

The Effectiveness and Safety of Moxibustion for Peripheral Facial Paralysis: A Protocol for Systematic Review and Meta-Analysis

Shanshan Xiang

Jiangxi University of Traditional Chinese Medicine

Ting Fang

Jiangxi University of Traditional Chinese Medicine

Changan Ren

Jiangxi University of Traditional Chinese Medicine

Junnan Qi

Jiangxi University of Traditional Chinese Medicine

Zheng Guo

Jiangxi University of Traditional Chinese Medicine

Fushui Liu (✉ lfstcm@163.com)

Jiangxi University of Traditional Chinese Medicine <https://orcid.org/0000-0002-8304-0889>

Wenlong Yang

Jiangxi University of Traditional Chinese Medicine

Protocol

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Abstract

Background: Moxibustion has been used in treating patients with Peripheral Facial Paralysis(PFP), but its effectiveness and safety have not been systematically evaluated. Therefore, the objective of this review is to comprehensively assess the effectiveness and safety of moxibustion for PFP.

Methods: We will conduct a systematic document retrieval of databases from inception to March 18, 2021, including Embase, Cochrane Library, Pubmed, Chinese databases SinoMed, Chinese National Knowledge Infrastructure (CNKI), Chinese Scientific Journals Database and Wanfang Data (WF). Reviewers will independently retrieve databases, identify trials, extract data, and evaluate the quality of eligible randomized controlled trials(RCTs). The outcomes will include: the effective rate, the House-Brackmann (H-B) score, Facial Disability Index (FDI), and side effects. The quality of eligible RCT will be assessed by the Cochrane risk-of-bias. Meta-analysis will be processed by the Cochrane Collaboration's RevMan 5.3.0.

Discussion: This review will provide comprehensive evidence of moxibustion for PFP.

Systematic review registration: PROSPERO CRD42020207068

1. Introduction

Peripheral facial paralysis(PFP) is a common clinical condition in which facial expression muscle paralysis is caused by facial nerve dysfunction, and also a cause of face disability and resulting in lower quality of life^[1-2]. Otherwise a prospective study indicated that PFP may have a negative impression to people's mental health^[3]. On the basis of epidemiological survey, the incidence of different populations is about 11.5 to 53.3 per 100,000 people^[4]. And research shows that suffers moderate to severe facial dissymmetry may persist impacting on PFP patients quality of life, which data in approximately 15-25%^[5-6]. Based on the literatures, the majority of patients diagnosed with PFP is between the ages of 20 and 40, with a higher incidence in men than women^[7]. According to clinical observations, the PFP can occur in any season, but autumn and winter are the peak seasons^[7].

Clinically, the clinical symptoms of PFP include inability to move the expression muscles, shallowing or disappearing off the frontal lines and nasolabial fold on the affected side, crooked mouth corners to the good side, incomplete eyelid closure, poor whistling, and bulging cheeks^[8]. The main pathological feature is characterized by edema and facial nerve primary or secondary ischemia cause nerve compression and hypoxia^[9]. The overwhelming majority of causing PFP is idiopathic Bell's palsy^[10], followed by traumatic causes accidental trauma leading to temporal bone fractures^[9]. Currently, the treatments of PFP include oral steroids, antiviral therapy combined antiviral-steroid treatment, facial nerve decompression surgical and physical therapy^[11-14]. However, there are still debate^[11, 12, 15, 16] on the effectiveness of these interventions and often accompanied by varying degrees of side-effects^[11, 12, 15, 16]. Consequently, PFP sufferers require alternative treatments.

Moxibustion is a method of treatment originally in traditional Chinese medicine(TCM), which is the moxa sticks burned on the skin. According to theory of TCM, moxibustion is a kind of warm stimulus, which can warm the meridians and dispel cold, promote blood circulation and relieving pain. Some Chinese studies by RCTs or clinical observations^[17-19]suggest that the moxibustion has the potential to be an effective and safe therapy for PFP, such as improving facial expression, adjusting the facial nerve function, improving face symptoms^[20].

With the deepening of research, it has been proved that moxibustion is effective on over 300 diseases, by accommodating circulatory, nervous system, immunologic function, and facilitating the formation of adaptation of huamn organisms^[21]. Moxibustion is applied more widely to treat PFP, and its curative effect is positive in the clinical research of TCM. Therefore, the review is based on an evidence-based methodology to evaluate the effectiveness and safety of moxibustion in the treatment of PFP, to provide a scientific basis for the clinicians treat PFP.

