Original Article

Systematic review and meta-analysis: the effectiveness and safety of acupuncture in the treatment of herpes zoster

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Background: The treatment of herpes zoster (HZ) by the traditional Chinese medicine of acupuncture is attracting attention. However, there is still a controversy about the effectiveness and safety of acupuncture treatment of HZ.

Methods: Articles on randomized controlled trials examining acupuncture and Western medicine treatments of HZ published since the establishment of the PubMed, Embase, Medline, and Chinese Biomedical Literature (CBM) databases to March 2021 were electronically retrieved. The Cochrane System Evaluation Manual was used for the data analysis with Review Manager 5.3 software, and the Cochrane Handbook version 5.3 systematic review writing manual was adopted to evaluate the risk of bias.

Results: In total, 11 articles, comprising 1,156 patients (585 in the experimental group and 571 in the control group) were included in the meta-analysis, and the results showed that the treatments used in the experimental and control groups were significant differences of total treatment efficiency [odds ratio (OR) =6.76; 95% confidence interval (CI): 3.46 to 13.21; P<0.05] in terms of the incidence of posterior neuralgia (OR =0.07; 95% CI: 0.02 to 0.21; P<0.05), pain-relief time [mean difference (MD) =−2.17; 95% CI: −2.90 to −1.44; P<0.05], shingles time (MD =−1.61; 95% CI: −2.84 to −0.38; P<0.05), and scabbing time (MD =−1.62; 95% CI: −2.64 to −0.61; P<0.05), and patients' visual analogue scale (VAS) pain scores improved [standard MD (SMD) =0.87; 95% CI: 0.01 to 1.73; P=0.05] was no significant difference.

Discussions: Compared to Western medicine treatments, acupuncture had a better effect on HZ, reduced the posterior neuralgia rate of patients, and shortened the course of treatment, but had no obvious effect on the relief of pain.

Keywords: Herpes zoster (HZ); acupuncture treatment; mate analysis; clinical efficacy

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Introduction

Herpes zoster (HZ) is a common skin disease caused by the reactivation of the varicella-HZ (VZV) virus, and is characterized by banded clusters of erythema blisters on the body, accompanied by severe neuralgia that seriously affects the patient's daily life (1). The VZV virus may reactivate due to age, stress, or decreased immunity, and spread along the sensory nerves to the skin, causing unique precursory pain followed by a rash. HZ can occur at any age, but is most common in elderly people (2). It is estimated that about 1/3 of the population will develop HZ during their lifetime (3). The incidence of HZ and HZ-associated complications increase with age (4,5). HZ may cause post-HZ neuralgia

(i.e., postherpetic neuralgia), which is the most common complication, and 10% of patients experience pain for more than a month, or even for years, which often leads to anxiety, insomnia and other problems that affect the normal life of patients (6,7). In Western medicine, HZ is mainly treated by antiviral and nutritional nerve drugs, Its treatment effect is poor (8). Over-the-counter or prescription painkillers are used when the pain is serious, but the side effects of some of the drugs are often difficult to ignore, and can include nausea, vomiting, and liver function damage (9,10).

Studies have shown that the treatment effects of acupuncture and moxibustion on HZ are certain, result in only minimal pain, have a quick effect, are acceptable to patients, and are widely used in clinical practice. Acupuncture treatment HZ can be adjusted to local qi and blood, dispersing silt and clearing away heat, shorten the course of disease, dredge meridians and blood, rapidly blocking further damage to nerve, having obvious analgesic effect and can reduce neuralgia (11). There is some evidence that acupuncture may be beneficial in the treatment of neurological pain (12). Additionally, acupuncture is known to be a safe treatment with few adverse reactions (13). The curative effect of acupuncture in the treatment of this disease is certain. Acupuncture can be administered in many ways (e.g., via electric needle, fire needle, warm moxibustion, plum needle, acupuncture cupping, surrounding thorn, and acupuncture injection), but the acupoints and methods used are different. Notably, fire needle, no needle, puncture, and other methods have a remarkable treatment effect on HZ, and can effectively relieve pain and promote HZ scabbing. However, very few studies have been conducted on acupuncture treatment in HZ patients, and the results of those studies have been controversial. Thus, there is a lack of extensive clinical research on this topic. This meta-analysis included randomized controlled clinical trials examining the use of acupuncture and Western medicine in the treatment HZ to compare the effectiveness of the two methods, the incidence of posterior neuralgia, visual analogue scale (VAS) pain scores before and after treatment, and pain-relief time, etc. We present the following article in accordance with the PRISMA reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-22-109/rc).

