


Efficacy of electroacupuncture on clinical signs and immunological factors in herpes zoster

The first systematic review, meta-analysis, and trial sequential analysis of randomized clinical trials

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Abstract

Background: Electroacupuncture (EA) is utilized to address various health conditions. Herein, we designed a systematic review and meta-analysis to evaluate the efficacy of EA on clinical and immunological factors in herpes zoster (HZ) based on randomized clinical trials.

Methods: Four international databases and 3 Chinese databases were searched until January 2024. We used RevMan 5.3 for meta-analysis and presented the data as standardized mean difference (SMD) or odds ratio (OR) and 95% confidence interval.

Results: A total of 1361 records were identified in the databases and at last, 19 articles were entered into the meta-analysis. The result shows a negative pooled SMD of -2.55 ($P < .00001$) for the VAS score. The pooled SMD for cessation of pustules time in the case group compared to the control group was -0.69 ($P = .0008$), for pain relief time was -1.36 ($P = .002$), for the time to scab was -0.47 ($P = .009$), and for time to remove scab was -1.01 ($P = .0003$). The pooled OR for the incidence of postherpetic neuralgia was 0.11 ($P < .00001$), and the total effective rate was 4.25 ($P < .00001$). The pooled SMD for the cluster of differentiation (CD)3 count was 2.59 ($P = .07$), for the CD4 count was 2.81 ($P = .04$), for the CD8 count was -0.75 ($P = .50$), and for the CD4/CD8 ratio was 1.12 ($P = .15$).

Conclusions: The results indicate that the EA treatment had several significant benefits compared to Western medicine (WM) in HZ patients in terms of clinical and immunological factors. But, the combination of treatments of EA with WM had better effects compared to EA treatment alone.

Abbreviations: CI = confidence interval, CD = cluster of differentiation, EA = electroacupuncture, HZ = herpes zoster, OR = odds ratio, PHN = postherpetic neuralgia, RCT = randomized controlled trial, RT = routine treatment, EA = electroacupuncture, HZ = herpes zoster, OR = odds ratio, PHN = postherpetic neuralgia, RCT = randomized controlled trial, SMD = standardized mean difference, TCM = traditional Chinese medicine, VAS = visual analog scale, WM = Western medicine.

Keywords: electroacupuncture, herpes zoster, meta-analysis, shingle, western medicine

1. Introduction

Herpes zoster (HZ), a medical condition instigated by the varicella-zoster virus, is widespread among all age groups, but it is most frequently detected in middle-aged and elderly people.^[1,2] The disease typically exhibits unique neuralgia, redness, and blisters that align with the path of single-sided peripheral nerves. The lifetime probability of contracting HZ is projected to be approximately 20% to 30%.^[3–5] Over a third of patients

endure continuous pain for more than a year.^[6] HZ and its subsequent complications can considerably affect a patient's quality of life, leading to a significant disease burden.^[7] Studies suggest that individuals with weakened immune systems or those receiving immunosuppressive therapy have a substantially higher occurrence of HZ compared to those with normal immune function.^[8,9]

If a patient with HZ does not get treatment promptly, they may suffer ongoing damage, leading to post-neuralgia and

QZ and MJ contributed to this article equally.

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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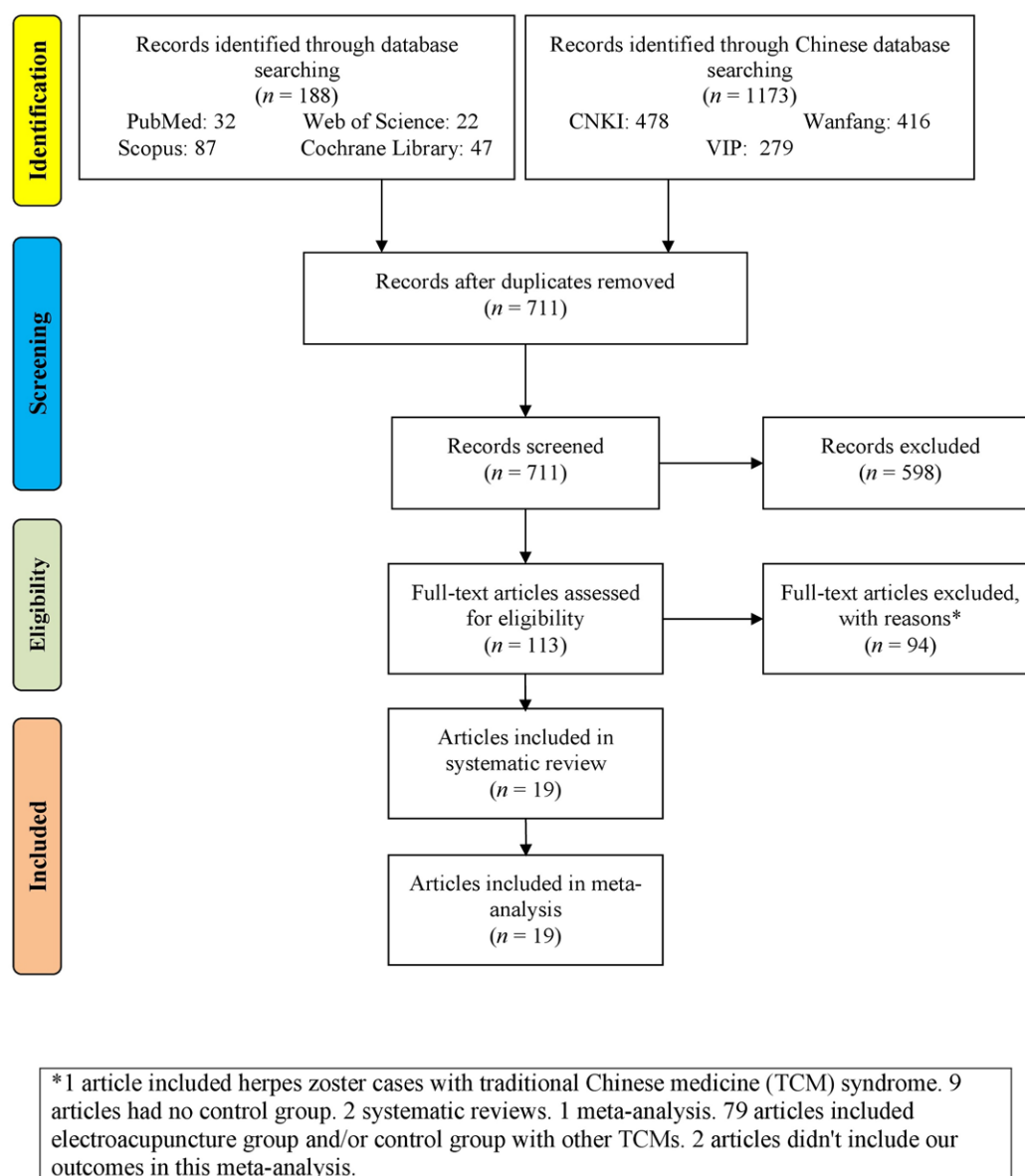