2. Objective

The objective of this review is to conclude the clinical evidence on the effectiveness and safety of moxibustion for the treatment of PFP and to provide credible proposals for clinicians.

3. Methods And Analysis

3.1. Protocol registration

The protocol for the systematic review and meta-analysis(SR-MA) documented in PROSPERO 2020 CRD42020207068, which could available from:

http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42020207068. The protocol is draw up following the principles that guide the SR-MA protocol (PRISMA-P) statement in the Cochrane Handbook^[22]. If there are any changes on the protocol, we will describe them in detail in the final draft.

3.2. Inclusion criteria of literature

3.2.1. Participants of studies

We will include PFP patients who have been diagnosed by clinicians, on the basis of the diagnostic criteria of PFP established by the American Academy of Neurology (AAN) or the Neurology Society of Chinese Medical Association. There will be no restriction on country, occupation, race, age, and gender.

3.2.2. Interventions of studies

Depending on the purpose of our review, RCTs with moxibustion in the treatment group will be included. The treatment group with moxibustion in spite of the shape, size and type of moxa, length of time. The

intervention group can treat with moxibustion or associate other interventions, while comparison group will only include other treatments.

3.2.3. Outcome measures of studies

3.2.3.1 Primary outcomes. Effective rate and the H-B score are regarded as the primary outcomes.

3.2.3.2. Secondary outcomes

(1) Quality of life

(2) Facial symptoms: FDI

(3) Side effects and adverse events, such as dizziness, nausea, scald, cough, vomiting and so on.

3.2.4. Design types of studies

All usable RCTs of moxibustion in the treatment of PFP will be included. The language of RCTs will be limited to Chinese and English.

3.3. Exclusion for study selection

1. Patients with another disease which would influence the outcome indicators.
2. Duplicate publications.
3. Specialist experience or theoretical research.
4. Result data is missing or unable to get complete data.

3.4. Literature retrieval and screening

3.4.1. Retrieval strategy

To obtain relevant RCTs comprehensively, we will search CNKI, China Biology Medicine, VIP, WF, PubMed, MEDLINE, Embase, Cochrane Library, and Web of Science systematically from their inception to March 18, 2021. The MeSH and non-MeSH terms will be adjusted according to different database, which including peripheral facial paralysis, facial paralysis, facial nerve disease, Bell palsy, facial nerve paralysis, Ramsay-Hunt syndrome, moxibustion, thunder fire moxibustion, Du moxibustion, suspended moxibustion, needle warming moxibustion, taiyi miraculous moxa roll, randomized, RCT. In addition, grey literature were searched for supplement. The gender, race, age, or country of the participants will not be restricted. The concrete search strategy for PubMed shows in Table 1. The search strategy for Pubmed.

3.4.2. Study selection

The search results will be imported into NoteExpress 3.2.0, excluding duplicate literature by it. Before literature selection, all reviewers will discuss and decide the selection criteria together. Firstly, two

reviewers will exclude articles which did not meet the inclusion criteria by reading the title and abstract individually. Then they will read the rest of the studies in full text to make the ultimate decision. If there are disagreements, we will discuss or negotiate with the three reviewer to reach a consensus. The process of document screening is shown in Figure 1.

3.5. Data extraction and analysis

3.5.1. Data management and extraction

Two reviewers will independently design an extraction form to collect general information from including RCTs, including author, country, year of publication, diagnostic criteria, sample size, intervention(s), control(s), treatment cycle(s), outcome measure(s), adverse events and other informations. In cases of any disagreement, we will consult and discuss with the three reviewer. When the RCTs' requisite data are incomplete or missing, we will contact the first or corresponding author via e-mail for obtaining the data.

3.5.2. Assessing the risk of bias in included studies

Two reviewers will independently evaluate the methodological quality of included RCTs which base on the Cochrane Risk of Bias Assessment tool of Cochrane Reviewer's Handbook 5.0.24^[23], as following: randomly generated sequence number, allocation sequence concealment, blinding of participants and personnel, blinding of outcome assessors, incomplete outcome data, selective outcome reporting and other sources of bias. The trial will be classified into each aspect " high, low or unclear risk ". The rating results will be cross-checked by two reviewers, and all disagreements will consult with the three reviewer.

3.5.3. Synthesis of results

RevMan 5.3 software will be prepare to conduct meta-analysis. If the result of overall effect test is $P < 0.5$, it means that difference is statistically significant. On the contrary, the difference is not statistically significant between the experimental group and control group. As for the index of effect size, we will use the Weighted Mean Difference (WMD) and 95% confidence intervals(CI) to evaluate the continuous variables, while using rate ratio(RR)and 95% CI for dichotomous variables. The results will be presented in the form of forest maps.