Methods

Strategy for article retrieval

The Embase, PubMed, Medline, and Cochrane Library databases were searched from January 1980 to March 2021 using the following search terms: “Acupuncture”, “Herpes zoster”, “treatment”, “ischemic”, “cerebrovascular”, “herpes”, “Pharmacoacupuncture”, and “Randomized controlled trial”. The terms were optimally combined to retrieve the most relevant articles. The search words had to appear in the scope of the title, keywords, or abstract. Some references in the included articles were also traced, and the full texts of the articles were manually searched and included in this study. After the retrieval, qualified randomized controlled trials were selected according to the inclusion and exclusion criteria for the meta-analysis.

Inclusion and exclusion criteria

To be eligible for inclusion in the study, the articles had to meet the following inclusion criteria: (I) be about clinical research; (II) include subjects who had been diagnosed with HZ; and (III) include an experimental group that received acupuncture therapy or acupuncture therapy combined with drug therapy, and a control group that received drug therapy.

Articles were excluded from the study if they met any of the following exclusion criteria: (I) was a literature review; (II) included animal subjects; (III) included repeated data; (IV) included acupuncture therapy combined with other treatments; (V) examined HZ combined with other diseases; and/or (VI) the full text of the article could not be obtained, or the data documents were incomplete.

Article screening and data extraction

The two researchers separately screened the articles according to the above-mentioned inclusion and exclusion criteria, and discussed any differences in opinions. If they could not reach a joint decision, a third researcher was asked to decide. The following data were extracted: the first author, publication year, basic data of research subjects, number of cases in experimental and control groups, treatment plan, and outcome indicators.

Literature bias risk and methodological quality evaluation

The quality evaluation was carried out according to the “bias risk assessment” recommended by Cochrane System Review Manual (version 5.3). In the evaluation, the following six questions were considered: how was the randomization generated? Was the assignment process biased? Did the researchers use blind methods in the study? Are the results

