

SOUTH BAYLO UNIVERSITY

**Effectiveness of Acupuncture on *Herpes zoster* Pain with Immunity Based on
Literature Review**

By

Randy K. Choi

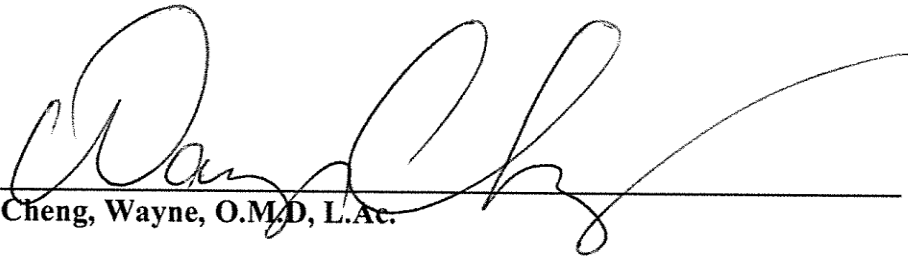
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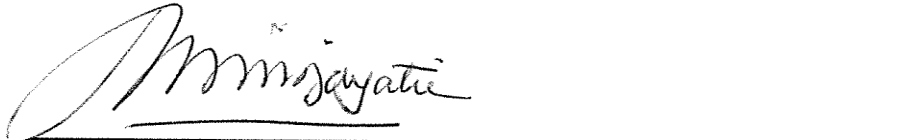
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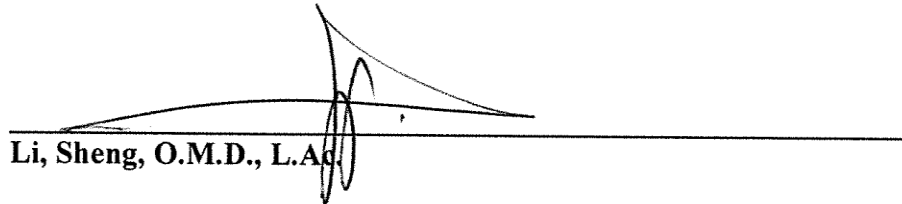
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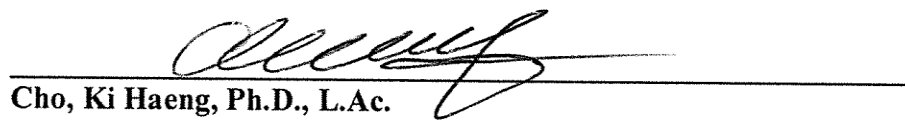
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SOUTH BAYLO UNIVERSITY AT ANAHEIM, 2018

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ABSTRACT

This narrative literature review is designed to provide a better effective acupuncture treatment protocol for treating *Herpes zoster* (HZ) pain. The objectives of this study are twofold: One is to present that acupuncture is effective in treating HZ pain; the other is to demonstrate the benefits of acupuncture on immunity as an integral aspect in the treatment of this disease. Literature search and identification of relevant studies were conducted through Internet search using the electronic databases or manual search. All the studies were thoroughly reviewed, and the extracted data was systemically and comparatively organized in order to demonstrate the effectiveness of acupuncture on HZ pain and the benefits of acupuncture on immunity in the treatment approaches. A total of 12 studies selected for the review. 4 RCTs and 1 meta-analysis for HZ pain which all showed acupuncture was an effective means of alleviating HZ pain. When acupuncture

combined with drug therapy had better results than drug only. With respect to acupuncture on immunity, 5 RCTs, 1 pilot study and 1 systematic review which all had a positive impact on the immune system, and expectedly ST 36 was the most chosen acupuncture point in all these studies. Since HZ pain affects the elderly most severely, acupuncture not only relieve pain which may also treat anxiety, depression, fatigue; therefore it is most ideal treatment for this patient population. One major limitation was that all the studies used for this review varied greatly in quality which partly could have affected the outcome of the results. The findings of this review showed acupuncture points LI 4, LI 11, SP 10 and ST 36 are the most effective points for treating HZ pain with the treatment approaches including acupoints for immunity as an integral aspect in the treatment protocol.

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I. INTRODUCTION

I.1. Research Background

Herpes zoster (HZ) or shingles is a viral disease that many people are afraid of because it often results in chronic painful debilitating condition called post-herpetic neuralgia (PHN) even long after the painful blisters have gone away. Pain relief is often unsatisfactory despite combinations of medications [1]. One of the main concerns of drug therapy using opioids for relieving pain is addiction. The use of opioids has become an alarming epidemic today affecting millions of Americans [2]. Moreover, HZ pain is a source of significant morbidity which results in substantial decline in the quality of life [3]. There is a growing need to find an alternative treatment that is safe and effective without relying on the use of opioids for advanced pain. Using acupuncture for alleviating HZ pain would be an alternative method, and it may also treat anxiety, depression, headaches or insomnia associated to the disease [4]. The highest incident of this disease occurs in people who have a weakened immunity most commonly seen in the elderly as well as people with immunosuppressed conditions [5].

