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Wet cupping therapy for treatment of herpes zoster: a systematic review of randomized controlled trials

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Abstract

Background—Wet cupping is a traditional Chinese medicine therapy commonly used in treating herpes zoster in China, and clinical studies have shown that wet cupping may have beneficial effect on herpes zoster compared with western medication.

Methods—We included randomized controlled trials on wet cupping for herpes zoster. We searched PubMed, the Cochrane Library (Issue 3, 2008), China Network Knowledge Infrastructure (CNKI), Chinese Scientific Journal Database (VIP), and Wan Fang Database. All searches ended in February 2009. Two authors extracted data and assessed the trials quality independently. RevMan 5.0.18 software was used for data analysis with effect estimate presented as relative risk (RR) and mean difference (MD) with a 95% confidence interval (CI).

Results—8 RCTs involving 651 patients were included, and the methodological quality of trials was generally fair in terms of randomization, blinding and intention-to-treat analysis. Meta-analyses showed wet cupping was superior to medications regarding the number of cured patients (RR 2.49, 95% CI 1.91 to 3.24, $p < 0.00001$), the number of patients with improved symptoms (RR 1.15, 95% CI 1.05 to 1.26, $p = 0.003$), and reducing the incidence rate of postherpetic neuralgia (RR 0.06, 95% CI 0.02 to 0.25, $p = 0.0001$). Wet cupping plus medications was significantly better than medications alone on number of cured patients (RR 1.93, 95% CI 1.23 to 3.04, $p = 0.005$), but no difference in symptom improvement (RR 1.00, 95% CI 0.92 to 1.08, $p = 0.98$). There were no serious adverse effects with related to wet cupping therapy in the included trials.

Conclusions—Wet cupping appears to be effective in treatment of herpes zoster. However, further large, rigorous designed trials are warranted.

Background

Herpes zoster, commonly with the pain and rash on skin, is caused by the infection of latent varicella zoster virus (VZV). VZV usually persists asymptotically in the dorsal root ganglia of anyone who has had chickenpox, reactivating from its dormant state in about 25% of people to travel along the sensory nerve fibres and cause vesicular lesions in the

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Potential conflict of interest

None known.

dermatome supplied by the nerve^[1]. The classical clinical presentation of herpes zoster starts with a mild-to-moderate burning or tingling in or under the skin of a given surface, often accompanied by fever, chills, headache, stomach upset and general malaise. The pain associated with shingles varies in intensity from mild to severe, the lesions usually begin to dry and scab 3–5 days after appearing. Total duration of the disease is generally between 7–10 days, and the most common complication associated with herpes zoster is the development of postherpetic neuralgia (PHN), a condition where pain accompanying the rash persists long after the lesions have healed.

Herpes zoster has a high infection rate, which is increasing by years. Some studies showed that the infection rate of herpes zoster and the intensity of the pain were relative with age, and the elderly were at greater risk for developing this disease. Early treatment can be more effective to release the pain and reduce the duration of disease^[2]. The objective of conventional therapy in the treatment of herpes zoster is to accelerate the healing of the lesions, reduce the accompanying pain, and prevent complications. Medications typically prescribed included antiviral agents, corticosteroids, analgesics, non-steroidal anti-inflammatory drugs, and tricyclic antidepressants^[3].

In Traditional Chinese Medicine, herpes zoster is called *She Chuan Chuang*, its pathological mechanism is insufficient of anti-pathogenic energy, toxin invades the body and transformation into heat, damp-heat spreading to the skin; or is stagnation of liver *qi*, and extreme heat generate wind, the fire depressed in skin; or is damp-heat in spleen and stomach, and spreading to the skin^[2]. The treatment including herbal decoction, Chinese formulated products, acupuncture, moxibustion, cupping therapy and so on.