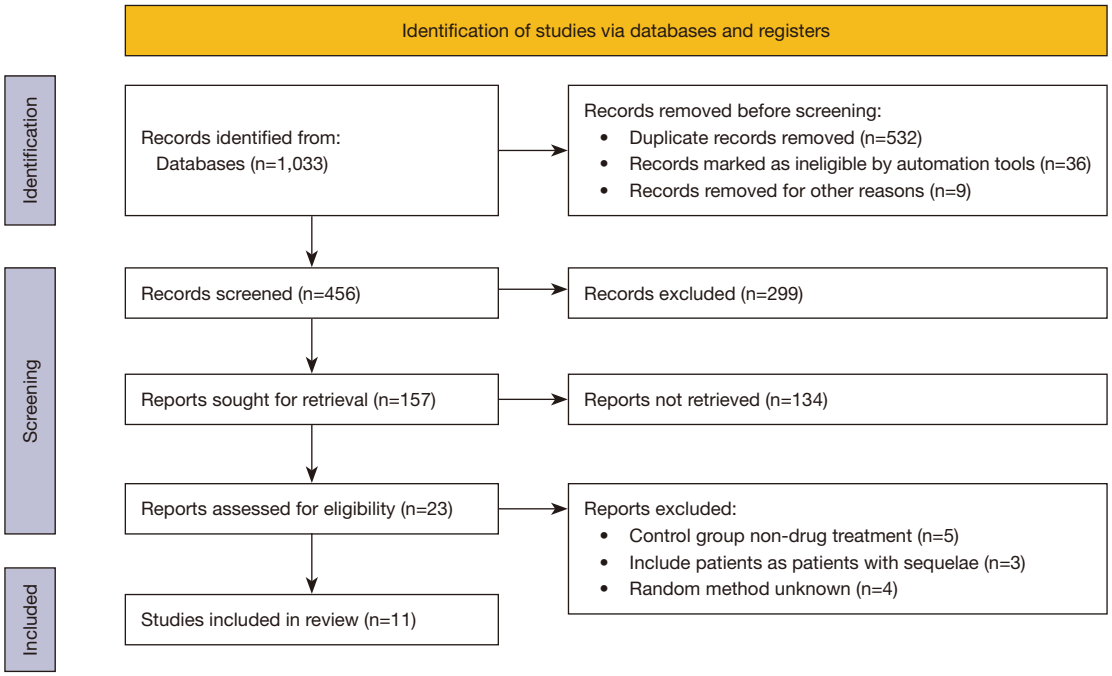

Figure 1 Flow chart of the article retrieval process.

and data complete? Were the study results selectively reported? Were there any other biases?

Statistical analysis

The Review Manager 5.3 software provided by the Cochrane Collaboration was used for the statistical analysis. Bin-classification variables were needed to calculate the odds ratio (OR) or risk ratio (RR), and continuity variables were needed to calculate the mean difference (MD), standard MD (SMD), and 95% confidence interval (CI), and express the results. A P value <0.05 was considered statistically significant. The heterogeneity of the articles was quantitatively evaluated using I^2. An I^2<50% indicated no significant heterogeneity, and a fixed-effects model was used. An I^2>50% indicated significant heterogeneity, and a stochastic-effects model was used. Funnel maps were drawn for the analysis of the publication bias of the included articles, and the symmetry of the funnel maps was evaluated to see if the sample was concentrated around the center line.

Results

Article retrieval

Based on the Cochrane system retrieval strategy, 157 documents were retrieved, duplicate documents were then removed, and the title, abstract and full text were carefully read. Ultimately, 11 articles were included in this study (14-24). There were 1,156 patients, including 585 patients in the experimental group and 571 patients in the control group. *Figure 1* shows the literature retrieval and screening flow. *Table 1* sets out the basic data of the included articles.

The literature quality evaluation

The results of the quality evaluation of the 11 articles are shown in *Figures 2,3*. Notably, none of the 11 articles included in this study used random-sequence generation (indicating selection bias) or allocation concealment (indicating selection bias). Li's research included incomplete outcome data (indicating a high risk of attrition bias) (20). Liu's research included incomplete outcome data and selective reporting (indicating a high risk of reporting bias) (18). Additionally, the other studies had low or unknown risks.

Total treatment efficiency

Of the 11 articles, 8 reported on total treatment efficiency. The differences between the acupuncture and control treatments in terms of total efficiency are shown in *Figure 4*.

Table 1 The basic characteristics of the included articles

Author	Publication year	Sample size (observation group/ control group)	Stochastic method	Experimental group interventions	Control group interventions	Outcome indicator
Zhu (14)	2019	30/30	Random digital tables method	Press needle around + medication	Oral varacyclovir, methyl cobalamin tablets, vitamin B1	③⑤⑥
Yang (15)	2012	60/60	Multi-center randomized control method	Pying cotton moxibustion	External acyclovir cream + oral facyclovir hydrochloride tablets, vitamin B1	①②③④⑤⑥
Ye (16)	2017	33/34	Random system software	Line incense moxibustion + thorn collaterals cupping	Oral acyclovir, vitamin B1, methyl cobalamine tablets + injection of interferon	①③⑤⑥
Hao (17)	2016	30/30	Random digital tables method	Pricking and cupping, pricking blood with cupping + encircling needling	Intravenous drip acyclovir + orally vitamin B1 and vitamin B12 tablets	②
Liu (18)	2009	31/22	Random digital tables method	Electric needle clip ridge hole + blood and cupping	Oral fluxiclovir hydrochloride, indindopecine, vitamin B1, vitamin B12, etc.	①
Ouyang (19)	2009	65/65	Random digital tables method	Pricking blood therapy + ultraviolet radiation	External acyclovir cream + oral acyclovir + intramuscular injection of vitamin B1, vitamin B12	①②④⑤⑥
Li (20)	2009	40/40	Random digital tables method	Electric needle clip + perithorn treatment	Oral vacyclovir, vitamin B1	①③
Tian (21)	2011	42/38	Random digital tables method	Need needle with thin cotton moxibustion	External acyclovir cream oral acyclovir + oral acyclovir	①④⑤⑥
Huo (22)	2007	120/120	Lottery	Needle thorns to put blood, supplemented by cupping, surround thorns	External acyclovir cream + oral acyclovir	①④⑤⑥
Dai (23)	2011	100/100	Simple randomization method	Meridian electrical information diagnosis and treatment + Assx and release blood	Oral acyclovir	①②
Ursini (24)	2011	34/32	Random system software	Acupuncture therapy	PreBahrain, gabapentin	②

