INPLASY PROTOCOL

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None.

Complementary and alternative therapies for non-alcoholic fatty liver disease: A Bayesian network meta-analysis protocol

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Review question / Objective: 1. Participants: Patients who have been diagnosed as non-alcoholic fatty liver disease (NAFLD) will be included. There are no restrictions on gender and age. Patients combined with other chronic liver diseases such as various viral hepatitis, alcoholic liver disease, autoimmune liver disease, drug-induced hepatitis will be excluded. Besides, liver cirrhosis, liver cancer, severe liver disease requiring liver transplantation, and other complicated and severe patients are also not included. 2.Interventions: NAFLD patients in the treatment group will be given complementary and alternative therapies, including dietary supplements, massage, acupuncture, acupoint injection, Chinese herbal medicine, psychotherapy, exercise therapy, etc. Different complementary and alternative therapies can be freely combined. What's more, they can be used based on the routine western medicine or independently. 3. Comparisons The control group will be treated with conventional western medicine. There is no limitation on the dosage form. 4. Outcomes (1). Primary outcomes: total effective rate, main blood lipid indexes (TC, TG), main liver function indexes (ALT, AST). (2). Secondary outcomes: TCM Syndrome Score Scale (TCMSSS), body mass index (BMI), fasting blood glucose, ultrasound imaging changes, and the incidence of adverse events, etc. 5. Type of study This study will include randomized controlled trials (RCTs) related to the treatment of NAFLD. The sample size of both the treatment group and the control group should be at least 30. The language will be restricted to Chinese or English.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 27 December 2020 and was last updated on 27 December 2020 (registration number INPLASY2020120136).

INTRODUCTION

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such as various viral hepatitis, alcoholic liver disease, autoimmune liver disease, drug-induced hepatitis will be excluded. Besides, liver cirrhosis, liver cancer, severe liver disease requiring liver transplantation, and other complicated and severe patients are also not included. 2.Interventions: NAFLD patients in the treatment group will be given complementary and alternative therapies, including dietary supplements, massage, acupuncture, acupoint injection, Chinese herbal medicine, psychotherapy, exercise therapy, etc. Different complementary and alternative therapies can be freely combined. What's more, they can be used based on the routine western medicine or independently. 3. Comparisons The control group will be treated with conventional western medicine. There is no limitation on the dosage form. 4. Outcomes (1). Primary outcomes: total effective rate, main blood lipid indexes (TC, TG), main liver function indexes (ALT, AST). (2). Secondary outcomes: TCM Syndrome Score Scale (TCMSSS), body mass index (BMI), fasting blood glucose, ultrasound imaging changes, and the incidence of adverse events, etc. 5. Type of study This study will include randomized controlled trials (RCTs) related to the treatment of NAFLD. The sample size of both the treatment group and the control group should be at least 30. The language will be restricted to Chinese or English.

Condition being studied: In a word, the current treatment strategy for NAFLD is mainly aimed at lifestyle intervention and controlling the risk of metabolism and complications. Although some progress has been made in treatment in recent years, the efficacy of related treatment options is still controversial. Thus, it is extremely urgent to find an effective and safe interventional therapy. Recently, it has been reported that the complementary and alternative therapies play an important role in NAFLD. Generally speaking, these therapies for NAFLD mainly contain dietary supplements, massage, acupuncture, acupoint injection, Chinese herbal medicine, psychotherapy, exercise therapy, etc. The latest research has shown that the mechanism of action of traditional Chinese medicine (TCM) intervention in NAFLD is mainly reflected in regulating lipid metabolism, increasing insulin sensitivity, inhibiting oxidative stress, improving the intestinal barrier, and improving inflammation. Besides, acupuncture and moxibustion also have a certain effect on the treatment of NAFLD.

METHODS

Participant or population: Patients who have been diagnosed as non-alcoholic fatty liver disease (NAFLD) will be included. There are no restrictions on gender and age. Patients combined with other chronic liver diseases such as various viral hepatitis, alcoholic liver disease, autoimmune liver disease, drug-induced hepatitis will be excluded. Besides, liver cirrhosis, liver cancer, severe liver disease requiring liver transplantation, and other complicated and severe patients are also not included.

Intervention: NAFLD patients in the treatment group will be given complementary and alternative therapies, including dietary supplements, massage, acupuncture, acupoint injection, Chinese herbal medicine, psychotherapy, exercise therapy, etc. Different complementary and alternative therapies can be freely combined. What's more, they can be used based on the routine western medicine or independently.

Comparator: The control group will be treated with conventional western medicine. There is no limitation on the dosage form.

