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Systematic Review

Is fire needle superior to Western medication for herpes zoster? A systematic review and meta-analysis

火针对比西药治疗带状疱疹的系统评价和Meta分析

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Abstract
Objective: To compare the effectiveness of fire needle versus Western medicine in the treatment of herpes zoster.
Methods: Randomized controlled trials comparing fire needle with Western medicine in the treatment of herpes zoster were identified using 8 databases. A meta-analysis was performed using RevMan 5.3 software.
Results: Eight trials involving 569 patients were included in this meta-analysis, and the results showed that fire needle was superior to Western medicine comparing the effective rate [risk ratio (RR)=1.13, 95% confidence interval (CI): 1.06 to 1.20; *P*=0.0002], the visual analog scale (VAS) score [mean difference (MD)=–7.95, 95% CI: –10.71 to –5.20; *P*<0.00001], time of pain disappearance (MD=–7.61, 95%CI: –9.38 to –5.84; *P*<0.00001), time of blister-stop (MD=–1.34, 95%CI: –1.51 to –1.18; *P*<0.00001), time of crusted scab (MD=–2.92, 95%CI: –3.62 to –2.23; *P*<0.00001), and time of scab off (MD=–4.64, 95%CI: –5.83 to –3.46; *P*<0.00001). In addition, a significantly lower incidence of postherpetic neuralgia was found in the fire needle group in 30 d (RR=0.23, 95%CI: 0.11 to 0.51; *P*=0.0002) and 60 d (RR=0.33, 95%CI: 0.12 to 0.91; *P*=0.03) after treatment.
Conclusion: Fire needle has a favorable effect in increasing the effective rate, relieving pain, recovering skin lesions and decreasing incidence of postherpetic neuralgia in the treatment of herpes zoster. However, considering the limitations in this study, the findings should be interpreted cautiously.

Keywords: Acupuncture Therapy; Fire Needle; Western Medication; Herpes Zoster; Neuralgia, Postherpetic; Randomized Controlled Trial; Meta-analysis; Systematic Review

【摘要】目的：比较火针与西药治疗带状疱疹的临床疗效。**方法：**检索 8 个数据库中关于火针对比西药治疗带状疱疹的随机对照试验，并采用 RevMan 5.3 进行 meta 分析。**结果：**纳入 8 项随机对照试验共 569 人。结果表明，火针治疗带状疱疹的有效率显著优于西药治疗组[RR=1.13, 95%CI(1.06, 1.20); *P*=0.0002]。与西药组比较，火针治疗在降低视觉模拟量表(VAS)评分[MD=–7.95, 95%CI(–10.71, –5.20); *P*<0.00001]，缩短疼痛时间[MD=–7.61, 95%CI(–9.38, –5.84); *P*<0.00001]以及止疱[MD=–1.34, 95%CI(–1.51, –1.18); *P*<0.00001]，结痂[MD=–2.92, 95%CI(–3.62, –2.23); *P*<0.00001]和脱痂时间[MD=–4.64, 95%CI(–5.83, –3.46); *P*<0.00001]方面具有显著优势。另外，火针能够显著降低随访第 30 天[RR=0.23, 95%CI(0.11, 0.51); *P*=0.0002]和第 60 天[RR=0.33, 95%CI(0.12, 0.91); *P*=0.03]带状疱疹后遗神经痛的发病率。**结论：**与西药相比，火针疗法在带状疱疹的有效率、疼痛、皮损以及后遗神经痛方面疗效更加显著。然而，由于本研究存在的局限性，这一结论应谨慎对待。

【关键词】针刺疗法；火针；西药；带状疱疹；神经痛，疱疹后；随机对照试验; Meta 分析；系统评价
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Herpes zoster (HZ) is the result of reactivation of the varicella zoster virus which represents a human neurotropic virus with distinctive capacity to persist in sensory ganglia after primary infection[1-2]. HZ stands for an acquired neurogenic viral infection which is described as drastic pain and aching vesicle on the skin and around the influenced sensory nerve[3]. Nowadays, HZ is becoming an important public health problem as its incidence has upraised over the past several decades, and about 1 million cases suffer from the disease in the USA per year[4]. The skin lesion caused by herpes is often accompanied by persistent or intermittent pain, algesia, dysesthesia or paresthesia, which not only affect the quality of life, but also cause physical disability or emotional disturbance[5-6]. In addition, HZ can lead to postherpetic neuralgia (PHN) and HZ

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ophthalmicus (HZO), even increase the risk of stroke, bringing on a heavy burden to social health care system[7].