The observation group received Western medicine treatment, the program with the control group. ① Total effective rate; ② incidence of posterior neuralgia; ③ VAS scores before and after treatment; ④ pain-relief time; ⑤ blistering-stop time; ⑥ scabbing time. VAS, visual analog scale. Among them, ② and ③ stand for the treatment safety evaluation indicators, the remaining ending indicators are used for efficacy assessment.

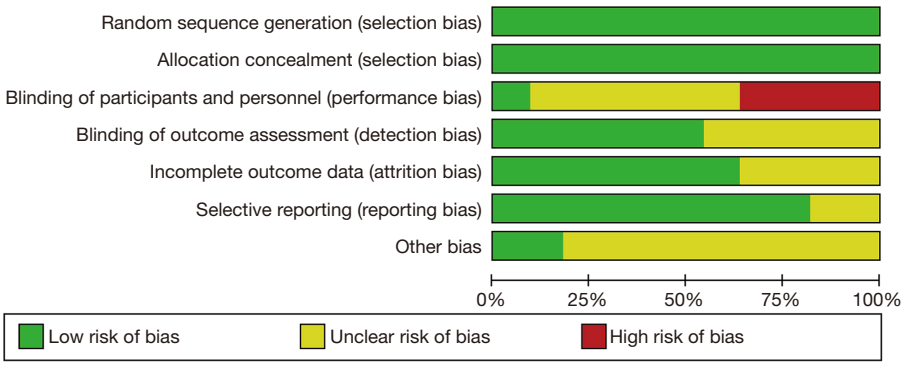

Figure 2 Assessment of the risk of bias of the included articles.

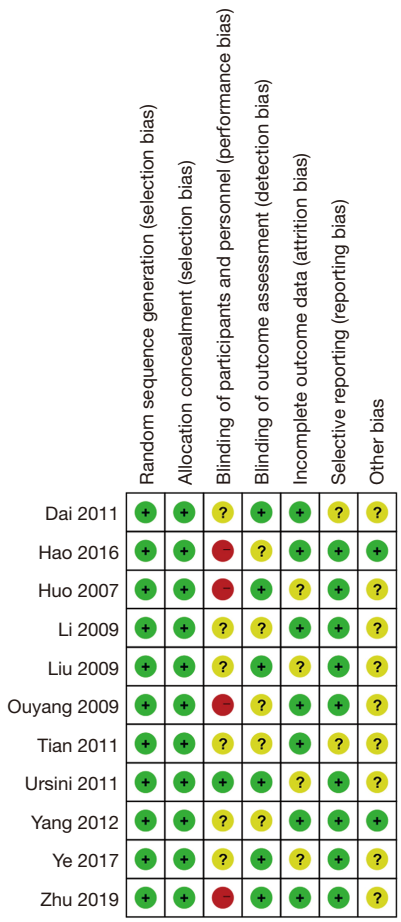

Figure 3 Multiple studies showed multiple risk biases.

