

# Acupuncture therapy for patients with hemifacial spasm

## A protocol of systematic review and meta-analysis

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### Abstract

**Background:** Hemifacial spasm (HFS) brings a lot of trouble to patients' daily life, having a severe influence on the psychological and physical wellbeing of patients. Relevant researches suggested that acupuncture therapy has potential benefits for HFS. However, there is no consistent conclusion. The purpose of our study is to assess whether acupuncture therapy is effective and safe for HFS.

**Methods:** To collect relevant randomized controlled trials (RCTs), the following electronic databases will be searched: Web of Science, the Cochrane Library, EMBASE, MEDLINE, ISI Web of Knowledge, PsycINFO, Allied and Alternative Medicine, Chinese National Knowledge Infrastructure, Wanfang data, and Chinese Scientific Journals Database. We will take the cure rate and the total effective rate as the primary outcomes, and change in intensity after treatment, change in frequency after treatment, the recurrence rate, and adverse events as secondary outcomes. Endnote software 9.1 will be used for study selection, Review Manager software 5.3, and STATA 13.0 software will be used for analysis and synthesis.

**Results:** Current relevant studies will be synthesized to assess whether acupuncture therapy is effective and safe for HFS.

**Conclusion:** Our research will provide evidence of acupuncture therapy for HFS.

**Registration:** International Prospective Register of Systematic Reviews (PROSPERO) CRD42019142473.

**Abbreviations:** HFS = hemifacial spasm, CIs = confidence intervals, CNKI = Chinese National Knowledge Infrastructure, GRADE = Grading of Recommendations Assessment, Development, and Evaluation, PRISMA-P = the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols, PROSPERO = International Prospective Register of Systematic Reviews, RCTs = randomized controlled trials, RevMan = Review Manager Software, SMD = standardized mean difference.

**Keywords:** acupuncture therapy, effectiveness, hemifacial spasm, meta-analysis, protocol, safety, systematic review

## 1. Introduction

Hemifacial spasm (HFS) is a neuromuscular disease that is featured by paroxysmal, involuntary twitching of unilateral, occasionally bilateral, facial muscles innervated by the facial nerve (seventh cranial nerve).<sup>[1]</sup> It is a chronic progressive disease that usually occurs in one's 40s to 70s,<sup>[2]</sup> but may also affect the

adolescents,<sup>[3]</sup> with higher prevalence in females (2:1).<sup>[4]</sup> As reported in previous studies, the prevalence in Asians is relatively higher than that of whites.<sup>[5,6]</sup> The common cause for HFS is compression on either the root exit of the facial nerve from the seventh brainstem or at its entering point to the auditory meatus.<sup>[7–12]</sup> There is a significant influence of HFS on the psychological and physical well-being such as emotional disturbance, visual or speech disability.<sup>[13–15]</sup> For instance, HFS might lead to impaired vision with drooping eyelids, which results in difficulties in reading and driving. Furthermore, involuntary facial spasm can evoke the risk of dysarthria.<sup>[3,16]</sup> Also, it causes a lot of social awkwardness.<sup>[16]</sup> HFS usually worsens gradually as the disease progresses, and is rarely self-limited,<sup>[17]</sup> so it is necessary to treat in time.

The treatment of HFS mainly includes oral medications, botulinum neurotoxin injections, and surgical management.<sup>[3]</sup> However, the currently existing treatment for HFS is unsatisfactory, due to limited effectiveness,<sup>[16]</sup> undesirable side effects,<sup>[18]</sup> the frequent repetition of procedures,<sup>[19]</sup> considerable risks, and postoperative complications.<sup>[20]</sup> Therefore, patients prefer seeking alternatives therapies for HFS.<sup>[21]</sup>

Acupuncture therapy, as a treasure of traditional Chinese medicine, has gained increasing attention worldwide. It has been used in a wide range of clinical situations and has achieved promising effectiveness. The advantages of acupuncture therapy in some other neurovascular conflict have been confirmed, such as trigeminal neuralgia,<sup>[22,23]</sup> facial paralysis,<sup>[24,25]</sup> and so on.

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There are studies suggesting that acupuncture therapy can be beneficial for HFS.<sup>[26,27]</sup> Whereas the effectivenesses and safeties of acupuncture therapy for HFS remain unclear due to lack of comprehensive synthesis and evaluation of existing evidence. Hence, the purpose of our research is to systematically synthesize all randomized controlled trials (RCTs) of acupuncture therapy for HFS to provide evidence for the clinical practice of HFS.