Cupping therapy is a method mainly using horn, bamboo or glass cups on patients' skin by creating minus pressure inside the cups, which exerts as an approach for diagnosis, treatment and prevention of diseases^[4]. There are many types of cupping therapy, but 8 types of cupping are commonly used in clinical practice, i.e., empty cupping, moving cupping, retained cupping, needle cupping, moxa cupping, wet cupping, herbal cupping and water cupping^[5]. Wet cupping, also called full (bleeding) cupping, was the most favored and practiced cupping method of all by the early practitioners, who particularly in Europe, employed the Bleeding cupping technique in order to purge foul blood, which was considered the source of disease, from the body. It can be used in the treatment of a sudden increase in blood pressure, and in discharging pus from boils and furuncles, which represents excess, with blood-heat and stagnation. Sterilize the selected points with alcohol and make a very small incision with a triangle-edged needle or, using a plum-blossom needle, firmly tap the point for a short time to cause bleeding. Once the point is bled, choose a cup and apply a strong cupping method to the point. The blood will quite quickly be observed being drawn slowly into the cup. If the incision is sufficient, blood with about 30–60 ml can be expected to be drawn into the cup. Remove the cup after 5 or 10 minutes with attention and care. Cupping regulates the flow of *qi* and blood. It helps to draw out and eliminate pathogenic factors such as damp and heat. Cupping also moves *qi* and blood and opens the pores of the skin, thus precipitating the removal of pathogens through the skin itself^[6].

From literature, we found some clinical trial reports on wet cupping therapy for herpes zoster, but there is no systematic review about the therapeutic effect of the therapy. Therefore, this review aims to evaluate the beneficial and harmful effects of wet cupping therapy for treatment of herpes zoster in randomized trials.

Methods

Inclusion Criteria

Parallel randomized controlled trials (RCTs) of wet cupping compared with no treatment, placebo or basic medical therapy in patients with herpes zoster and PHN were included. Combined therapy of wet cupping and other interventions compared with other interventions in RCTs was also included. Outcome measures include reductions in severity of pain, duration of relief of pain, percentage of cured patients and the incidence rate of PHN. Multiple publications reporting the same groups of participants were excluded. Combined therapy of wet cupping and acupuncture compared with medication or other interventions except acupuncture was also excluded. There was no limitation on language and publication type.

Identification and selection of studies

We searched China Network Knowledge Infrastructure (CNKI) (1979–2009), Chinese Scientific Journal Database VIP (1989–2009), Wan Fang Database (1985–2009), PubMed (1966–2009) and the Cochrane Library (Issue 3, 2008), all the searches ended at February 2009. The search terms included “post-herpetic neuralgia”, “PHN”, “herpes zoster”, “zona”, or “shingles” combined with “venesection”, “phlebotomy therapy”, “three edged needle”, “triangle-edged needle”, “ventouse”, “cupping” or “blood-letting”. Two authors (HJ Cao and CJ Zhu) selected studies for eligibility and checked against the inclusion criteria independently.

Data extraction and quality assessment

Two authors (HJ Cao and CJ Zhu) extracted the data from the included trials independently. Quality of the included trials was evaluated according to following categories [7]. Category A (good): studies have the least biases and their results are considered valid. These studies are likely to consist of (1) clear description of the population, setting, interventions and comparison groups; (2) appropriate measurement of outcomes; (3) appropriate statistical and analytical methods; (4) no reporting errors; (5) less than 20 percent dropouts; (6) clear reporting of dropouts; and (7) appropriate consideration and adjustment for potential confounders. Category B (fair): studies are susceptible to some degrees of biases that are not sufficient to invalidate the results. These studies may have sub-optimal adjustments for potential confounders and may also lack certain information that is needed to assess limitations and potential problems. Category C (poor): studies have significant biases which may invalidate the results. These studies either do not consider potential confounders or do not make adjustments for them appropriately. These studies may have critical flaw in design, analysis and/or reporting, missing information and/or discrepancies in reporting.

Data analysis

Data were summarized using relative risk (RR) with 95% confidence intervals (CI) for binary outcomes or mean difference (MD) with 95% CI for continuous outcomes. Revman5.0.18 software was used for data analyses. Meta-analysis was used if the trials had a good homogeneity on study design, participants, interventions, control, and outcome measures. Publication bias was explored by funnel plot analysis.