The heterogeneity test (I^2=50%; P=0.05) indicated heterogeneity between the studies, and thus the random-effects model was used. The effect value of the OR was 6.76 (95% CI: 3.46 to 13.21). The transverse line fell on the right side of the invalid vertical line. The statistical test results were Z=5.59 and P<0.00001, indicating that the experimental treatment was significantly more efficient than the control treatment (P<0.05).

Rate of posterior legacy neuralgia

A total of 3 articles reported on the occurrence of posterior neuralgia in patients. The differences between the acupuncture and control groups were compared, and the results are shown in *Figure 5*. Based on the heterogeneity test (I^2=43%; P=0.18), there was no heterogeneity between the studies, and thus the fixed-effects model was used. The effect value of the OR was 0.07 (95% CI: 0.02 to 0.21). The transverse line fell on the left side of the invalid vertical line. The statistical test results were Z=4.76 and P<0.00001, indicating that the incidence rate of the experimental group was significantly lower than that of the control group (P<0.05).

VAS pain score before and after treatment

A total of 6 articles evaluated the VAS scores before and after treatment, but only 4 articles stated the standardized average difference of the improved VAS score before and after treatment; the other 2 only stated the average score number and standard difference before and after treatment, and thus were excluded from the comparison. The comparison results are shown in *Figure 6*. The results were I^2=92% and P<0.00001; thus, a random-effects model was used. The SMD was 0.87 (95% CI: 0.01 to 1.73). The statistical test results showed P=0.05, and were not statistically significant in experimental group and control group.

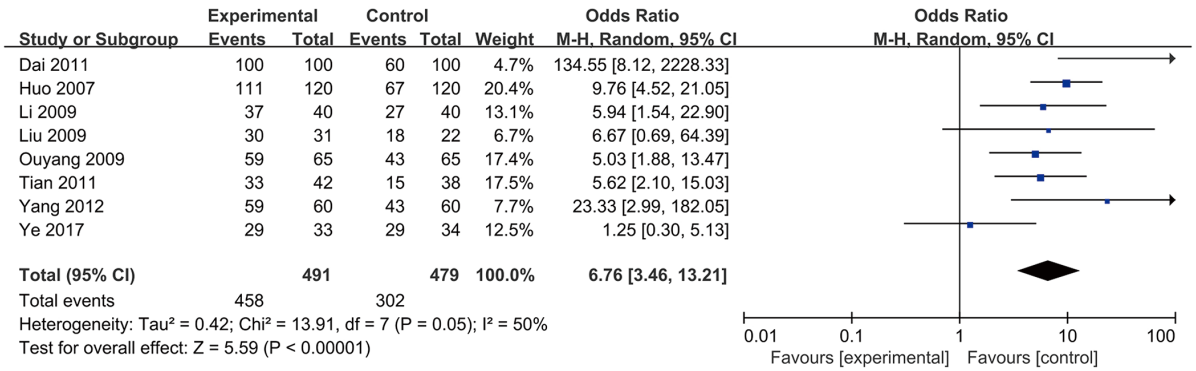

Figure 4 Forest map comparing total treatment efficiency. CI, confidence interval.

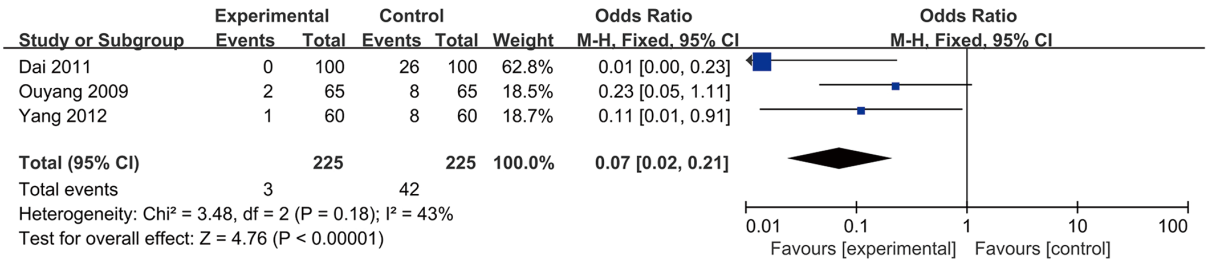

Figure 5 Forest map comparing the incidence of posterior neuralgia. CI, confidence interval.

