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The Effectiveness of Acupuncture for Post-herpetic Neuralgia: a Narrative Review

By

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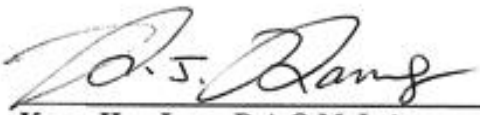

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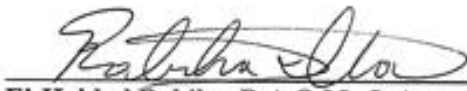

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SOUTH BAYLO UNIVERSITY at Anaheim, 2018

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ABSTRACT

Post-herpetic neuralgia (PHN) is the most common complication of *Herpes* zoster which persistent pain lasts for months to years after lesion is healed. About 10 to 20% of the elderly patients suffer from PHN in every year and PHN seriously decreases patients' quality of life, has impact on the physical and psychologic health, and increases costs related to treatments to relieve pain and to improve the quality of life. The purpose of this narrative literature review are to evaluate the effectiveness of acupuncture for PHN based on clinical evidences and to establish the method of effective acupuncture treatment for PHN through the comprehensive review on randomized controlled trials and case studies. This literature review was searched and collected by using six main databases from January 1999 to December 2017: EBSCO, PubMed, PubMed Central, MEDLINE and Google scholar. Initially, 610 studies were found and five randomized controlled trials and five case series, a total of ten studies which met the inclusion criteria were reviewed. The research inclusion criteria included: 1) published in English 2) full text available 3) any forms of acupuncture 4) randomized controlled trials (RCTs), non-

randomized trials, case series and reports 5) pain after lesion is healed; the exclusion criteria included: 1) published in other than English 2) systematic and narrative literature reviews and meta-analysis 3) acute stage of *Herpes* zoster studies. 4) all animal studies. After analyzing the acupuncture points that were used in five RCTs and five case series, LV3,LI4, Hua Tuo Jia Ji points, ST36, SJ5, GB34 were used most often and were most significant acupuncture points to treat PHN. It was concluded that acupuncture is potent therapeutic method in relieving symptoms of PHN with minimal adverse effects based on some significant evidence. Also, when acupuncture treatments are combined with western medicine, the effectiveness is amplified.

Keyworlds: Acupuncture, Post-herpetic neuralgia, cupping, and TCM

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I. INTRODUCTION

Post-herpetic neuralgia (PHN) is the most common chronic complication of *Herpes* zoster and the most common neuropathic pain resulting from infection affecting between 10% to 20% of people over 50 years of age. The risk of PHN increases with age and it is not common under the age of 40 years. [1-2, 30]. *Herpes* zoster, also commonly known as shingles, results from reactivation of late *Varicella* zoster virus (VZV) in a sensory ganglion and it is characterized by a painful, blistering skin eruption following dermatome distribution which usually resolves within 2-4 weeks. VZV usually persists asymptomatically in the dorsal root ganglia who has had chickenpox during childhood. After the primary infection of VZV that causes chicken pox, the virus is implanted in neural ganglions [3-5]. *Herpes* zoster generally resolve within few weeks, however, approximately 18% to 41% of patients suffering with *Herpes* zoster experience intense or serious intense pain at presentation, frequently persisting long after the lesions have healed. In about 50% of HZ patients who are over 60 years of age and 75% of HZ patients who are over 70 years of age have experience of PHN [8].

PHN is defined that *Herpes* zoster pain persists for months or years after the lesions have healed [1, 6]. However, there is no standardized clinical definition of the length of time for a diagnosis of PHN; currently, it is controversial for the definition of the length of time required after *Herpes* zoster onset for a diagnosis of PHN [7-9]. PHN often defined as pain persisting or resuming at least 30 days after rash healing or pain

persisting more than 3 months after the onset of the rash but the presence of neuralgia one month after onset of *Herpes* zoster is often used as a cut-off clinically [7, 8].

PHN may persist or recur for months, years, or for life, and it is occurred in 4 over 1000 people per year, which increases to 12 over 1000 among people aged over 80 years [9]. Post-herpetic neuralgia can result in severe pain; patients feel pain when they wear clothing that comes in contact with the lesions or to be outside in the wind because of the sensitivity of the skin on the thorax and face. There may be loss of vision or even loss of the eye and facial scarring. Also, it is rare but it could result inflammation of the spinal cord, brain and meninges, and facial paralysis [10].

The most relevant risk factor of PHN is old age; 99% of adults over 40 years have been exposed to VZV in the United States [31, 32]. The incidence of post-herpetic neuralgia rises from 10% among people of all ages to as high as 40% among those 50 years and older. People with PHN can develop other symptoms other than chronic pain such as decreased appetite, impaired sleep, diminished libido, depression, fatigue, severe psychosocial dysfunction, interfering with physical, emotional, and social functioning. About 43% of people with PHN has moderate anxiety. Also, PHN may severely impact on quality of life and healthcare costs. According to the American Society of Regional Anesthesia, post-herpetic neuralgia is the leading cause of suicide in chronic pain patients in elder populations [7, 11, 12, 29]. The annual healthcare costs for PHN range from $2,159 to $5,387 per person and are much greater than the healthcare costs for acute *Herpes* zoster pain in patients which range from $757 to $1,313 per person [14].

It is difficult to diagnose PHN because the pain persists after rash has cleared up and there is no significant test or examination to diagnose PHN; therefore, patient history and physical examination are important steps to diagnose PHN. Presence of antibodies to *Herpes* zoster could support diagnosis of *Herpes* zoster infection [11, 32].

The western medicine treatments for *Herpes* zoster and PHN generally include one or more of antiviral medications such as famciclovir and valacyclovir, tricyclic antidepressants, opioid analgesics, anticonvulsants and topical applications such as lidocaine patches or capsaicin lotion. Tricyclic antidepressants, and anticonvulsants (Gabapentin, Pregabalin, and Lidocaine patch 5%) were recommended as first-line therapies in US, European, Canadian guidelines and international expert consensus recommendations and Opioids, Tramadol, topical capsaicin were recommended as second-line or third-line therapy [2].