**2. Methods**

**2.1. Study registration**

The protocol of our study has been registered on the International Prospective Register of Systematic Reviews (PROSPERO) (registration number, CRD42019142473). The protocol is reported strictly according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) guidelines.

**2.2. Eligibility criteria**

**2.2.1. Type of study.** We will include the RCTs of acupuncture therapy for patients with HFS.

**2.2.2. Type of participant.** The study involved participants who had been diagnosed with HFS. Diagnostic criteria for HFS, according to “Neurology,<sup>[28]</sup>” “Clinical Neurosurgery,<sup>[29]</sup>” and “Clinical Pain Therapy<sup>[30]</sup>” include uncontrollable spasm on one side of the face, early manifestation as intermittent spasm of orbicularis oculi muscle, and gradually extends to mouth and finally affect the entire face; the severity of spasm varies and can be aggravated by stress, exhaustion, talking, and so on; spasm terminates when patients are asleep; also, there is no positive sign from neurologic examinations. There is no restriction of age, sex, or race.

**2.2.3. Type of intervention.** Our research will include studies that took acupuncture therapy as the main treatment in the intervention group, such as acupuncture, auricular acupuncture, electroacupuncture, fire needle, scalp acupuncture, acupoint injection, press needle, acupressure, acupoint catgut embedding, among others. Meanwhile, the control group used nonacupuncture therapy (pharmacological treatments, conventional treatment, placebo, or waiting-list) or sham acupuncture.

**2.2.4. Types of outcome measurements**

**2.2.4.1. Primary outcome.**

- The cure rate (number of participants who made a full recovery/ total number of participants in this group);
- The total effective rate (number of participants who showed a positive response to therapy/ total number of participants in this group).

**2.2.4.2. Secondary outcomes.**

- Change in intensity after treatment;
- Change in frequency after treatment;
- The recurrence rate (number of people who relapsed during follow-up/ total number of participants in this group);
- Adverse events related to interventions.

**2.2.5. Exclusion criteria.**

- Participants with the unclear diagnosis;
- Studies that did not use acupuncture therapy as primary treatment in the intervention group;

- Data that cannot be extracted;
- Duplicated data;
- The studies where full text is unavailable.

**2.3. Search methods for identification of studies**

**2.3.1. Electronic data sources.** The following 10 electronic databases from inception to November 2019 will be searched: Web of Science, the Cochrane Library, EMBASE, MEDLINE, ISI Web of Knowledge, PsycINFO, Allied and Alternative Medicine, Chinese National Knowledge Infrastructure, Wanfang data and Chinese Scientific Journals Database.

**2.3.2. Other resources.** We will review and screen the relevant references. Furthermore, the following registration website of the clinical trial will be searched: WHO ICTRP, <http://www.chictr.org.cn>, <http://www.ClinicalTrial.gov>, and ISRCTN Register. In addition, we will search for the relevant gray literature from the Health Management Information Database, OpenSIGLE Database, and the National Technical Information Service. Experts in the field will be consulted for relevant studies.

**2.4. Search strategy**

We will combine subject words with text words for the search strategy. The search terms will be expanded around: acupuncture therapy, HFS, and randomized controlled trial. It will not be restricted with publication dates and languages. Use MEDLINE as an example, the specific searching strategy, as stated in Table 1.

**Table 1**

**Search strategy for the MEDLINE database.**

Number	Search items
1	Facial nerve diseases/
2	Facial spasm.af.
3	Facial paralysis/or hemifacial spasm/
4	((bell\$ or facial\$ or hemifacial\$ or cranial\$) adj3 (pals\$ or paraly\$ or paresis\$ or spasm\$)).tw.
5	or/1-4
6	Exp acupuncture/
7	Acupuncture therapy/
8	Exp acupuncture points/
9	Exp acupuncture ear/
10	Exp auriculotherapy/
11	Exp electroacupuncture/
12	Exp electric stimulation therapy/
13	Exp acupressure/
14	Exp moxibustion/
15	(Acupuncture\$ or electroacupuncture\$).tw.
16	(Acupuncture\$ or moxibustion).tw.
17	or/6-16
18	Randomized controlled trial.pt.
19	Controlled clinical trial.pt.
20	Randomized.ab.
21	Placebo.ab.
22	Drug therapy.fs.
23	Randomly.ab.
24	Trial.ab.
25	Groups.ab.
26	or/18-25
27	Exp animals/ not humans.sh.
28	26 not 27
29	5 and 17 and 28

The searching strategy will be modified by the characteristic of the different databases.

