk". Any disagreement will be resolved through discussion amongst review authors (JP Liu, Xun Li, J Li, RX Zheng). Revman 5.3 software will be used to pool the data. For dichotomous outcomes, the risk ratio (RR) with 95% confidence interval (CI) will be used, and for continuous outcomes, the mean difference (MD) with 95% CI or standardized mean difference (SMD) with 95% CI. A meta-analysis will be performed for trials that had a similar study design, participants, interventions, control, and outcome measurements. The analysis will be based on intention to treat (ITT) analysis on each outcome when possible. If no significant heterogeneity is identified (I2 lower than 50%), a fixed effects model will be used to pool the data and a random effects model when the heterogeneity is significant. If I2 is greater than 75%, as there might be a high level of heterogeneity, a narrative description will be presented instead of meta-analysis. Heterogeneity across studies will be tested by using the Z score and chi-square test with significance being set at $P \leq 0.01$.

Subgroup analysis: The subgroup analysis will be based on patient's severity, comparisons, and comparator(s) (such as ART or placebo).

Sensitivity analysis: Where I2 is greater than 50%, further investigation of potential heterogeneity sources will be conducted using sensitivity analysis. For the primary outcome, sensitivity analyses will be performed to determine whether the review conclusions will be different if eligibility is restricted to trials with low risk in selection bias.

Language: The language in this review will be limited to Chinese and English.

Country(ies) involved: China, United Kingdom.

Keywords: Systematic review; Chinese Medicine; Tangcao tablets; Antiviral therapy; HIV/AIDS; clinical trials.

Contributions of each author:
Author 1 - Ruo-xiang Zheng.
Author 2 - Xun Li.
Author 3 - Jing Li.
Author 4 - Zhen-wei Liu.
Author 5 - Feng Jiang.
Author 6 - Nicola Robinson.
Author 7 - Jian-ping Liu.