Results

Description of studies

After primary searches from seven databases, 389 citations were identified, and the majority was excluded due to obvious ineligibility, and full text papers of 14 studies were retrieved.

At last, 8 [8–15] trials were included in this review, 5 trials [16–20] were excluded as they used wet cupping therapy combined with acupuncture or moxibustion compared with other medications, 1 trial [21] was excluded due to the ineligible data reporting (Figure 1: The process of including and excluding studies). The characteristics of included and excluded trials were listed in Table 1 (Characteristics of included studies) and Table 2 (Studies excluded from the review and reasons for exclusion).

The 8 trials involved a total of 651 patients with herpes zoster. The variation in the age of subjects was 12–82 years and disease duration was from 1 day to 14 days. Five trials specified four diagnostic criteria, including two criteria in different kind of text books in China, two national criteria in China. The interventions included wet cupping therapy (prick on lesion with triangle-edged needle, plum needle, or seven-star needle), wet cupping therapy plus conventional medications or acupuncture. The controls included medications or acupuncture. The total treatment duration ranged from 7 days to 10 days. All the included trials used two, three or four of four classes to evaluate treatment effects including cure, markedly effective, effective/improve, and ineffective according to the degree of overall symptom improvement.

Methodological quality

According to our pre-defined quality assessment criteria, all the included trials had clear description of the population, setting, interventions and comparison groups, appropriate statistical and analytical methods, the sample size varied from 30 to 50 participants, with average of 43 patients per group, though none of the trials reported sample size calculation, method for allocation concealment and blinding. Two trials [8, 9] described the randomization procedure, using random number table, and drawing. All the included trials chose the improvement of the symptoms as the outcome measurement, but whether the assessors of outcome were blinding were not reported in all the 8 trials. There was no participant dropped during all the studies, only two trials [9, 13] mentioned follow-up, but intention-to-treat was not used. No trials had appropriate consideration and adjustment for potential confounders. It has high potential to have some degrees of biases that are not sufficient to invalidate the results, so we generally concluded that all the 8 trials (100%) were evaluated as fair (B).

Effect estimates (Table 3: Effect of estimates of wet cupping treatment in 8 RCTs)

Wet cupping versus medications—Four trials [9–11, 13] compared wet cupping with medications. Three of them [9–11] showed that wet cupping therapy was significantly better than medications on increasing the number of patients whose herpes zoster were cured (RR 2.49, 95%CI 1.91 to 3.24, $p < 0.00001$), and also on increasing the number of patients whose symptom was improved after treatment (RR 1.15, 95%CI 1.05 to 1.26, $p = 0.003$), though one trial's result showed not estimable [10].

Three trials [9, 10, 13] reported the incidence rate of PHN after treatment. The meta-analysis showed that wet cupping therapy was significantly more effective to prevent the complications (RR 0.06, 95%CI 0.02 to 0.25, $p = 0.0001$).

One trial [10] reported the average cure time, which showed no significant difference between wet cupping with medications (MD -3.14 , 95%CI -6.45 to 0.17 , $p = 0.06$).

Wet cupping plus other interventions versus other interventions—Five trials [8, 10, 12, 14, 15] compared wet cupping therapy plus other interventions versus other interventions alone. Result of meta-analysis showed significant difference between wet cupping plus medications or ultraviolet radiation compared with the same interventions on

increasing the numbers of patients whose herpes zoster were cured (RR 1.93, 95%CI 1.23 to 3.04, $p=0.005$). Four trials' [8, 10, 14, 15] results about number of patients whose symptom was improved after treatment were also be synthesized, but three of them showed not estimable, only one trial [8] showed no positive result of this comparison (RR 1.00, 95%CI 0.92 to 1.08, $p=0.98$).

Two trials [8, 10] reported the average cure time, and the meta-analysis showed significant difference between wet cupping plus medications compared with medications alone on accelerating the time of cure (MD -2.67 , 95%CI -3.97 to -1.37 , $p<0.0001$).