However, approximately a half of PHN patients did not satisfy with these medications to relieve pain and also, there are many side effects of these medications such as sedation, xerostomia, confusion, dysrhythmia, weight gain, dizziness, somnolence, fatigue , and ataxia. Particularly in elderly patients, it is very limited to use the western medicines due to side effects [7]. The effectiveness of current medications on post-herpetic neuralgia is limited, and have side effects; more effective and have less side effects methods are needed to treat or reduce post-herpetic neuralgia pain. Acupuncture is one of alternative methods to treat PHN patients and it is widely used in China [4].

Traditional Chinese Medicine (TCM)

In TCM, *Herpes* zoster is called snake string sores, fire belt sores, spider sores, snake burrow sores, and lumbus-binding fire cinnabar PHN is caused by evil toxins, aging, unregulated eating, drinking, etc,. The mechanisms of PHN is that due to wei qi weakness, evil toxins enter the body or emotional stress may affect liver and gallbladder to produce heat. Also, excessive eating of sweet, oily, spicy caused spleen damp-heat to cause PHN. Evil qi, dampness, or heat causes qi and blood stagnation. Moreover, qi deficiency results poor blood moving which leads to heat stagnation and damp heat [4, 27].

Post-herpetic neuralgia is diagnosed as follow: liver and gallbladder fire, spleen damp-heat, and qi and blood stagnation [27]. First, liver and gallbladder fire type of PHN has burning heat and prickling pain with bitter taste in the mouth, and red tongue with yellow tongue coating. Second type is spleen damp-heat PHN which has severe aching pain, heaviness with loose stools, and white or yellow greasy tongue coating. Last type is qi and blood stagnation which is most common type of PHN that has severe fixed pain with hard to bear, and purplish tongue color.

Many different kinds of acupuncture methods such as regular acupuncture, electroacupuncture, cupping, bloodletting cupping, plum blossom needles, fire needles, laser acupuncture, etc., are in use for the treatment PHN pain in hospitals in China for long time. Although there are many different kinds of acupuncture methods for treating PHN, many clinical studies showed that acupuncture treatment methods are effective [15].

Many studies were published regarding acupuncture for treating both acute and chronic *Herpes* zoster related pain and studies showed that acupuncture are effective for PHN but most of them are not translated in English. No literature reviews and meta-analysis were published on the effectiveness of acupuncture for PHN until 2017; only one systematic literature review's protocol is available but it was not completed its research yet. There is no comprehensive literature review or meta-analysis on this topic previously. Only some randomized control trials and case series were done and published in English. Due to a limitation of quantity of meta-analysis, case series or case studies are valuable to evaluate the effectiveness of acupuncture and it is necessary to integrate RCTs and case series. A comprehensive review for acupuncture treatment is required to provide the alternative effective treatment for PHN.

The purpose of this literature review is to evaluate the effectiveness of acupuncture for post-herpetic neuralgia from clinical evidences. Also, this review is aimed to establish the method of effective acupuncture treatment for post-herpetic neuralgia through the comprehensive review on randomized controlled trials and case studies. The significance of this study is to provide comprehensive guideline of treating PHN through updated reviews on the current evidence of using acupuncture to treat post-herpetic neuralgia.

II. MATERIALS AND METHODS

Six electronic databases were searched from January 1999 to December 2017 for literature selection: English databases included EBSCO, PubMed, PubMed Central, MEDLINE and Google Scholar. The following keywords combinations were used for search: “Acupuncture”, “Cupping”, AND “Post-herpetic neuralgia”, “*Herpes* zoster related pain”,

The initial search yielded 610 total articles through the databases specified above. Many articles are not related to acupuncture; from initial search, 335 articles were eliminated based on subject relevance. 187 duplicates and articles which only abstracts’ are available were eliminated. All animal studies, articles which written in other than English were eliminated. After elimination, 10 studies were remaining: 5 randomized control trials studies and 5 case series. Figure 1 shows a summary of the selection process.