**2.5. Data collection**

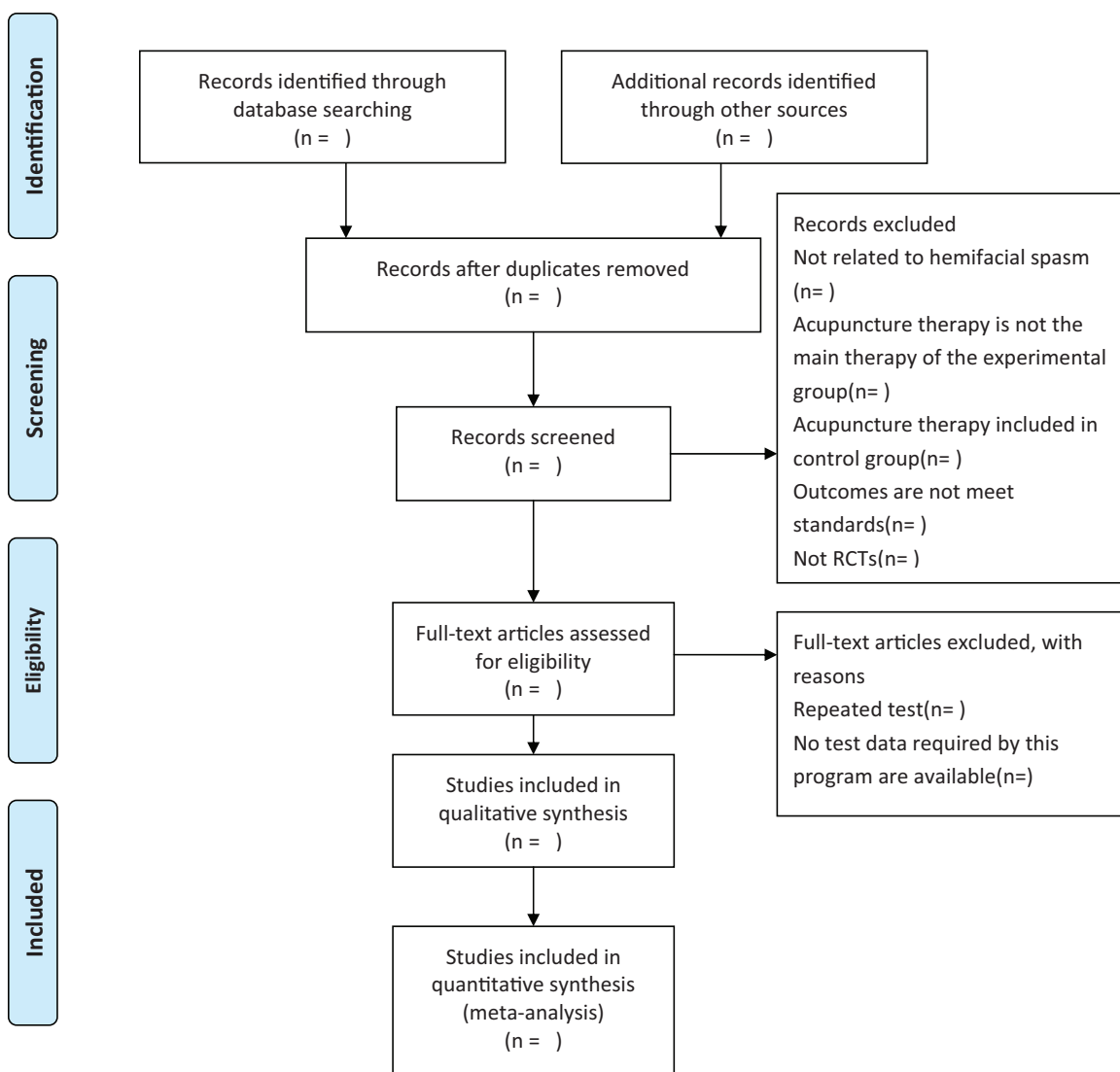
**2.5.1. Selection of studies.** We will import the retrieved studies in Endnote software 9.1 to remove duplicates. According to the established inclusion and exclusion criteria, 2 researchers (JZ and ZHY) will screen the titles and abstracts independently. After that, the full text will be screened as a second filtration. Two researchers will crosscheck the included studies, and the third researcher (FRL) will be involved if disagreements occur. The detailed screening process will be shown in the following PRISMA-P flow diagram (Fig. 1).

**2.5.2. Data extraction and management.** The other 2 researchers (DLZ and GXX) will extract data independently to fill out the predesigned form. The information includes author, country, publication year, methodological quality, characteristics

of participants, the details of intervention and comparisons, outcomes, the specific data, results, conclusions, follow-up, adverse events, conflicts of interest, sources of funds, and ethical approval. The extracted data will be cross-checked by the 2 researchers. A third researcher (FRL) will be involved if a disagreement occurs. The authors of the studies included will be contacted for further information when necessary.

