INPLASY PROTOCOL

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None declared.

Efficacy and safety of Chinese herbal medicine combined with Sorafenib in the treatment of primary liver cancer: A protocol for systematic review and meta-analysis

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Review question / Objective: **The aim of this systematic review is to compare Chinese herbal medicine combined with Sorafenib in terms of efficacy and acceptability in the primary liver cancer to better inform clinical practice. To this end, the proposed systematic review will address the following question: Which is the best choice to reduce Efficacy and safety in Patients with primary liver cancer, Chinese herbal medicine combined with Sorafenib or Sorafenib.this systematic review and meta-analysis will evaluate the efficacy and Sorafenib combined with Chinese herbal medicine in the treatment of PLC.**
Information sources: **We will search the following databases from inception up to September 8, 2021: PubMed, Web of Science, Embase, AMED, Cochrane Library, CNKI, VIP, CBM, and Wanfang. There will be no restrictions regarding publication date or language. We will apply a combination of medical keywords and words, including "Sorafenib", "Chinese herbal medicine" and "primary liver cancer". Additionally, we will manually search all reference lists from relevant systematic reviews to find other eligible studies.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 08 September 2021 and was last updated on 08 September 2021 (registration number INPLASY202190024).

INTRODUCTION

Review question / Objective: **The aim of this systematic review is to compare Chinese herbal medicine combined with Sorafenib in terms of efficacy and acceptability in the primary liver cancer to better inform clinical practice. To this end, the proposed systematic review will address the following question: Which is the best choice to reduce Efficacy and safety in Patients with primary liver cancer,**

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Chinese herbal medicine combined with Sorafenib or Sorafenib.this systematic review and meta-analysis will evaluate the efficacy and Sorafenib combined with Chinese herbal medicine in the treatment of PLC.

Condition being studied: Primary liver cancer (PLC) is a common cancer, and its morbidity and mortality are ranked 6th and 3rd in the world for malignant tumors, respectively. According to statistics, there were 841,080 new cases and 781,631 deaths in 2018, accounting for 4.8% and 8.2% of all new cancer cases in the world, and this number is still on the rise, seriously endangering people's health. Although there are many treatment methods, such as surgical treatment, chemotherapy, interventional therapy, and molecular targeted therapy, they have many limitations in the scope of application (such as liver function Child-Push score and tumor staging). Moreover, the efficacy of the above treatments did not meet expectations, so the mortality and prognosis of PLC still have not been improved. In short, the difficult-to-treat characteristics of PLC have caused a major global health and economic burden. As a complementary and alternative medicine, Chinese herbal medicine has gradually shown advantages in the treatment of PLC, which is one of the current research hotspots. Sorafenib is a commonly used anti-tumor drug. As the only PLC systemic drug in the last ten years of 2007, its efficacy in the treatment of PLC has been confirmed. However, its drug resistance is also an issue that cannot be ignored. In recent years, Chinese herbal medicine combined with sorafenib has been widely used in the treatment of PLC, and there are few restrictions. Chinese herbal medicine can also improve the resistance of sorafenib to a certain extent. However, there is no obvious evidence to show the effectiveness of Sorafenib and Chinese herbal medicine for PLC and the incidence of its side effects. This is also an important reason that prevents it from spreading to the Western world for its treatment of PLC. Therefore, this systematic review and meta-analysis will evaluate the efficacy and Sorafenib combined with Chinese herbal medicine in the treatment of PLC.

METHODS

Search strategy: We will search the following databases from inception up to September 8, 2021: PubMed, Web of Science, Embase, AMED, Cochrane Library, CNKI, VIP, CBM, and Wanfang. There will be no restrictions regarding publication date or language. We will apply a combination of medical keywords and words, including "Sorafenib", "Chinese herbal medicine" and "primary liver cancer". Additionally, we will manually search all reference lists from relevant systematic reviews to find other eligible studies.

Participant or population: Patients with primary liver cancer who have undergone Chinese herbal medicine combined with Sorafenib treatment or Sorafenib. There are no restrictions on race, age, gender, etc.

Intervention: Chinese herbal medicine combined with Sorafenib.

Comparator: Sorafenib.

Study designs to be included: Randomized controlled study.

Eligibility criteria: The inclusion criteria were as follows: (1) the study was a randomized controlled study (RCT); (2) the included patients had PLC; (3) the experimental group is treated with Chinese herbal medicine and sorafenib, the control group is treated with sorafenib, and supportive treatment is the basic treatment method of the two groups. The exclusion criteria were as follows: (1) metastatic liver cancer; (2) other treatments in the experimental group and the control group; (4) the literature is not the type of included research.

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or language. We will apply a combination of medical keywords and words, including "Sorafenib", "Chinese herbal medicine" and "primary liver cancer". Additionally, we will manually search all reference lists from relevant systematic reviews to find other eligible studies.

Main outcome(s): The short-term curative effect is effective, the quality of life is stable, and the survival rate of patients is six months and one year.

Additional outcome(s): The occurrence of side effects, such as fever, nausea and vomiting, incidence of liver damage, etc.

Quality assessment / Risk of bias analysis: The two authors will use the Cochrane risk bias assessment tool to separately assess the quality of randomized studies.[13] The Cochrane bias risk assessment tool consists of six parts: selection bias (random sequence generation), selection bias (distribution hiding), implementation bias, measurement bias, follow-up bias, reporting bias, and other biases. Each item is divided into high-risk and low-risk. The three options are not clear. When the evaluation quality of the same study was inconsistent, it was resolved through consensus among all authors.

Strategy of data synthesis: We will use the random effects model in Review Manager software (REVMAN v5.3 Cochrane Collaboration) for meta-analysis, and $P<0.05$ was considered statistically significant. Two authors will perform data extraction and input independently, the third author will check the data, and the other two authors will perform data calculations. Evaluate the hazard ratio of the 95% confidence interval or the standardized mean difference of 95% CI for binary classification results or continuous results, respectively. We will use I2 statistics to detect clinical heterogeneity. If there was a high degree of heterogeneity between trials ($I2 \geq 50\%$), we tried to determine the source of heterogeneity through subgroup analysis, meta-regression and sensitivity analysis.

Subgroup analysis: We will use subgroup analysis based on different interventions, controls, and outcomes.

Sensitivity analysis: Sensitivity analysis will be performed by removing low methodological quality studies. We will be able to assess the impact of individual studies on the overall results and determine whether the results are strong.

Language: There will be no restrictions regarding language.

Country(ies) involved: China.

Keywords: Chinese herbal medicine, efficacy, meta-analysis, primary liver cancer, protocol, systematic review, Sorafenib.

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