Concerning the treatment of this disease, the clinical guideline recommends antiviral therapy for HZ[8]. However, antiviral therapy may lead to many side effects such as gastrointestinal irritation and damage to kidneys[9-10]. Moreover, the most common complication of HZ is PHN, a highly debilitating chronic neuropathic pain, and approximately 20%-30% of the patients affected by HZ may develop PHN[11]. A recent study reported that antiviral therapies were ineffective in reducing the incidence of PHN[12].

Fire needle therapy, a special method of acupuncture, has a long history of being used to treat pain[13], and its efficacy for HZ has also been reported[14]. Fire needle has a different operation method from common acupuncture in needle depth and retention time. After heated, fire needle is used to prick the selected acupoints by depth of 0.3-0.5 cun, and then removed immediately[15]. The synergistic effect of heat and stimulation on acupoints can produce analgesic effect, improve blood circulation, and eliminate blood stasis promptly. Therefore, fire needle is used not only for the acute stage of HZ, but also for PHN[16].

However, no review or meta-analysis articles have been published to compare the effectiveness of fire needle and Western medication for HZ, so it is still unclear whether fire needle is superior in the treatment of HZ. Therefore, we conducted this systematic review and meta-analysis to evaluate the efficacy of fire needle versus Western medication, to help physicians make better treatment strategy for patients with HZ.

1 Methods

1.1 Data retrieval

The following databases were searched to retrieve records from their inception till August 1st, 2018: PubMed, Cochrane Library, Excerpta Medica Database (EMBASE), Chinese Biomedical Literature Database (CBM), Web of Science, China National Knowledge Infrastructure (CNKI), Chongqing VIP Database (CQVIP), and Wanfang Academic Journal Full-text Database (Wanfang). The searching was conducted using medical subject headings (MeSH) and key words. The search strategy included the following group terms in English database: (fire needle OR fire needle treatment) AND (antiviral agents OR antiviral therapy OR acyclovir OR valaciclovir OR famciclovir) AND (herpes zoster OR acute posterior ganglionitis OR zona ignea) AND clinical trial. In Chinese databases, we used the following strategy: (Huo Zhen OR Huo Zhen Liao Fa) AND (Kang Bing Du Yao OR Kang Bing Du Liao Fa OR A Xi Luo Wei OR Fa Xi Luo Wei OR Fan Xi Luo Wei) AND (Dai Zhuang Pao Zhen OR She Chuan Chuang) AND Sui Ji Dui Zhao Shi Yan. Our search language was restricted to English and Chinese. The references in the located literatures were also manually searched for more relevant articles. After finishing the search, two reviewers independently checked the titles and abstracts of the articles to select the potential ones. Then, the full texts of the chosen articles were screened according to the inclusion and exclusion criteria, and the divergence was checked by a third reviewer.

1.2 Inclusion criteria

Randomized controlled trials (RCTs); trials comparing fire needle with Western medication; the included patients were diagnosed with herpes zoster in acute stage (painful rash stage 7-10 d)[17]; trials with complete data.

1.3 Exclusion criteria

Duplicate studies; fire needle or Western medicine was not used as the only intervention.

1.4 Data extraction

Two reviewers independently worked on data extraction and collected the following information: basic characteristics, including author name, study design, participants, interventions, outcomes, and adverse events; outcome measurements, including effective rate, visual analog scale (VAS), time of pain disappearance, time of blister-stop, time of crusted scab, time of scab off, and the incidence of PHN.

1.5 Quality assessment

The Cochrane Risk of Bias Tool was used for quality assessment of the included studies, which was carried out independently by two reviewers, and the disagreements were checked by a third reviewer. Risk of bias included the following items: random sequence generation; allocation concealment; blinding of participants and personnel; blinding of outcome assessment; incomplete outcome data; selective reporting bias; other bias. The judgments were categorized as 'low risk', 'high risk', or 'unclear'.

1.6 Statistical analysis

A meta-analysis was carried out using Review Manager Version 5.3 (The Nordic Cochrane Centre, Copenhagen, Denmark). Continuous variables (VAS, time of blister-stop, crusted scab, scab off, and pain disappearance) were analyzed using the mean difference (MD) with its 95% confidence interval (CI), and the dichotomous data (effective rate and incidence of PHN) were analyzed using the risk ratio (RR) and its 95%CI. The heterogeneity was quantified by calculating the value of I^2, and $I^2 \geq 50\%$ indicated a substantial level of heterogeneity. Fixed effects model was used when there was no significant heterogeneity between trials, otherwise random effects model was employed. Besides, the subgroup analysis and sensitivity analysis were applied when a substantial level of heterogeneity was detected. $P<0.05$ was indicative of significant difference between the fire needle group and Western

medication group.

