INPLASY PROTOCOL

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Corresponding author:
Yuli Sun

sunyulijn@126.com

Author Affiliation:
Affiliated Hospital of Shandong University of Traditional Chinese Medicine.

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None declared.

Efficacy and safety of Yangzheng xiaoji capsule combined with TACE for intermediate and advanced hepatocellular carcinoma：A protocol for systematic review and meta-analysis

Sun, YL[1]; Li, M[2]; Tan, ZF[3]; Wang, LJ[4]; Liu, DD[5]; Sun, JG[6].

Review question / Objective: **Yangzheng Xiaoji Capsules combined with TACE play an important role in the treatment of intermediate and. However, its exact clinical efficacy and safety are still not well studied. Therefore, we use the method of meta-analysis to summarize the efficacy and safety of Yangzheng Xiaoji Capsules combined with TACE in the treatment of intermediate and.advanced hepatocellular carcinoma.**
Information sources: **We will comprehensively search the Cochrane Library, PubMed, Embase, ClinicalTrials foreign databases, and CNKI, Wanfang database, Weipu database, China Biomedical database. The search strategy will be constructed in the form of Medical Subject Headings (MeSH) combine with keywords. We will also search ongoing trial registers in the trial registry websites.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 October 2021 and was last updated on 18 October 2021 (registration number INPLASY2021100066).

INTRODUCTION

Review question / Objective: **Yangzheng Xiaoji Capsules combined with TACE play an important role in the treatment of intermediate and. However, its exact clinical efficacy and safety are still not well studied. Therefore, we use the method of meta-analysis to summarize the efficacy and safety of Yangzheng Xiaoji Capsules combined with TACE in the treatment of**

intermediate and.advanced hepatocellular carcinoma.

Condition being studied: Hepatocellular carcinoma (HCC), most of which has the background of chronic liver disease, is known as the king of cancers due to its characteristics of insidious onset, high incidence, high recurrence rate and high mortality rate. It is a major public health problem facing the world at present and in the coming decades. According to statistics, there were about 854,000 new cases of HCC in 2015, while there are an estimated 810,000 HCC related deaths each year, with a mortality ratio of close to 1. Worldwide, ASMR is close to ASIR, reflecting that HCC is a highly lethal tumor. Hepatitis B virus (HBV) is the leading cause of HCC and death worldwide (33%), followed by alcohol (30%), hepatitis C virus (HCV) (21%) and other causes (16%). The global incidence of HCC is uneven due to different potential risk factors. It is estimated that the highest is in East Asia and Africa, with 72% of cases in Asia (over 50% in China), and about 60% of the population attributed to hepatitis B virus infection. However, only 20% of cases in the Western world can be attributed to HBV infection, and chronic HCV is the most common underlying etiology of liver disease. Obesity may account for 16% of HCC cases in Europe, and obesity and/or diabetes account for 37% of HCC cases in the United States. In addition, there is a causal relationship between alcohol consumption and its associated cirrhosis and the development of HCC. According to statistics, the global incidence of HCC has increased by 75% between 1990 and 2015. Based on this trend, the number of new cases and deaths from HCC is expected to increase from 841,080 and 781,631 in 2018 to 1,361,836 and 1,284,252 in 2040. In the United States, the incidence of HCC due to NAFLD will increase by 122% between 2016 and 2030, from 5,510 to 12,240 cases. Therefore, the treatment of HCC is one of the focus of global medical attention. Hepatocellular carcinoma (HCC) is a kind of invasive liver tumor, the vast majority of chronic liver disease or with liver fibrosis and cirrhosis of the liver, appears most early in patients with asymptomatic or nonspecific discomfort, such as abdominal pain, abdominal distension, jaundice and weight loss, the main is ultrasonic and AFP monitoring, because of the sensitivity is not high and poor compliance, HCC found most middle-late, 5-year survival rate is very low, about 18%. Due to the influence of tumor size and location, as well as basic liver lesions, liver function and the overall condition of the patient, advanced HCC is not suitable for surgical resection, usually with poor prognosis and low 5-year survival rate.