**2.5.3. Assessment of risk of bias in included studies.**

According to the guidance from the Cochrane Handbook of Systematic Reviews of Interventions,<sup>[31]</sup> 2 researchers (HY and JL) will evaluate the risk of bias of the included RCTs independently. We will evaluate from the following 6 parts: selection, performance, attrition, detection, reporting, and other sources of bias. We will rate the risk of bias into 3 levels: when meets none of the criteria, it will be regarded as high; when meets all criteria, it will be regarded as low; when study without sufficient information to determine, it will be regarded as unclear.



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

**Figure 1.** The Preferred Reporting Items for Systematic Reviews and Meta-analyses Protocols flow diagram of the study selection process.

After the assessment, it will be cross-checked by 2 researchers. The third researcher (FRL) will be involved if a disagreement occurs.

### 2.6. Data synthesis

Review Manager software (RevMan5.3) and STATA 13.0 software will be used to conduct all data analyses if it is possible to perform a meta-analysis. Data synthesis will be performed with a random-effects model if significant statistical heterogeneity is detected. Otherwise, the data will be processed with a fixed-effects model. Furthermore, the descriptive analysis will be conducted if there is significant statistical heterogeneity.

**2.6.1. Measures of treatment effect.** For continuous outcomes (the change in intensity after treatment, the change in frequency after treatment), we will use mean difference to evaluate the extracted data. For dichotomous outcomes (the cure rate, the total effective rate, the recurrence rate, and adverse events), we will analyze the rate ratio. The confidence intervals (CIs) will be set to 95% for both continuous outcomes and dichotomous outcomes.

**2.6.2. Management of missing data.** For the insufficient or missing data, the related corresponding author will be contacted. If we cannot get accurate data after contacting the corresponding author, these studies will be excluded.

**2.6.3. Assessment of heterogeneity.** We will conduct the qualitative analysis by comparing the characteristics of included researches and quantitative analysis by using the  $I^2$  test and the  $\chi^2$  test to assess the heterogeneity. If the values of  $I^2$  are  $>50\%$ , the significant heterogeneity will be thought to exist.

**2.6.4. Assessment of reporting biases.** When the quantity of the included RCTs  $\geq 10$ , we will select funnel plots to evaluate the potential publication bias. Otherwise, we will use STATA 13.0 software to perform the Egger test.

**2.6.5. Subgroup analysis.** According to different kinds of acupuncture therapy applied, different interventions of the control group, and different time points for evaluating outcomes after treatment, subgroup analysis will be performed.

**2.6.6. Sensitivity analysis.** Based on the risk of bias, insufficient data, and sample size, we will perform a sensitivity analysis to evaluate the robustness if significant statistical heterogeneity existed.

### 2.7. Grading the quality of evidence

According to the Grading of Recommendations Assessment, Development, and Evaluation,<sup>[32]</sup> we will assess the each outcome's quality of evidence from the 5 aspects (limitation of study design, inconsistency, indirectness, imprecision, and bias of publication) and rank the quality into 4 levels (very low, low, moderate, and high).

### 2.8. Ethics and dissemination

There is no necessity to gain ethical approval considering our research has no connection with individual patient data. The results of our research will be reported in a peer-reviewed journal

or relevant conferences and evaluate the implication of acupuncture therapy for patients diagnosed with HFS.

## 3. Discussion

HFS brings a lot of trouble to patients' daily life, having a severe influence on the psychological and physical well-being of patients. At present, the optimum treatment for HFS is still controversial. Acupuncture therapy may be an effective and safe treatment for HFS, which may work through regulating humoral immunity and auto cell immunity.<sup>[33]</sup> However, there is no definitive conclusion. Following the Cochrane Handbook for Systematic Reviews of Interventions<sup>[31]</sup> strictly, the systematic review and meta-analysis will be conducted based on the existing RCTs to assess whether acupuncture therapy is effective and safe for HFS, aiming to provide evidence for clinical practice and to facilitate future researches.

### Author contributions

The idea of this study was put forward by Han Yang and Dongling Zhong. The protocol was drafted by Han Yang and Jun Zhou. The whole process was supervised by Fanrong Liang. The manuscript was revised by all authors. The final version was approved by all authors.

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**Supervision:** Fanrong Liang.

**Writing – original draft:** Han Yang, Jiao Chen, Dongling Zhong.

**Writing – review & editing:** Han Yang, Jun Zhou, Juan Li.

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