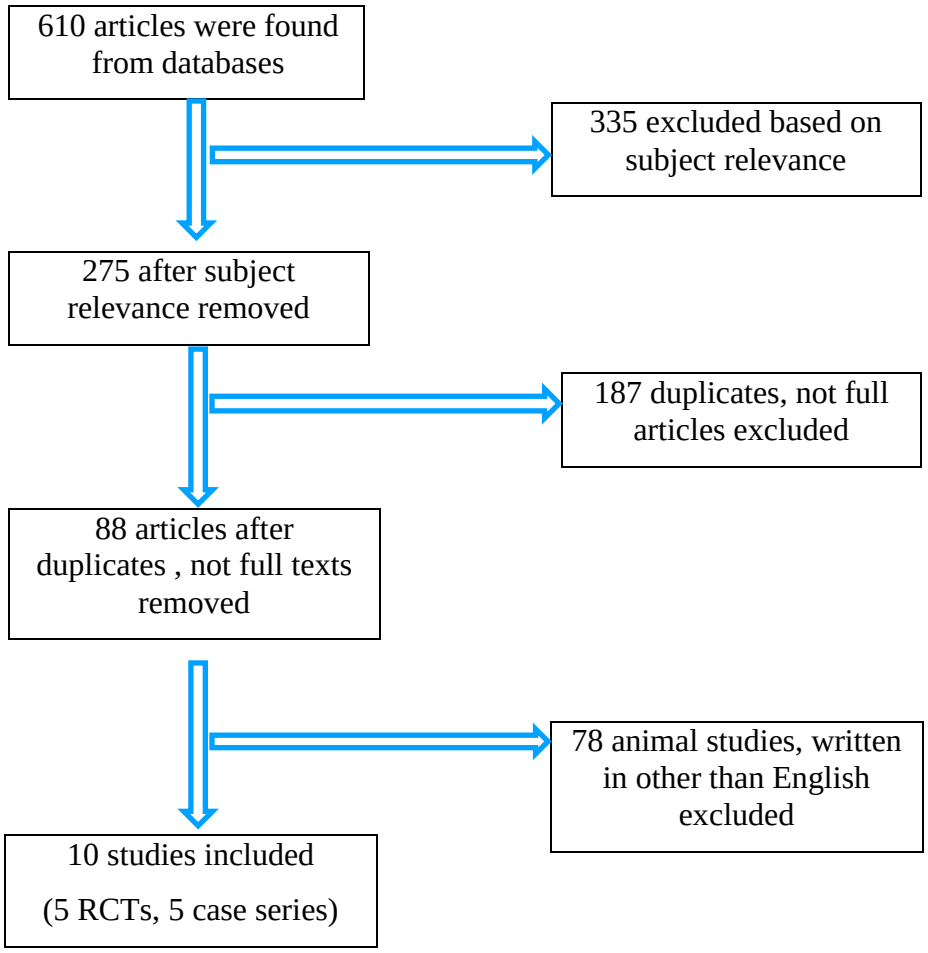

Figure 1. Articles Selection Flow Chart

Inclusion and Exclusion Criteria

This narrative study were allowed all types of studies included randomized controlled trials (RCTs), non-randomized trials, case series and reports which written in English but systematic and narrative review and meta-analysis were excluded. Patients of any age, race and gender were included. Only *Herpes* zoster related pain after lesions were healed were included. Any form of acupuncture treatment that stimulates acupoints were included such as solid needles, electroacupuncture, warm needles, dry acupuncture, auricular acupuncture, laser acupuncture, three-edged needles, plum blossom needles (sever-star needles), moxibustion, bloodletting cupping, and dry cupping. Any acupuncture techniques were included. Sham or fake acupuncture treatment with or without standard care were included as control interventions. Studies of acupuncture combined with Chinese herbal formulas were included. Acupuncture combined with western medicine were included. Studies were published in English only was included. Studies were published from January 1999 to December 2017 were included.

Studies involving any form of massage, acupressure and gua-sha were excluded. No acute *Herpes* zoster studies were excluded. Also, all animal studies were excluded. Any forms of non-proved opinions, non-scientific, studies and studies that only available abstracts or proposals were excluded.

Data Analysis

Based on the inclusion and exclusion criteria, only full texts of studies were obtained from six databases and were reviewed. Author(s), publication year, study design, number of participants, outcomes, treatment duration, and major results were extracted from each study. All 5 RCTs, Visual analogue scale (VAS) scores or Linkert pain scale scores were measured for pain intensity. The VAS score or Linkert pain scale was compared between the observation groups and the control groups in RCTs. VAS score and Linkert pain scale scores are very similar that the scale 0 to 10 were used to measure pain; 0 means no pain and 10 means not bearable pain. All $p<0.05$ or less was considered as significant. 1 RCT used the Medical Outcomes Study-Short Form 36 to measure the health related quality of life and used the Depression scale to measure depression level. 1 other RCT used the international criteria for sleep efficacy. For case series, two studies used VAS scores or Linkert pain scales to measure pain and all studies used the therapeutic effect criteria to evaluate pain for PHN.

III. RESULTS

Ten articles were found that five were the randomized controlled trials and five were the case series which had more than twenty participants participated in the study. As shown in Table 1 and 2, total 591 participants were participated from ten studies. All ten articles were published in last 20 years.

Table 1. Summary of 5 RCTs

Author, publication year	Duration of pain (Average)	Duration of treatment	Number of Participants (group)	Age (Average or mean)	Gender (M/F)
Hui, 2012	At least 30 days	Not specified (3,6,9 weeks follow up)	59 (A:32/B:27)	69.8 (mean)	A: 14/18 B: 10/17
Liu, 2014	A: 5 days-6.3 months (5.3 weeks) B: 7 days-5.7 months (5.1 weeks)	2 courses (7 times is 1 course	130 (A:65/B:65)	A: 28-81 (47.6) B: 28-79 (45.5)	A: 30/35 B: 29/36
Garrido-Suarez, 2017	<6 months	15 days	68(A:26/B:21/C:21)	A: 77.65±1.6 B: 75.81±1.9 C: 73.48±1.3	A: 15/11 B: 9/12 C: 10/11
Li, 2014	2 months-3 years	2 courses (10 times is 1 course)	120(A:60/B:60)	A: 40-74 (62.3) B: 42-68 (58.2)	A: 23/37 B: 31/29
Fang, 2011	2-10 weeks	4 courses (7 times is 1 course)	24(A:12/B:12)	A: 71±6 B: 72±7	A: 8/4 B: 7/5

Table 1. ***Continued.***

Author, publication year	Intervention	Acupuncture points	Results
Hui, 2012	Acupuncture, neural therapy, bloodletting cupping, TCM herbs	LV3, LI4, ST36	The mean pain level decreased significantly from 7.5 to 2.3.
Liu, 2014	A: Floating-acupuncture laser + bloodletting cupping B: Electroacupuncture	LI4, LV3, SJ6, LI11, ST36, Hua Tuo Jia ji	The total effective rate of the floating-acupuncture laser w/ bloodletting cupping was 98.5% and the total effective rate of the electroacupuncture was 78.5%.
Garrido-Suarez, 2017	A: Electroacupuncture B: EA + Ketamine C: Sham EA + Ketamine	GB30, GB34, UB25, UB40	Combined the electroacupuncture with ketamine was most effective than electroacupuncture alone or sham acupuncture-kemaine.
Li, 2014	A: Fire needle + Linggui Bafa therapy B: Simple fire needle	ST36, GB34, LV3, SP6, Ashi	The total effective rate of the fire needles with Linggui Bafa was 93.3% and the total effective of the fire needle alone was 76.7%
Fang, 2011	A: Acupuncture B: Brufen (NSAID), Famotidine, Vit. B_1 and B_{12} injection	Hua Tuo Jia Ji	The total effective rate of the acupuncture group was 91.6% which was higher than the medication group (83.3%).

Table 2. Summary of 5 Case Series

Author, publication year	Duration of pain (Average)	Duration of treatment	Number of Participants (group)	Age (Average or mean)	Gender (M/F)
Zhang Y, 2004	Not specified	10 times (everyday) for acupuncture; 5 times (every other day) for cupping	56	42-72 (57.8)	35 M/21 F
Huang, 2014	2-10 months	10 times (everyday) for two courses	27	61-70 (56±5)	15 M/ 12 F
Hui, 1999	20.4 months (average)	3-34 sessions (Average 12.5)	56	Predominantly 65 yrs or older (Average 72.7)	31 M/ 25 F
Zhang D. 2005	1 month-6 years	3 courses (10 times per course)	21	69-80	13 M/ 8 F
Wang, 2008	2 months-2 years	2 courses (10 times per course)	30	48-78	17 M/ 13 F

Table 2. - continued.

