INPLASY PROTOCOL

To cite: Han et al. Comparison of efficacy and safety of complementary and alternative therapies for essential hypertension with anxiety or depression disorder A Bayesian network meta-analysis protocol. Inplasy protocol 202120068. doi: 10.37766/inplasy2021.2.0068

Received: 20 February 2021

Published: 20 February 2021

Corresponding author:
Qiming Zhang

zhang_917@126.com

Author Affiliation:
Shandong University of Traditional Chinese Medicine, Jinan, Shandong Province, China.

Support: **National Key R&D Program.**

Review Stage at time of this submission: **The review has not yet started.**

Conflicts of interest:
None declared.

Comparison of efficacy and safety of complementary and alternative therapies for essential hypertension with anxiety or depression disorder A Bayesian network meta-analysis protocol

Han, XY[1]; Liu, XX[2]; Zhong, FX[3]; Wang, Y[4]; Zhang, QM[5].

Review question / Objective: **1. Participants: (1) Patients who were diagnosed EH (SBP≥140 mmHg or DBP≥90mmHg, according to the diagnostic criteria of the Guidelines for Prevention and Control of Hypertension in 2010), with anxiety or depression disorder. (2) It is not affected by the age, sex and region of the included patients. 2. Intervention: The treatment group was treated with complementary replacement therapies on the basis of the control group. The complementary replacement therapies include biological-based therapies, traditional Chinese medicine (TCM), acupuncture, massage, qigong, moxibustion, yoga, Chinese herbal medicines, music therapy, five-animal exercises, cognitive-behavioral therapy, relaxation training, tai chi, mindfulness meditation, and so on. They can also be used without conventional hypotensive drugs. 3. Comparison: The control group was treated with or without conventional hypotensive drugs, at the same time, with or without anti-anxiety drugs or antidepressants. 4. Outcomes: Primary outcomes include the change of SBP and DBP, the change in score of any validated scales, such as HAMA, HAMD, or SAS, SDS, which can assess severity of anxiety or depression. The total efficacy rate, stationarity of hypotension, adverse effects, and TCM symptoms score, are Secondary outcomes. 5. Study design: the type of study is RCTs related to complementary and alternative therapies for EH complicated with anxiety or depression disorder, and the languages are Chinese and English.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 20 February 2021 and was last updated on 20 February 2021 (registration number INPLASY202120068).

INTRODUCTION

Review question / Objective: **1. Participants: (1) Patients who were diagnosed EH (SBP≥140 mmHg or DBP ≥ 90mmHg, according to the diagnostic criteria of the Guidelines for Prevention and Control of Hypertension in 2010), with**

anxiety or depression disorder. (2) It is not affected by the age, sex and region of the included patients. 2. Intervention: The treatment group was treated with complementary replacement therapies on the basis of the control group. The complementary replacement therapies include biological-based therapies, traditional Chinese medicine (TCM), acupuncture, massage, qigong, moxibustion, yoga, Chinese herbal medicines, music therapy, five-animal exercises, cognitive-behavioral therapy, relaxation training, tai chi, mindfulness meditation, and so on. They can also be used without conventional hypotensive drugs. 3. Comparison: The control group was treated with or without conventional hypotensive drugs, at the same time, with or without anti-anxiety drugs or antidepressants. 4. Outcomes: Primary outcomes include the change of SBP and DBP, the change in score of any validated scales, such as HAMA, HAMD, or SAS, SDS, which can assess severity of anxiety or depression. The total efficacy rate, stationarity of hypotension, adverse effects, and TCM symptoms score, are Secondary outcomes. 5. Study design: the type of study is RCTs related to complementary and alternative therapies for EH complicated with anxiety or depression disorder, and the languages are Chinese and English.

Condition being studied: EH with anxiety or depression belongs to the category of psycho-cardiology. In terms of treatment, we should not only treat hypertension, but also pay more attention to psychological diseases in order to achieve a good antihypertensive effect. Western medicine is often combined with anti-anxiety drugs or antidepressants, although the anxiety and depression of patients are alleviated to some extent, but many adverse reactions such as respiratory inhibition, mental fatigue, addiction, gastrointestinal reactions and so on are bad for the quality of life of patients. Another significant problem in the treatment of anti-anxiety drugs or antidepressants is poor compliance, with about 50% of patients discontinuing prescription drugs in the first month of medication. Studies have shown that tricyclic antidepressants and antidepressants that lower adrenaline and serotonin may lead to grade 1 hypertension in patients. Supplementary and replacement therapies have accumulated rich experience in clinical practices, which can reduce side effects and improve clinical efficacy.

METHODS

Participant or population: Inclusion criteria: (1) Patients who were diagnosed EH (SBP≥140 mmHg or DBP≥90mmHg, according to the diagnostic criteria of the Guidelines for Prevention and Control of Hypertension in 2010), with anxiety or depression disorder (according to the score of any validated scales). (2) It is not affected by the age, sex and region of the included patients. Exclusion criteria: (2) The subjects included were diagnosed patients with secondary hypertension; (3) Patients without anxiety or depression.

Intervention: The treatment group was treated with complementary replacement therapies on the basis of the control group. The complementary replacement therapies include biological-based therapies, traditional Chinese medicine (TCM), acupuncture, massage, qigong, moxibustion, yoga, Chinese herbal medicines, music therapy, five-animal exercises, cognitive-behavioral therapy, relaxation training, tai chi, mindfulness meditation, and so on. They can also be used without conventional hypotensive drugs.

