Original Article
The effect of acupuncture on Bell’s palsy: an overall and cumulative meta-analysis of randomized controlled trials

Xiao-Wen Zhang¹, Fu-Ming Wang², Sha-Sha Yu¹, Qing-Hui Zhou¹

¹Changhai Hospital of Traditional Chinese Medicine, Second Military Medical University, Shanghai, China; ²Kaifeng Children’s Hospital, No.87, Zijyou Road, Gulou District, Kaifeng, Henan province, China. *Equal contributors.

Received May 27, 2017; Accepted December 22, 2017; Epub April 15, 2018; Published April 30, 2018

Abstract: Background: Whether acupuncture is effective for Bell’s palsy is controversial, and potential modifiers exist according to previous studies. Objectives: An overall and cumulative meta-analysis was conducted to evaluate and quantify this efficacy. Study appraisal and synthesis methods: Searches of PubMed, EMBASE, Wanfang database and the Cochrane Central Register of Controlled Trials were performed up to July 2016, and a random-effect model was used to yield summary relative risks (RRs). Results: Compared to conventional treatments, RRs for total effective rate and cured rate of acupuncture are 1.11 (95% confidence interval (CI)=1.05-1.17) and 1.56 (95% CI=1.30-1.87), respectively. Cumulative meta-analysis revealed that the efficacy of Bell’s palsy have a stable and preferable variation tendency over time. Subgroup and sensitivity analyses suggested comparisons, acupuncture regimens and disease stages are potential confounding factors. Conclusion: In conclusion, we failed to draw a conclusion that the acupuncture is effective for facial paralysis since these limited methodological quality studies and potential biases, there need to be validated by more well designed and large sample size RCTs.

Keywords: Acupuncture, Bell’s palsy, total effective rate, total cured rate, meta-analysis

Introduction
Bell’s palsy, also known as acute idiopathic facial palsy, is an acute peripheral facial neuropathy which is the most common cause of lower motor neuron facial palsy [1]. Its characterized clinical symptoms include a rapid onset, unilateral, lower motor neuron-type facial weakness accompanying post auricular pain, dysgeusia, subjective change in facial sensation and hyperacusis [2]. Although Bell’s palsy is uncommon, it affects people across children to adults [3], with incidence up to 53.3 per 100,000 person years in different population [4-6].

For etiology of Bell’s palsy, several plausible mechanisms have been proposed, such as herpes simplex type-1 [7], nerve compression [8], autoimmunity [9]. Relevant therapies containing antiviral medicine [10], corticosteroids [11], surgery [8] and acupuncture treatment [12] are commonly applied to Bell’s palsy patients. The acupuncture is a practical and cost-effective intervention with few adverse side effects which is useful for many disorders. The efficacy of acupuncture treatment on Bell’s palsy have been examined for many times by meta-analyses [12-14] from Cochrane database, in spite of that, no conclusion was drawn due to restricted quality of included studies. Recently, a meta-analysis was conducted on this topic [15], which cautiously supported acupuncture curative effect. However, the high heterogeneity was found among included studies, raising concerns about the reliability of its summary results. In addition, sample size, baseline data, and intervention measures, as well as the variable evaluation criterion across different trials, may be responsible for the unstable results.

Acupuncture is among the oldest healing practices in the world. In the United States, it has been considered as one of the major therapies in complementary and alternative medicine (CAM) [16]. With arousing considerable atten-
Acupuncture on Bell’s palsy

tion to the acupuncture treatment for Bell’s palsy, investigating its efficacy and potential modifiers is critical for a better understanding of this traditional Chinese medicine therapy method. Therefore, we conduct an update meta-analysis of randomized controlled trials (RCTs) to comprehensively investigate whether Bell’s palsy patients would benefit from acupuncture treatment, and to further investigate confounding factors.

Materials and methods

Search strategy

This meta-analysis was performed in adherence to PRISMA statement [17]. Systematic literature searches of PubMed, EMBASE, Wanfang database and the Cochrane Central Register of Controlled Trials were conducted up to July 2016. The search strategy is showed in the Supplementary List 1 in detail. We checked the reference lists of included studies and previous meta-analysis [15, 18] for additionally eligible studies. No attempt was made to identify unpublished reports. If necessary, the original authors were contacted to obtain extra information via e-mails.