Author, publication year	Intervention	Acupuncture points	Results
Zhang Y, 2004	Acupuncture + bloodletting cupping	Hua Tuo Jia Ji	The total effective rate was 94.6%
Huang, 2014	Electroacupuncture+ analgecine	Ashi points around pain	The total effective rate was 85.19%.
Hui, 1999	Acupuncture + bloodletting cupping + local anesthetic+ TCM herbs	LV3, GB34, ST36, PC6, SJ5, LI4, LI11	The average reduction in pain was 72.1%.
Zhang D. 2005	Warm needle acupuncture	Hua Tuo Jia Ji, SJ5, LV3, GB41	The total effective rate was 95.2%.
Wang, 2008	Acupuncture + point injection	Ashi points	The total effective rate was 90%.

A randomized controlled trial #1 [8]

This RCT trial was performed by Hui Fred et. al. [8] that 59 patients were participated for this study and they were randomly assigned into two groups: group A and group B. Group A (n=32) was an immediate treatment group which was received the TCM intervention once daily, five days per week, for three week. Group B was a wait-list (delayed treatment) group (n=27), and used as a control group that received the same treatment starting three weeks after randomization. Hui Fred et. al., defined PHN as the presence of PHN one month after onset of *Herpes* zoster.

The objective of this study was to determine whether a similar TCM protocol could significantly reduce the level of pain associated with PHN. 10-point Likert pain scale was used to measure the change in pain from baseline to three weeks for the primary outcome measure; o is no pain and 10 is most pain. Also, they measured health-related quality of life which measured by the Medical Outcomes Study-Short Form 36 and depression which was measured by the Centre for Epidemiological Studies Depression Scale.

Acupuncture points that the treatment groups were received were received LI4, LV3, and ST36 and local ashi points. For cupping and bleeding, the skin was pricked with a sterile needle and using a plastic suction cup with a vacuum seal that was placed over the bleeding site. Also, neural therapy consisted of a 1% of procaine injected into the affected dermatome to allow for painless pricking for bloodletting cupping. Moreover, participants in the trial all receive herbal formulas either Long Dan Xie Gan

Wan or Zhi Bat Di Huang Wan depend on patients' tongues' conditions: patients with thickly coated tongues received Long Dan Xie Gan Wan and patients who had scanty tongue coating received Zhi Bai Di Huang Wan.

There was a significantly reducing in pain in the immediate treatment group and also the wait-list group reduced the pain level after they received the treatments. As shown in table 3, the pain level was decreased significantly in the immediate treatment group from 7.5 to 2.3 after the patients were treated for three weeks and the pain level in the wait-list control group remained about same as the baseline until they get the treatments; when the wait-list group started to receive the treatments, the pain level started to decrease. Moreover, participants' physical and mental health-related quality of life and depression improved throughout the treatment period. In both groups, all improvements persisted for up to two years.

Table 3. Pain, Physical and Mental Health-related Quality of Life and Depression at Baseline, 3, 6, 9 weeks for Both Immediate Treatment Group and Wait-list Group [8]

	Baseline	3 weeks	6 weeks	9 weeks
Pain level				
Immediate	7.5	2.3	3.5	3.5
Wait-list	7.8	7.2	4.5	4.9
Physical health				
Immediate	35.3	40.5	45.5	45.2
Wait-list	34.5	33.6	38.5	38.5
Mental health				
Immediate	39.1	49.8	50.7	55.5
Wait-list	37.7	41.1	48.8	52.2
Depression				
Immediate	18.9	10.8	7.9	6.4
Wait-list	20.4	18.1	10.0	9.8

*Pain level used a Likert Pain Scale (0=no pain, 10=strongest pain), physical and mental component summaries of the SF-36, depression measured by Centre for Epidemiological Studies Depression Scale.

A randomized controlled trial #2 [17]

This trial was performed by Min-juan Liu. 130 participants were divided randomly into two groups; group A was a floating-acupuncture laser with bloodletting cupping and group B was an electroacupuncture group. The objective of this study was to observe the clinical efficacy of treating PHN by combining floating-acupuncture laser with bloodletting cupping and electric acupuncture.

30 male and 35 female patients in group A, whose ages ranged from 28 to 81, with an average of 47.6 years old and the duration of pain was from 5 days to 6.3 months

after lesions were healed. In group B, 29 male and 36 females were involved, whose ages were from 28 to 79, with an average of 45.5 years old and the duration of pain was from 7 days to 5.7 months. There was no obvious difference between the two groups in gender, age, duration of pain (all $P>0.05$).

Liu, the author defined PHN as 1) suffer from pain for 1 month to 2 years after lesions were healed, with a past medical history of *Herpes zoster*; 2) a sense of pain distributed in line with the innervation area, and the sense of touch is abnormal, with chromatosis in local part; 3) the pain is paroxysmal or lightning pain , or constant burning pain and packing pain; 4) obvious discomfort after nerve damage in affected area: tickle, packing feeling and formication, etc.; 5) the patient is depressed, with heavy psychological burden.

For group A, all participants received acupuncture treatments every other day, with 7 times a course and two courses were given. Acupuncture needles were inserted on the pain points and after they were retained for 10 min, they were taken out and then the laser acupotome therapeutic apparatus was connected for 20 min. After needling, bloodletting cupping was performed around the neuropathic pain sites. For group B, electroacupuncture was applied on acupoints LI4, LV3, SJ6, LI11, Hua Tuo Jia ji and ST36. The needles were retained for 30 min with 30 Hz of wave and it was conducted once a day with 7 times as a course for 2 courses of treatments.

Visual analogue scale (VAS) was adopted in the pain rating that “0” is no pain, “10” is the strongest pain. VAS scores are in table 4. This study collected VAS scores before treatment, after one course of the treatment, end of the treatment and 3 months after the treatment. VAS scores after end of treatment and 3 months after the treatment in

both groups in comparison with VAS score of before treatment were significant (both group A and B were $P<0.01$).

Table 4. VAS scores in the Two Groups A and B Comparison [17]

Group	Before treatment	After 1 course of the treatment	End of the treatment	3 months after the treatment
A	8.4±0.7	3.7±0.9	1.4±1.1	1.2±0.8
B	8.3±0.8	5.8±1.0	2.8±0.9	3.2±0.7

The comparison of group A and B for the effectiveness is shown in table 5. From group A, 31 patients were cured, 33 patients had less pain and only 1 patient had no difference; the total effective rate in group A was 98.5%. From group B, 16 patients were cured, 35 patients had less pain and 14 patients were ineffective; the total effective rate in group B was 78.5%.