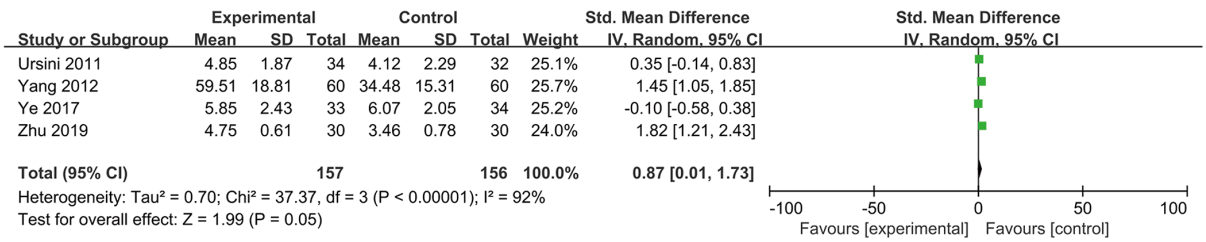

Figure 6 Forest map comparing VAS scores. VAS, visual analog scale; CI, confidence interval.

Pain-relief time

Pain-relief time was reported in 4 articles. The comparison results are shown in *Figure* 7. The heterogeneity test results (I^2=72%; P=0.01) indicated heterogeneity differences among the studies, and thus the stochastic-effects model was used. The results showed that the effect value of the MD was −2.17 (95% CI: −2.90 to −1.44). The transverse line fell on the left side of the invalid vertical line. The statistical test results were Z=5.85 and P<0.00001, indicating that the pain-relief time was significantly shorter in the experimental group than the control group significant (P<0.05).

Shingles time

In total, 6 articles reported on the blistering-stop time of patients. The comparison results are shown in *Figure 8*. The heterogeneity test results (I^2=96%; P<0.00001) indicated heterogeneity between the studies, and random-effects model was used. The results showed that the effect value of the MD was −1.61 (95% CI: −2.84 to −0.38). The transverse line fell on the left side of the invalid vertical line. The

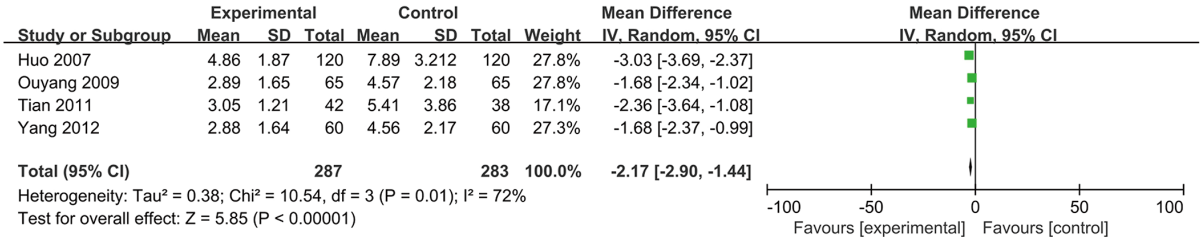

Figure 7 Forest map comparing pain-relief time. CI, confidence interval.

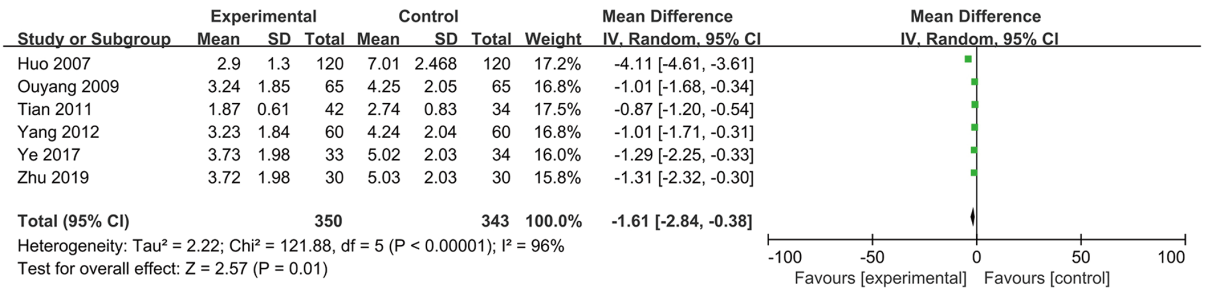

Figure 8 Forest map comparing blister-stopping time. CI, confidence interval.

