

INPLASY PROTOCOL

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The authors have no conflicts of interest to disclose.

Comparison of efficacy and safety of complementary and alternative therapies for Primary Trigeminal neuralgia: A Bayesian network meta-analysis protocol

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Review question / Objective: 1. Participants (1) Patients diagnosed as primary trigeminal neuralgia; (2) No restrictions on gender, age, race, nationality, etc; 2. Intervention: complementary therapy and alternative therapies on the basis of conventional western medicine, or be used alone. Complementary therapy and alternative therapies include Chinese herbal medicine, acupuncture, moxibustion, massage, acupoint injection, psychotherapy and so on. 3. Comparison: western medicine or other methods based on western medicine. Other method include microvascular decompression, radiofrequency thermocoagulation, radiotherapy, local blocking therapy 4. Outcomes: The primary outcomes include the total efficiency rate and the visual analogue scale (VAS). The secondary outcomes include pain numerical rating scale, analgesic dose, recurrence rate, pain duration, and the incidence of toxic and side effects. 5. Study design: RCTs and systematic review/meta-analysis of supplementary and alternative treatments in PTN treatment. Case reports, reviews, animal experiments, non-RCT or semi-RCT trials, will not be included in this study. The language will be restricted in Chinese or English.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 05 December 2020 and was last updated on 05 December 2020 (registration number INPLASY2020120026).

INTRODUCTION

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race, nationality, etc; 2. Intervention: complementary therapy and alternative therapies on the basis of conventional western medicine, or be used alone. Complementary therapy and alternative

therapies include Chinese herbal medicine, acupuncture, moxibustion, massage, acupoint injection, psychotherapy and so on. 3. Comparison: western medicine or other methods based on western medicine. Other method include microvascular decompression, radiofrequency thermocoagulation, radiotherapy, local blocking therapy 4. Outcomes: The primary outcomes include the total efficiency rate and the visual analogue scale (VAS). The secondary outcomes include pain numerical rating scale, analgesic dose, recurrence rate, pain duration, and the incidence of toxic and side effects. 5. Study design: RCTs and systematic review/meta-analysis of supplementary and alternative treatments in PTN treatment. Case reports, reviews, animal experiments, non-RCT or semi-RCT trials, will not be included in this study. The language will be restricted in Chinese or English.

Condition being studied: In short, PTN is mainly treated by western medicine, MVD, RFT, GKSR and local blocking therapy. These therapies lack specific treatment, and also have adverse effects such as hearing loss, dizziness, sensory and motor nerve damage. Therefore, it is a treatment trend to seek green therapy with little trauma, better curative effects and fewer side effects. Nowadays complementary and alternative therapies have been widely used with significant clinical effects, that usually include Chinese herbal medicine, acupuncture, moxibustion, massage, acupoint injection, psychotherapy and so on. It is pointed out that acupuncture and traditional Chinese medicine have obvious advantages in treating PTN disease, which can not only reduce the pain degree and side effects of western medicine, but also improve the clinical curative effect, thus improving the quality of life of patients. TCM contains multiple components, which can target different pain pathological mechanisms. TCM can significantly improve the curative effect and help predict the risks of pain through various components and targets[7, 8]. Latest research indicates that acupuncture, a traditional Chinese practice, is much less

stressful, safer and cheaper than medication or surgery.

METHODS

Search strategy: We will search all related RCTs according to the complementary and alternative therapies for PTN from inception to November 2020 in the following databases: PubMed, Cochrane Library, Cochrane Central Register of Controlled Trials, Web of Science, EMBASE, Chinese Biomedical Literature Database (SinoMed), CNKI, VIP Database, Wanfang Database. Meanwhile, we will follow up the references included in the systematic review/meta-analysis. The search strategy will be constructed by MeSH and keywords.

Participant or population: Basic information of participants, including gender, age, sociodemographic characteristics, sample size, source of research subjects, inclusion criteria, exclusion criteria, course of treatment, people lost to follow-up or dropped out.

Intervention: Complementary therapy and alternative therapies on the basis of conventional western medicine, or be used alone. Complementary therapy and alternative therapies include Chinese herbal medicine, acupuncture, moxibustion, massage, acupoint injection, psychotherapy and so on. The information include therapeutic method, frequency, duration of treatment.

Comparator: Western medicine or other methods based on western medicine. Other method include microvascular decompression, radiofrequency thermocoagulation, radiotherapy, local blocking therapy. The information include therapeutic method, frequency, duration of treatment.

Study designs to be included: RCTs and systematic review/meta-analysis of supplementary and alternative treatments in PTN treatment. Case reports, reviews, animal experiments, non-RCT or semi-RCT trials, will not be included in this study. The

language will be restricted in Chinese or English.

