INPLASY PROTOCOL

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Review Stage at time of this submission: **The review has not yet started.**

Conflicts of interest:
None declared.

A retrospective integrated analysis evaluate the effect and safety of Combination therapy of fenofibrate and ursodeoxycholic acid in patients with primary biliary cirrhosis who respond incompletely to UDCA monotherapy

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Review question / Objective: **The efficacy and safety of UDCA combined with fenofibrate in the treatment of PBC patients with poor response to UDCA were evaluated by meta-analysis, so as to provide relevant suggestions for the clinical treatment of PBC.**
Condition being studied: **Primary biliary cholangitis (PBC), also known as primary biliary cirrhosis, is a chronic intrahepatic cholestatic disease, which is mainly characterized by progressive non suppurative inflammatory reaction of intrahepatic bile duct, and can develop into hepatic fibrosis and cirrhosis.**
Eligibility criteria: **1) A randomized controlled trial or clinical controlled trial comparing UDCA alone with UDCA combined with fenofibrate.2) PBC diagnosis meets any two of the following: 1 There is a biochemical basis for cholestasis. 2. Anti mitochondrial antibody was positive. 3. Histologically consistent with the diagnosis.3) All patients did not use other liver disease drugs.4) The research report shall include at least one of the indexes to evaluate the curative effect, such as biochemical and / or immunological indexes, survival rate, etc. 5) For the research results of the same team, the results with the most cases and the most complete data are taken.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 March 2022 and was last updated on 21 March 2022 (registration number INPLASY202230111).

INTRODUCTION

Review question / Objective: **The efficacy and safety of UDCA combined with fenofibrate in the treatment of PBC patients with poor response to UDCA were evaluated by meta-analysis, so as to**

provide relevant suggestions for the clinical treatment of PBC.

Condition being studied: Primary biliary cholangitis (PBC), also known as primary biliary cirrhosis, is a chronic intrahepatic cholestatic disease, which is mainly characterized by progressive non suppurative inflammatory reaction of intrahepatic bile duct, and can develop into hepatic fibrosis and cirrhosis.

METHODS

Search strategy: For literature on ursodeoxycholic acid combined with fenofibrate in the treatment of adverse PBC published before December , 20th, 2021, search databases will include Google Scholar, EMBASE, Web of Science, PubMed, the CNKI, VIP, Wanfang, and Cochrane Library.to identify systematic reviews or metaanalyses. The following search terms and their derivatives were used in multiple combinations: "Primary Biliary Cirrhosis", "Ursodeoxycholic Acid", "Fenofibrate", "原发性胆汁性胆管炎", "非诺贝特", "熊去氧胆酸".

Participant or population: PBC diagnosis meets any two of the following: 1 There is a biochemical basis for cholestasis. 2. Anti mitochondrial antibody was positive. 3. Histologically consistent with the diagnosis. And all patients did not use other liver disease treatment drugs,. Or other liver diseases.

Intervention: UDCA combined with fenofibrate

Comparator: UDCA monotherapy.

Study designs to be included: RCT.

Eligibility criteria: 1) A randomized controlled trial or clinical controlled trial comparing UDCA alone with UDCA combined with fenofibrate.2) PBC diagnosis meets any two of the following: 1 There is a biochemical basis for cholestasis. 2. Anti mitochondrial antibody was positive. 3. Histologically consistent with the diagnosis.3) All patients did not use other liver disease drugs.4) The research report shall include at least one of the indexes to evaluate the curative effect, such as biochemical and / or immunological indexes, survival rate, etc.5) For the research results of the same team, the results with the most cases and the most complete data are taken.

Information sources: For literature on mindfulness practice for adolescent emotional disorders published before December , 20th, 2021, search databases will include Google Scholar, EMBASE, PubMed, the CNKI, the Chinese Science and Technology Periodical Database, VIP, Wanfang, and Cochrane Library.

Main outcome(s): The changes of biochemical levels such as ALP, alt, AST, GGT, TG IgM and the occurrence of major adverse events such as pruritus were included.

Quality assessment / Risk of bias analysis: The quality of the included meta-analysis and systematic evaluation was assessed by using the Cochrane systematic evaluation tool. Two researchers will assess the quality of the study and any differences will be resolved by the third author.

Strategy of data synthesis: Use revman5 4 conduct meta-analysis. For the binary counting data, the or value and 95% confidence interval (95% CI) of each literature were calculated. For continuous variable data, mean difference (MD) and 95% CI were used. We mainly use q test and I2 test to test heterogeneity. When p value < 0.10 or I2 value > 50% is considered to have significant heterogeneity, we use random effect model analysis. The fixed effect model was used when p value > 0.10 and I2 value < 50%. Subgroup and sensitivity analysis were used when necessary. Funnel plot was made to evaluate publication bias.

Subgroup analysis: When the heterogeneity was large, we performed subgroup analysis. According to the characteristics of the collected articles. We will conduct

grouping analysis to determine the differences between different drug doses, treatment time, etc.

Sensitivity analysis: Sensitivity analysis will be performed by excluding tests one by one and observing whether there is a significant change in the synthesis results. If I^2 ≥ 50% for the primary outcome, further analysis will be performed of each risk factor. The sensitivity of the article was analyzed by the change of effect quantity after deleting one report.

Language: English.

Country(ies) involved: China.

Keywords: primary biliary cholangitis, randomized controlled trial, fenofibrate, odds ratio, combination therapy, monotherapy, meta-analysis.

Contributions of each author:
Author 1 - Guoyun Xuan - Author 1 drafted the manuscrip.
Author 2 - Liu Ning - The author provided statistical expertise.
Author 3 - Ding Dawei - The author contributed to the development of the selection criteria, and the risk of bias assessment strategy.
Author 4 - Xu Ang - The author read, provided feedback and approved the final manuscript.
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