Study selection

Two investigators (Fu-ming Wang and Sha-sha Yu) independently selected the suitable publications according to following inclusion criteria: (1) Participants: subjects diagnosed with Bell’s palsy. (2) Intervention: manual acupuncture or electric acupuncture. (3) Control: other therapy regimens except acupuncture. (4) Outcome: Adjusted risk estimates with 95% confidence interval (CI) on the association of acupuncture and efficacy of Bell’s palsy included cured rate and effective rate. (5) Study design: RCTs. The criteria were determined with reference to the House-Brackmann judging and grading system of facial nerve function. There are 4 levels, respectively, cured, markedly effective, effective, and ineffective. The percentage of cured was called cure rate, and the percentage of markedly effective or effective were called total effective rate.

Data extraction and risk of bias assessment

Data extraction was conducted by one investigator (Fu-ming Wang), the n independently checked by another investigator (Sha-sha Yu) for the accuracy. The following information was extracted: first author, publication year, study location, sample size, mean age, disease stage.

Two investigators (Fu-ming Wang and Sha-sha Yu) independently assessed the quality of included studies using the Cochrane Handbook for Systematic Reviews of Interventions [19]. Seven aspects were evaluated as following: 1) Selection bias: random sequence generation, allocation concealment; 2) Performance bias: Using blind method to researchers and subjects; 3) Detection bias: The evaluation results of the study by the method for the blind; 4) Attrition bias: The data results integrity; 5) Reporting bias: Report the results of the study selectively; 6) Other bias: In addition to the above bias, the information provided can whether evaluate other causes of bias or not. If problems or factors are first mentioned in the protocol, those should give the corresponding answers. The “high”, “moderate”, “low” was allocated for each item. Any controversies on the results of data extraction and quality assessment were resolved by further discussion.

Data synthesis and analyses

In this meta-analysis, relative risk (RR) with 95% confidence intervals (CI) was considered as common measure of the association between acupuncture therapy and total effective rate or total cured rate. A random-effect model [20] was used to pool RRs to obtain the overall effect size. The between-study heterogeneity was assessed by Q statistic ($Q_{Heterogeneity}$<0.10 suggesting statistically significant) and the $I^2$ [21] (high heterogeneity, $I^2$≥75%; moderate heterogeneity, 50.0%<$I^2$<75%; low heterogeneity, $I^2$<50% [22]).

To identify potential modifiers, the study-level subgroup analysis was performed stratified by age, contrast design, acupuncture design, sample size, therapy period, disease stage, respectively, and a $P_{interaction}$ between subgroups was calculated by meta-regression [23]. To further analysis the heterogeneity between eligible studies and check the stability of pooled results, three sensitivity analyses were conducted as following: omitting a single study in turn; repeating analyses by the fixed-effects model; and employing various eligibility criteria.

Additionally, cumulative meta-analysis was conducted to evaluate the efficacy of acupuncture therapy. Eligible studies were added 1 at a
Potential publication bias was assessed by Begg rank correlation test [24] and Egger linear regression test [25]. All analyses were conducted using STATA version 12.0 (StataCorp, College Station, TX) and RevMan 5.3 (The Nordic Cochrane Centre, Copenhagen, Denmark). *P*<0.05 was considered statistically significant. All statistical tests were two-sided.

**Results**

**Study selection and characteristics**

A flowchart of search selection and results is shown in Figure 1. We identified 244 potential-
# Acupuncture on Bell’s palsy

