

INPLASY PROTOCOL

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submission:** Preliminary
searches.

Conflicts of interest:
None declared.

INTRODUCTION

Review question / Objective: To determine whether Tenofovir Disoproxil Fumarate Combined with Fuzheng Huayu shows superior efficiency, compared with Tenofovir Disoproxil Fumarate alone, for the treatment of chronic HBV-related liver fibrosis and the recovery of liver function.

Fuzheng Huayu Combined with Tenofovir Disoproxil Fumarate for Hepatitis B: A Systematic Review and Meta-Analysis

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Review question / Objective: To determine whether Tenofovir Disoproxil Fumarate Combined with Fuzheng Huayu shows superior efficiency, compared with Tenofovir Disoproxil Fumarate alone, for the treatment of chronic HBV-related liver fibrosis and the recovery of liver function.

Information sources: The databases, including PubMed, Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI) database, Wanfang Data Knowledge Service Platform, the VIP information resource integration service platform (cqVIP), and China Biology Medicine Disc (Sino Med) were searched to collect randomized control trials (RCTs) from inception to November 2021.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 01 November 2021 and was last updated on 01 November 2021 (registration number INPLASY2021110002).

Condition being studied: Chronic hepatitis B virus (HBV) infection is a major global health problem, affecting an estimated 257 to 291 million people worldwide, and causes significant morbidity and mortality due to clinical complications such as liver cirrhosis and hepatocellular carcinoma. The induction of long-term suppression of HBV replication represents the main endpoint of current treatment strategies. TDF is a

potent nucleoside analogue with high barrier to resistance, which can inhibit reverse transcription of pregenomic RNA to HBV DNA. However, despite long-term therapy, liver-related complications, such as liver fibrosis, can still occur even with sustained viral suppression. Advanced liver fibrosis results in cirrhosis, liver failure, and portal hypertension and often requires liver transplantation. Therefore, anti-fibrosis is extremely important to improve intermediate prognosis, and overall health outcomes. The purpose of this study was to evaluate the efficacy of Fuzheng Huayu (FZHY) plus Tenofovir Disoproxil Fumarate (TDF) in regression of liver fibrosis and improvement of liver function in chronic hepatitis B (CHB) patients.

METHODS

Search strategy: Search terms were “hepatitis b” OR “hepatitis b virus infection” OR “chronic hepatitis b” OR “hepatitis b virus” OR “type b hepatitis”, “Tenofovir Disoproxil Fumarate” OR “TDF”, “Fuzheng Huayu” OR “FZHY” OR “Fuzheng Huayu capsule” OR “Fuzheng Huayu tablet” OR “Fuzheng Huayu recipe” OR “Fuzheng Huayu formula”, and “randomized controlled trial” OR “randomized” OR “placebo”, which was composed of subject words and free words with no language restrictions.

Participant or population: Inclusion: Patients, of any age and gender, with chronic hepatitis B, diagnosed according to established diagnostic criteria. Exclusion: Liver damage caused by other viruses, autoimmunity, alcohol and drugs.

Intervention: Fuzheng Huayu combined with Tenofovir Disoproxil Fumarate.

Comparator: Tenofovir Disoproxil Fumarate alone.

Study designs to be included: Only randomized controlled trials (RCT) will be included.

Eligibility criteria: Included if the following conditions are met: (1) Research type:

RCTs; (2) Participants: Patients had an established diagnosis of hepatitis b virus infection; (3) Intervention: The experimental group was treated with FZHY combined with TDF, while the control group was only treated with TDF. There were no limitations in terms of gender, race, or country.

Information sources: The databases, including PubMed, Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI) database, Wanfang Data Knowledge Service Platform, the VIP information resource integration service platform (cqVIP), and China Biology Medicine Disc (Sino Med) were searched to collect randomized control trials (RCTs) from inception to November 2021.

Main outcome(s): Liver fibrosis index (Hyaluronic Acid, Type III Procollagen, Type IV Collagen, Laminin).

Additional outcome(s): Liver function index (Alanine Transaminase, Aspartate Aminotransferase, Albumin, Total Bilirubin).

Quality assessment / Risk of bias analysis: Two researchers independently assessed the risk of bias of each included literature according to the Cochrane Handbook 5.1.0, and the divergence will be resolved through discussion or consultation with a third party.

Strategy of data synthesis: The Review Manager version 5.4 software was adopted for statistical analysis. For dichotomous variables, we used relative risk (RR) with 95% confidence intervals (CI) as the effect measure. For continuous variables, we used mean difference (MD) or standardized mean difference (SMD) with 95% CI as the effect measure. We assessed the heterogeneity of the included studies by Cochrane χ^2 test and I^2 test. The value of $P > 0.1$ and $I^2 < 50\%$ indicated low heterogeneity, and in this case a fixed effect model was applied. Otherwise, a random effect model was used. Subgroup and sensitivity analysis were used to find the source of heterogeneity. If there is still considerable heterogeneity, we will mainly describe the results. The funnel plot was

used to assess the potential publication bias.

Subgroup analysis: Subgroups by degree of disease progression, gender, years with HBV, type of treatment and others characteristics will be conducted.

Sensitivity analysis: The studies were excluded one by one, and then the meta-analysis was performed in the remaining studies.

Country(ies) involved: China.

Keywords: Systematic review; meta-analysis; Fuzheng Huayu; Tenofovir Disoproxil Fumarate; Liver fibrosis index; Liver function index.

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