3.5.4. Heterogeneity test

I^2 will be applied to assess the heterogeneity for included RCTs. When $P > 0.1$ and $I^2 \leq 50$, it is indicated that the merged studies with a lower heterogeneity, we will use the fixed-effects model. Oppositely, it means that the heterogeneity of the merged studies is higher, we will choose the fixed-effects model. When heterogeneity is apparent, we will perform subgroup analysis or sensitivity analysis to explore the source of heterogeneity and its impact on the research results.

3.5.5. Evaluation of reporting bias

When the number of eligible RCTs ≥ 10 , publication bias will be evaluated by funnel plot developed by Egger^[24]. If the funnel plot appeared to be symmetric, showing that studies are lower with publication bias; If to be asymmetric, showing that studies are higher with publication bias.

3.5.5. Analysis of sensitivity If heterogeneity is significant in combination of different research data, we will conduct sensitivity analysis in line with sample size, methodological components, quality of RCTs, and study characteristics. Sensitivity analysis will be applied to assess whether the results are stable.

3.5.6. Analysis of subgroup If the data of eligible RCTs are reliable, we will conduct subgroup analysis based on age, course, frequency of treatment, treatment cycle, interventions for the control group and so on. For instance, if included RCTs were divided into 2 subgroups basis of different moxibustion type, and the 2 subgroups put on heterogeneity test which had been proved to be homogeneous. If the data of the 2 subgroups were apparent heterogeneity, it revealed that moxibustion type was the source of heterogeneity. Conversely, it showed that the type has little impact on the study results.

3.5.7. Grading the quality of evidence

Two reviewers will independently assess the quality of eligible RCTs evidence by the software of GRADE profiler 3.6. The specific quality of the included RCTs will be evaluated in 5 dimensions (inconsistency, limitations, imprecision, indirectness, and publication bias), and ultimately the quality of RCTs outcome measure will be defined as 4 levels, expressed as high, moderate, low, or very low^[25].

4. Discussion

Peripheral Facial Paralysis(PFP) is a disease with multiple pathogenic factors and complicated nosogenesis. However, the exact pathogenesis of PFP remains controversial. Clinically, most PFP cases have been uncovered without determining a exact causation. Therefore, a new study analyze the actuality of theories regarding the causes of PFP in five aspect: cold stimulation, ischemia, anatomical, viral infection, and inflammation^[26]. Currently, it is generally agreed that inflammation and edema of the facial nerve leading to entrapment within the facial canal, which also is main pathological manifestations of early PFP^[26]. According to pathological manifestations of PFP, the most commonly accepted theories that cold stimulation lead to the microenvironment change of the facial microvascular neuron, which also an important factor causes inflammation and edema of the facial nerve^[27, 28].

Moxibustion, as one of the oldest traditional therapies, has been used to treat various diseases including PFP for many years. Moxibustion is a warm stimulus produced by burning moxa, which with the effect of removing pathogenic wind and dampness^[29]. Literature research showed that moxibustion which can expand the diameter of face capillaries, improve blood circulation, and relieve facial nerve and blood vessel spasm^[30]. Moxibustion can inhibits the release of inflammation at the branch of the facial nerve, which plays a critica role in eliminate the inflammation and edema of facial nerve^[31, 32].

PFP is a disease which influences a persons life via causing face modality change. Conventional treatments and operative intervention are helpful but at same time have their limitations. Recently, some clinical reports have showed that using moxibustion for PFP could contribute to both modality and functional aspects. However, there is no SR-MA on the effectiveness of moxibustion in the treatment of PFP so far. Based on the latest data, we hope that this study will provide clinicians and other workers with new ideas and programs for the treatment of PFP, and ultimately make thorough with the objective of reducing the physical damage and mental distort of patients.

Abbreviations

CI = confidence intervals, CNKI = China National Knowledge Infrastructure, PFP = Peripheral Facial Paralysis, MeSH = Medical Subject Headings, PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses, RCTs = randomized controlled trials, RoB = risk of bias, TCM = traditional Chinese Medicine, WF = Wanfang Data, systematic review and meta-analysis = SR-MA.

Declarations

Ethics approval and consent to participate

No ethics approval is required for this systematic review because we will be using information from published documents. Our findings will be published in a peer-reviewed journal according to the PRISMA guidelines.