## Table 1. Characteristics of 20 eligible RCTs

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Bell’s Palsy ascertainment</th>
<th>Efficacy assessment</th>
<th>Acupuncture type</th>
<th>Comparison</th>
<th>Outcome Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liu et al. 1996 China</td>
<td>130</td>
<td>Clinical diagnosis: Symptom, Sign, EMG</td>
<td>Clinical diagnosis: Symptoms, Signs, Electromyography</td>
<td>Multi-needle shallow puncture</td>
<td>Acupuncture: needles inserted with manual stimulation till elicited de qi; 30 min×10 treatment sessions; vs. Drug group: prednisone 20 mg three times/day, vitamin B+, dibazol</td>
<td>Total effective rate; The cured rate</td>
</tr>
<tr>
<td>Yu et al. 1999 China</td>
<td>50</td>
<td>Clinical diagnosis: Symptom, Sign</td>
<td>NR</td>
<td>Multi-needle shallow puncture</td>
<td>Acupuncture group: conventional acupuncture 20 min/day×10 sessions; vs. Drug group: vitamin B, steroid, traditional Chinese medicine</td>
<td>Total effective rate</td>
</tr>
<tr>
<td>Shao et al. 1999 China</td>
<td>108</td>
<td>NR</td>
<td>NR</td>
<td>Combined group: conventional acupuncture once/day×15 d/session, rested for 4 days, another cycle; vs. Drug group: dexamethasone + vitamin B1 + vitamin B12 + citicoline + ribavirin</td>
<td>Electroacupuncture group: needles inserted with manual stimulation till elicited de qi, electroacupuncture for 30 min/d×10 treatment sessions; vs. Observed group: therapeutic apparatus was applied for 2 min/d×10 sessions</td>
<td>Total effective rate</td>
</tr>
<tr>
<td>Yang et al. 2001 China</td>
<td>60</td>
<td>NR</td>
<td>Electroacupuncture</td>
<td>Manual stimulation</td>
<td>Electroacupuncture + routing group: electroacupuncture 30 min/d×13 sessions for a cycle, rested for 2 days, another cycle, and routing group; vs. Routing group: acyclovir, traditional Chinese medicine, physical therapy</td>
<td>Total effective rate; The cured rate</td>
</tr>
<tr>
<td>Zhu et al. 2004 China</td>
<td>57</td>
<td>Facial paralysis scale</td>
<td>Electroacupuncture</td>
<td>Electroacupuncture group: 20 min/d×5 days/week, rested for 2 days, a total of 4 weeks; vs. Control group: Chinese traditional manipulation</td>
<td>Total effective rate</td>
<td></td>
</tr>
<tr>
<td>Ma et al. 2004 China</td>
<td>195</td>
<td>Clinical diagnosis: Symptom, Sign</td>
<td>Clinical diagnosis: Symptoms, Signs, facial muscle function</td>
<td>Manual acupuncture</td>
<td>Acupuncture group: needles inserted with manual stimulation till elicited de qi; 30 min/d×5 treatment sessions/week, rested for 2 days, total 6 weeks; vs. Drug group: vitamin B1 100 mg/d×5 times/week, vitamin B12 250 ug/d×5 times/week, rested for 2 days, total 6 weeks</td>
<td>Total effective rate</td>
</tr>
<tr>
<td>Li et al. 2005 China</td>
<td>94</td>
<td>NR</td>
<td>Electroacupuncture</td>
<td>Electroacupuncture group: electroacupuncture 20-30 min/other day×10 sessions for a cycle; vs. Stellate ganglion block group: 10 g/L lidocaine 6-8 mL, injected at the basal of sixth cervicalvertebra transverse process</td>
<td>Total effective rate; The cured rate</td>
<td></td>
</tr>
<tr>
<td>Zhao et al. 2005 China</td>
<td>42</td>
<td>The Facial Movement Score</td>
<td>The Facial Movement Score</td>
<td>Electroacupuncture</td>
<td>Electroacupuncture group: electroacupuncture 20-30 min/other day×10 sessions for a cycle; vs. Stellate ganglion block group: 10 g/L lidocaine 6-8 mL, injected at the basal of sixth cervicalvertebra transverse process</td>
<td>Total effective rate; The cured rate</td>
</tr>
<tr>
<td>Liang et al. 2006 China</td>
<td>480</td>
<td>House-Brackmann grading scale</td>
<td>The House-Brackmann grading scale The FDI scale</td>
<td>Manual acupuncture</td>
<td>Acu-moxibustion group: filiform needle plus moxibustion; vs. Basic treatment group: prednisone, vitamin B1, vitamin B12 and dibazol</td>
<td>The cured rate The markedly relived rate The improved rate</td>
</tr>
<tr>
<td>Zhu et al. 2006 China</td>
<td>108</td>
<td>Clinical diagnosis: Symptom, Sign</td>
<td>The Facial paralysis scale</td>
<td>Manual acupuncture</td>
<td>Acupuncture group: shallow needles inserted, 30 min/d×5 treatment sessions for acute stage, 30 min/d×10 treatment sessions, rested for 2-3 days, 2 cycles for resting stage and restoration stage; vs. Drug group: prednisone 5 mg three times/d</td>
<td>Total effective rate; The cured rate</td>
</tr>
<tr>
<td>Yang et al. 2006 China</td>
<td>320</td>
<td>The facial paralysis diagnostic criteria</td>
<td>Clinical diagnosis: Symptoms, Signs</td>
<td>Horizontal and shallow needles inserted</td>
<td>Combined group: horizontal and shallow needles inserted, 30 min/d×10 treatment sessions, rested for 2 days, total 4 cycles, and drugs; vs. Drugs group: Steroids, Antiviral drugs, Vasodilators and neurotrophic drugs</td>
<td>Total effective rate and the cured rate</td>
</tr>
<tr>
<td>Fu et al. 2007 China</td>
<td>52</td>
<td>Traditional Chinese medicine criteria and Western medicine criteria</td>
<td>Efficacy of Traditional Chinese Medicine</td>
<td>Light stimulation method Electroacupuncture</td>
<td>Acupuncture group: acupuncture during the acute stage, drugs, acupuncture, microwave therapy electroacupuncture the acute stage vs. Drugs group: the same methods as the treatment group but acupuncture was not given at the acute stage</td>
<td>Total effective rate The cured rate</td>
</tr>
<tr>
<td>Author</td>
<td>Year</td>
<td>China</td>
<td>Journal</td>
<td>Study Design</td>
<td>Treatment and Medication</td>
<td>Outcome Measures</td>
</tr>
<tr>
<td>-------------------</td>
<td>------</td>
<td>-------</td>
<td>---------</td>
<td>--------------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------------------------</td>