Table 5. Comparison of Group A and B for the Effectiveness [17]

Group	# of patients	Cured	Markedly effective	Effective	Ineffective	Total effective rate (%)
A	65	31(47.7)	25(38.5)	8(12.3)	1(1.5)	98.5
B	65	16(20.5)	20(30.8)	15(23.1)	14(21.5)	78.5

According to Liu's study [17], both floating acupuncture laser with bloodletting cupping and electroacupuncture were effective to reduce or relieve PHN pain; however,

floating acupuncture laser with bloodletting cupping is more effective than electroacupuncture only.

A randomized controlled trial #3 [18]

In this study, 68 patients were randomized into three groups: group A (26 patients), group B (21 patients), group C (21 patients). Group A received electroacupuncture treatments only, group B received combination of electroacupuncture and ketamine and group C received sham electroacupuncture-ketamine for 15 days. According to Garrido-Suarez et al. [18], PHN is defined as pain that persists 120 days or more after rash onset. The objective of this study was to examine the potential anti-hyperalgesic effects the electroacupuncture and the combination electricacupuncture and ketamine in patients with PHN. Ketamine is a N-methyl-D-aspartate (NMDA) receptor antagonist which can provide short-term relief of refractory neuropathic pain in some patients but frequent use of ketamine can result long-lasting memory impairment and altered prefrontal dopaminergic function.

Group A received an electric acupuncture 10 Hz treatment every day for 20 minutes for 15 days. Group B was received an electroacupuncture with ketamine hydrochloride (0.25-0.5 mg/kg) was injected for 15 days. Group C was received Sham electroacupuncture with ketamine injection. The needles located into small adhesive cylinders were placed without perforating the skin. Same acupuncture points were used as group A.

In this study, the results were measured the change in the average daily pain score (ADPS) using the Likert pain scale that 0 means pain-free and 10 indicated unbearable pain.

Table 6. Change in Average Daily Pain Score (ADPS) for Group A, B, C. Score Range is 0 to 10. 0 is No Pain, 10 is the Strongest Pain [18]

	0 day	15 days	30 days	60 days	90 days
EA (A)	7.8	6.8	5.3	4.3	3.5
EA-ketamine (B)	8	3.5	3	2.5	2
Sham EA-ketamine (C)	8	6.5	5	4.1	3.5

Table 6 showed that, in group A, pain reduced and in group C, pain reduced. However, group B, the combination electroacupuncture-ketamine reduced pain significantly ($P<0.001$). Using electroacupuncture combined with ketamine was more efficient to reduce pain compared using electroacupuncture alone and using sham-ketamine. There was a synergetic effect when electroacupuncture was used with ketamine. The combination electroacupuncture and ketamine was superior compared with other groups.

However, adverse effects such as nausea, vomiting, constipation and sedation were observed in patients receiving ketamine.

A randomized controlled trial #4 [19]

120 PHN patients were participated in this study and they were divided randomly into two groups: an observation and control group. Each group had 60 patients. Li J., Liu Z., and Pang R. [19], defined PHN as the pain had lasted for one month or more since the rash was cured. VAS scored was used to measure the level of pain before and after treatment. The objective of this study was that to observe the clinical effect of fire needle combined with Linggui Bafa for PHN.

For the observation group (group A), the fire needle therapy and Linggui Bafa therapy were given to patients. Fire needle therapy is that the each needle was heated at the outer flame of the alcohol lamp until it became reddish and pierced rapidly at acupoints and withdrawn swiftly. For fire needle therapy, ST36, GB34, LV3, SP6 and local ashi points were used. Linggui Bafa therapy is one of the classical acupuncture therapies in TCM which combines the eight-diagram, nine-palaces theory and eight traditional acupoints (the joint points of 12 meridians and eight extra meridians, including UB62, KD6, GB41, SP4, SJ5, PC6, SI3, LU7) and the acupoints are selected based on the time deduced by the heavenly stems and earthly branches. For Linggui Bafa therapy, the acupuncture points SP4, PC6, GB41, SJ5, UB62, SI3, KD6, LU7 were used. All patients in the observation group were received the fire needles with Linggui Bafa every other day, 10 times for each course for 2 courses of treatment.

For the control group (group B), patients received simple fire needle treatments using same acupoints as the observation group once every other day, 10 times for each course for 2 course of treatment.

Table 7. VAS Scores for Two Groups before and after Treatment [19]

Groups	Number of patients	Before treatment	After treatment
Observation	60	6.12±1.96	2.28±2.08
Control	60	6.07±2.02	3.62±2.90

In this study, VAS scores were used to measure pain level to compare the two groups before and after treatment. Table 7, showed that VAS scores for the two groups: the observation and the control group. The pain was decreased in both the observation and the control group; however, fire needles with Linggui Bafa were more effective than simple fire needles. The VAS scores dropped significantly from 6.12 to 2.28 in the observation group ($P<0.01$).

As shown in table 8 below, the total effective rate of the observation group was 93.3% from 60 patients and the control group's total effective rate was 76.7%. The effective rate of the control group was still high but the effective rate of the observation group was higher than the control group.

Table 8. Therapeutic Effect for Two Groups [19]

Groups	Number of patients	Cured	Markedly effective	Effective	Ineffective	Total effective rate (%)
Observation	60	15 (25.0%)	35 (58.3%)	6 (10.0%)	4 (6.7%)	93.3
Control	60	6 (10.0%)	26 (43.3%)	14 (23.3%)	14 (23.3%)	76.7

A randomized controlled trial #5 [20]

In this trial, 24 inpatients were randomized into two groups: an acupuncture and a medication group. The objective of this trial was to observe the clinical efficacy of acupuncture therapy for PHN in the elders.

