INPLASY PROTOCOL

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The authors do not have any conflicts of interest to report.

Efficacy and safety of ShenSongYangXin Capsule combined with antiarrhythmic drugs for atrial fibrillation - A protocol for systematic review and network meta-analysis

Shi, QS[1]; Shi, JJ[2]; Jia, QL[3]; Shi, S[4]; Yuan, GZ[5]; Hu, YH[6].

Review question / Objective: **Is Shensong Yangxin capsule (SSYX) combined with anti-arrhythmic drugs (AADs) effective in reducing the frequency of atrial fibrillation (AF) attack? Is SSYX combined with AADs effective to relieve the clinical symptoms of AF patients? Compared with using AADs alone, is SSYX combined with AADs effective in reducing the adverse events?**
Condition being studied: **AF is the most common clinical arrhythmia characterized by the high-frequency electrical activity of the atrium and unsynchronized atrial contraction. With a global prevalence of 33.5 million, the number of AF patients is continuously increasing and is estimated to rise to 12.1 million in the United States by 2030. SSYX is a Chinese patent medicine, which combined with AADs in the treatment of AF has been widely applied in clinical practice, but the results are controversial. This study aims to conduct a network meta-analysis based on data from the randomized controlled trials to evaluate the efficacy and safety of SSYX combined with ADDs in the treatment of AF.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 August 2020 and was last updated on 18 August 2020 (registration number INPLASY202080075).

INTRODUCTION

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METHODS

Participant or population: All adult patients diagnosed with AF (aged 18 and over, with no upper age limit) will be included in the study. We will follow the 2016 European Society of Cardiology preliminary criteria for the clinical diagnosis of AF and the AHA/ACC/HRS 2019 guidelines for the management of patients with AF.

Intervention: Both the experimental group and the control group routinely treated for basic cardiovascular diseases, including antihypertensive, anticoagulant, lipid-lowering, diuretic and other treatments. According to the literature, the intervention methods were designed into following groups:1) SSYX with Amiodarone; 2) SSYX with Propafenone; 3) SSYX with Metoprolol; 4) SSYX with Bisoprolol; 5) others: alternative AADs.

Comparator: Patients in the control group are those who only have received AADs treatment without SSYX.

Study designs to be included: RCTs regarding SSYX combined with AADs for AF will be included without language restriction.

Eligibility criteria: The following were the inclusion criteria: a) study design: RCTs regarding SSYX combined with AADs for AF will be included without language restriction. b) population: All adult patients diagnosed with AF (aged 18 and over, with no upper age limit) will be included in the study. We will follow the 2016 European Society of Cardiology preliminary criteria for the clinical diagnosis of AF and the AHA/ACC/HRS 2019 guidelines for the management of patients with AF. c) intervention: the intervention methods were designed into following groups:1) SSYX with Amiodarone; 2) SSYX with Propafenone; 3) SSYX with Metoprolol; 4) SSYX with Bisoprolol; 5) others: alternative AADs. d) control: Patients in the control group are those who only have received AADs treatment. e) outcomes: The primary outcomes will be the frequency of AF attack and P-wave dispersion, which will be measured by electrocardiogram or 24hours dynamic electrocardiogram result.

Information sources: In this study, we will search seven commonly used databases: Cochrane Library, PubMed, Web of Science, EMBASE, Chinese Biomedical Literature Database (SinoMed), CNKI and WanFang database. The retrieval time begins on the database's build date and ends in December 2019.The references of included studies will be tracked and those meeting the inclusion criteria will be supplemented. The search strategy will be adjusted according to the characteristics of different databases.

Main outcome(s): The primary outcomes will be the frequency of AF attack and P-wave dispersion, which will be measured by electrocardiogram or 24hours dynamic electrocardiogram result.

Additional outcome(s): The secondary outcomes will be:1) Symptom improvement, including palpitations, chest tightness, dizziness, blackness, fatigue and other symptoms; 2) Left atrial diameter that measured by echocardiography; 3) adverse events.

Quality assessment / Risk of bias analysis: The quality of the included studies will be assessed according to the Cochrane collaboration's risk of bias tool. The evaluation contents include random sequence generation, allocation concealment, participants and personnel blindness, outcome evaluation blindness, incomplete outcome data and selective reports. The risk of bias will be classified as “high risk”, “low risk” and “unclear risk”.

Strategy of data synthesis: Standard pairwise meta-analysis will be performed using Stata V.14.0 software. Odds ratio (OR) will be used as the effect size for enumeration data, mean difference (MD) will be used for measurement data, and 95% confidence interval (CI) will be used for interval estimation. To explore between-study variability, the Cochrane Q statistic with the χ2 test and the Higgins I2 test for heterogeneity will be used. WinBUGS 1.4.3 will be used for network statistical analysis , in which the posterior parameters will be calculated by Markov chain Monte Carlo methods. After an initial burn-in of 50,000, we will operate another 100,000 iterations.Surface under the cumulative ranking probabilities (SUCRA) values will be applied to rank the examined treatments, with SUCRA values of 100% and 0% assigned to the best and worst treatments, respectively. The network geometry will be drawn by Stata 14.0. The larger arm indicates a larger amount of basic data of the intervention, and the larger circle area indicates a better effectiveness of the intervention.Besides, a comparison-adjusted funnel plot was used to test for the publication bias.

Subgroup analysis: To assess the impact of covariates and areas (e.g., gender distribution, Severity of illness graded) of heterogeneity in our sample, we will explore subgroup analysis and/or use meta regression.

Sensibility analysis: We will conduct a sensitivity analysis to exclude each study sequentially and combine the remaining studies to identify the impact of each study on the overall outcome.

Country(ies) involved: China.

Keywords: Shen-song-yang-xin Capsule; atrial fibrillation; antiarrhythmic drugs; randomized controlled trials; network meta-analysis; protocol.

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