<td>-----------------------------------------</td>
</tr>
<tr>
<td>Wang et al. 2007</td>
<td>60</td>
<td>China</td>
<td>The Latest Medical Diagnostic Criteria at Home and Abroad</td>
<td>Symptoms and Signs House-Brackmann scale Manual acupuncture Acupuncture and medicine group: needles inserted with manual stimulation till elicited de qi; 30 min/d×6 treatment sessions/week, rested for a day, total 2 cycles, and drugs; vs. Medicine Drugs group: dexamethasone 10 mg/d×4 d, Vitmin B12 0.5 mg/d + Vitamin B1 100 mg×4 days (im)</td>
<td>Total effective rate</td>
<td></td>
</tr>
<tr>
<td>Hou et al. 2008</td>
<td>97</td>
<td>China</td>
<td>Practical Medicine</td>
<td>Clinical diagnosis: Symptom, Sign Light stimulation method Combined group: acupuncture at main points in combination with He-Ne laser radiation; VS. Medicine group: Intravenous dripping of low molecular dextran, compound Danshen and ATP injections, VitBl and VitBl2, and oral administration of oryzanol and prednisone</td>
<td>Total effective rate The cured rate</td>
<td></td>
</tr>
<tr>
<td>Dai et al. 2009</td>
<td>72</td>
<td>China</td>
<td>Traditional Chinese medicine criteria and Western medicine criteria</td>
<td>Clinical diagnosis: Symptom, Sign Shallow needles inserted Electroacupuncture Combined group: shallow needles inserted, electroacupuncture 20-30 min/other day×10 sessions for a cycle; vs. Medicine group: prednison 1 mg/Kg/d×7 d, Vitamin B12 0.5 mg/d, Vitamin B1 100 mg×4-5 weeks (im)</td>
<td>Total effective rate</td>
<td></td>
</tr>
<tr>
<td>Tong et al. 2009</td>
<td>119</td>
<td>China</td>
<td>The facial paralysis diagnostic criteria of ENT surgeons</td>
<td>House-Brackmann scale; The degree and speed of recovery Manual acupuncture Acupuncture group: needles inserted with manual stimulation till elicited de qi; vs. Medicine group: predni- solone 30 mg twice daily×1 week + pepcidine 20 mg twice daily×1 week</td>
<td>Total effective rate The cured rate</td>
<td></td>
</tr>
<tr>
<td>Xie et al. 2010</td>
<td>120</td>
<td>China</td>
<td>Standard of clinical common diseases diagnosis and treatment</td>
<td>House-Brackmann scale Shallow needles inserted Combined group: shallow needling combined with acupoint application + the routine medication; vs. Medicine group: routine medication</td>
<td>Total effective rate The cured rate</td>
<td></td>
</tr>
<tr>
<td>Liu et al. 2010</td>
<td>131</td>
<td>China</td>
<td>The diagnostic criteria of Traditional Chinese Medicineand Western Medicine</td>
<td>House-Brackmann scale Horizontal and shallow needles inserted Acupuncture group: horizontal and shallow needles inserted, 30 min/d×5 treatment sessions, rested for 2 days, total 4 cycles; vs. Medicine group: prednisone and Acyclovir (po) Vitamin B1 and Vitamin B12 (im) in acute stage, acupuncture during quiescent and recovery stages</td>
<td>Total effective rate The cured rate</td>
<td></td>
</tr>
<tr>
<td>Zhang et al. 2013</td>
<td>60</td>
<td>China</td>
<td>The diagnostic criteria of Traditional Chinese Medicineand Western Medicine</td>
<td>House-Brackmann scale Shallow needles inserted and subexcite Continued group: drugs, acupuncture and microwave therapy during the acute stage, EA, acupoint injection, electrotherapy and massage during the convalescence stage; vs. Medicine group: ‘Shuxuening’, dehydrohydrocortisone, vit B1, vit B12, bendazol</td>
<td>Total effective rate The cured rate</td>
<td></td>
</tr>
<tr>
<td>Jin et al. 2015</td>
<td>156</td>
<td>China</td>
<td>Traditional Chinese medicine criteria and Western medicine criteria</td>
<td>Symptoms + Signs House-Brackmann scale Manual acupuncture Continued group: needle stimulation till elicited de qi; 30 min/d×5 treatment sessions/week, rested for a day, total 4 cycles; vs. Medicine group: steroid, Vitamin B1 and Vitamin B2</td>
<td>Total effective rate The cured rate</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: EMG, electromyography; ENT, ear-nose-throat department; IM, intramuscular; PO, per os; EA, electro-acupuncture; FDI, facial deformity index.
ly relevant articles from PubMed (48), EMBASE (41) and the Cochrane Central Register of Controlled Trials (155) . Of these, only 21 articles were retained for further review through removing 81 duplications and 142 articles of which themes were not relevant. After browsing the full text for more details, three articles were excluded: one study with mixed interventions both of acupuncture group and the control group [26]; two studies compared different types of the efficacy of acupuncture [27, 28]. Therefore, of the 21 full-text publications obtained, only 18 [29-46] RCTs met our inclusion criteria. By referring to previous meta-analysis and related reviews, the another 2 [47, 48] RCTs were included. Finally, a total of 20 studies were included in our meta-analysis. The characteristics of the 20 included RCTs were summarized in Table 1, where they were stratified by chronological order. All these included studies were conducted in China and published from 1996 to 2015. Eighteen studies were written in Chinese and two in English [30, 34]. A total of 2511 participants were enrolled in this meta-analysis with sample sizes ranging from 42 to 480. The patients were randomly assigned to acupuncture group (Intervention group) or control group, with their age ranging from 6 to 72. The average time of appearing facial nerve paralysis relevant clinical symptoms ranges from 1 day to 6 months. Eleven studies compared acupuncture against other interventions: nine RCTs used drug therapy as a control; one RCT used Chinese traditional manipulation [41]; one RCT used stellate ganglion block therapy as a control [47]. In addi-