Figure 1. Flowchart of the study selection.

intense inflammation.^[10] Presently, Western Medicine (WM) mainly employs antiviral and pain-relieving medications to ease acute rashes and pain and to avert certain complications.^[10] Acyclovir and ibuprofen are frequently used treatments that can be effective, but they may also have specific side effects. Traditional Chinese medicine (TCM) is becoming increasingly popular due to its notable clinical impacts.^[7,11] Electroacupuncture (EA), a common pain management method in TCM hospitals, has demonstrated superior therapeutic effects on both acute and chronic pain.^[12–14] Recent studies suggest that EA can relieve pain by activating various bioactive chemicals through peripheral and central mechanisms, thereby bypassing the adverse effects of potentially harmful pharmaceuticals.^[15]

T cells hold a crucial function in the immune system.^[16] There are several types of T cells, such as cluster of differentiation (CD)4 + T cells, CD8 + T cells, and CD3 + T cells.^[17] It has been observed that the burden of HZ increases as the patient's immunity diminishes.^[18]

A meta-analysis has suggested that EA might offer benefits in managing acute pain in patients suffering from herpetic

neuralgia, although these conclusions are constrained by small sample sizes, a variety of study designs, and inconsistent methodological quality.^[19] A systematic review has proposed that the efficacy of EA at Jiaji points, when used in conjunction with other treatments, could potentially exceed that of WM alone in treating HZ.^[20] However, the evidence backing this assertion is of inferior quality. Therefore, there is a demand for more extensive, meticulously designed randomized controlled trials (RCTs).^[20] In light of this, we have structured the first systematic review and meta-analysis to assess the effectiveness of EA on both clinical symptoms and immunological factors (e.g. CDs) in HZ based on RCTs, incorporating a greater number of randomized trials and performing subgroup and meta-regression analyses to determine the factors that influence the outcomes.

2. Materials and methods

This systematic review and meta-analysis followed the preferred reporting items for systematic reviews and meta-analyses (PRISMA) Statement 2020 guidelines.^[21] The protocol was not registered.

Table 1 Characteristics of the studies.						
The study, publication yr	No. of case/control	Case intervention	Control intervention	Outcomes	Mean age ± SD of case/control, yr	Male: female in case/control EA features
Aizhen, 2012a ^[30]	50/50	EA + RT	RT: Famciclovir 0.25 g, orally administered once every 8 h; Methylcobalamin 0.5 mg, take orally 3 times a day; Vitamin B110mg, take orally 3 times a day; Acyclovir ointment, apply to the affected area 5 times a day.	Cessation of pustules time the time to scab time to remove scab pain relief time	52.24 ± 5.56/52.58 ± 5.80	Injection point: Fengchi, Taiyang, Cuanzhu, Xiaguan, Hegu, Wai Guan, Jiaji or Beishu, back shu, Yanglingquan, Zusanli, Sanyinjiao Treatment duration: 7 days
Aizhen, 2012b ^[31]	50/50	EA + RT	RT: Famciclovir 0.25 g, orally administered once every 8 h; Methylcobalamin 0.5 mg, One taken orally 3 times a day; Vitamin B110 mg, taken orally 3 times a day; Acyclovir ointment, apply to the affected area 5 times a day.	CDs	56.5 ± 4.23/58 ± 4.46	Injection point: Fengchi, Taiyang, Cuanzhu, Xiaguan, Gu, Waiguan, Jiaji, back Yu, Zhigou, Yanglingquan, Tachong, and Sanyinjiao Treatment duration: 7 days
Bin, 2023 ^[32]	40/40	EA + RT	RT: Acyclovir and ibuprofen, A Xi Lowe (Manufacturer: Chifeng Mengxin Pharmaceutical Co., Ltd.; Snopharm H1993894), 0.2 g/time, 5 times/d, 10 d as 1 treatment Procedure. Ibuprofen (Manufacturer: Xiu Xiu pharmaceutical group Changchun high-tech pharmaceutical Co., Ltd.; National Drug approval number H22022803), 0.2 g/time, 2 times a day	VAS score total effective rate	60.50 ± 3.25/61.50 ± 3.87	Injection point: Jiaji Treatment duration: 7 days
Cheng, 2018 ^[33]	25/29	EA + RT	RT: Valaciclovir, 0.3 g, orally twice daily for 10 d; methylcobalamin, 0.5 mg, orally 3 times for 10 d; If the pain were severe, oxycodone (10 mg) would be used	VAS score incidence of PHN	51.40 ± 3.12/61.1 ± 2.13	Injection point: Jiaji and Ashi Frequency: 2 Hz Treatment duration: 10 d Injection point: Ashi, Jiaji, Zhigou, and Houxi Frequency: 2/100 Hz Treatment duration: 10 d Injection point: Jiaji, Ashi, Zhigou, and Houxi Frequency: 2/100 Hz Treatment duration: 10 d
Guohua, 2011 ^[34]	30/32	EA	RT: Valacyclovir hydrochloride Livzon Vitamin B1 taken orally, 300 mg/time, 2 times/d; Vitamin B1 taken orally, 10 mg/time, 3 times/d. Topical skin treatment for herpes: keep the skin clean and protect skin damage. Course of treatment: a total of 1 course of treatment.	Cessation of pustules time the time to scab time to remove scab	Range: 18 to 70	NA
Hong, 2018 ^[35]	40/40	EA	RT: Valacyclovir hydrochloride, 300 mg, 2 times/d; vitamins B1, 10 mg, 3 times/d; taken orally.	total effective rate	38.10 ± 5.65/ 37.49 ± 5.72	24:16/23:17
Jianmin, 2002 ^[36]	63/53	EA + RT	RT: Oral acyclovir tablets 0.2/time each time, 5 times a day, indomethacin tablets 25 mg/time 3 times a day.	cessation of pustules time the time to scab time to remove scab pain relief time	42 ± 12.01/40.5 ± 11.26	40:23/34:19
Jun, 2019 ^[37]	58/57	EA	RT: valacyclovir hydrochloride tablets (chengdu times produced by Te Pharmaceutical Co., Ltd., approval number: National Drug approval number H20066855) Oral, 2 times a day, 0.3 g each time; Methylcobalamin tablets (Microbao, manufactured by Eisai China Pharmaceutical Co., Ltd., batch number: 20,143,107, 0.5 mg × 20 tablets) Oral, 3 times a day, each time 0.5 mg.	VAS score pain relief time cessation of pustules time the time to scab time to remove scab total effective rate	49.11 ± 13.77/47.71 ± 13.82	27:31/25:32 Injection point: Jiaji, Ashi, Zhigou, and Yanglingquan frequency: 120 Hz treatment duration: 14 d