For the acupuncture group, patients were received the acupuncture treatments every day for seven days; seven days considered as one course and four courses were given, with a three day interval between courses. Hua Tuo Jia Ji, the extra points were used for the treatment: C2-C4 for Face, T4-11 for chest and upper back, T10-L2 for abdomen and lower back, C5-T2 for upper limbs, L1-L5 for lower limbs. Also, ashi points and Longyan, the extra point (located between the second and third phalanges of the small fingers, at the end of the transverse crease when clenching the fist) were used. The needles were retained for 20-30 minutes. For the medication group, 300 mg Brufen, one of the nonsteroidal anti-inflammatory drug (NSAID) was orally taken with Famotidine for stomach discomforts, 100mg of vitamin B_1 injection and 0.5 mg of

vitamin B_{12} twice a day for seven days which was considered as one course for 4 course with a three day interval between courses.

Fang used VAS score to evaluate the pain and sleep was assessed by the international criteria for sleep efficacy. For pain, 0 means no pain, 10 is most pain and for sleep, 0 means cannot sleep, 10 means well sleep (Table 9).

Table 9. Comparison VAS Scores of Pain and Sleep in the Acupuncture and Medication Groups before and after Treatment [20]

	Acupuncture group		Medication group	
	Before treatment	After treatment	Before treatment	After treatment
Pain	7.2±1.6	3.9±1.2	7.1±1.5	5.1±1.4
Sleep	1.6±1.2	7.3±1.3	1.3±1.1	4.9±1.7

By comparing the acupuncture group with the medication group, although both groups' pain scores were decreased ($P<0.05$), the pain score of the acupuncture group was dropped significantly ($P<0.05$) (Table 10).

Table 10. Comparison of the Effectiveness between the Two Groups [20]

Group	Number of patients	Cure	Markedly effective	Effective	Ineffective	Total effective rate (%)
Acupuncture	12	8	2	1	1	91.7
Medication	12	4	4	2	2	83.3

The total effective rate was also higher in the acupuncture group than in the medication group; the total effective rate of the acupuncture group was 91.7% and the total effective rate of the medication group was 83.3%. The medication was also effective, however, there were 3 cases in the medication group had stomach discomforts. No side effects were reported in the acupuncture group.

Case Series #1 [21]

According to Zhang Y, 35 males and 21 females, ages from 42 years old to 72 years old, total 56 PHN patients were treated with acupuncture and bloodletting cupping in this series. Hua Tuo Jia ji points were mainly used correspondingly affected segments and also ashi points were used for the acupuncture treatments. The needles were retained for 20 minutes, once every day for ten times. Using the three edged needles, tapped the tenderness spots 3-5 consecutive times, and then followed by cupping to bloodletting; two or three spots were selected every time, once every other day for five times. There is a criteria of therapeutic effect into three: recovery, effective and no effect. "Recovery" means that the pain was completely disappeared, "effective" means the pain alleviated but still have little pain left, and "no effect" means the pain remained same. As a result, recovery for 36 cases, effective for 17 cases, no effective for 3 cases. Thus, the total effective rate was 94.6% from 56 PHN patients.

Case Series #2 [24]

In this case series, 27 cases were involved; 17 males and 12 females whose ages from 61 to 70. The duration of pain was 2 to 10 months after herpes scabs. In this series, the Huang used electroacupuncture and acupoint injection. The needles were inserted around the lesion edge and then connected to 20 Hz electroacupuncture; the needle was retained for 30 minutes, once a day for 10 days. About 0.5 to 1 ml of Analgecine was injected to each acupoint, once a day for 10 times. Each therapy was done for 2 courses

that one course is considered 10 times of treatment. The location of acupoints were not specified in this case series.

Huang, Y., adopted VAS scores to evaluated pain and VAS scores in Table 11 in comparison of before and after treatment, pain dropped significantly after treatment ($P<0.01$).

Table 11. VAS Scores before and after Treatment [24]

Groups	Number of patients	Before treatment	After treatment
Observation	27	8.21±2.15	0.95±0.57

From 27 cases, 10 cases were markedly effective, 13 cases were effective, 4 cases were ineffective. Therefore, the total effective rate was 85.19. According to the result, electroacupuncture combined with Analgecine injection on acupoints was effective for PHN. Combined use of them results in better clinical effect to treat PHN.

Case Series #3 [22]

According to Hui, F., this case series consisted of 56 PHN patients, their average age was 72.7 years old, predominantly 65 years old or older. All patients were treated minimum 3 sessions to maximum 34 sessions, average 12.5 sessions until they had no pain. For each session, each patient received acupuncture, local anesthetic infiltration and nerve block, bloodletting cupping, meditation and Chinese herbs. The following

acupuncture points were used for the acupuncture therapy: LV3, GB34, ST36, PC6, SJ5, LI4, and LI11. All needles were retained for 10 minutes. 1% of procaine was used to infiltrate the nerve root on the affected dermatome for painless bloodletting cupping and helped facilitate long term healing. For the bloodletting cupping, the pain area was pricked by a needle and then cupping. Each patient learned how to meditate and encouraged them to do meditation at home twice daily for 20 minutes. Also, each patient took Chinese herbs depend on their additional symptoms: Long Dan Xie Gan Tang for irritability, Jin Gui Shen Qi Wan for lethargy, Zhi Bai Di Huang Wan for dryness, Xiao Yao Wan for depression.

As a result, the average reduction in pain was 72.1%. Hui, F., used the pain scale 0 to 10 that 0 is no pain and 10 is unbearable pain. The average pain level was 7.29 before treatment and the pain level went down to 2.0 after treatment. 24 patients out of 56 patients (43%), reported more than 90 % reduction in pain at the end of all sessions. 37 patients(67%) reported more than 70% reduction in pain at the end of all sessions. From this case series, acupuncture, and bloodletting cupping were effective for PHN patients to reduce pain. There was no significant adverse effect during the acupuncture treatments and Chinese herbs. Chinese herbs were used for specific symptoms such as irritability, lethargy and depression and they were not used as primary treatment method to treat PHN.

Case Series #4 [23]

According to Zhang, D., there were 21 cases in this case series that 13 males and 8 females, ages from 69 to 80 years old. The duration of pain was from 1 month to 6 years. Each patient received the acupuncture treatment with warm needles once a day for 10 days, 10 days is one course and total three courses had done; 3 days of interval was done between the courses. Main acupuncture points that were used were Hua Tuo Jia ji, SJ5, LV3, GB41 and ahsi points. Also, some more points were added depend on the affected area; ST44 for abdomen, UB60 for back, LV2 for hypochondriac.