Adverse effect—Outcome of adverse effect with related to wet cupping therapy was described in two trials [10, 13], but no adverse effect was observed in wet cupping group. One trial [13] reported one patient with diabetes had several depressed scars on lesion skin in aciclovir group ($n=48$).

As each comparisons included in this review had less than five trials, it was not meaningful to conduct a funnel plot analysis.

Discussions

Based on the meta-analyses, the results showed that compared with medications, wet cupping therapy was significant better on healing the lesions and reducing the accompanying pain, and the combination of other interventions appears more effective than those interventions alone, though it is possible that the beneficial effect from wet cupping was overvalued because of the small sample size, insufficient reporting of methodology of the included trials.

There are several limitations in this review. First, the quality of the included studies is generally fair, which may cause moderate risk of bias. Because of inadequate application of randomization and lack of blinding in majority trials, it was possible for potential performance bias and detection bias due to patients and researchers being aware of the therapeutic interventions for the subjective outcome measures. Intention-to-treat analysis was not applied in data analyses in the included trials. Though the funnel plot can not be generated due to the limited number of trials in the meta-analysis, all studies reported the positive result favoring the treatment group, it may have publication bias. Further more, all the included trials were published in Chinese, it may also affect the possibility of selection bias. Second, one trial [9] included only the middle-age and senile patients with herpes zoster, one trial [15] only included the patients with head-face herpes zoster, and there were different type of needles used in the trials, included triangle-edged needle in 4 trials, plum-blossom needle in 2 trials, filiform needle in 1 trials, and seven-star needle in 1 trial. Seven trials applied the pricking bloodletting on lesion of skin, 1 trial pricking and cupping on DU14, BL13, BL17, BL18 and bloodletting on ear apex. The variance of participates and the detail of interventions may create the heterogeneity among the included trials, and affect the meta-analysis of therapeutic effect. Forth, the use of composite outcome measures in 8 trials to evaluate overall improvement of symptoms limits the generalization of the findings. The classification of cure, markedly effective, effective or ineffective is not internationally recognized, and it is hard to interpret the effect. We suggest future trials to comply with international standards in the evaluation of treatment effect. Although there is not major statistical heterogeneity among the data analyses, we realized that the clinical heterogeneity would be very significant due to the variations in study quality, participants, intervention, control and outcome measures. The interpretation of the positive findings from the meta-analyses needs to be incorporated with the clinical characteristics of the included trials and evidence strength. Therefore, the conclusion of the beneficial effect of wet cupping therapy

for herpes zoster needs to be confirmed in large and rigorously designed randomized controlled trials.

Our searches identified one review of acupuncture and cupping therapy for herpes zoster [22]. It published in Chinese in 2008 included 399 trials, and the purpose of that review was to assess the quality of literature of clinical studies on acupuncture and cupping therapy in treatment of herpes zoster. It reported that in all 399 trials, 86 trials only used acupuncture as the treatment intervention, and 187 of the left 313 trials used wet cupping therapy. It showed that as a very commonly used method in treating herpes zoster, wet cupping therapy combined with acupuncture may have more markedly effect. In our systematic review, we excluded 5 trials which used wet cupping therapy combined with acupuncture to treat herpes zoster compared with medications alone, but all the 5 excluded trials showed positive result of the therapeutic effect of interventions. Therefore the further rigorous trials are warranted to testify this conclusion.