(Continued)

Table 1
(Continued)

The study, publication yr	No. of case/control	Case intervention	Control intervention	Outcomes	Mean age \pm SD of case/control, yr	Male: female in case/control	EA features
Li, 2009 ^[39]	40/40	EA	RT: oral administration of valacyclovir hydrochloride 300 mg/time 2 per day times; Vitamin B1 is taken orally 10 mg/time 3 times a day.	VAS score total effective rate	46.36 \pm 10.21/44.79 \pm 9.43	15:25/19:21	Injection point: Jiaji and Ashi Frequency: 2/100 Hz treatment duration: 10 d
Li, 2011 ^[38]	27/31	EA + RT	RT: valacyclovir hydrochloride (trade name, Livzonvir), 6 tablets per box, 0.3 g per tablet, manufacturer: Livzon Pharmaceutical Co., Ltd., batch number: H10960079L, 0.3 g each time, 2 times a day. Oral administration of vitamin B1, 10 mg each time, 3 times a day.	VAS score cessation of pustules time the time to scab time to remove scab incidence of PHN	48.39 \pm 17.06/49.61 \pm 16.34	16:11/24:7	Injection point: Ashi, Zhigou, and Houxi Frequency: 2/100 Hz Treatment duration: 10 days
Lin, 2015 ^[40]	27/27	EA + RT	RT: Valacyclovir hydrochloride (trade name, Livzonvir, specifications. 6 tablets per box, 0.3 g per tablet, manufacturer: Livzon Pharmaceutical Co., Ltd.; batch number: H10960079L, 0.3 g each time, 2 times a day, oral administration of vitamin B1, 10 mg each time, 3 times a day	VAS score	Range: 18 to 80	14:13/13:14	Frequency: 2 Hz treatment duration: 7 days
Rong, 2017 ^[41]	13/12	EA + RT	RT: diclofenac sodium sustained-release tablets (75 mg, daily 1 time), methylcobalamin tablets (0.5 mg, 3 times a day), valacyclovir hydrochloride tablets (0.25 g, 3 times a day), apply 3% boric acid solution externally to the red and swollen parts of the skin	VAS score cessation of pustules time the time to scab time to remove scab	47.28 \pm 10.41/47.14 \pm 10.34	6:7/5:7	Injection point: Jiaji frequency: 60 Hz Treatment duration: 10 d
Shiqing, 2019 ^[42]	44/44	EA + RT	RT: Extensive Aciclovir tablets (National Drug Approval No. H20083370) are taken orally, 0.25 g each time, Once every 8 h; Methylcobalamin tablets (National Drug approval number H20143107) Take orally, 0.5 mg each time, 3 times a day; vitamin B1 tablets (approved by the state of the art no. H42020611) Orally, 10 mg each time, 3 times a day; Acyclovir Cream (National Drug approval no. H1999049) is applied topically, once a day.	VAS score total effective rate CDs	60.25 \pm 5.14/ 60.83 \pm 5.24	26:18/27:17	Injection point: Jiaji Frequency: 5/100 Hz Treatment duration: 7 days
Shuying, 2015 ^[43]	30/30	EA	RT: Oral valacyclovir hydrochloride (Lizhuvin): 300 mg·time-1, 2 times/d-1; Vitamin B1: Orally: 10 mg, 3 times/d	VAS score total effective rate	42.32 \pm 7.62/42.32 \pm 7.62	14:16/13:17	Injection point: Jiaji and Ashi
Song, 2009 ^[44]	30/30	EA	RT: Valacyclovir, 300 mg, orally 3 times daily for ten days; vitamin B1, 10 mg, orally 3 times daily for 10 d	VAS score cessation of pustules time the time to scab time to remove scab incidence of PHN	42.23 \pm 14.98/43.47 \pm 13.57	16:14/15:15	Injection point: Jiaji, Zhigou, and Houxi Frequency: 2/100 Hz Treatment duration: 10 d
Xiangpeng, 2019 ^[45]	45/45	EA + RT	RT: Valacyclovir hydrochloride tablets (Li Kefen 0.3 g \times 6 tablets/box) 1 tablet each time, take it twice a d for a total of 7 d; Adenosylcobalamin (produced by North China Pharmaceutical Co., Ltd. 0.25 mg \times 100 tablets/bottle) 2 tablets each time, 3 times a d. for a total of 2 wk; Preba Lin (Lyric 75 mg \times 10 capsules/box), 2 tablets each time, 2 times a day	VAS score	57.89 \pm 8.22/56.53 \pm 9.15	20:25/22:23	Injection point: Jiaji and local points of rash Frequency: 2 Hz Treatment duration: 14 d
Xin, 2016 ^[46]	40/40	EA + RT	RT: Valacyclovir hydrochloride 300mg orally before meals 2 times/d, Vitamiv B1 10mg 3 times/d	incidence of PHN total effective rate	45.4 \pm 15/46.03 \pm 15.50	21:19/23:17	Frequency: 220 Hz Treatment duration: 10 d
Zhixiang, 2017 ^[47]	36/36	EA	RT: Valacyclovir hydrochloride tablets (trade name: Lizhuwei) 0.3 g each time, 2 times a day; Vitamin B1 Tablets, 10 mg each time, 3 times a day.	VAS score pain relief time cessation of pustules time the time to scab time to remove scab CDs	Range: 50 to 70	16:20/17:19	Injection point: Ashi Frequency: 2/100 Hz
Zhou, 2015 ^[48]	23/23	EA	RT: Oral acyclovir tablets (Jiangsu Pingguang Pharmaceutical Co., Ltd., national drug approval number H20059233) 0.3 g, 3 times/d, Methylcobalamin Capsules (Yangzijiang Pharmaceutical Group Nanjing Hailing Pharmaceutical Co., Ltd. Production, national drug approval number H20052315) 0.5 mg 3 times/d; Kumasi Ping (produced by Qiliu Pharmaceutical Co., Ltd., national drug approval number H37021328) 0.1 g, 1 time/d.		54.04 \pm 10.87/50.09 \pm 12.92	11:12/13:10	Injection point: Jiaji Treatment duration: 10 d

CD = cluster of differentiation, EA = electroacupuncture, NA = not available, PHN = postherpetic neuralgia, RT = routine treatment, VAS = visual analogue scale.

