INPLASY PROTOCOL

Corresponding author:
Qian Wu

2958552563@qq.com

Author Affiliation:
Beijing University of Chinese Medicine

Review Stage at time of this submission: Preliminary searches.

Conflicts of interest: None.

Efficacy and safety analysis of combined Chinese and Western medicine in the treatment of lung cancer with brain metastasis

Wu, Q[1]; Duan, H[2]; Zhou, T[3].

Review question / Objective: The combination of traditional Chinese and Western medicine in the treatment of brain metastasis of lung cancer has gradually shown greater advantages, but its exact efficacy lacks the strong support of multi center and large sample clinical trials. This study intends to use the method of systematic evaluation to retrieve the clinical randomized controlled trials for the treatment.The purpose of the analysis is to further evaluate the clinical efficacy of the combination of Chinese and Western medicine in the treatment of brain metastasis of lung cancer so as to provide evidence-based basis for the rational use of drugs for clinicians.

INTRODUCTION

Review question / Objective: The combination of traditional Chinese and Western medicine in the treatment of brain metastasis of lung cancer has gradually shown greater advantages, but its exact efficacy lacks the strong support of multi center and large sample clinical trials. This study intends to use the method of systematic evaluation to retrieve the clinical randomized controlled trials for the treatment.The purpose of the analysis is to further evaluate the clinical efficacy of the combination of Chinese and Western medicine in the treatment of brain metastasis of lung cancer so as to provide evidence-based basis for the rational use of drugs for clinicians.

Rationale: It is the first time to systematically evaluate the efficacy and

safety of integrated Chinese and Western medicine in the treatment of lung cancer with brain metastasis.

Condition being studied: Brain Metastases (BMs) is an important cause of lung cancer morbidity and death. About 20% of patients with lung cancer had Brain Metastases at the time of first diagnosis, which greatly affects the quality of life and prognosis of patients and endangers their lives. Moreover, the median overall survival (mOS) of BMs patients with lung cancer is less than 3 to 6 months.It is difficult for some chemotherapy drugs to pass through the blood-brain barrier (BBB). Nowadays, only one single treatment method is rarely used clinically, but a comprehensive treatment method is adopted, such as surgical treatment combined with chemotherapy, surgical treatment combined with radiotherapy, radiotherapy combined with radiotherapy, and targeted therapy.In recent years, integrated Traditional Chinese and western medicine has been widely used in lung cancer with brain metastasis, and has played an important role in improving clinical symptoms, reducing side effects of radiotherapy, improving quality of life, and prolongating survival.

METHODS

Search strategy: We will search the following electronic bibliographic databases from their inception to January 2020:PubMed, EMBASE, The Cochrane Library(the Cochrane Database of Systematic Reviews, the Cochrane Central Register of Controlled Trials(CENTRAL), and the Cochrane Methodology Register), Chinese National Knowledge Infrastructure(CNKI), Wanfang Database, Chinese Biology Medical Database (CBM) and Chinese Scientific Journal Database (VIP).The language is restricted to Chinese and English.All literature reviews were performed by two independent researchers.

Participant or population: English databases (PubMed, Embase, Cochrane Library) and Chinese databases (CnKI, Wanfang, Viper and Chinese Biomedical Literature System) were searched by computer, and the retrieval time was from 2020-05-30 with no language restriction.Use the combination of subject words and free words.Keywords: Lung Neoplasms, Pulmonary Neoplasms, Neoplasm, Lung, Brain metastasis, Integrated Traditional Chinese AND Western Medicine, etc.Chinese search words: "lung cancer brain metastasis", "lung cancer brain metastasis", "lung cancer", "brain metastasis", "Traditional Chinese and Western medicine", etc.

Intervention: Patients received integrated traditional Chinese and Western Medicine.

Comparator: Patients received standard western medicine treatment alone.

Study designs to be included: Only clinical randomized controlled trials (RCTs) were eligible.

Eligibility criteria: Brain metastasis of lung cancer was confirmed by histology or pathology. There was no restriction on age, gender or race. The experimental group was integrated traditional Chinese and Western medicine treatment group, while the control group was pure Western medicine treatment group.Only randomized controlled studies were included.