![Figure 2. Meta-analysis on acupuncture for total effective rate of Bell’s palsy, with the area reflecting the weight assigned to the study. The horizontal line across each square represents the 95% confidence interval. The diamond represents the summary relative risk of total effective rate on acupuncture, with width representing 95% confidence interval.](image-url)
Acupuncture on Bell’s palsy

Figure 3. Meta-analysis on acupuncture for cured rate on Bell’s palsy, with the area reflecting the weight assigned to the study. The horizontal line across each square represents the 95% confidence interval. The diamond represents the summary relative risk of cured rate on acupuncture, with width representing 95% confidence interval.

As an outcome measure. Meanwhile, fifteen studies used the cured rate [29-33, 35-40, 42, 46-48] and one study used the course of cured patient [31] as an outcome measure. Only one RCT referred to adverse effects and/or complications during acupuncture [47]. The others didn’t mention about side effects and/or complications. Potential risk of bias was found by reviews’ judgment’s about each risk of bias item for each included study (Supplementary Figure 1).

Primary Outcome: total effective response rate and total cured rate

All the selected 20 studies were used to calculate the pooled estimate for assessing the total effective rate. In total, there were 973 cured individuals among 1004 patients in the acupuncture group (96.90%) and 817 individuals among 945 patients in the control group.
The criteria were determined with reference to the House-Brackmann judging and grading system of facial nerve function. We defined total cure rate and total effective rate as our end-points. A random-effect model was applied to pool the results (Figure 2): acupuncture therapy was associated with an increased total effective response rate (RR=1.11, 95% CI: 1.05-1.17), with significant heterogeneity ($I^2=77.1\%$, $P_{Heterogeneity}<0.001$). A cumulative meta-analysis was conducted to evaluate the total effective rate in chronological order (Figure 3). The results indicated that: 1) The point estimation value of RR and confidence interval tend to be stable and have a preferable variation tendency over time. 2) On the premise of the selected test level, the time of reaching statistical significance began with Yang et al. [39] (RR=2.13, 95% CI: 1.16-3.89).

