INPLASY PROTOCOL

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Corresponding author:
Li-dan Zhang

13253619363@163.com

Author Affiliation:
Institute of Basic Chinese Medicine, Chinese Academy of Chinese Medical Sciences

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There is no conflict of interest.

Efficacy and Safety of Xuebijing Injection in the Treatment of Adult Severe Pneumonia Systematic Evaluation and Meta-analysis

Zhang, LD[1]; Chai, Y[2]; Lyu, J[3]; Zhang, C[4]; Xie, YM[5].

Review question / Objective: **The current clinical treatment for adult severe pneumonia often involves the maintenance of vital signs, a large number of antibiotics and hormones and other methods. However, due to the increase of the high-risk host of infection, multiple infections, bacterial resistance, multidrug resistance, and other phenomena are becoming more and more serious. The therapeutic effect is not obvious, while the Xuebijing injection, which contains safflower, red peony root, Chuanxiong (Ligustricum striatum), red sage (Salvia miltiorrhiza) and angelica, is based on the theory of promoting blood circulation and removing blood stasis. All these ingredients promote blood circulation and removing blood stasis. They have good clinical efficacy for diseases such as febrile disease and systemic inflammatory response syndrome, etc.In view of this situation, this study used the method of systematic evaluation to collect the published randomized controlled trials of the Xuebijing injection in the treatment of adult severe pneumonia, and to further evaluate and explore the clinical efficacy and safety of Xuebijing injection in the treatment of severe pneumonia in adults.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 13 August 2020 and was last updated on 13 August 2020 (registration number INPLASY202080056).

INTRODUCTION

Review question / Objective: **The current clinical treatment for adult severe pneumonia often involves the maintenance of vital signs, a large number of antibiotics and hormones and other methods. However, due to the increase of the high-risk host of infection, multiple infections, bacterial resistance, multidrug resistance, and other phenomena are becoming more and more serious. The therapeutic effect is not obvious, while the Xuebijing injection, which contains safflower, red peony root, Chuanxiong (Ligustricum striatum), red sage (Salvia miltiorrhiza) and angelica, is based on the theory of promoting blood circulation and removing blood stasis. All**

these ingredients promote blood circulation and removing blood stasis. They have good clinical efficacy for diseases such as febrile disease and systemic inflammatory response syndrome, etc.In view of this situation, this study used the method of systematic evaluation to collect the published randomized controlled trials of the Xuebijing injection in the treatment of adult severe pneumonia, and to further evaluate and explore the clinical efficacy and safety of Xuebijing injection in the treatment of severe pneumonia in adults.

Rationale: This study used meta-analysis to evaluate the efficacy and safety of the Xuebijing injection in the treatment of severe pneumonia in adults and to provide reference for the treatment of new coronavirus pneumonia.

Condition being studied: Eight Chinese and English databases were mechanically searched, including Chinese periodical full-text database (CNKI), WanFang database, VIP database, Chinese BioMedical Database (CBM), PubMed, EMbase, web of science, and Cochrane Library. A randomized controlled trial of the Xuebijing injection in the treatment of severe pneumonia in adults was comprehensively conducted. The evaluation was performed according to the Cochrane evaluation criteria and tools, and meta-analysis was performed with RevMan5.3 software.

METHODS

Search strategy: Electronic databases, including CNKI, Wan Fang, CBM, PubMed, EMBASE, Web of Science, and the Cochrane Library were systematically searched for entries added between inception and May 2020, and not subject to published language restrictions. The following search terms were used separately or in combination: 'Xuebijing' or 'Xuebijing injection' AND 'Severe pneumonia' or 'sever pneumoniae'.

Participant or population: Adult severe pneumonia.

Intervention: Xuebijing injection plus routine Western-medicine treatment group.

Comparator: Western-medicine treatment group.

Study designs to be included: A randomized controlled trial of the Xuebijing injection in the treatment of severe pneumonia in adults was comprehensively conducted.

Eligibility criteria: 1) the study was performed as a randomized controlled trial (RCT)2) The subjects were defined as adults with severe pneumonia and met the diagnostic criteria for severe pneumonia. 3) Interventions: The control group was treated with routine treatment (cough, spasmolytic, anti-asthmatic, etc.) or 1-2 other kinds of western medicine on the basis of routine treatment. The experimental group was treated with Xuebijing injection, or combined with Xuebijing injection on the basis of the control group. 4) Main outcome indicators: Total effective rate, Mortality rate. Secondary outcomes included laboratory findings and adverse events.

Information sources: Chinese periodical full-text database (CNKI), WanFang database, VIP database, Chinese BioMedical Database (CBM), PubMed, EMbase, web of science, and Cochrane Library.

Main outcome(s): Total effective rate (total effective rate = (number of effective cases) / total number of cases × 100); Mortality rate.

Additional outcome(s): Secondary outcomes included laboratory findings and adverse events. The laboratory tests included white blood cell count (WBC), oxygenation index (Pao2/ Fio2), C-reactive protein (CRP) and any adverse drugs events/reactions (ADEs/ADRs).

Quality assessment / Risk of bias analysis: according to the bias-risk assessment tool of Cochrane collaboration network, the quality of the literature was evaluated. The

quality evaluation includes the following items: 1) Random sequence generation; 2) Allocation concealment; 3) Blinding of participants and personnel; 4) Blinding of outcome assessment; 5) Incomplete outcome data; 6) Selective reporting; 7) Other bias. The methodological quality of the included studies was evaluated by making high-risk, low-risk, uncertain risk judgments for each entry bias.

Strategy of data synthesis: The RevMan 5.3 software provided by Cochrane Collaboration was used to analyze the data. The relative ratio (RR) and 95% CI were used for binary outcomes while the weighted mean difference and 95% CIs were used for continuous outcomes. If there was no significant heterogeneity among the studies ($I^2 \leq 75\%$), the data were quantified by meta-analysis; if $I^2 \leq 25\%$, we use the fixed effect model for analysis; if $25\% \leq I^2 \leq 75\%$, indicating a certain degree of statistical heterogeneity between studies, we use the random effects model; if the heterogeneity was greater than 75%, indicating a statistically significant heterogeneity, a meta-analysis was not performed.

Subgroup analysis: Subgroup analysis was not used in this study.

Sensibility analysis: Meta reliability and stability of the results are inferred by sensitivity analysis. When the results of the sensitivity analysis show significant differences, the results of the meta analysis are considered to be of poor stability and low credibility, conclusions should be drawn with caution, and sensitivity can be carried out to identify the main factors that may affect the stability and authenticity of the results. if the results of sensitivity analysis and meta analysis are not significantly different, it is considered that the results of meta analysis are stable and reliable.

Language: English.

Country(ies) involved: China and the United States.

Keywords: Xuebijing injection; Severe pneumonia; COVID-19;Systematic evaluation; meta analysis.

Contributions of each author:
Author 1 - Li-dan ZHANG.
Author 2 - Yan CHAI.
Author 3 - Jian-LYU.
Author 4 - Cheng ZHANG.
Author 5 - Yan-ming XIE.