Study designs to be included: This study will include randomized controlled trials (RCTs) related to the treatment of NAFLD. The sample size of both the treatment group and the control group should be at least 30. The language will be restricted to Chinese or English.

Eligibility criteria: 1. Type of study This study will include randomized controlled trials (RCTs) related to the treatment of NAFLD. The sample size of both the

treatment group and the control group should be at least 30. The language will be restricted to Chinese or English. 2. Participants: Patients who have been diagnosed as non-alcoholic fatty liver disease (NAFLD) will be included. There are no restrictions on gender and age. Patients combined with other chronic liver diseases such as various viral hepatitis, alcoholic liver disease, autoimmune liver disease, drug-induced hepatitis will be excluded. Besides, liver cirrhosis, liver cancer, severe liver disease requiring liver transplantation, and other complicated and severe patients are also not included. 3.Interventions: NAFLD patients in the treatment group will be given complementary and alternative therapies, including dietary supplements, massage, acupuncture, acupoint injection, Chinese herbal medicine, psychotherapy, exercise therapy, etc. Different complementary and.

Information sources: The search databases are as follows: PubMed, Cochrane Library, Cochrane Controlled Trial Center Registration, EMBASE, CNKI, Wanfang Database, VIP Database. We will collect all relevant RCTs about the treatment of NAFLD. The search time is from the inception of database to November 2020. We will optimize the retrieval strategy according to the characteristics of diverse databases. The search strategy will be in the form of medical subject headings (MeSH) and keywords. Furthermore, we will continue to follow up literature in the systematic review/meta-analysis. The terms to be searched are as follows: "non-alcoholic fatty liver disease", " NAFLD ","Fatty Liver" "Non-alcoholic Steatohepatitis" and so on.

Main outcome(s): Total effective rate, main blood lipid indexes (TC, TG), main liver function indexes (ALT, AST).

Quality assessment / Risk of bias analysis: In this study, we will use the GRADE method to evaluate the quality of evidence and strength of recommendations. It is much appropriate for systematic reviews, health technology assessments and clinical practice guidelines. Nowadays, GRADE is the most valuable tool for assessing the quality of NMA evidence, which can be divided into high, medium, low and very low.

Strategy of data synthesis: 1. Pairwise meta-analysis For the direct comparison results from the literature, we will conduct a conventional paired meta-analysis. Continuous data are represented by weighted mean difference (WMD), standardized mean difference (SMD) and 95 % confidence interval (CI), while dichotomous data will be calculated by risk ratio (OR) and 95 % CI. 2. NMA We will use STATA 16.0 and WinBUGS 1.4.3 for NMA to compare direct and indirect evidence. In WinBUGS 1.4.3 software, the Bayesian framework is simulated by Markov-chain-Monte-Carlo (MCMC) . After statistical analysis, the potential scale reduction factor (PSRF) will be applied to evaluate convergence. When the result is closer to 1, the convergence and the conclusion are more credible. If the PRSF exceeds this range, we will continue to manually increase the number of iterations until the FRSF is within this range. In addition, we will adjust the number of iterations and annealing times according to the actual situation. Numerical variables will be represented by SMD with 95%CI. Then, WinBUGS 1.4.3 software will be utilized to rank the effectiveness of different interventions. This study will adopt the subsurface cumulative ranking curve value to predict and rank the treatment effect. The higher the percentage, the better the intervention effect will be. Besides, we will analyze the consistency model of the main outcome indicators and the probability ranking of the optimum treatment measures. Considering there is a closed loop, we will apply the node splitting method to estimate the inconsistency between indirect comparison and direct comparison.

Subgroup analysis: When I2> 50% and P value <0.1, there is obvious heterogeneity between the studies, so it is necessary to analyze the reasons for heterogeneity. We will conduct a subgroup analysis based on the characteristics of the research related

to heterogeneous sources. Given the difference of methodology quality, subgroup analysis will be carried out in the light of the quality. Moreover, due to the heterogeneity caused by different designs, we will conduct subgroup analysis according to age, gender, treatment type, and the disease duration.

Sensibility analysis: Sensitivity analysis will be evaluated by excluding literature one by one to determine whether the literature has an impact on heterogeneity. When the heterogeneity of research changes after excluding a literature, the literature may be the source of the heterogeneity, and we will further analyze the following factors, such as the difference in sample size, the reference standard of the outcomes, etc. Otherwise, it indicates that the sensitivity is low, and the results are more stable and reliable.

Country(ies) involved: China.

Keywords: non-alcoholic fatty liver disease, Bayesian, network meta-analysis, complementary and alternative therapies, protocols.

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