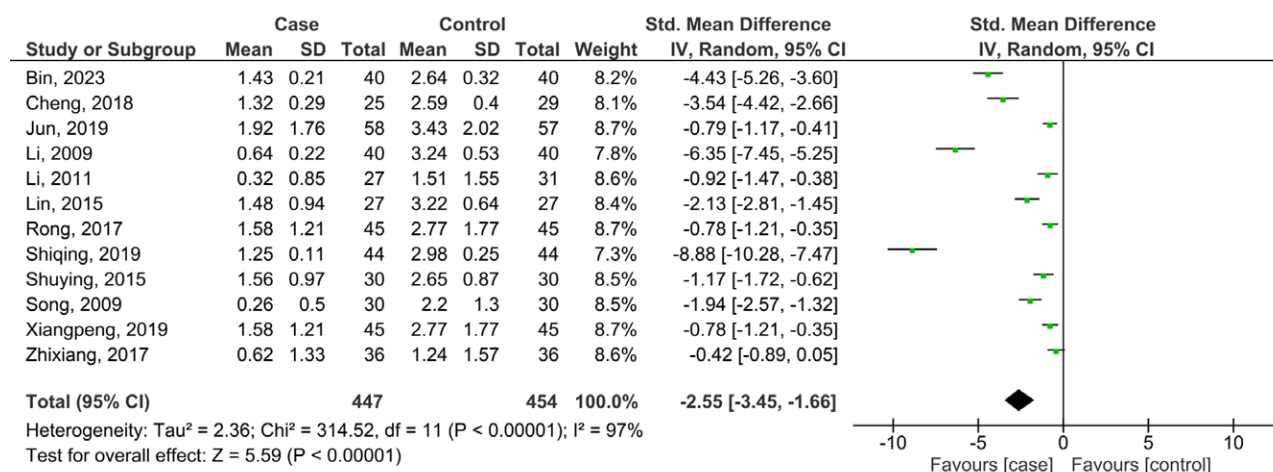


Figure 2. Forest plot of VAS score. Standardized mean differences of VAS score in the case group compared with the control group. VAS = visual analog scale.

2.1. Literature search

Four electronic databases (PubMed, Web of Science, Scopus, and Cochrane Library) and 3 Chinese databases (CNKI, VIP, and Wanfang) were searched through January 26, 2024, without any restrictions. The search terms were (“electroacupuncture” or “electro-acupuncture”) and (“HZ” or “zoster” or “shingles” or “varicella-zoster virus” or “postherpetic neuralgia” or “postherpetic neuralgia” or “PHN”). We also went through the references of eligible studies and manually reviewed articles to identify possible relevant publications, as well as through electronic sources such as Google Scholar. The ethical approval was not required as this study involved the data from previously published studies.

2.2. Study selection

The PICOS framework was utilized as the inclusion criteria for this study. The population (P) consisted of adult participants over 18 years old who were diagnosed with HZ. All patients were in the acute phase of the disease (<2 weeks) and had not received any treatment. The intervention (I) was the application of EA. The comparison (C) involved a case group receiving EA or EA combined with routine treatment (RT), compared to a control group receiving RT and/or sham EA. The outcome (O) measures included the visual analog scale (VAS) score, cessation of pustules time, time to scab, time to remove scab, time to pain relief, the incidence of postherpetic neuralgia (PHN), and the total effective rate. The study design (S) was RCT. The RT for HZ in this meta-analysis typically involved the use of antiviral medications or other forms of WM.

The criteria for inclusion encompass all RCTs that have an HZ group as a case group receiving EA or EA combined with RT, and a control group receiving RT. The criteria for exclusion consist of studies that involve participants with a history or diagnosis of any systemic diseases that overlap with HZ, HZ cases that are undergoing therapies other than WM, case reports or articles that lack statistical data, and articles without a control group. Other types of documents excluded are reviews, meta-analyses, letters to the editors, book chapters, and articles devoid of any data.

2.3. Data extraction

Two authors independently conducted a review of the literature and data extraction to maintain consistency in the screening core criteria and data collection process. In cases where there were differing opinions, further discussions were held, or an

additional individual was invited to join the discussions until a consensus was achieved. The analyses were independently carried out by 2 authors, with all decisions being agreed upon unanimously.

2.4. Statistical analysis and data synthesis

We used Review Manager, version 5.3 for meta-analysis and presented the data as standardized mean difference (SMD) or odds ratio (OR) and 95% confidence interval (CI) to evaluate the relationships between the levels and incidence of outcomes and HZ, respectively. To report mean \pm standard deviation on the graphs, we utilized GetData Graph Digitizer software version 2.26.0.20.^[22]

The studies' heterogeneity was evaluated using the I^2 statistic, with the significance level set at $P < .05$. Considering the likely heterogeneity of the studies, a random-effects model or a fixed-effect model based on I^2 cutoff was utilized.^[23] The presence of publication bias was assessed using a funnel plot and Begg and Egger tests, with the significance level set at $P < .10$.^[24] The comprehensive meta-analysis version 3.0 (CMA 3.0) software was employed to conduct bias analyses, meta-regression, and sensitivity analyses.

The “risk-of-bias tool” recommended by the Cochrane Handbook for Systematic Reviews of Intervention was used to assess the methodological quality of the included studies. This 2-part tool concentrates on 6 distinct areas.^[25] Each area includes 1 or more specific entries. The second part of the tool involves making a judgment about the risk of bias for that entry.^[26,27]

A trial sequential analysis (TSA) was performed using TSA software (version 0.9.5.10 beta).^[28] The necessary information size (RIS) for was determined with an alpha risk of 5% and a beta risk of 20%. More information is located in the articles of Golshah et al.^[24,29]

3. Results

3.1. Study selection

The flowchart (Fig. 1) indicates that 188 records were identified from various databases, including PubMed, Web of Science, Cochrane Library, and Scopus. Additionally, 1173 records were identified through Chinese databases (CNKI, VIP, and Wanfang). After removing duplicates, 711 records were remaining. These records were screened for relevance. In this stage, full-text articles (113 in total) were assessed for eligibility. Out of these, 94 articles were excluded for various reasons. Finally, 19 RCTs^[30–48] were included in both the systematic review and meta-analysis.