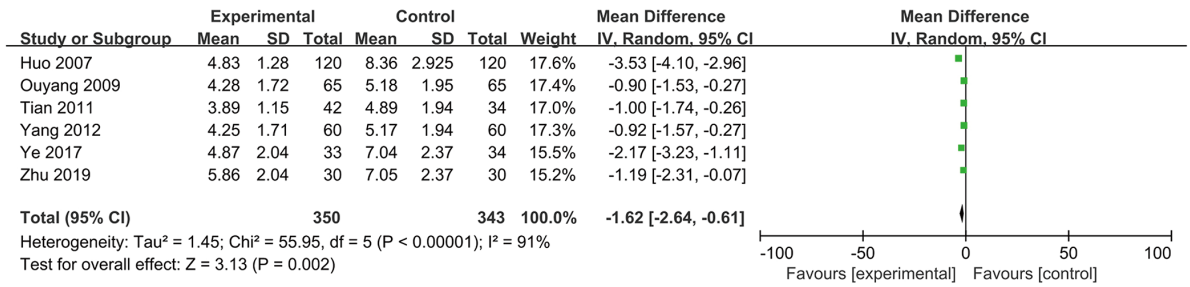

Figure 9 Forest map comparing scabbing time. CI, confidence interval.

results were Z=2.57 and P=0.01, indicating that the time was significantly shorter in the experimental group than the control group (P<0.05).

Scabbing time

A total of 6 documents reported on patients' scabbing time. The comparison results are shown in *Figure 9*. The heterogeneity test (I^2=91%; P<0.00001) indicated that there was heterogeneity between the studies, and random-effects model was used. The results showed that the effect value of the MD was –1.62 (95% CI: –2.64 to –0.61). The transverse line fell on the left side of the invalid vertical line. The statistical results were Z=3.13 and P=0.002, indicating that the scabbing time was significantly shorter in the experimental group than the control group (P<0.05).

Analysis of literature publication bias

An inverted funnel plot of the total efficiency of acupuncture in treating HZ and the improvement in VAS pain scores was produced to determine whether the articles had any publication bias. As *Figure 10* shows, the total efficient graphic was asymmetrical, and almost all of the included studies fell within the inverted funnel plots. Only few studies did not fall into the inverted funnel plot. The possible

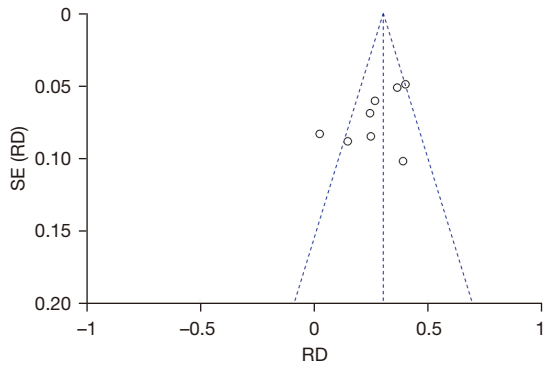

Figure 10 Total efficient publication bias funnel diagram. SE, standard error; RD, risk difference.

reasons were few literatures included in the meta-analysis and the heterogeneity between the articles. The funnel graph shape exhibits a symmetrical blade leakage, so incorporate research does not present literature publication bias.