2 Results

2.1 Identification of the relevant studies

A total of 1 231 articles were identified in our initial search, from which 459 articles were excluded for duplication. In the remaining 772 articles, 52 review articles and 30 case reports were excluded, and 152 were excluded for lacking of a control group and 274 were excluded for irrelevant topics after titles and abstracts were checked. The full texts of the remaining 264 articles were obtained to check eligibility, in which 23 were excluded because Western medication was not the only intervention in the control group and 233 were excluded because fire needle was not the only intervention in the observation group. Finally, 8 trials[18-25] were included in our final analysis. Figure 1 shows the selection process for relevant studies.

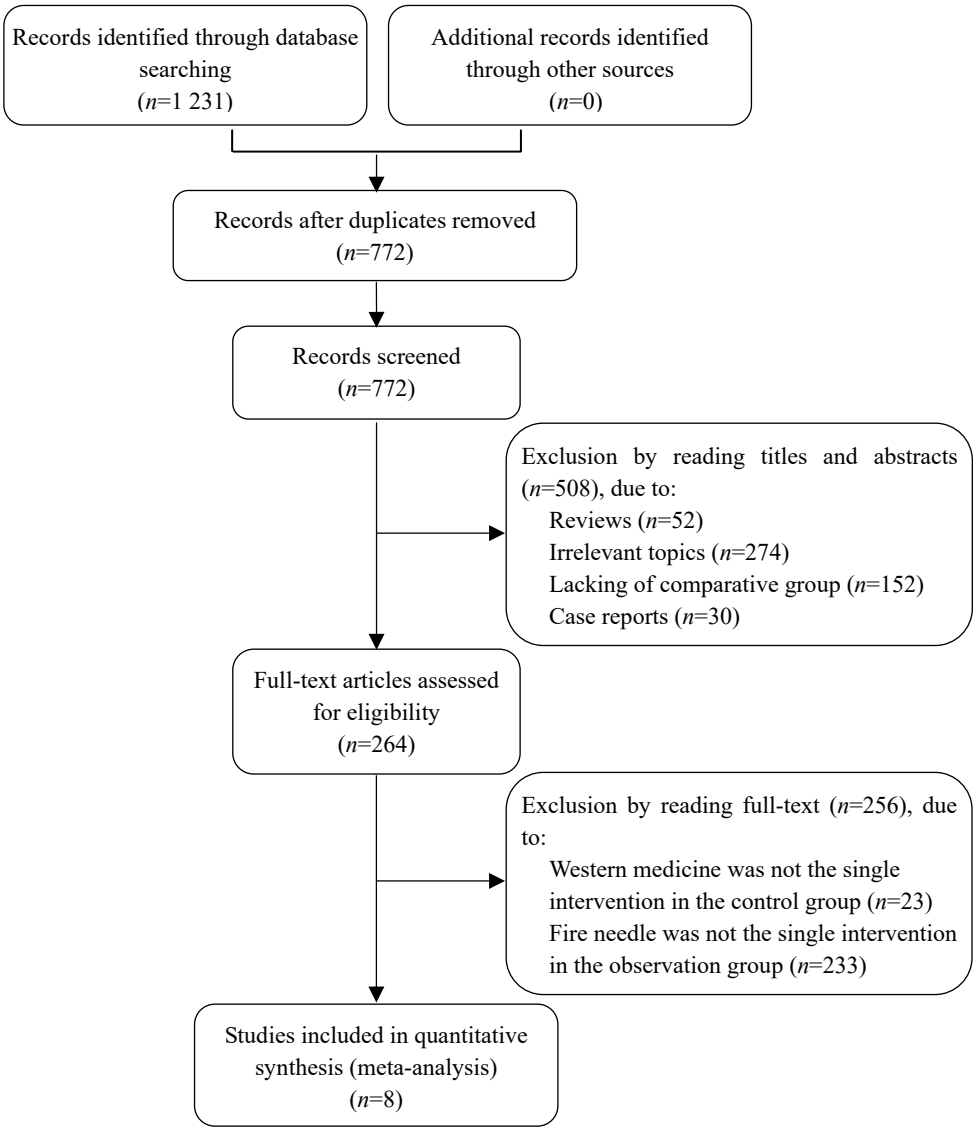

Figure 1. Literature screening and outcome

2.2 Characteristics of the included trials

The 8 trials, which were published in Chinese, involved 569 patients, and the sample size ranged from 44 to 103 cases. All trials[18-25] employed fire needle as the only intervention in the observation group and Western medication as the only intervention in the control group. Different types of fire needles were used, 4 trials[19-20,24-25] employed middle-size needles (diameter: ≥0.8 mm, but <1.1 mm), 1 trial[22] employed large-size needles (diameter: ≥1.1 mm), and 3 trials[18,21,23] did not mention the fire needle type. Regarding the Western medication, 4 trials[19-20,24-25] used valacyclovir plus vitamin B_1; 1 trial[22] used acyclovir plus vitamin B_1; 1 trial[21] used valaciclovir plus

vitamin B_1, mecobalamin and tylox; 1 trial[23] used acyclovir plus vitamin B_1, mecobalamin and loxoprofen sodium; and 1 trial[18] used acyclovir alone. The characteristics of the included studies are presented in Table 1.

Table 1. Characteristics of the included trials

Trial	Study design	Gender (case)		Mean age (year)		Sample size	Interventions		Outcomes
		FNG (M/F)	WMG (M/F)	FNG	WMG	FNG/ WMG	FNG	WMG	
Wang YZ 2014[22]	RCT	49	31	42.5±3.8		40/40	Ashi points, Jiaji (EX-B 2), Zhigou (TE 6), and Houxi (SI 3) on the affected side	Acyclovir, vitamin B_1, and gentamicin (external use)	①③④⑤⑥
Chen X 2014[18]	RCT	24/20	21/23	N/A		44/44	Ashi points	Acyclovir-injection (IV drip); acyclovir ointment (external use)	①