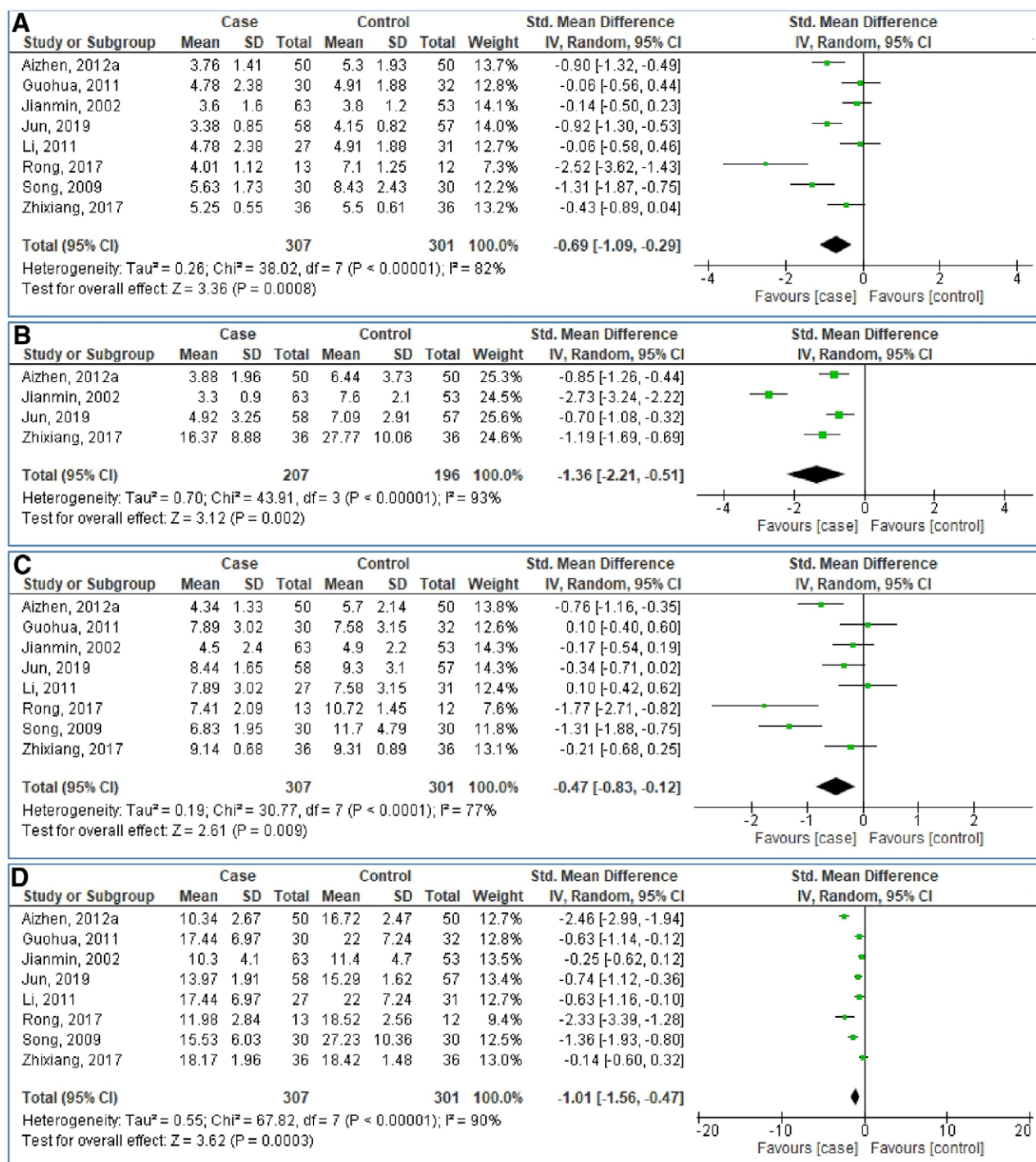


Figure 3. Forest plot of standardized mean differences of 4 variables in the case group compared with the control group. (A) cessation of pustules time. (B) pain relief time. (C) the time to scab. (D) time to remove scab.

3.2. Characteristics of studies

Table 1 provides a summary of various studies on the effects of EA in HZ patients compared to the control group. The studies were conducted between 2002 and 2023. The number of cases and controls in each study ranged from 12 to 63 cases. The interventions used in the case group were either EA alone or a combination of EA and RT. The control groups primarily received RT. The outcomes measured varied across studies and included variables such as VAS scores, cessation of pustules time, time to scab, time to remove scab, pain relief time, total

effective rate, and incidence of PHN. The mean age of participants ranged from around 38 to 61 years. The gender distribution varied across studies. The EA features, including injection points and treatment duration, also varied across studies.

3.3. Pooled analyses

Figure 2 shows a statistical summary of twelve studies for VAS scores in the case group compared with the control group. The result shows a negative SMD of -2.55 with a 95% CI of

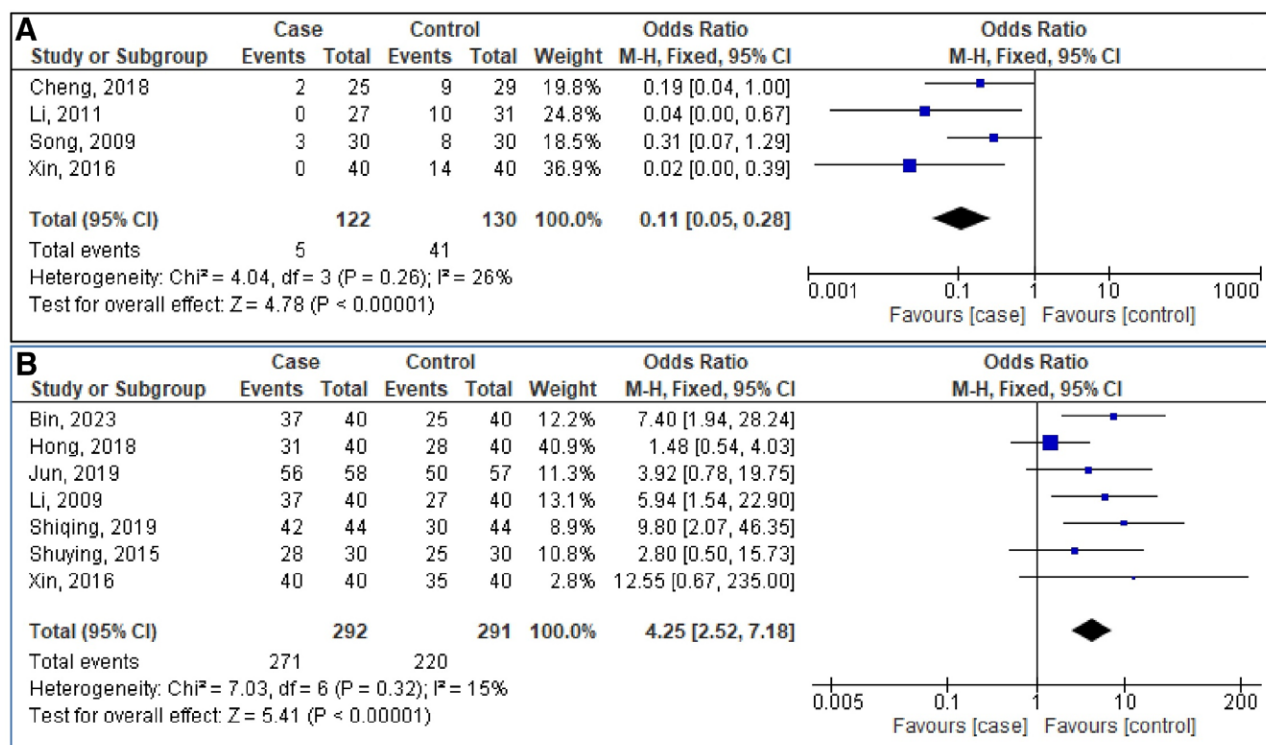


Figure 4. Forest plot of odds ratios of 2 variables in the case group compared with the control group. (A) incidence of postherpetic neuralgia. (B) total effective rate.