Zhang, D., used the therapeutic effect which is recorded as pain disappeared, obviously alleviated pain but still have little pain, and slightly alleviated pain. After three courses of treatments, 16 cases reported pain disappeared, 4 cases obviously alleviated pain and 1 case slightly alleviated pain. Based on this study, acupuncture with warm needles was effective to relieve PHN pain without any obvious side effects. Acupuncture with warm needles helped to warm and promote qi and blood circulations of nerve roots to eliminate pain.

Case Series #5 [25]

According to Wang, S., 30 cases were done in this study that 17 cases were male and 13 cases were female, from age 48 to 78 years old. The duration of pain was from 2 months to 2 years. Each patient received acupuncture treatment that was used ashi points around the diseased region, Hua Tou Jia Ji, GB34, LV3, ST36, PC6 and LI4; the needles

were retained for 30 minutes. Additional to the acupuncture therapy, the point injection to each Huo Tou Jia Ji points and around pain region; 5 ml 2% lidocaine and 2 ml vitamin B1 solution were injected. Both the acupuncture therapy and the point injection were done once daily, 10 days as a one course for two courses; there was 3 day interval between courses.

Wang, S., used the therapeutic effect criteria as cure, improvement, effectiveness, and ineffectiveness; cure means pain completely disappeared, improvement means pain obviously alleviated but still has little pain, effectiveness means pain was improved, and ineffectiveness means no changes. Among 30 cases, 18 cases were cured, 5 cases were improved, 4 cases were effective and 3 cases were ineffective; the total effective rate was 90% of 30 cases. Combine the acupuncture therapy with the point injection were effective to treat PHN. The point injection was used for pain reduction but they were applied to the Hua Tou Jia Ji points to emphasize the functions of that specific acupuncture points to treat PHN effectively.

IV. DISCUSSION

Total 591 participants were participated from ten studies: 5 randomized controlled trails and 5 cases series. Each study used different types of acupuncture such as regular acupuncture, floating acupuncture, bloodletting cupping, electroacupuncture, fire needles and TCM herbs. Two most frequent type of acupuncture were bloodletting cupping and electroacupuncture. Some unique types they used were floating acupuncture with laser, fire needle, Linggui Bafa and warm needles. Most of studies used two or more types of acupuncture except 2 studies: Fang's RCT and Zhang D.'s case series. When Fang treated patients with acupuncture, he only used regular acupuncture and Zhang D treated his patients with warm needles. 5 out of 10 studies used either acupuncture alone or combinations of two or more types of acupuncture. Other 5 studies used some types of acupuncture combined with western medications such as procaine, ketamine, analgecine, anesthetic, and lidocaine or herbal formulas.

In RCT #1, all participants received either Long Dan Xie Gan Wan or Zhi Bai Di Huang wan three times a day based on their tongue coating; participants with thickly coated tongues received Long Dan Xie Gan Wan and participants with scanty coated tongues received Zhi Bai Di Huang Wan. Long Dan Xie Gan Tang is for liver and gallbladder fire and it is commonly used for PHN. Zhi Bai Di Huang Wan is for liver and kidney yin deficiency with heat and it is not often to prescribe for PHN patients; however, Fred Hui prescribed it based on participants' tongue coating.

The most frequent used one that was the bloodletting cupping which could help to remove chronic qi and blood stagnation in area of PHN which caused the pain and

regulate meridians, promotes qi and blood circulations and remove the inflammation of the nerve root [16, 21]. Also, bloodletting cupping can help strengthen the body immunity and has an analgesic effect [17]. The electroacupuncture is a modern acupuncture type which makes quicker to make "arrival of qi" and does strong stimulant; it is used widely for neurological pain [18]. The warm needle that Zhang D. used in his case series that warm and promote qi and blood circulations, dredge the meridians and regulate Zang-Fu organs to eliminate pain and remove pathogenic factors [23]. The fire needle which inserting red hot needle to body can help to transmit heat into the body at specific points. Linggui Bafa is one of the classical method in TCM that pick eight points linked with extraordinary meridians according to time [19]. The floating acupuncture is a modern acupuncture technique that is based on theory of cutaneous regions, adjacent point selection, theory of painful locality taken as an acupoint and the Emperor's Inner Classic; it is similar to puncture on ashi points [17].

All 5 RCTs randomly assigned participants into two or three groups: the observation group and the control/sham group. RCT #1 compared the immediate treatment group with the wait-list group. Both groups received the same treatments of acupuncture, neural therapy, bloodletting cupping and TCM herbs but the wait-list group did not have any treatment until 3weeks were passed. The reduction of pain in the immediate treatment group was significantly decreased while the wait-list group did not receive the treatments. Also, the reduction of pain in the wait-list group was decreased after the patients received the acupuncture treatments. RCT #2 compared the floating acupuncture with laser and bloodletting cupping to electroacupuncture. The floating acupuncture with laser combined with bloodletting cupping was more effective than the

electroacupuncture alone. However, electroacupuncture treatments were effective as well. RCT #3 had 3 groups to compare: 1) electroacupuncture 2) electroacupuncture with Ketamine 3) sham electroacupuncture and Ketamine. All three groups have positive results but the second group which was electroacupuncture with Ketamine was significantly effective to treat PHN. The first group which used electroacupuncture alone and the third group which used sham electroacupuncture with Ketamine, both groups were also effective but combine electroacupuncture with Ketamine was most effective. When electroacupuncture was used with Ketamine, the synergetic effect was occurred. RCT #4 compared the fire needle plus Linggui Bafa therapy group with the simple fire needle group. The fire needle alone groups had a decent total effective rate 76.7% but when the fire needle combined Linggui Bafa therapy, the total effective rate became 93.3%. RCT #5 compared the acupuncture group with the medication group. The author used NSAID medication for the medication group. By comparing, the acupuncture treatments were more effective than the western medication.

In RCT #3 and #5, there were some side effects were reported when they used western medications. In RCT #3, the side effects of nausea, vomiting, constipation, and sedation were observed in patients receiving ketamine. Also, in RCT5, stomach discomforts were observed in patients receiving NSAID, Famotidine, Vit. B1 and B12 injection; Famotidine was for the stomach discomforts, however, some participants still have the stomach discomforts. However, no side effects of acupuncture were observed in all ten studies.

Each study used different types of acupuncture but used similar acupuncture points to treat PHN. As shown in Table 11. Many same points were used in all 10

studies. LV3, Hua Tuo Jia Ji points, LI4, ST36, SJ5, GB34, and PC6 were used repeatedly throughout 10 studies.