Liu Y 2015[20]	RCT	18/17	20/15	N/A		35/35	Ashi points and Jiaji (EX-B 2)	Valaciclovir; vitamin B_1	①
Yu GH 2016[23]	RCT	12/10	11/11	48.5±1.5	43.5±1.6	22/22	Ashi points and area around the points	Acyclovir powder (IV drip); mecobalamine; vitamin B_1; loxoprofen sodium	①
Qiu CZ 2017[21]	RCT	32/23	30/18	63.7±2.4	63.4±2.9	55/48	Ashi points, the center of the herpes, Jiaji (EX-B 2), Houxi (SI 3) and Zhigou (TE 6)	Valaciclovir; vitamin B_1; tylox; mecobalamine;	①
Zhong ZM 2012[24]	RCT	14/19	10/21	41.97±14.70	47.61±14.25	33/31	Topical points; Jiaji (EX-B 2), Zhigou (TE 6) and bilateral Houxi (SI 3)	Valaciclovir; vitamin B_1	③④⑤⑥⑦
Dong F 2013[25]	RCT	9/21	11/19	50.20±14.54	46.90±16.48	30/30	Ashi points, Jiaji (EX-B 2), Zhigou (TE 6) and Houxi (SI 3)	Valaciclovir; vitamin B_1	②③④⑤⑥⑦
Kong MJ 2012[19]	RCT	7/23	11/19	44.63±15.99	49.07±16.33	30/30	Ashi points, Jiaji (EX-B 2), Zhigou (TE 6) and Houxi (SI 3)	Valaciclovir; vitamin B_1	①②③④⑤⑥⑦

Note: FNG=Fire needle group; WMG=Western medication group; M/F=Male/Female; RCT=Randomized controlled trial; N/A=Not applicable; ①=Effective rate; ②=Visual analog scale; ③=Time of pain disappearance; ④=Time of blister-stop; ⑤=Time of crusted scab; ⑥=Time of scab off; ⑦=Incidence rate of postherpetic neuralgia

2.3 Quality assessment

The patients in the 8 trials were randomly assigned to groups, and 5 trials[18-19,21,24-25] which used random number table were defined as low risk of bias for random sequence generation. The other studies[20,22-23] did not provide sufficient information about random method, and were considered to be unclear risk of bias. None of the included trials mentioned the details of allocation, and were evaluated as unclear risk for allocation concealment. Without mentioning blinding of participants and personnel, all trials were defined as unclear risk of bias for blinding. Two trials[19,24] which reported blinding of outcome assessment were evaluated as low risk of bias for this domain, while the others were considered as unclear risk of bias due to insufficient details. Furthermore, all the included trials reported complete data, and were defined as low risk of bias. Besides, all of the trials did not provide the details of selective reporting outcomes, and thus were evaluated as unclear risk of bias. The results are summarized in Figure 2 and Figure 3.