(−3.45 to −1.66) and $I^2 = 97\%$. Therefore, the case group had significantly a lower VAS score compared to the control group ($P < .00001$).

Figure 3 shows the forest plots of SMDs of 4 variables in the case group compared with the control group. The pooled SMD for cessation of pustules time was −0.69 (95% CI: −1.09 to −0.29; $P = .0008$; $I^2 = 82\%$), for pain relief time was −1.36 (95% CI: −2.21 to −0.51; $P = .002$; $I^2 = 82\%$), for the time to scab was −0.47 (95% CI: −0.87 to −0.12; $P = .009$; $I^2 = 77\%$), and for time to remove scab was −1.01 (95% CI: −1.56 to −0.47; $P = .0003$; $I^2 = 90\%$). The results indicate that the case group had a shorter cessation of pustules time compared to the control group, the case group had a pain relief time compared to the control group, the case group had a shorter time to scab on average compared to the control group, and the case group had a shorter time to remove scab on average compared to the control group.

Figure 4 shows the forest plots of ORs of 2 variables in the case group compared with the control group. The pooled OR for the incidence of PHN was 0.11 (95% CI: 0.05–0.28; $P < .00001$; $I^2 = 26\%$), and for the total effective rate was 4.25 (95% CI: 2.52–7.18; $P < .00001$; $I^2 = 15\%$). The results showed that the case group had a lower incidence of PHN compared to the control group and the case group had a higher total effective rate compared to the control group.

Figure 5 shows the forest plot of SMDs of the level of CDs in the case group compared with the control group. The pooled SMD for CD3 level was 2.59 (95% CI: −0.21 to 5.40; $P = .07$; $I^2 = 98\%$), for CD4 count was 2.81 (95% CI: 0.08–5.53; $P = .04$; $I^2 = 98\%$), for CD8 was −0.75 (95% CI: −2.94 to 1.45; $P = .50$; $I^2 = 98\%$), and for CD4/CD8 ratio was 1.12 (95% CI: −0.42 to 2.65; $P = .15$; $I^2 = 96\%$). There was no significant difference in terms of CD3, CD8, and CD4/CD8 ratio counts between the case and control groups, but the CD4

count in the case group was significantly higher than the control group.

3.4. Risk of bias

Seven studies didn't report random sequence generation, all studies didn't report allocation concealment, and performance and assessment biases, and 2 studies had attrition bias (Fig. 6).

3.5. Subgroup analysis

A subgroup analysis was performed based on several variables (Table 2). The injection point on VAS score, treatment duration on the time to scab, and frequency of EA on total effective rate were significant factors.

3.6. Meta-regression analysis

A meta-regression analysis was performed based on several variables (Table 3). The results reported that the mean age was a confounding factor for the total effective rate.

3.7. Sensitivity analysis

The sensitivity analyses reported that all pooled results (SMDs and ORs) were stable.

3.8. Trial sequential analysis

Figures S1 to S7, Supplemental Digital Content (<http://links.lww.com/MD/O437>), show TSA plots in the case group compared with the control group. The results indicated that there is sufficient evidence to conclude a significant effect for the VAS

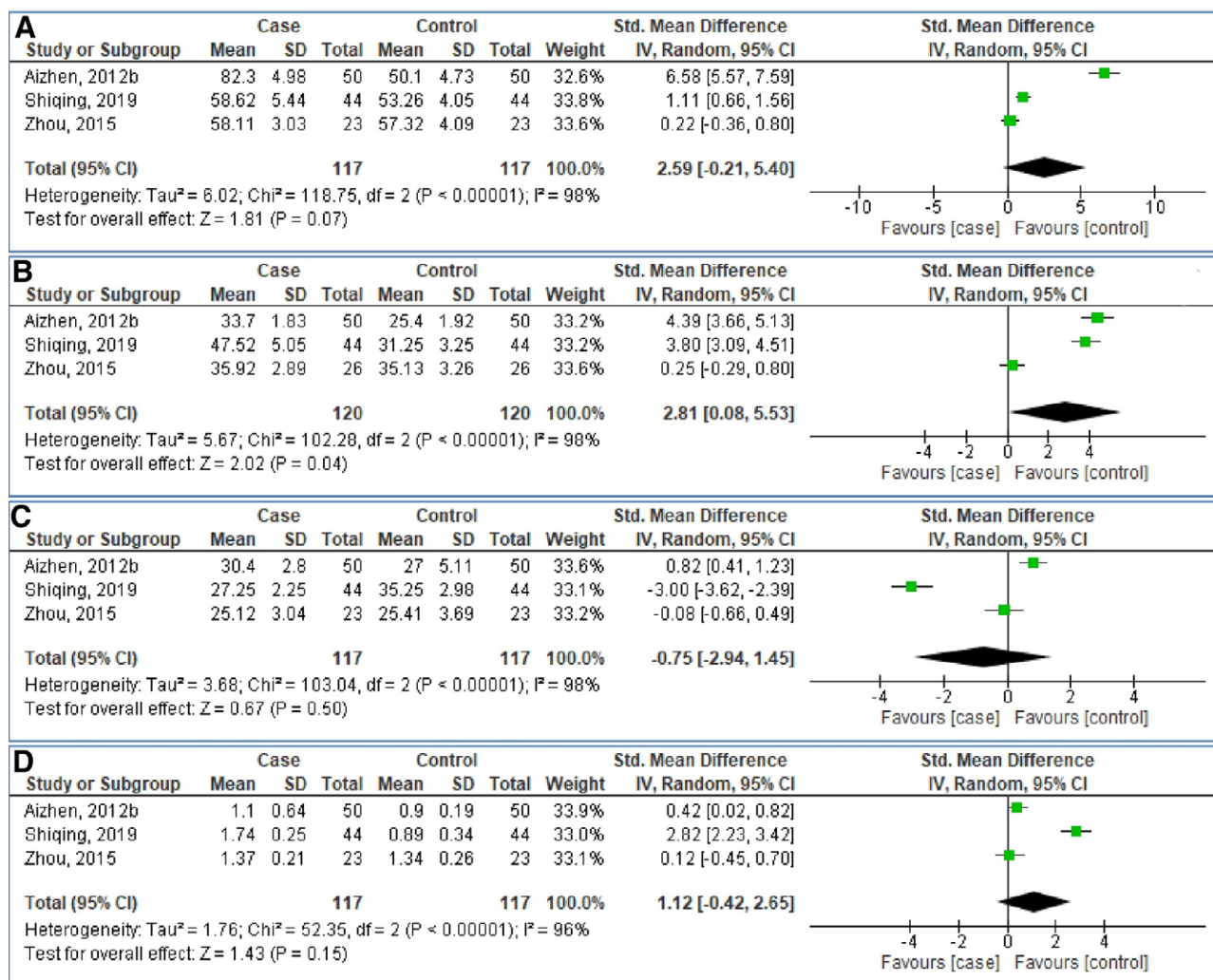


Figure 5. Forest plot of standardized mean differences of level of 4 variables in the case group compared with the control group. (A) CD3 count. (B) CD4 count. (C) CD8 count. (D) CD4/CD8 ratio.

score, cessation of pustules time, pain relief time, time to remove scab, incidence of PHN, and total effective rate. This is because the Z-curve (cumulative Z-score) crossed the RIS line for these outcomes, suggesting that the required information size has been reached and the findings are likely conclusive. However, for the time to scab, the Z-curve did not cross the RIS line. This suggests that the current information size (i.e., the number of participants in the studies analyzed) may not be sufficient to draw a definitive conclusion. More studies may be needed to confirm the effect of this outcome.