A total of 15 RCTs were used to calculate the pooled estimate for assessing the cured rate. A random-effect model was used to estimate the results (Figure 4): Overall, the total cured rates in the acupuncture and control groups were 61.64% and 38.28%, respectively. Acupuncture therapy was associated with an increased total cured rate (RR=1.56, 95% CI: 1.30-1.87, $P<0.000$), with significant heterogeneity among the included studies ($I^2=69.5\%$, $P_{Heterogeneity}<0.001$). Figure 5 showed the results of the cumulative meta-analysis for the total cured rate between the acupuncture group and the control group, which is similar to the total effective rate: 1) Significantly stability can be observed on the point estimation value of RR and its confidence interval over time. 2) On the premise of the selected test level, the time of reaching statistical significance began with Ma et al. [42] (RR=1.27, 95% CI: 1.03-1.57).
Secondary outcomes

Only one RCT referred to adverse effects and/or complications during acupuncture [47]. The others didn’t mention about side effects and/or complications. Thus, an evaluation of the incidence of complications was not available, owing to insufficient data.

Subgroup analyses and sensitivity analyses

Several subgroup analyses were conducted to assess the stability of the meta-analysis’s results (Table 2). Except for electro-acupuncture and acupuncture with moxibustion or He-Ne laser radiation versus medicines subgroups, significant associations between acupuncture and total effective rate or cured rate for Bell’s palsy remained in the rest subgroups (Table 2). Pooled hazard ratios from the random-effects model and fixed-effects model were virtually identical. Omitting a single study in turn did not significantly change the summary risk estimate of either effective rate or cured rate (Supplementary Figures 2 and 3). Repeating meta-analyses according to various inclusion or exclusion criteria did not change our results, either (Supplementary Table 1).

Substantial publication bias was found in acupuncture-Bell’s palsy association (P for Begg test=0.03; P for Egger test=0.001) for total effective rate, while no evidence of publication bias was found in cured rate (all P>0.1).

Discussion

This meta-analysis included 20 RCTs with 2508 Bell’s palsy patients and reported the efficacy of acupuncture on Bell’s palsy through comparing total effective rate and cured rate with traditional drug treatment. Our study revealed a more convincing positive association between acupuncture and treatment of Bell’s palsy, because we contained new researched literature published after 2009 which previous studies did not, and we conducted a cumulative meta-analysis trial according to chronological order. In cumulative analysis, we observed that the RR value of treatment efficacy of acupuncture for Bell’s palsy tended to be more stable and CIs became more narrowed. Especially,
Acupuncture on Bell’s palsy

this change performed significantly after 2006 of which sample size was high to 908, 36% of total sample size from 1996 to 2015. In despite of these, substantial heterogeneity also existed in this current meta-analysis, and subgroup analyses as well as sensitivity analyses were conducted to explore the potential modifiers.

Jingluo, namely, a system of internal main and collateral channels, regarded as a network of energy passages, along with acupuncture points distributed [49]. Some new research on theory of main and collateral channels with many clinical experiences have fully proved that main and collateral channels is not entirely unreal [50]. It is a functional collection of the nervous system, circulatory system, lymph system, endocrine system, muscle tissue and so on [51, 52]. The acupuncture points, in essence, is a series of micro-vascular with synchronous diastole and contraction [53, 54]. The mechanism of acupuncture treatment could be explained in terms of neurology [55] and microcirculation theories [53, 54] such as activation of receptors, transmission of signals along afferent nerve fibers, projecting into central nervous systems, efferent control mechanisms, improving microcirculation, elimination of inflammation, absorption of edema, strengthening the body resistance and so on. It has been hypothesized that part of the effects of acupuncture may be attributed to diminishment of the muscle tone induced by various motor reflexes [28]. This is especially true for muscles under continuous tonic contraction. The inhibition of the muscle tone by acupuncture stimulation may be related to the functional recovery of the facial nerve and associated muscles. However, these theories are not currently fully established.

Most cases (approximately 70%) of Bell’s palsy can recover within 6 months spontaneously. Conventional medical options for Bell’s palsy are limited which include care of eyes, corticosteroid or antiviral medications, physical therapy, surgery, and acupuncture. Eye ointment is widely used to avoid trauma and corneal drying. Corticosteroids have been used in facial nerve paralysis, due to powerful anti-inflammatory effect, and have been proven to be an effective treatment. Regarding to facial nerve injury, electrical response grading is superior to the House-Brackmann scale in efficacy and reliability, and can conveniently assess the degree of facial nerve injury. The House-Brackmann scale is suitable for the patients with mild facial nerve injury, but its evaluated quality for severe facial nerve injury is poor [56]. According to a recent study, the effect of steroids on acute Bell’s palsy within 72 h of the onset of symptoms is clinically effective, but steroids have not been used on Bell’s palsy for long time [57].