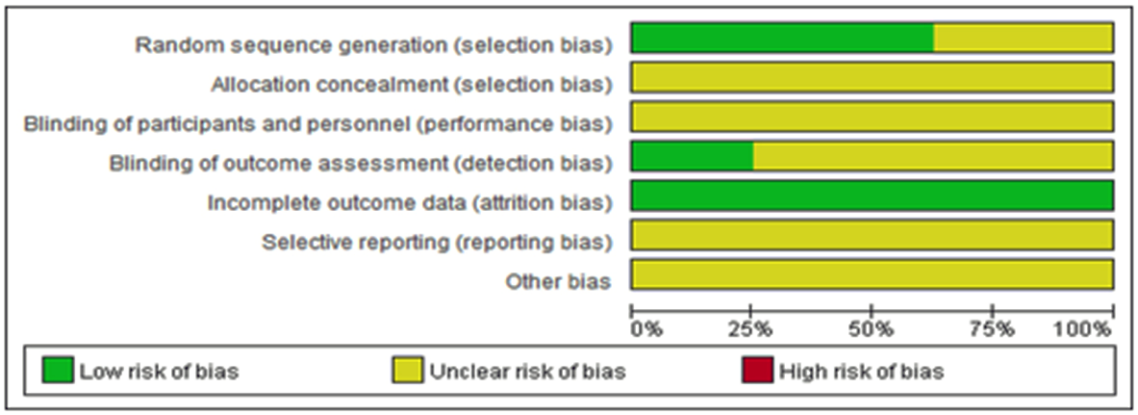

Figure 2. Summary of risk of bias in the included studies

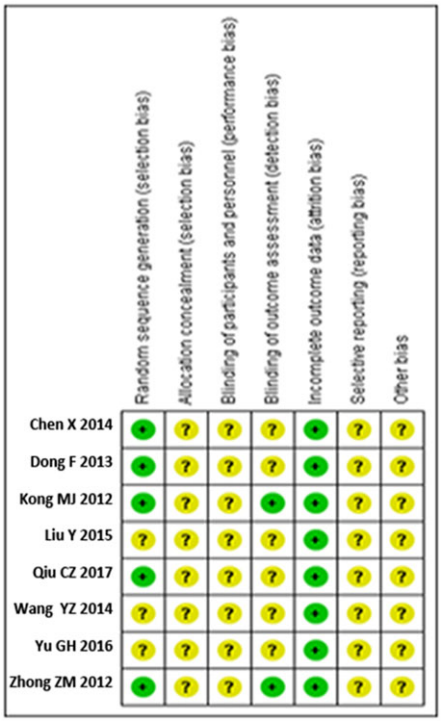

Figure 3. Risk of bias in the included studies

3 Outcome Measures

3.1 Effective rate

Six trials[18-23] reported effective rate. As shown in Figure 4, compared with Western medication, fire needle produced a significantly higher effective rate (RR=1.13, 95%CI: 1.06 to 1.20; *P*=0.0002).

3.2 Measure of pain

3.2.1 VAS

VAS was reported in 2 trials[19,25], which showed a significant difference between fire needle and Western medication (MD=–7.95, 95%CI: –10.71 to –5.20; *P*<0.00001), demonstrating a lower VAS score in the fire needle group (Figure 5).

3.2.2 Time of pain disappearance

Data regarding the time of pain disappearance were available in 4 trials[19,22,24-25]. As shown in Figure 6, the time of pain disappearance was significantly shorter in the fire needle group (MD=–7.61, 95%CI: –9.38 to –5.84; *P*<0.00001).

3.3 Measure of skin lesion

3.3.1 Time of blister-stop

Four trials[19,22,24-25] reported the time of blister-stop. As shown in Figure 7, the time of blister-stop in the fire needle group was significantly shorter than that in Western medication group (MD=–1.34, 95%CI: –1.51 to –1.18; *P*<0.00001).