3.9. Publication bias

Figures S1 to S11, Supplemental Digital Content (<http://links.lww.com/MD/O438>), show the funnel plots in the case group compared with the control group. Egger ($P < .001$) and Begg ($P < .0001$) tests showed publication bias for VAS score, Begg test ($P = .0477$) showed publication bias for time to remove scab, Begg test ($P = .0415$) for pain relief time, Egger test ($P = .0117$) for incidence of PHN, and Egger test ($P = .0048$) for CD4 count.

4. Discussion

The case group receiving EA had a significantly lower VAS score compared to the control group with RT. The case

group also had a shorter cessation of pustules time, a shorter time to scab, and a shorter time to remove scab compared to the control group. However, the control group experienced pain relief sooner than the case group. The case group had a lower incidence of PHN and a higher total effective rate compared to the control group. CD4 count in the case group was significantly higher than the control group. The injection point on VAS score, treatment duration on the time to scab, and frequency of EA on total effective rate were significant factors. Mean age was a confounding factor for the total effective rate. There is sufficient evidence to conclude a significant effect for the VAS score, cessation of pustules time, pain relief time, time to remove scab, incidence of PHN, and total effective rate. However, more studies may be needed to confirm the effect of the time to scab. There was publication bias for the VAS score and time to remove scab.

It is worth mentioning that EA is beneficial in treating acute pain in patients with PHN. Earlier research indicates that EA is linked with a decrease in chronic pain conditions, such as cervical myofascial pain syndrome and knee osteoarthritis.^[14,49] Furthermore, some studies suggest that EA is connected with a reduction in acute pain, including acute postoperative pain.^[50] The current meta-analysis validates the positive impact of EA on the VAS score and the duration of pain relief in HZ patients.

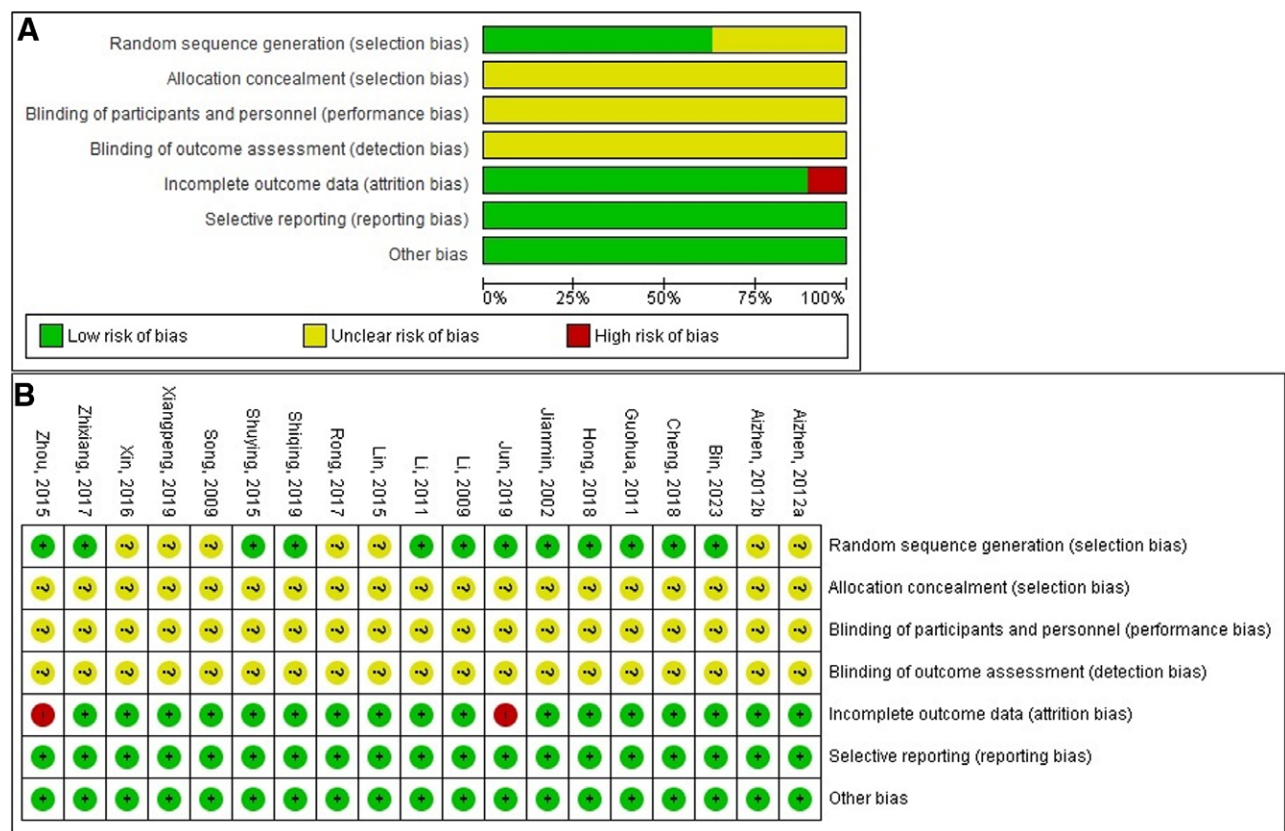


Figure 6. Bias risk assessment. (A) Risk of bias summary and (B) risk of bias graph.

The findings of this study align with previous research, which suggests that the analgesic effect of EA is more potent when alternating between low and high frequencies, compared to a constant frequency.^[51–53] The subgroup analysis in this meta-analysis indicated that the frequency of EA was a significant factor influencing the total effective rate.

Earlier research has demonstrated that EA applied to Jiaji (EX-B2) points can alleviate neuropathic pain.^[54] Numerous studies have indicated that EA on “Jiaji” points can mitigate various pain conditions, including persistent tissue damage (inflammation), nerve damage (neuropathy), cancer, and visceral pain.^[55–58] The subgroup analysis in the current meta-analysis revealed that the injection point significantly influenced the VAS score, and EA on the Ashi point reduced the VAS score more than either the Jiaji (EX-B2) point or a combination of Ashi and Jiaji (EX-B2) points.