Discussion

HZ is a common disease in elderly people, and occurs as age increases and immunity drops. The activation of the VZV can cause skin blisters, acute attacks, and pain. If it is not treated in time, it will cause chronic refractory neuralgia. Self-limiting herpes caused by VZV infection is characterized by local burning, pain, intense neuralgia, skin damage, and scabs. The earlier pain relief is provided, the less patients suffer. Drugs can effectively treat HZ, but it is not good to improve neuralgia. A large proportion of patients (18–41%) experience severe or very severe pain, which usually persists after the rash has healed (25-27). The acute and chronic pain of post-HZ neuralgia may seriously affect patients' quality of life, carry high medical costs, and interfere with patients' physical, emotional and social functions (28).

Western medicine treatments of HZ focus on anti-inflammation, infection prevention, shortening the course of the disease, and symptomatic treatment, and generally use antiviral drugs, B vitamins, corticosteroid hormones, transfer factors and interferons. Presently, antiviral drugs are considered an important step in the treatment of HZ, and the timely application of effective antiviral drugs, such as valaciclovir, acyclovir, and famciclovir, can prevent the destruction of the nerve, control acute symptoms, and prevent the occurrence of posterior neuralgia. However, such drugs have high medical cost and certain side effects. Clinically, 10–15% of patients treated with antiviral drugs still experience severe neuralgia after the complete healing of skin lesions, and the incidence of post-HZ neuralgia has been reported to be as high as 50–85% (29).

Acupuncture has unique advantages and good efficacy, and offers a variety of clinical treatment options. Acupuncture may play an analgesic role by reducing central and peripheral sensitization, inhibiting glial activity, and regulating pain-related cell signaling pathways and the expression of receptors. Acupuncture has great advantages in the treatment of primary menstrual pain, cancer pain, nerve pain, and other pain diseases (30).

We conducted a meta-analysis of 11 studies, comprising 1,156 patients (585 in the experimental group and 571 in the control group). The studies examined the total efficiency, posterior pain rate, pain time, blistering time, scabbing time, and VAS pain score. The results showed that acupuncture and moxibustion treatments have obvious advantages in terms of both their efficiency, and in reducing the incidence of posterior neuralgia. Additionally, acupuncture treatment also quickly reduces the pain of patients and shortens the course of the treatment.

The following limitations may explain the biases found in this study. First, only 11 studies were included in the meta-analysis. Second, no unified indicators were used to assess the effect of acupuncture on HZ, and most of the results varied in the articles. Third, as acupuncture and moxibustion are external treatment methods, it was difficult to achieve the application of the blind method, which could have led to a bias in the results. Fourth, there are many specific methods of acupuncture. The literature included in this article is acupuncture, but the specific method has distinctiveness. Due to the constraint limitations of the article, it is impossible to discuss the acupuncture method of the literature. Fifth, the treatment times differed, which may have caused bias. Sixth, only 1 of the included article was published in English, and 1 in Italian, and the rest were published in Chinese, which may lead to language and regional biases. Finally, 1 of the experimental groups used acupuncture combined with Western medicine, but the other groups only used a simple acupuncture treatment, which may have led to bias in the results.

Conclusions

To systematically assess the effectiveness of acupuncture compared to Western medicine in the treatment of HZ, 11 articles on randomized clinical trials were included

in this meta-analysis. The results showed that the total efficiency of acupuncture treatment was significantly higher in the experimental group than the control group, and the incidence of neuralgia post treatment, the pain-relief time, blistering time, and the scabbing time were lower in the experimental group than the control group. Thus, acupuncture had a good effect on HZ, quickly reduced patient pain, shortened the course of the treatment, and reduce the incidence of posterior neuralgia. In relation to the VAS score, there was no difference between acupuncture and moxibustion and the degree of pain.

In summary, acupuncture has significant advantages in terms of its total efficiency and in the treatment of posterior neuralgia. Patients' pain is quickly reduced after acupuncture treatment. To address the limitations of this study, a set of standard evaluation criteria should be set, and the standard system should be designed according to the requirements of clinical randomized control trials, and multi-center large sample-size studies should be conducted to increase the accuracy and reliability of the results.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-22-109/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-22-109/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work, including ensuring that any questions related to the accuracy or integrity of any part of the work have been appropriately investigated and resolved.

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