3.3.2 Time of crusted scab

In terms of the time of crusted scab, the data of 4 trials[19,22,24-25] were merged for analysis, which showed the time was significantly shorter in the fire needle group (MD=–2.92, 95%CI: –3.62 to –2.23; *P*<0.00001), (Figure 8).

3.3.3 Time of scab off

Four trials[19,22,24-25] reported the time of scab off. A significant difference was found between the fire needle group and the Western medication group (MD=–4.64, 95%CI: –5.83 to –3.46; *P*<0.00001), and the fire needle group presented a shorter time of scab off (Figure 9).

3.4 Incidence of PHN

Three trials[19,24-25] reported the incidence of PHN 30 d, 60 d and 90 d respectively after treatment. A significantly lower incidence of PHN was found in the fire needle group 30 d (RR=0.23, 95%CI: 0.11 to 0.51; *P*=0.0002) and 60 d (RR=0.33, 95%CI: 0.12 to 0.91; *P*=0.03) after treatment, but no significant difference was found between the two groups 90 d after treatment (RR=0.29, 95%CI: 0.07 to 1.15; *P*=0.08), (Figure 10).

3.5 Adverse events

As for adverse events, 4 trials[20-23] did not mention the adverse events and 4 trials[18,19,24-25] reported no adverse events.

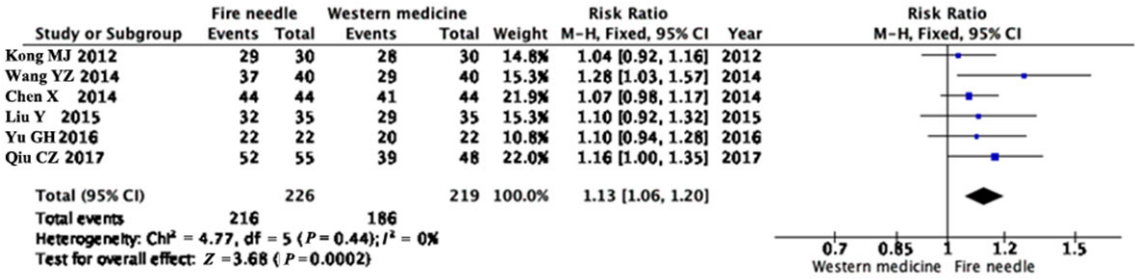

Figure 4. Comparison between the fire needle group and the Western medication group in effective rate

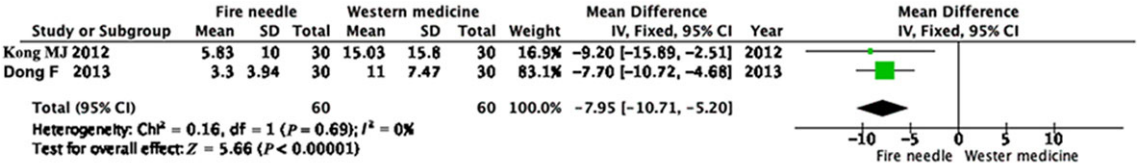

Figure 5. Comparison between the fire needle group and the Western medication group in VAS

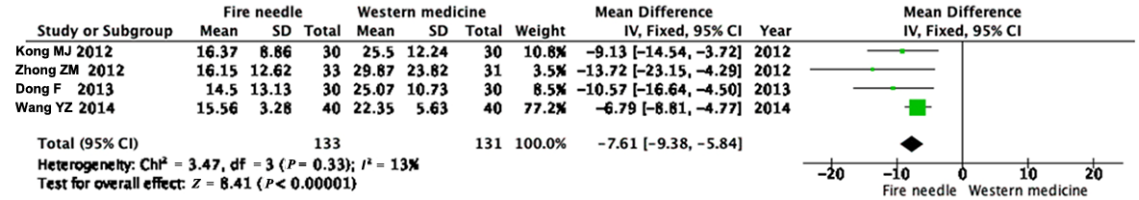

Figure 6. Comparison between the fire needle group and the Western medication group in the time of pain disappearance

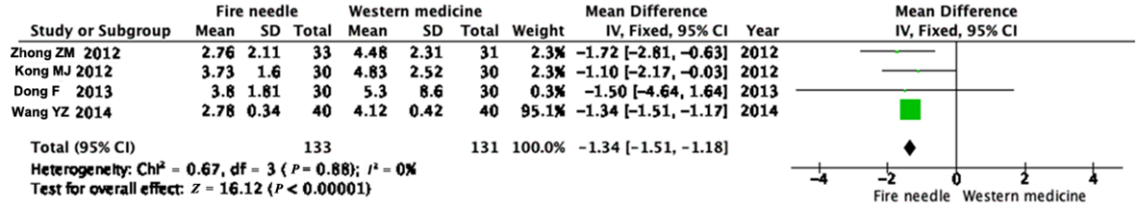

Figure 7. Comparison between the fire needle group and the Western medication group in time of blister stop