Most of existing trials are of small size and some risk of bias. Further high quality studies of larger sample size are needed to confirm the effectiveness of wet cupping therapy in treating herpes zoster. Randomization methods need to be clearly described and fully reported. Although blinding of the patients and practitioners might be very difficult, blinding of outcome assessors should be attempted as far as possible to minimize performance and assessment biases. Choosing outcome measures should be according to the international standards, the continuous data may include change in average daily pain score from the baseline week to the final study week, measured on Visual Analogue Scale (VAS), Short Form-36 (SF-36) Quality of Life Questionnaire, Profile of Mood States (POMS), and the Present Pain Intensity (PPI) score [23], the binary outcomes may include the burden of illness due to herpes zoster, and the incidence of postherpetic neuralgia [24], et al. Analysis of outcomes based on intention-to-treat principle is important. In addition, well-defined diagnostic criteria should be employed to make a precise clinical diagnosis of herpes zoster, and hence increase the comparability between trials. In its classical manifestation, the signs and symptoms of zoster are usually distinctive enough to make an accurate clinical diagnosis once the rash has appeared, but in some cases, particularly in immunosuppressed persons, the location of rash appearance might be atypical, or a neurologic complication might occur well after resolution of the rash. In these instances, laboratory testing might clarify the diagnosis [25]. Reporting of trials should follow by the Consolidated Standards of Reporting Trials (CONSORT) [26] to explicitly explain the process of the treatment, so that the clinicians or other researchers can possibly practice. Since herpes zoster may wax and wane with or without treatment, and it may have complications such as postherpetic neuralgia, a longer follow-up period with serial measurement of outcomes is important to determine the effectiveness and long-term effect of wet cupping therapy.

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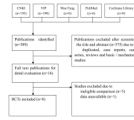


Figure 1.
The process of including and excluding studies

Table 1

Characteristics of included studies

Trials	Patients (M/F)		Average age (y)	Diagnostic criteria	Interventions		Duration of treatment	Outcome measure
	treatment	control			Cupping treatment	Control		
Guo L 2006 [8]	19/17	17/18	unclear	Chinese criteria for diagnosis	Prick with triangle-edged needle and cupping on lesion for 10 minutes, once every two days, plus aciclovir 200mg 3 times daily, VitB ₁ 100mg, VitB ₁₂ 250mg injection once daily.	Aciclovir 200mg 3 times daily, VitB ₁ 100mg, VitB ₁₂ 250mg injection once daily.	10 days	* Cure, improve, ineffective; average time of cure.
Jin M 2008 [9]	26/19	25/20	55.5	Professional criteria in China	Prick with seven-star needle and cupping on the lesion for 10–15min, once daily for first 3 days, then once every two days and last for 4 days	Aciclovir capsule 0.2g five times daily, cimetidine 0.2g three times daily, indometacin tablet 50mg three times daily, Mecobalamin daily, Mecobalamin tablets 0.5mg three times daily, washout with calamin and use aciclovir cream	10 days	* Cure, improve, ineffective. Incidence rate of postherpetic neuralgia (PHN)
Lin L 2003 [10]	28/22	19/15	55.1	Criteria in text book in China	Group 1: prick with plum needle on lesion then cupping on the same place for 10–15min, once every two days, plus aciclovir 0.2g five times daily, VitB ₁ 20mg three times daily, VB12 500mg injection once every two days, 2%–3% aciclovir cream for external use.	Aciclovir 0.2g five times daily, VitB ₁ 20mg three times daily, VB12 500mg injection once every two days, 2%–3% aciclovir cream for external use.	10 days	** cure, markedly effective, ineffective. The average time of cure. Incidence rate of PHN.
	16/14	19/15	54.2		Group 2: prick with plum needle on lesion then cupping on the same place for 10–15min, once every two days.	Aciclovir 0.2g five times everyday, VitB ₁ 20mg three times everyday, VB12 500mg injection once every two days, 2%–3% aciclovir cream for external use.		
Liu Q 2004 [11]	32	32	55.6	unavailable	Prick with triangle-edged needle and cupping on lesion.	Aciclovir 1.2g five times everyday, poly I-C injection 2mg once every two days.	10 days	** cure, markedly effective, ineffective.
Long W 2003[12]	34	30	44.5	unavailable	Prick with plum needle on lesion then cupping on the	Ultraviolet radiation once every two days.	10 days	Times of treatment for * cured