Availability of data and materials

Not applicable.

Consent for publication

Not applicable.

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Declaration of Competing Interest

The authors have no conflicts of interest to declare.

Author contributions

Shanshan Xiang, Ting Fang, and Fushui Liu designed the study. Changan Ren, Junnan Qi, Zheng Guo, and Wenlong Yang drafted the manuscript.

All authors approved the manuscript.

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Table

Due to technical limitations, table 1 is only available as a download in the Supplemental Files section.

Figures

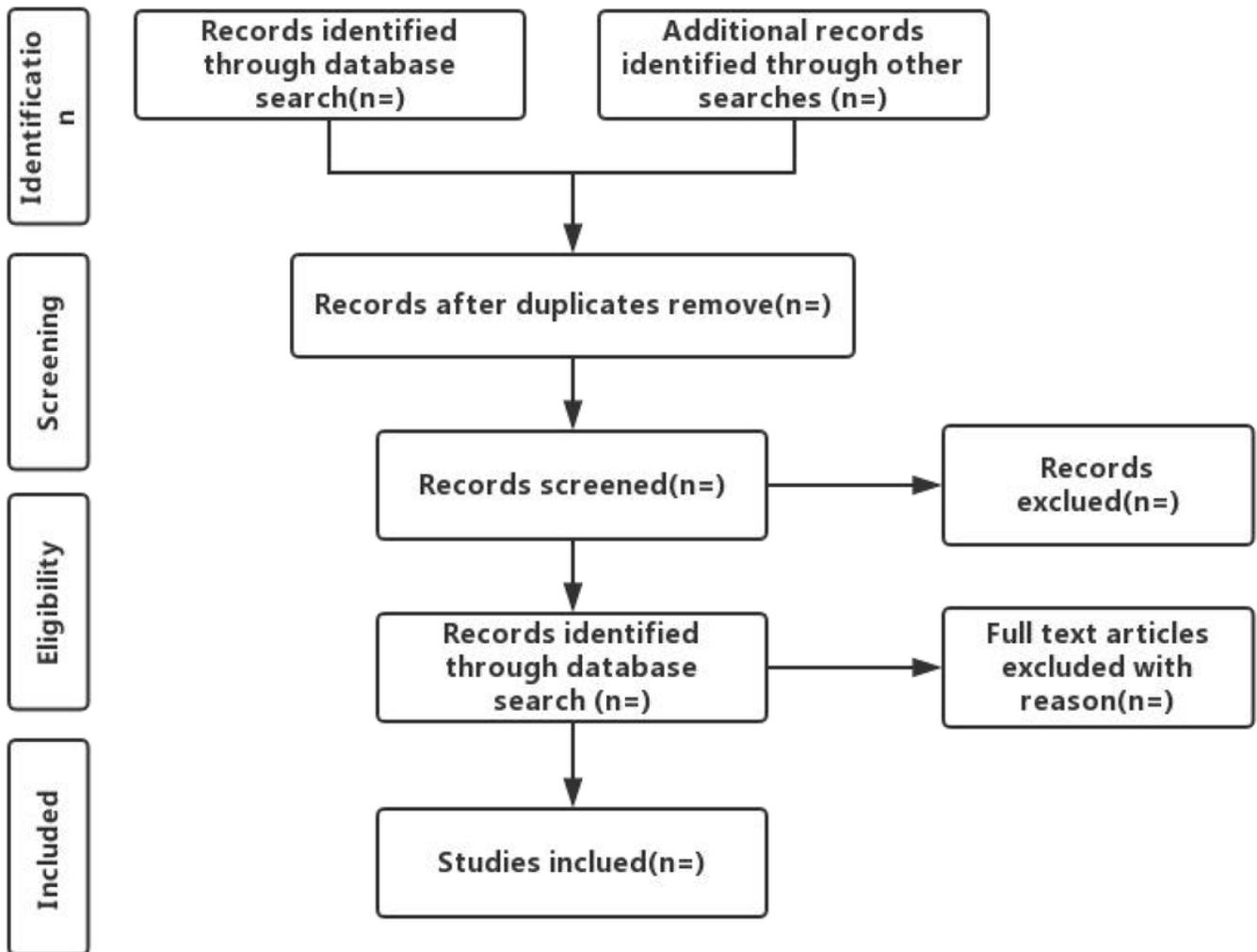


Figure 1

Flowchart of literature selection

Supplementary Files

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- [Table1ThesearchstrategyforPubmed.pdf](#)

- [PFPPRISMAPchecklist.doc](#)