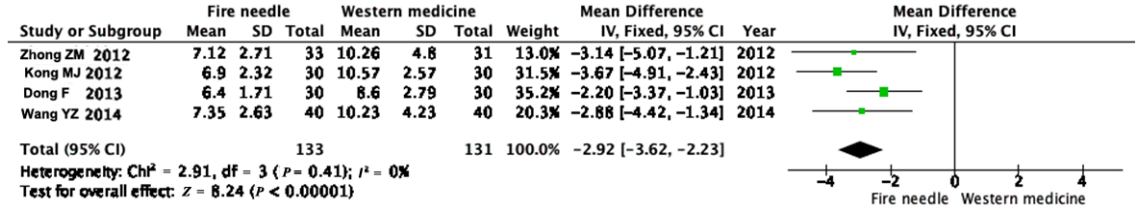

Figure 8. Comparison between the fire needle group and the Western medication group in time of crusted scab

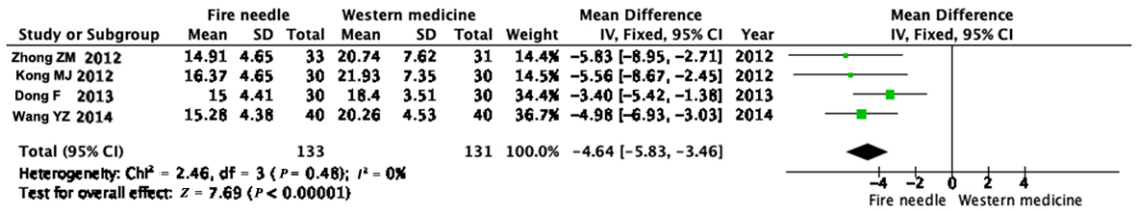

Figure 9. Comparison between the fire needle group and the Western medication group in time of scab off

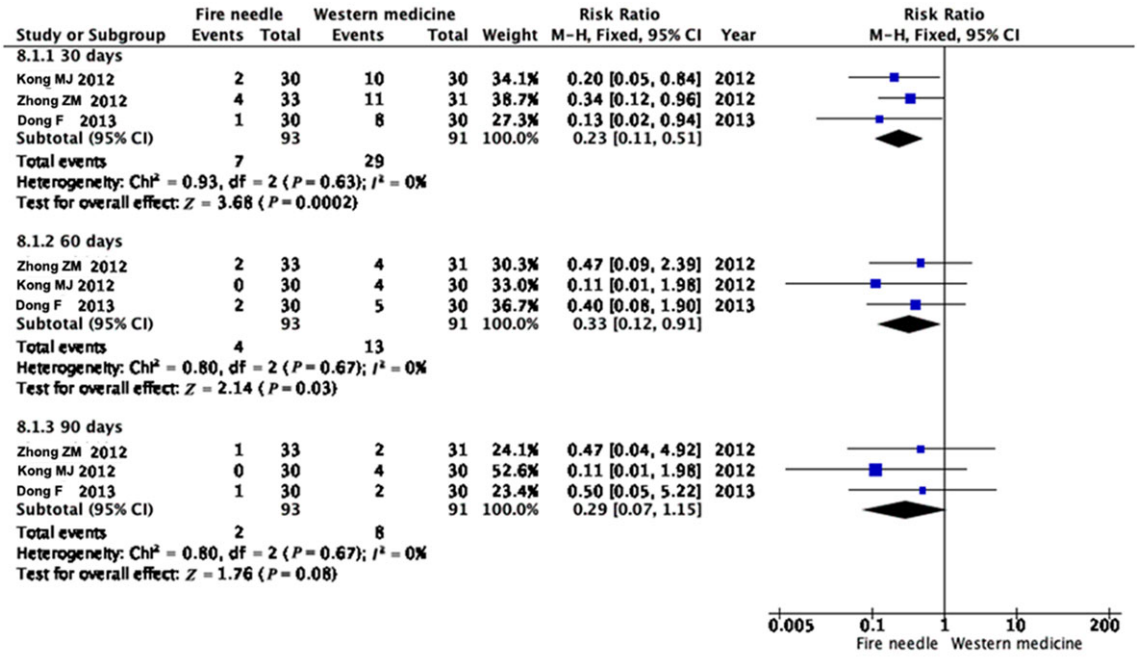

Figure 10. Comparison between the fire needle group and the Western medication group in the incidence of postherpetic neuralgia