Trials	Patients (M/F)		Average age (y)	Diagnostic criteria	Interventions		Duration of treatment	Outcome measure
	treatment	control			Cupping treatment	Control		
Xiong Z 2007 ^[13]	20/28	16/24	49	Criteria in text book in China	Prick on lesion and cupping for 5 minutes.	Aciclovir plus normal saline 250ml intravenous drip once daily.	7 days	Incidence rate of PHN.
Xu L 2004 ^[14]	20/20	21/19	unclear	unavailable	Prick with triangle-edged needle and cupping on lesion for 15min, aciclovir cream for external use plus aciclovir 0.5g and glucose 250ml intravenous drip twice daily.	Aciclovir cream for external use plus aciclovir 0.5g and glucose 250ml intravenous drip twice daily.	7 days	* cure, improve, effective, ineffective. Scores given by patients according to their symptom of disease. Average dry up time of lesion; average time of pain disappear
Zhang Q 2008 ^[15]	14/26	12/28	unclear	Criteria in text book in China	Aciclovir 200mg five times daily, acupuncture beside the lesion 30min once daily, plus prick with triangle-edged needle on Dazhui, Feishu (double), Ganshu (double) and cupping for 10min once every two days, blood-letting on auditive apex twice every week	Aciclovir 200mg five times daily, acupuncture beside the lesion 30min once daily	14 days	* cure, improve, effective, ineffective.

Definition of "cure", "markedly effective", "effective", and "ineffective":

* cure: rash totally faded, the clinical symptoms are disappeared, no accompanying pain.
 markedly effective: rash faded more than 70% (including 70%), the accompanying pain was almost disappeared.
 improved: rash faded 30%–69%, the accompanying pain was obviously alleviated.
 ineffective: rash faded less than 30%, no alleviation of the accompanying pain.

** cure: rash totally fade, no accompanying pain.
 markedly effective: rash faded more than 50%, the accompanying pain was almost disappeared.
 effective: rash faded 10%–50%, the accompanying pain was alleviated a little.
 ineffective: rash faded less than 10%, no alleviation of the accompanying pain.

Table 2

Studies excluded from the review and reasons for exclusion

Study	Reasons for exclusion
Cai P 2006[16]	Randomized controlled trial (RCT) which used wet cupping therapy combined with acupuncture compared with western medications
Huo H 2007[17]	RCT which used wet cupping therapy combined with acupuncture and needle prick round the rash compared with western medications
Lao S 2008[18]	RCT which used wet cupping therapy combined with moxibustion compared with western medications
Pang S 2003[19]	RCT which used wet cupping therapy combined with needle prick round the rash compared with western medications
Wang H 2007[20]	RCT which used wet cupping therapy combined with acupuncture compared with western medications
Zhang J 2004[21]	RCT but data were not available for analysis due to inadequate reporting