LV3 was the most frequently used acupuncture point and Hua Tuo Jia ji points and ST36 were the second most frequent use. LV3 is a yuan primary point, which clears heat from liver and regulated liver and gallbladder. 3 RCTs and 3 case series , total 6 studies out of 10 used LV3. 3 studies used the combination of LV3 and LI4. The combination of LV3 and LI4 is called the four gates which opens up circulation of qi and blood throughout the entire body and clear heat. Use LV3 and LI3 together results more effective. Also, both LV3 and LI4 increase endorphins which help to relive pain [8].

Hua Tuo Jia Ji points were used in 4 studies which are the second most frequently used, warm and promote qi and blood circulations of nerve roots, expel pathogenic factors from skin, improve the immunity. Both western medicine and TCM believe PHN resulted when the immunity is weak; therefore, HTJJ points are helpful to resolve qi and blood stagnation and boost immunity to relived PHN pain [17, 20, 21, 23].

Also, ST36 was the second most frequently used point which were used in 4 studies. ST36 strengthens vital qi and eliminating pathogens and improves the immunity. ST36 is the best point in TCM for tonify qi and boosts immunity [8, 25]. For increasing immunity. ST36 is the most important acupuncture point.

GB34 was used in 3 studies and it was often combined with LV3. GB34 clears heat toxin in liver and promotes smooth flow of LV qi. The combination of GB34 and LV3 work together to clear heat toxin in liver meridian strongly [22, 25]. Both PC6 and SJ5 used in 2 studies. PC6 regulates qi and blood, regulate and clear the San Jiao. SJ5 clears and activates the Shaoyang meridian and Yang link vessel. [21, 23, 25]. Also, ashi

points where pain is located, were used often in these 10 studies; putting needles on or around pain remove stasis and promotes qi and blood circulation on that area.

Table 11. Points Selection for Each Group

Author, year	Acupoints						
Hui, 2012	**LV3***	**LI4***	**ST36***				
Liu, 2014	**LV3***	**LI4***	**ST36***	**HTJJ***			
Garrido-Suarez, 2017	GB30	UB40	UB25	**GB34***			
Li, 2014	**LV3***	SP6	**ST36***	**GB34***			
Fang, 2011	**HTJJ***						
Zhang Y. 2004	**HTJJ***						
Huang, 2014	Ashi points						
Hui, 1999	**LV3***	**LI4***	**ST36***	**GB34***	**SJ5***	**PC6***	LI11
Zhang D, 2005	**HTJJ***	**LV3***	**SJ5***	GB41			
Wang, 2008		**LV3***	**PC6***	ST36	**GB34***		

*HTJJ means Hua Tuo Jia Ji

*Commonly used acupuncture points were marked with asterisks.

Throughout the databases, five RCTs were found and five case series were found which were related to this review's topic. Case series were not randomized or have

control groups to compare with. However, these case series are unique and give important results to future RCT studies.

Limitations

Many studies of *Herpes* zoster treating with acupuncture and cupping were published but compare to HZ studies include acupuncture and cupping, the number of PHN studies treating with acupuncture and cupping are limited. Moreover, there is no standardization of outcome measures for PHN. The existing RCTs and case studies on PHN with acupuncture treatments used different outcome measures for PHN. Standardized outcome measurement are required to evaluate the effectiveness of acupuncture in post-herpetic neuralgia accurately. Also, there were no studies have a long-term follow-up after

Proposal of Treatment Protocols

Based on this literature review, the following treatment protocol is proposed to treat post-herpetic neuralgia patients. First of all, diagnosis of patient is most important in Traditional Chinese Medicine. PHN patients should treat different ways depend on diagnosis. The patterns of PHN are LV and GB fire, SP dampness, and qi and blood stagnation.

The treatment principles of LV and GB fire pattern PHN are to clear LV and GB fire, relieve pain, and transform toxins. I will use LV3, LI4, SJ5, GB34, and some ashi points on local area to treat PHN with LV and GB fire. In addition to regular

acupuncture, electroacupuncture will be used if it is necessary. The acupuncture points LV3, LI4, SJ5, and GB34 will clear heat in LV and GB and transform toxin to treat PHN. Moreover, the herbal formula Long Dan Xie Gan Tang may help in addition to acupuncture treatment. Long Dan Xie Gan Tang also drain excess fire from LV and GB.

The treatment principles of SP dampness pattern PHN are drain dampness and clear heat, relieve pain, and transform toxins. The acupuncture points ST36, SP9, SP6, LI4, LI11 and ashi points will be used. ST36, SP9, and SP6 drain dampness, LI4 and LI11 clear heat from SP and ST. In this case, ST36 is the only frequent point based on this review; 10 studies which were reviewed here more focused on stagnation and heat and did not mention about SP damp-heat. The herbal formula Si Miao San Jia Wei could be used to support the acupuncture treatment if necessary; Si Miao San Jia Wei is for draining dampness and clearing heat.

The treatment principles of qi and blood stagnation type PHN are promote circulation of qi and blood, remove stasis, relieve pain, and transform toxins. In this case, the acupuncture points Hua Tuo Jia Ji (HTJJ) points and bloodletting cupping on local area will used. HTJJ points and bloodletting cupping quickens qi and blood circulation and remove stagnation. HTJJ was the second most frequently used point in this review. Depends on the location pain, different HTJJ points will be used: C2-C4 for face, T4-T11 for chest and upper back, T10-L2 for abdomen and lower back, C5-T2 for upper limbs, L1-L5 for lower limbs.

V. CONCLUSION

This research evaluated the effectiveness of acupuncture for post-herpetic neuralgia. Acupuncture could be an effective alternative treatment for post-herpetic neuralgia other than the western medications. Acupuncture is safe and adverse effects are very minimal. Based on this research, acupuncture is effective for post-herpetic neuralgia. Also, two or more types of acupuncture combinations are more effective than use one type of acupuncture. Moreover, when acupuncture is used with western medication, the synergetic effect is occurred to treat PHN faster and more effective.

There are many options to select acupuncture points when treating PHN patients; however, LV3,LI4, Hua Tuo Jia Ji points, ST36, SJ5, GB34 are the best acupuncture points to treat PHN patients.

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