INPLASY PROTOCOL

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Review Stage at time of this submission: **Preliminary searches.**

Conflicts of interest:
None.

Meta-analysis of Probiotics Combined with Pelyene phosphatidylcholine in the Treatment of Nonalcoholic Fatty Liver Disease

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Review question / Objective: **What are the effects of probiotics combined with pelyene phosphatidylcholine in the treatment of nonalcoholic fatty liver disease?**
Condition being studied: **Nonalcoholic fatty liver disease（NAFLD） is one of the most common chronic liver diseases in the world. NAFLD is characterized by a large spectrum of liver disease, from isolated steatosis to steatohepatitis, and can progress to cause hepatic fifibrosis formation and cirrhosis.In addition to existing drugs for the treatment of NAFLD, new therapeutic targets for NAFLD still need to be found. Existing studies have found that there is a relationship between NAFLD and gut microbiota dysbiosis (Mouzaki et al. 2019, Wigg et al. 2001, Zhu, L.et al.2013, Knight et al.2017). Probiotics have a certain effect on the treatment of NAFLD, but the single use of probiotics has a poor effect on the treatment of NAFLD. It is a worthy question to observe the efficacy of the combination of probiotics and polyene phosphatidylcholine in the treatment of NAFLD.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 May 2020 and was last updated on 21 May 2020 (registration number INPLASY202050078).

INTRODUCTION

Review question / Objective: **What are the effects of probiotics combined with pelyene phosphatidylcholine in the treatment of nonalcoholic fatty liver disease?**

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METHODS

Search strategy: The English literatures mainly searches Cochrane Library, Pubmed, EMBASE, and Web of Science. While the Chinese literatures come from CNKI, CBM, VIP and Wangfang database. The databases will be searched using the following terms: "Probiotics", "Polyene phosphatidylcholine", "Non-alcoholic Fatty Liver Disease", and their synonyms. Research will be limited to humans, regardless of the language of the studies analyzed. We will retrieve each database from the built-in until December 2019.The reference lists of all selected studies will be checked as well as the gray literature.

Participant or population: Patients with nonalcoholic fatty liver disease.

Intervention: Probiotics combined with pelyene phosphatidylcholine in the treatment of nonalcoholic fatty liver disease.

Comparator: Control group-pelyene phosphatidylcholine in the treatment of nonalcoholic fatty liver disease.

Study designs to be included: Clinical randomized controlled trials (RCTs).

Eligibility criteria: The study only selects randomized controlled trials of probiotics combined with pelyene phosphatidylcholine in the treatment of nonalcoholic fatty liver disease published in both Chinese and English. However, animal experiments, reviews, case reports and non-randomized controlled trials are excluded.

Information sources: The English literatures will retrived from Cochrane Library, Pubmed, EMBASE, and Web of Science. While the Chinese literatures come from CNKI, CBM, VIP and Wangfang database. The databases will be searched using the following terms: "Probiotics", "Polyene phosphatidylcholine", "Non-alcoholic Fatty Liver Disease", and their synonyms. Research will be limited to humans, regardless of the language of the studies analyzed. We will retrieve each database from the built-in until December 2019.The reference lists of all selected studies will be checked as well as the gray literature.

Main outcome(s): The primary outcomes include serological markers (AST,ALT, GGT,TG,TC,LDL, HDL), MBI, endotoxin, HOMA-IR and inflammatory factors (TNF-α, IL-6).

Additional outcome(s): None.

Data management: Two investigators independently extract all data from each article, including: first author's name, publication year, study, sample size, age, sex.When disagreement in the collection of data occur, it will be resolved through discussion. If the data are missing or can not be extracted directly, we will contact the corresponding authors to ensure that the information is integrated.

Quality assessment / Risk of bias analysis: The quality assessment of RCTs adopts the risk of bias (ROB) assessment tool provided by the Cochrane Handbook. The following seven items, such as random sequence generation , allocation concealment, blinding of participants and personnel,blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other bias, are evaluated by three grades of "low bias", "high bias" and "unclear bias". The

Cochrane Collaboration's risk of bias tool will be used (RevMan 5.3). The discrepancies will get a consistent conclusion by discussing between both reviewers or seeking the third-party consultation.

Strategy of data synthesis: Review Manager software version 5.3 provided by the Cochrane Collaboration will be performed for data synthesis and analysis. The data will be analyzed by mean and standard deviations to derive a standard mean difference (SMD)or weighted mean difference (WMD)with 95% confidence intervals.If there is no heterogeneity ($I2 < 50\%$, $P > 0.1$), the data is synthesized using a fixed effect model. Otherwise ($I2 \geq 50\%$, $P \leq 0.1$), a random effect model is used to analyze. If a meta- analysis cannot be performed, it will be replaced by a general descriptive analysis.

Subgroup analysis: None.

Sensibility analysis: If necessary, sensitivity analysis using standards will be performed.

Country(ies) involved: China.

Other relevant information: None.

Keywords: Probiotics pelyene phosphatidylcholine nonalcoholic fatty liver disease meta-analysis.

Dissemination plans: None.

Contributions of each author:
Author 1 - Dan Wang - Study design, data collection, statistical analysis, writing of manuscript.
Author 2 - Jinzhong Li - Study design, data extraction.
Author 3 - Ranran Yang - Revising the manuscript.
Author 4 - Xiaobing Gong - Revising the manuscript.