Comparator: The control group was treated with or without conventional hypotensive drugs, at the same time, with or without anti-anxiety drugs or antidepressants.

Study designs to be included: The type of study is RCTs related to complementary and alternative therapies for EH complicated with anxiety or depression disorder, and the languages are Chinese and English.

Eligibility criteria: 1. Type of study: The type of study is RCTs related to complementary and alternative therapies for EH complicated with anxiety or depression disorder, and the languages are Chinese and English. 2. Participants: (1) Patients who were diagnosed EH (SBP≥140 mmHg or DBP≥90mmHg, according to the diagnostic criteria of the Guidelines for Prevention and Control of Hypertension in 2010), with anxiety or depression disorder (according to the score of any validated scales). (2) It is not affected by the age, sex and region of the included patients. 3. Interventions: The control group was treated with or without conventional hypotensive drugs, at the same time, with or without anti-anxiety drugs or antidepressants. The treatment group was treated with complementary replacement therapies on the basis of the control group. The complementary replacement therapies include biological-based therapies, traditional Chinese medicine (TCM), acupuncture, massage, qigong, moxibustion, yoga, Chinese herbal medicines, music therapy, five-animal exercises, cognitive-behavioral therapy, relaxation training, tai chi, mindfulness meditation, and so on. They can also be used without conventional hypotensive drugs. 4. Outcomes: Primary outcomes include the change of SBP and DBP, the change in score of any validated scales, such as HAMA, HAMD, or SAS, SDS, which can assess severity of anxiety or depression. The total efficacy rate, stationarity of hypotension, adverse effects, and TCM symptoms score, are Secondary outcomes.

Information sources: Chinese and English databases such as MEDLINE, PubMed, Embase, ClinicalTrials.gov, PsycINFO, Web of Science, Cochrane Library, Biosis, CNKI, Wanfang Database, Weipu Database and China Biology Medicine disc (CBMdisc) and so on will be searched by two independent researchers. RCTs, related to supplementation and replacement therapies of EH with anxiety or depression disorder, which were published from initial state to February 2021 will be collected in the form of computer retrieval. For the researches on the incomplete informations or some problems in the data, the corresponding author will be contacted to supplement the missing information as much as possible. At the same time, references of systematic review/meta-analysis as well as registered and ongoing trials will be traced.

Main outcome(s): Primary outcomes include SBP and DBP, the change in score of any validated scales, such as HAMA, HAMD, or SAS, SDS, which can assess severity of anxiety or depression.

Additional outcome(s): The total efficacy rate, stationarity of hypotension, adverse effects, and TCM symptoms score, are Secondary outcomes.

Quality assessment / Risk of bias analysis: The quality of literature will be scored according to the Jadad scale. The Jadad score of the selected literature should be greater than or equal to 3. In case of disagreement, consult the third party to decide. The funnel chart will be drawn, and the publication bias of the included data will be tested by Stata 16.0 to evaluate whether the inclusion studies have publication bias and effect of small sample size. If the included studies are concentrated near the midline and basically symmetrically distributed, it shows that the publication bias has little influence on this research. The quality of evidence is divided into five levels - risk of bias, indirectness, inconsistency, imprecision, and publication bias - in NMA according to Grading of Recommendations Assessment, Development and Evaluation (GRADE). GRADE is used to evaluate the level of evidences and recommendation intensity.

Strategy of data synthesis: 1. Pairwise meta-analysis: Stata 16.0 software will be used for statistical analysis. The ratio (OR) will be used as the index for the counting data, and the mean difference (MD) will be used for the measurement data. The 95% confidence interval (95% CI) of each effect size will be given. A p-value <0.05 will be considered significant. We will combined

with I2 to quantitatively judge the size of heterogeneity. 2. Network meta-analysis: In this paper, the NMA is mainly based on the Bayesian theory to compare all the intervention measures and make a comprehensive evaluation at the same time. The Markov chain Monte Carlo (MCMC) will be selected as the method. MCMC is a method of the joint posterior distribution by constructing simulation parameters of Markov-chain. The steps are as follows: checking model logic and syntax, importing data, and compiling. In this study, three chains will be selected for simulation, with 40000 iterations and 10,000 annealing times. Brooks-Gelman-Rubin will be used to evaluate the convergence of the model. The higher the surface under the cumulative ranking curve values (SUCRA) indicates that the better the efficacy of the intervention. And then efficacy of the intervention measures included in the end will be ranked.

Subgroup analysis: We will divided data into smaller units according to different design scheme, quality of literature, publishing year, etc. to make a further comparison.

Sensitivity analysis: After excluding the studies with abnormal results, the NMA will be carried out again, and the results are compared with the results of NMA which does not exclude the studies with abnormal results, so as to probe the influence of the studies on the merger effect. The methods of sensitivity analysis include excluding unpublished studies, including or excluding those controversial studies on whether they meet the inclusion criteria, excluding studies with low quality, using different statistical methods to re-analyze data, and so on.

Language: Chinese and English.

Country(ies) involved: China.

Keywords: essential hypertension, anxiety, depression, network meta-analysis, complementary and alternative therapies.

Contributions of each author:
Author 1 - Xueyan Han.
Author 2 - Xinxin Liu.
Author 3 - Fengxing Zhong.
Author 4 - Yiguo Wang.
Author 5 - Qiming Zhang.