4 Discussion

This review first evaluated the efficacy of fire needle versus Western medication in the treatment of HZ. Since we only included trials that used fire needle or Western medication as the only intervention, different outcomes were assessed, and the heterogeneity of the included trials was low, so we believe that the review may facilitate physicians to better understand the efficacy of fire needle in treating HZ. Besides, we conducted this research on the basis of comprehensive search of English and Chinese databases, which consolidated the credibility of our results.

In the eight included trials, four reported the comparison of analgesic effect between fire needle and Western medication including acyclovir or valaciclovir plus vitamin B_1, and fire needle showed a favorable effect in VAS score and time of pain disappearance. These drugs do not have analgesic effect, but they can act on pain indirectly by antivirus and improving the nerve function, and they work slowly. By contrast, fire needle can inhibit the discharge of nerve and promote the content of neurotransmitters such as substance P (SP), endorphins, opioid peptide and encephalin[26-27], and integrate the stimulus information and regulate the function of pain network in the central nervous system[28]. In addition, the high temperature of fire needle can cause necrosis of cells and proteins in local lesions, activate the function of macrophages and reduce local inflammatory reaction[26]. Subsequently, fire needle showed a better analgesic effect.

Moreover, this review evaluated the time of blister-stop, crusted scab and scab off between fire needle and acyclovir or valaciclovir plus vitamin B_1, demonstrating that fire needle can promote the healing of skin lesions. The high skin temperature caused by fire needle can accelerate local blood circulation, promote the metabolism and repair of cells[28-29]. Meanwhile, fire needle can enhance human immune function by regulating the endocrine system and cytokines, then accelerate the regeneration of tissues and repair of skin lesions[28-29]. These factors may be the explanation for the better effect of fire needle in accelerating the healing of skin lesions.

Clinically, patients with HZ have a high rate of PHN[30]. The persistent pain stimulates central nervous system, leading to central sensitization, and subsequently produce PHN[31]. Fire needle can prohibit the transportation of neurotransmitters and reduce the inflammation, and then facilitate to decrease the occurrence of PHN[26-27]. Besides, a previous study showed that patients with PHN had a higher cytokine level[32], which was closely associated with the occurrence of PHN[33]. The level of interleukin (IL)-6 can be used as an index to evaluate the treatment of PHN[34], while fire needle can down-regulate it[35]. On the contrary, a meta-analysis revealed that antiviral therapy could not reduce the incidence of PHN[36]. In our meta-analysis, the results demonstrated that fire-needle significantly reduced the incidence of PHN 30 d and 60 d after treatment, compared with Western medication. At 90 d after treatment, the incidence of PHN was lower in the fire needle group, but no significant difference was found between the two

groups, which may be attributed to the small sample size of the included trials.

In clinic, antiviral drugs have been widely used to treat HZ with many known side effects. According to our research, fire needle was superior to Western medication in most outcomes for HZ. In addition, fire needle has advantages of lower medical cost, easier operation and no obvious complications. Consequently, we suggest fire needle to be used as a regular treatment for HZ.

However, this review has several limitations. First, the methodological quality of the included trials was low, as no trial mentioned allocation concealment and blinding method. Second, the sample size of the included trials was small. Third, the risk of publication bias could not be excluded, as all the trials were published in China. Fourth, effective rate was used as outcome measurement in six trials, but it is not recognized internationally. In addition, two trials that used loxoprofen sodium or tylox in the Western medication group did not compare the analgesic effect, so the differences in analgesic effect between fire needle and these two analgesics are still unclear.

5 Conclusion

In brief, our meta-analysis shows that compared with Western medication, fire needle has a favorable effect in increasing effective rate, relieving pain, recovering skin lesions and decreasing incidence of postherpetic neuralgia in the treatment of HZ. However, considering the limitations of our study, the findings should be interpreted cautiously. In the future, more rigorously designed trials with higher quality and larger sample size should be carried out to provide a stronger evidence for the effectiveness of fire needle for HZ.

Conflict of Interest

The authors declared that there was no potential conflict of interest in this article.

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