Previous studies have shown that some patients of bell’s palsy in presence of herpes simplex virus infection [16, 26, 56, 58, 59]. Namely, antiviral agents can be applied in some cases. As optional treatments of Bell’s palsy, no particular benefits of physical therapy or surgical operation have been reported [19, 59, 60]. Acupuncture is known as a safe treatment used for a wide range of symptoms over all stages associated with Bell’s palsy [61]. Acupuncture for the disease, by contrast, has advantage for efficacy, safety, simple, little side effects and wide clinical applications.

Significant heterogeneity was found in included studies. After conducting subgroup analyses and sensibility analyses stratified by age, the heterogeneity decreased to 0% on the subgroup of age more than 40. In respect to contrast design, of the studies with acupuncture plus drug versus only drug treatment, heterogeneity in total effective rate decreased by about 43% while not showed in cured rate, whose comparison is more reasonable [62]. As for sample size and therapy period, we only observed significant decline of heterogeneity in total effective rate or cured rate since limited sample size, methodology defects and mixed treatment restrict our analyses. In addition, heterogeneity in studies stratified by disease stage shrinks both in total effective rate and cured rate, which plausibly owed to this self-limited characteristic. Besides, sensitivity analyses indicated that heterogeneity in the studies evaluating efficacy by facial paralysis score or House-Brackmann scoring lower by at least 63% which were also suggested by recent guideline [63]. In conclusion, acupuncture type, disease stage and evaluated criterion of efficacy of acupuncture possibly are potential modifiers.

Strength and limitation

Clearly the major strength of this meta-analysis is that we have analyzed what we believe to be all available data from comprehensive litera-
Acupuncture on Bell’s palsy

Data capture is perhaps the most important aspect of comprehensive meta-analysis with such large combinations of data across an extensive number of studies. Additionally, our analysis showed a modest effect for acupuncture compared with control group, cumulative meta-analyses were first to be conducted. Superior efficacy for Bell’s palsy being suggested in previous meta-analyses [15] can’t explain the high heterogeneity between studies, further analyses were carried out, such as subgroup analyses and sensitivity analyses. To shrink this heterogeneity, attentions were proposed for later studies.

We acknowledge several limitations of our analysis. Firstly, poor methodological quality of eligible studies raised concerns of reliability for our results, what’s more, increasing bias risk. Then, definitions of efficacy in different studies varied, and we cannot exclude misclassification. In addition, many variables had influenced on outcomes, such as course or duration of treatment, characteristic of subjects and disease stages. We were unable to perform dose-response meta-analysis due to insufficient data and Bell’s palsy is a self-limited disease affecting observation of efficacy. Lastly, publication bias existed in our meta-analysis.

Conclusion

In summary, different comparisons, acupuncture regimens and disease stages showed opposite results on efficacy of Bell’s palsy. Therefore, RCTs should not combine these when examining acupuncture’s efficacy. Meanwhile, we can’t draw a conclusion since these findings should be interpreted with caution due to limited methodological quality studies and potential biases, and need to be validated by more well designed and large sample size RCTs.

Acknowledgements

This study was supported by grants from Three-year Action Plan for Traditional Chinese Medicine Development in Shanghai (ZY3-CC-CX-3-7002).

Disclosure of conflict of interest

None.

Abbreviations

RCT, randomized controlled trial; RR, relative risk; CI, confidence interval.

References

Acupuncture on Bell’s palsy


[41] Li J. Comparison of the efficacy between acupuncture and manipulation for Bell’s palsy. Chinese Clinical Medicine Research 2005; 41: 1715-1716.

Acupuncture on Bell’s palsy


[45] Shao SF, WZ WL. Acupuncture treatment combined with Western medicine for peripheral nerve paralysis of 58 cases. New Med (Chinese). 1999; 16.