Table 3

Effect of estimates of wet cupping treatment in 8 RCTs

Trials	Comparisons	Effect Estimates([95%CI])	P Value
3.1 Numbers of cured patients			
<i>3.1.1 wet cupping plus other interventions versus other interventions alone</i>			
Guo L 2006[8]	Wet cupping plus aciclovir, VitB ₁ , VitB ₁₂ versus aciclovir, VitB ₁ , VitB ₁₂	RR 1.48 [1.05, 2.09]	
Liu L 2003[10]	Wet cupping plus aciclovir, VitB ₁ , VitB ₁₂ and aciclovir cream versus aciclovir, VitB ₁ , VitB ₁₂ and aciclovir cream	RR 3.83 [2.07, 7.06]	
Long W 2003[12]	Wet cupping plus ultraviolet radiation versus ultraviolet radiation alone	RR 1.30 [1.06, 1.59]	
Xu L 2004[14]	Wet cupping plus aciclovir cream, aciclovir 0.5g and glucose 250ml intravenous drip versus aciclovir cream, aciclovir 0.5g and glucose 250ml intravenous drip	RR 1.35 [0.93, 1.97]	
Zhang Q 2008[15]	Wet cupping and blood-letting on auditive apex plus aciclovir and acupuncture versus aciclovir and acupuncture	RR 4.17 [1.92, 9.05]	
	meta-analysis	RR 1.93 [1.23, 3.04]*	0.005
<i>3.1.2 wet cupping versus medications</i>			
Jin M 2008[9]	Wet cupping versus aciclovir, cimetidine, indometacin, mecobalamin, calamin and aciclovir cream.	RR 2.15 [1.54, 3.00]	
Liu L 2003[10]	Wet cupping versus aciclovir, VitB ₁ , VitB ₁₂ and aciclovir cream	RR 2.83 [1.47, 5.46]	
Liu Q 2004[11]	Wet cupping versus aciclovir and poly I-C injection	RR 2.90 [1.71, 4.91]	
	meta-analysis	RR 2.49 [1.91, 3.24]	<0.00001
3.2 Numbers of patients with PHN after treatment			
Jin M 2008[9]	Wet cupping versus aciclovir, cimetidine, indometacin, mecobalamin, calamin and aciclovir cream.	RR 0.09 [0.01, 1.60]	
Liu L 2003[10]	Wet cupping versus aciclovir, VitB ₁ , VitB ₁₂ and aciclovir cream	RR 0.06 [0.00, 1.09]	
Xiong Z 2007[13]	Wet cupping versus aciclovir plus normal saline 250ml intravenous drip	RR 0.05 [0.01, 0.38]	
	meta-analysis	RR 0.06 [0.02, 0.25]	0.0001
3.3 Numbers of patients with improved symptom after treatment			
<i>3.3.1 wet cupping plus other interventions versus other interventions alone</i>			
Guo L 2006[8]	Wet cupping plus aciclovir, VitB ₁ , VitB ₁₂ versus aciclovir, VitB ₁ , VitB ₁₂	RR 1.00 [0.92, 1.08]	
Liu L 2003[10]	Wet cupping plus aciclovir, VitB ₁ , VitB ₁₂ and aciclovir cream versus aciclovir, VitB ₁ , VitB ₁₂ and aciclovir cream	Not estimable	
Xu L 2004[14]	Wet cupping plus aciclovir cream, aciclovir 0.5g and glucose 250ml intravenous drip versus aciclovir cream, aciclovir 0.5g and glucose 250ml intravenous drip	Not estimable	
Zhang Q 2008[15]	Wet cupping and blood-letting on auditive apex plus aciclovir and acupuncture versus aciclovir and acupuncture	Not estimable	
	meta-analysis	RR 1.00 [0.92, 1.08]	0.98

Trials	Comparisons	Effect Estimates([95%CI])	P Value
3.3.2 wet cupping versus medications			
Jin M 2008[9]	Wet cupping versus aciclovir, cimetidine, indometacin, mecobalamin, calamin and aciclovir cream.	RR 1.07 [0.98, 1.17]	
Liu L 2003[10]	Wet cupping versus aciclovir, VitB ₁ , VitB ₁₂ and aciclovir cream	Not estimable	
Liu Q 2004[11]	Wet cupping versus aciclovir and poly I-C injection	RR 1.27 [1.05, 1.54]	
	meta-analysis	RR 1.15 [1.05, 1.26]	0.003
3.4 Average cure time			
3.4.1 wet cupping plus other interventions versus other interventions alone			
Guo L 2006[8]	Wet cupping plus aciclovir, VitB ₁ , VitB ₁₂ versus aciclovir, VitB ₁ , VitB ₁₂	MD -2.10 [-3.55, -0.65]	
Liu L 2003[10]	Wet cupping plus aciclovir, VitB ₁ , VitB ₁₂ and aciclovir cream versus aciclovir, VitB ₁ , VitB ₁₂ and aciclovir cream	MD -5.08 [-8.04, -2.12]	
	meta-analysis	MD -2.67 [-3.97, -1.37]	<0.0001
3.4.2 wet cupping versus medications			
Liu L 2003[10]	Wet cupping versus aciclovir, VitB ₁ , VitB ₁₂ and aciclovir cream	MD -3.14 [-6.45, 0.17]	0.06

RR: Relative Risk MD: Mean Difference CI: Confidence Interval

* : Random model for data analysis