Eligibility criteria: 1. Type of study This study will include RCTs and systematic review/meta-analysis of supplementary and alternative treatments in PTN treatment. Case reports, reviews, animal experiments, non-RCT or semi-RCT trials, will not be included in this study. The language will be restricted in Chinese or English. 2. Participants (1)Patients diagnosed as primary trigeminal neuralgia; (2)No restrictions on gender, age, race, nationality, etc; 3. Interventions In the treatment group, PTN must be treated with complementary therapy and alternative therapies on the basis of conventional western medicine, or be used alone. The control group should be treated with western medicine or other methods based on western medicine. 4. Outcomes The primary outcomes include the total efficiency rate and the visual analogue scale (VAS). VAS is a useful and reliable tool to determine the severity of pain, that ranges from 0 (no pain) to 10 (unbearable pain). The secondary outcomes include pain numerical rating scale (NRS), analgesic dose, recurrence rate, pain duration, and the incidence of toxic and side effects. Total efficiency rate will be calculated according to the total number of random patients.

Information sources: We will search all related RCTs according to the complementary and alternative therapies for PTN from inception to November 2020 in the following databases: PubMed, Cochrane Library, Cochrane Central Register of Controlled Trials, Web of Science, EMBASE, Chinese Biomedical Literature Database (SinoMed), CNKI, VIP Database, Wanfang Database. Meanwhile, we will follow up the references included in the systematic review/meta-analysis. Two reviewers (Tianqi Zhang and Tiefeng Zhang) will independently screen and extract data. We will resolve disagreements through discussion, or, if necessary, we will consult the third reviewer (Chuancheng Li). If the required information is not complete,

we are going to contact the corresponding author.

Main outcome(s): The primary outcomes include the total efficiency rate and the visual analogue scale (VAS).

Additional outcome(s): The secondary outcomes include pain numerical rating scale (NRS), analgesic dose, recurrence rate, pain duration, and the incidence of toxic and side effects.

Data management: According to the above strategy, we will retrieve all related papers from the database and then import the research into Endnote X9. Then, two reviewers (Tianqi Zhang and Tiefeng Zhang) will independently screen and extract data. All titles and abstracts of documents will be searched and irrelevant documents will be ruled out. For all abstracts deemed eligible for inclusion during the first level of review, full-text articles will be retrieved and reviewed. Full-text screening will be conducted by two independent investigators(Tianqi Zhang and Tiefeng Zhang). We will resolve disagreements through discussion, or, if necessary, we will consult the third reviewer (Chuancheng Li). If the required information is not complete, we are going to contact the corresponding author.

Quality assessment / Risk of bias analysis: For articles with more than 10 researches, a comparison-correction funnel chart will be established for the outcome indicators. If the funnel plot is symmetric, there is no significant publication bias. If it is asymmetric, there is a publication bias, it indicates that there may be publication bias and then we will analyze the reasons for that. We will assess the quality of evidence by GRADE, which includes risk of bias, indirectness, inconsistency, imprecision, and publication bias.

Strategy of data synthesis: 1.Pairwise meta-analysis We will carry out STATA15.0 software for pairwise meta-analysis. Bivariate and continuous variables are represented by OR and MD respectively. We will analyse 95% CI for each effect

indicator and calculate I² for assessing the heterogeneity among studies. 2. Network meta-analysis We will adopt STATA 16.0 to draw a network diagram to compare the intervention measures of each outcome indicator. In addition, we are going to utilize WinBUGS1.4.3 software to analyze the data, using the Bayesian Markov Chain Monte Carlo (MCMC) random effect model. Bayesian NMA can settle statistical processing in sophisticated evidence networks, so it is much more flexible and efficient. Meanwhile, the posterior probabilities obtained can be used to rank all intervention from good to bad. When working WinBUGS1.4.3 program, for every MCMC, the number of iterations will be set to 50,000, of which the first annealing is set to 20,000 times to remove the influence of the initial value, as well as the final 30,000 times are sampled. We will assess convergence of the iteration by the Brooks-Gelman Rubin method. If the potential scale reduction factor (PSRF) tends to 1, it means that the convergence of the model is more reliable. What's more, we will modulate the iteration times and annealing times in terms of the actual situation, and calculate the corresponding effective value of 95% CI. Moreover, the intervention measures will be ranked by using the cumulative ranking curve (SUCRA) values. 3. Assessment of inconsistency If NMA is closed loop, inconsistency will be estimated. Hence, we will calculate the difference between direct and indirect comparative evidence by the node splitting method. Then we will adopt the P value to conform whether there is.

Subgroup analysis: Assuming heterogeneity exists in the research, we will deal with it in subgroup analysis according to various sources of heterogeneity. Besides, for different design schemes, we will make subgroup analysis in the light of design scheme, country, publication year, age, onset time and duration.

Sensibility analysis: In addition, we will analyze the sensitivity of all outcome indicators by the exclusion method to. If the heterogeneity changes after excluding

an article, then this article is the cause of the heterogeneity. It can be discussed in terms of sample size, experimental design, result indicators, evaluation criteria, etc. On the contrary, if the heterogeneity still the same, then the result is stable and reliable.

Language: The language will be restricted in Chinese or English.

Country(ies) involved: China.

Keywords: primary trigeminal neuralgia, Bayesian, network meta-analysis, complementary and alternative therapies, protocol.

Contributions of each author:

Author 1 - Tianqi Zhang.

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