Information sources: We will seek missing data by contacting the original authors whenever possible.If we failed to obtain the missing data, those data will be excluded from the analysis.

Main outcome(s): (1)ORR: Complete response (CR), partial response (PR), no progression (SD), worsening (PD) according to the world Health Organization (WHO) general evaluation indicators of objective efficacy of solid tumor.ORR=(CR+PR)/ (CR+PR +SD+PD) ×100%.CR: Tumor lesions were completely disappeared and maintained above 4W;PR: The product of the maximum diameter and the maximum vertical transverse diameter of tumor lesions decreased by more than 50%, while other lesions did not increase

and no new lesions appeared, maintaining over 4W.(2)OS: median survival, 1-year survival, 2-year survival.

Additional outcome(s): (1)ORR: Complete response (CR), partial response (PR), no progression (SD), worsening (PD) according to the world Health Organization (WHO) general evaluation indicators of objective efficacy of solid tumor.ORR=(CR+PR)/ (CR+PR +SD+PD) ×100%.CR: Tumor lesions were completely disappeared and maintained above 4W;PR: The product of the maximum diameter and the maximum vertical transverse diameter of tumor lesions decreased by more than 50%, while other lesions did not increase and no new lesions appeared, maintaining over 4W.(2)OS: median survival, 1-year survival, 2-year survival.

Data management: Literature screening and data extraction were conducted independently by 2 researchers according to the inclusion criteria, including the first author, year of publication, sample size, age, gender, pathology, brain metastasis site, intervention measures and outcome indicators.If there are doubts, they are discussed or resolved by a third person.

Quality assessment / Risk of bias analysis: The quality of the included RCTS was assessed using Cochrane Systematic Review Manual 5.1(Insert literature) and evaluated from seven aspects: RCTS, allocation concealment, blind participants and researchers, blind outcome evaluation, incomplete outcome indicators, selective reporting, and other biases.According to the evaluation results, the included literatures were divided into "high risk", "low risk" and "unknown situation". When the number of literature studies ≥10, funnel plot was used for publication bias analysis.

Strategy of data synthesis: Data were analyzed using RevMan 5.3.Dichotomous data will be expressed as the risk ratio (RR), and continuous outcomes will be presented as the weighted mean difference (MWD). 95% confidence intervals (95% CI) will be calculated for both types of data .Survival data were assessed with the

hazard ratios (HRs) and 95% CIs.A Cochran's Q-test with P>0.10 and an I² of no more than 50% indicated that statistical homogeneity was acceptable.When the heterogeneity exists (I² > 50% or P < 0.1), random effects model was applied to estimate the data synthesis, otherwise a fixed effects model for meta-analysis was used.Descriptive analysis will be performed on data that cannot be synthesized.

Subgroup analysis: Subgroup analysis will be conducted when there is significant clinical heterogeneity in the included studies, such as different dosage and comparative interventions and so on.

Sensibility analysis: Sensitivity analysis will be conducted when there is significant clinical heterogeneity in the included studies, such as different dosage and comparative interventions and so on.

Language: Both Chinese and English can be included in the study.

Country(ies) involved: China.

Keywords: Integrated Chinese and Western medicine treatment; Lung cancer with brain metastasis; Meta analysis.

Contributions of each author:
Author 1 - Qian Wu - The data were extracted by two reviewers(Qian Wu and Hua Duan) independently. The extracted data are mainly as follows: title, author, publication time, sample size, intervention measures, control measures, outcomes, etc.
Author 2 - Hua Duan - The data were extracted by two reviewers (Qian Wu and Hua Duan) independently.The extracted data are mainly as follows: title, author, publication time, sample size, intervention measures, control measures, outcomes, etc.
Author 3 - Tian Zhou - The data were extracted by two reviewers(Qian Wu and Hua Duan) independently. The extracted data are mainly as follows: title, author, publication time, sample size, intervention measures, control measures, outcomes, etc.