METHODS

Participant or population: The population includes advanced liver cancer diagnosed according to any international or nationally recognized diagnostic criteria (such as the Chinese Society of Clinical Oncology Guidelines for the Diagnosis and Treatment of Primary Liver Cancer, the American Society of Clinical Oncology Guidelines for the Treatment of Hepatocellular Carcinoma, etc.)

Intervention: Patients in the experimental group with intermediate and advanced hepatocellular carcinoma must be treated with Yangzheng Xiaoji Capsules combined with TACE.

Comparator: The control group only received TACE treatment.

Study designs to be included: We will include all RCTs that use Yangzheng Xiaoji Capsules in combination with TACE for the treatment of intermediate and advanced hepatocellular carcinoma.

Eligibility criteria: We include studies if they meet the following criteria: 1) Patients diagnosed with intermediate and advanced hepatocellular carcinoma according to international or nationally recognized diagnostic criteria; 2) The experimental group was treated with Yangzheng Xiaoji Capsules combined with TACE; 3) The control group was treated with TACE;

4)study types are randomized controlled trials.

Information sources: We will comprehensively search the Cochrane Library, PubMed, Embase, ClinicalTrials foreign databases, and CNKI, Wanfang database, Weipu database, China Biomedical database. The search strategy will be constructed in the form of Medical Subject Headings (MeSH) combine with keywords. We will also search ongoing trial registers in the trial registry websites.

Main outcome(s): Overall response rate (ORR, complete response + partial response) and disease control rate (DCR, complete response + partial response + stable disease); QoL as evaluated by Karnofsky score; Clinical symptoms, such as abdominal pain, distension, fatigue, fever, and loss of appetite.

Additional outcome(s): Immune function indicators: CD3+, CD4+, CD8+, natural killer (NK) cells percentage, and CD4+/CD8+ cell ratios, and serumcytokines level [Interleukin-2 (IL-2), Interleukin-4 (IL-4),Interferon-g (IFN-g) and tumor necrosis factor-a (TNF-a)]; Liver function: ALT, AST, TBIL, DBIL, IBIL, ALB;Adverse events: toxicity was graded from 0 to IV in severity on the basis of the WHO recommendations.

Data management: The included literature must cover one or more main indicators.

Quality assessment / Risk of bias analysis: The quality of each trial will be assessed by two researchers independently based on the Cochrane Risk of Bias Risk Assess ment Tool recmmenedby Cochrane Handbook version. Use the decision words "high risk", "low risk", and "unclear risk" to evaluate the quality of the input article in 7 aspects, including: whether the random sequence is sufficient; whether there is hidden allocation; whether blinding is used; whether the result data is complete; Whether there is selective reporting; whether there is publication bias; others.

Strategy of data synthesis: We will utilize Review Manager 5.3 and Stata 14.0 statistical software to pool the data and carry out the data analysis. For continuous data, the extracted data will be presented as standardized mean difference (SMD) with their confidence intervals (CIs). Dichotomous data will be recorded as risk ratio (RR) with 95% CIs. A two-tailed P<.05 was considered statistically significant.

Subgroup analysis: Subgroup analysis: Subgroup analysis will be considered if sufficient data is available.

Sensitivity analysis: Sensibility analysis: Sensitivity analysis will be conducted with symptom improvement rate to evaluate clinical similarity and methodology of included studies to determine the reliability of the results of this study.

Country(ies) involved: China.

Keywords: Yangzheng xiaoji capsule; intermediate and advanced hepatocellular carcinoma; clinical symptoms;quality of life; Protocol.

Contributions of each author:

Author 1 - Yuli Sun.
Email: sunyulijn@126.com
Author 2 - Min Li.
Author 3 - Zhaofeng Tan.
Author 4 - Lijun Wang.
Author 5 - Danan Liu.
Author 6 - Jianguan Sun.