The immune system is vital in managing and warding off HZ. Nonetheless, individuals with weakened immune systems, due to factors such as aging, immunodeficiency disorders, autoimmune diseases, HIV, cancer, or organ transplantation, face an increased risk of HZ.^[59] A study indicated that EA stimulation at the ST36 acupoint boosted the level of immune cytokines and splenic CD4 + T cells via transient receptor potential vanilloid channels in this system.^[60] A case report described a patient with disseminated HZ, who had a reduced CD4 count.^[61] According to our meta-analysis, there was a significant increase in CD4 count by EA.

Limitations: The number of studies reported in most analyses was limited, implying that the existing evidence may not be robust enough to form conclusive results for certain variables. Several analyses were subject to publication bias. The methodological standards of the studies were somewhat lacking.

5. Conclusions

The results indicate that the EA treatment had several significant benefits for HZ. EA reduced cessation of pustules time, pain relief time, time to scab, and time to remove scab compared to the control group, and also, EA reduced the incidence of PHN and increased total effective rate and CD4 count in the HZ patients compared to the control group. But, the combination of treatments of EA with WM had better effects compared to EA treatment alone.

The EA may offer certain benefits over WM for the specific conditions studied, such as quicker recovery times and lower incidence of PHN. However, it’s important to note that more research may be needed, particularly given the publication bias detected in the study. The clinical significance would also consider the practicality of implementing EA in various healthcare settings and its acceptability to patients.

Author contributions

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Table 2
Subgroup analysis.

			95% CI		Z-value	P-value	I ²	
Variable	Subgroup, N	SMD	Min.	Max.				
VAS score	Frequency	2 Hz (3)	−2.11	−3.67	−0.56	2.67	.008	94%
		2/100 Hz (4)	−2.02	−3.61	−0.43	2.49	.01	97%
		120 Hz (1)	−0.79	−1.17	−0.41	4.09	<.0001	–
	Type of treatment for case group	EA (5)	−2.04	−3.30	−0.78	3.17	.002	96%
		EA + RT (7)	−2.95	−4.33	−1.58	4.21	<.0001	97%
	Treatment duration	7 d (3)	−5.09	−8.33	−1.85	3.08	.002	97%
		10 d (8)	−1.89	−2.75	−1.03	4.31	<.0001	95%
	Injection point	Jiaji (3)	−4.65	−8.77	−0.53	2.21	.03	99%
		Ashi (1)	−0.42	−0.89	0.05	1.77	.08	–
		Jiaji and Ashi (3)	−3.65	−6.55	−0.76	2.47	.01	97%
Cessation of pustules time	Frequency	2/100 Hz (4)	−0.45	−0.99	0.09	1.64	.10	78%
		120 Hz (1)	−0.92	−1.30	−0.53	4.66	<.00001	–
	Type of treatment for case group	EA (4)	−0.67	−1.17	−0.17	2.64	.008	78%
		EA + RT (4)	−0.75	−1.47	−0.04	2.06	.04	87%
	Treatment duration	7 d (1)	−0.90	−1.32	−0.49	4.30	<.0001	–
		10 d (5)	−0.87	−1.52	−0.21	2.59	.010	86%
The time to scab	Frequency	2/100 Hz (4)	−0.32	−0.93	0.29	1.03	.30	83%
		120 Hz (1)	−0.34	−0.71	0.02	1.84	.07	–
	Type of treatment for case group	EA (4)	−0.43	−0.94	0.09	1.62	.11	80%
		EA + RT (4)	−0.54	−1.12	0.04	1.83	.07	81%
	Treatment duration	7 d (1)	−0.76	−1.16	−0.35	3.65	.0003	–
		10 d (5)	−0.57	−1.18	0.03	1.85	.06	84%
Time to remove scab	Frequency	2/100 Hz (4)	−0.68	−1.16	−0.19	2.72	.007	72%
		120 Hz (1)	−0.74	−1.12	−0.36	3.83	.0001	–
	Type of treatment for case group	EA (4)	−0.70	−1.15	−0.25	3.05	.002	72%
		EA + RT (4)	−1.38	−2.54	−0.22	2.33	.02	94%
	Treatment duration	7 d (1)	−2.46	−2.99	−1.94	9.20	<.00001	–
		10 d (5)	−1.00	−1.43	−0.56	4.48	<.00001	68%
Total effective rate	Frequency	2/100 Hz (2)	2.56	1.18	5.56	2.38	.02	62%
		120 Hz (1)	3.92	0.78	19.75	1.66	.10	–
		220 Hz (1)	12.55	0.67	235.00	1.69	.09	–
	Type of treatment for case group	EA (4)	2.80	1.47	5.34	3.12	.002	0%
		EA + RT (3)	8.90	3.41	23.20	4.47	<.00001	0%
	Treatment duration	7 d (2)	8.41	3.05	23.17	4.12	<.0001	0%
		10 d (4)	3.20	1.64	6.24	3.41	.0007	25%

CI = confidence interval, EA = electroacupuncture, RT = routine treatment, SMD = standardized mean difference.

Bold number mean statistically significant datum ($P < .05$).**Table 3**
Random meta-regression analysis.

Variable	Outcome	Coefficient	Standard error	95% lower	95% upper	Z-value	P-value
Publication yr	VAS score	0.0031	0.0028	−0.0025	0.0086	1.08	.2788
	Cessation of pustules time	−0.0009	0.0020	−0.0049	0.0031	−0.44	.6618
	The time to scab	−0.0013	0.0017	−0.0046	0.0021	−0.75	.4560
	Time to remove scab	0.0016	0.0022	−0.0028	0.0060	0.70	.4843
	Total effective rate	−0.0009	0.0010	−0.0030	0.0011	−0.91	.3643
Mean age, yr	VAS score	−0.1991	0.1113	−0.4172	0.0190	−1.79	.0736
	Cessation of pustules time	−0.0062	0.0847	−0.1722	0.1599	−0.07	.9420
	The time to scab	0.0196	0.0706	−0.1189	0.1580	0.28	.7817
	Time to remove scab	−0.1138	0.0940	−0.2982	0.0705	−1.21	.2260
	Total effective rate	0.0710	0.0324	0.0076	0.1345	2.19	.0282
Number of cases	VAS score	0.0106	0.0348	−0.0577	0.0788	0.30	.7616
	Cessation of pustules time	0.0141	0.0099	−0.0054	0.0336	1.42	.1556
	The time to scab	0.0117	0.0083	−0.0046	0.0280	1.41	.1583
	Time to remove scab	0.0106	0.0108	−0.0105	0.0318	0.99	.3243
	Total effective rate	−0.0011	0.0214	−0.0429	0.0408	−0.05	.9608

VAS = visual analogue scale.

Bold number mean statistically significant datum ($P < .05$).**References**

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