Supplementary List 1-Search Strategy

Pubmed (n=48)

#1: “Search acupuncture [Title/Abstract]”
#2: “Search acupuncture therapy [Title/Abstract]”
#3: “Search (acupuncture [Title/Abstract]) OR acupuncture therapy [Title/Abstract]”
#4: “Search Bell’s palsy [Title/Abstract]”
#5: “Search facial paralysis [Title/Abstract]”
#6: “Search idiopathic facial paralysis [Title/Abstract]”
#7: “Search herpetic Facial Paralysis [Title/Abstract]”
#8: “Search (((Bell's palsy [Title/Abstract]) OR facial paralysis [Title/Abstract]) OR idiopathic facial paralysis [Title/Abstract]) OR herpetic Facial Paralysis [Title/Abstract]”
#9: “Search ((acupuncture [Title/Abstract]) OR acupuncture therapy [Title/Abstract]) AND (((Bell's palsy [Title/Abstract]) OR facial paralysis [Title/Abstract]) OR idiopathic facial paralysis [Title/Abstract]) OR herpetic Facial Paralysis [Title/Abstract]”
#10: “Search ((acupuncture [Title/Abstract]) OR acupuncture therapy [Title/Abstract]) AND (((Bell's palsy [Title/Abstract]) OR facial paralysis [Title/Abstract]) OR idiopathic facial paralysis [Title/Abstract]) OR herpetic Facial Paralysis [Title/Abstract]) Filters: Randomized Controlled Trial”
#11: “Search ((acupuncture [Title/Abstract]) OR acupuncture therapy [Title/Abstract]) AND (((Bell's palsy [Title/Abstract]) OR facial paralysis [Title/Abstract]) OR idiopathic facial paralysis [Title/Abstract]) OR herpetic Facial Paralysis [Title/Abstract]) Filters: Randomized Controlled Trial; Clinical Trial”
Acupuncture on Bell’s palsy

EMBASE (n=41)

#1. ‘acupuncture’: ab, ti
#2. ‘acupuncture therapy’: ab, ti
#3 #1 OR#2
#4. ‘bell palsy’: ab, ti
#5. ‘facial paralysis’: ab, ti
#6. ‘idiopathic facial paralysis’: ab, ti
#7. ‘herpetic facial paralysis’: ab, ti
#8. #4 OR#5 OR#6 OR#7
#9. #3 AND #8
#10. #9 AND (controlled clinical trial)/lim OR [randomized controlled trial]/lim.
Acupuncture on Bell’s palsy

Cochrane library (n=155)

#1 “acupuncture”: ti, ab, kw
#2 acupuncture therapy: ti, ab, kw
#3 #1 or #2
#4 Bell’s palsy: ti, ab, kw
#5 “facial paralysis”: ti, ab, kw
#6 idiopathic facial paralysis: ti, ab, kw
#7 herpetic Facial Paralysis: ti, ab, kw
#8 #4 or #5 or #6 or #7
#9 #3 and #8 in Trials.
Acupuncture on Bell’s palsy

WanFang (n=38)

(title or key words: (Bell’s palsy) + title or key words: (facial paralysis) + title or key words: (idiopathic facial paralysis) + title or key words: (Bell’s palsy) + title or key words: (facial paralysis)) and (title or key words: (acupuncture) + title or key words: (acupuncture therapy) + title or key words: (electroacupuncture) + title or key words: (acupuncture and moxibustion)) and (title or key words: (randomized controlled trial) + title or key words: (randomized controlled trial) + title or key words: (RCT)).
Supplementary Figure 1. Risk of bias summary: review authors’ judgments about each risk of bias item for each included study.

Supplementary Figure 2. Sensitivity analysis on acupuncture for total effective rate of Bell’s palsy.

Supplementary Figure 3. Sensitivity analysis on acupuncture for cured rate of Bell’s palsy.
# Supplementary Table 1. Sensitivity analysis

<table>
<thead>
<tr>
<th></th>
<th>Total effective rate</th>
<th>Total cured rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td><strong>Random effect model</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>1.11 (1.05, 1.17)</td>
</tr>
<tr>
<td><strong>Fixed effect model</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>1.12 (1.09, 1.15)</td>
</tr>
<tr>
<td><strong>Within</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Using facial paralysis or House-Brackmann scoring</td>
<td>10</td>
<td>1.05 (1.02, 1.09)</td>
</tr>
<tr>
<td>Reported both effective rate and cured rate</td>
<td>15</td>
<td>1.11 (1.07, 1.16)</td>
</tr>
<tr>
<td><strong>Without</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sample size &lt;100</td>
<td>10</td>
<td>1.09 (1.03, 1.16)</td>
</tr>
<tr>
<td>Extra therapy method¹</td>
<td>17</td>
<td>1.10 (1.05, 1.15)</td>
</tr>
<tr>
<td>Therapy period &gt;1 month</td>
<td>14</td>
<td>1.08 (1.03, 1.14)</td>
</tr>
</tbody>
</table>

Abbreviations: N, number of studies; CI, confidence interval; RR, relative risk. ¹moxibustion or He-Ne laser radiation.