I.2. Research Scope and Significances

The scope of this research included standard acupuncture and related modalities such moxibustion, laser acupuncture, electro-acupuncture, pharmaco-acupuncture, certain acupuncture techniques and comparison of drug therapy for herpes zoster pain against standard acupuncture alone or combinations of acupuncture related modalities as described above. The significance of this review was that several studies on HZ pain had

been previously done but the conclusions were inconclusive due to lack of quality and the amount of evidence. However in a recent meta-analysis published in 2017 in the “*Journal of Pain*”, it presented acupuncture was effective for treating variety of chronic pain [15] including PHN. Another review article entitled “*Acupuncture and Immunity*” from PubMed provided evidence that ST 36, which has been widely applied in various immune-related diseases, strengthen the immune system by increasing T cells [6]. Examining the point prescriptions currently used in standard acupuncture books, there was no emphasis with adding immunity points e.g. ST 36, LU 7, LI 11 and KD 27, which were in fact beneficial in the treatment of HZ. Part of the focus of this review was to demonstrate that if these immunity points were added, it may significantly decrease the severity and shorten the duration of HZ pain.

I.3. Research Objectives

This study is a narrative literature review and the objectives of this study are twofold: One is to present that acupuncture is effective in treating HZ pain; the other is to demonstrate the benefits of acupuncture on immunity is an integral aspect in the treatment of this disease.

I.4. Research Outline

The main framework of this study is shown in Figure I-1. Literature search and identification of relevant studies were firstly conducted for data collection. All the selected studies were thoroughly reviewed, and key information was extracted for analysis and integration of data. Finally, data was systemically and comparatively

organized in order to synthesize the effectiveness of acupuncture on HZ pain and treatment approaches.

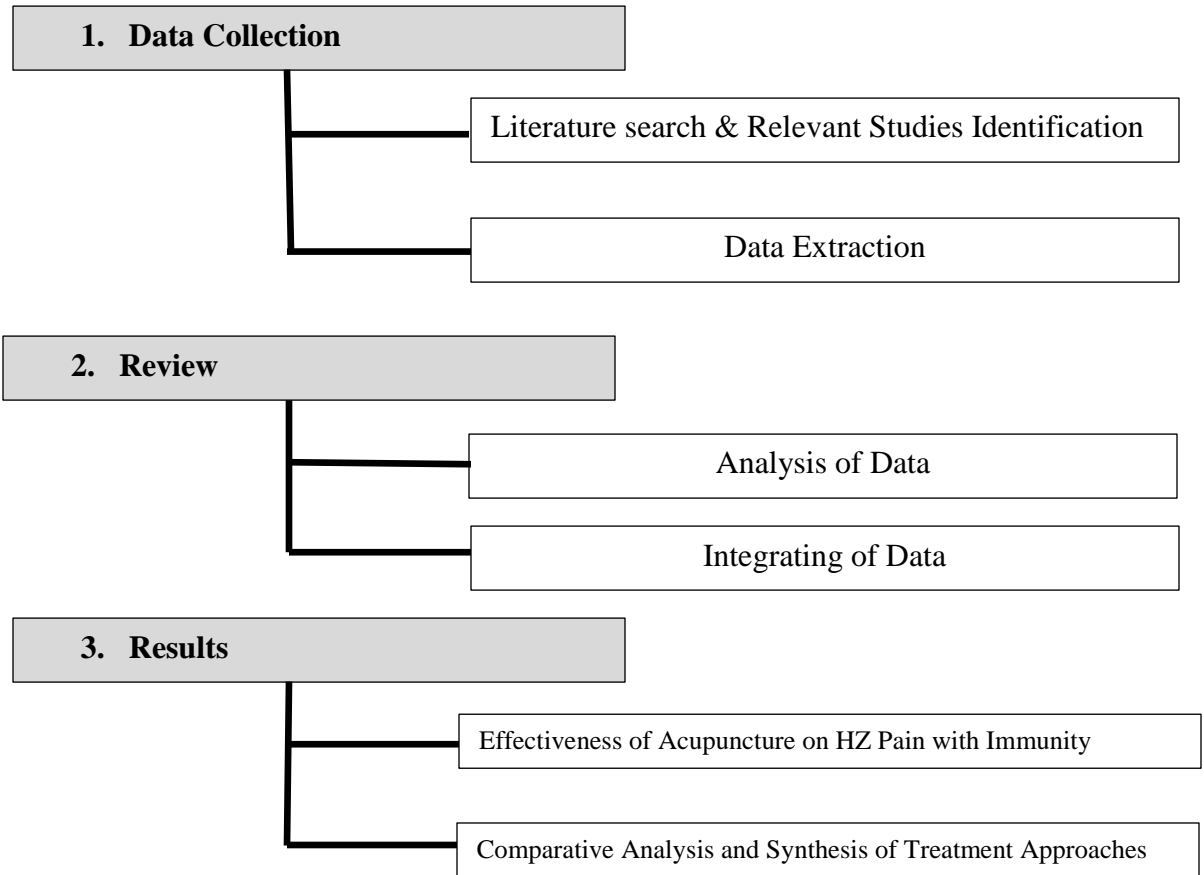


Figure I-1. Research Outline

II. LITERATURE REVIEW

II.1. Pathogenesis and Incidence of *Herpes zoster* Disease

Herpes zoster (HZ) is caused by the herpes varicella-zoster virus (VZV), the same virus that causes chickenpox. According to the Centers for Disease Control and Prevention (CDC), although the HZ vaccine has been proven to be effective in prevention, the incidence of HZ has not been declined and estimated that approximately 30% of Americans will experience herpes zoster in their lifetime [6]. The virus remains dormant within the dorsal root ganglia of the spinal cord and or cranial nerves until it reactivates later in life causing the disease. It can affect any part of the body but areas commonly affected include the chest, back, abdomen and in some cases, even the face or eyes. This disease starts with pain along the distribution of a nerve, dermatome, later develops into a rash which then turn into itchy blisters over the course of several days to weeks. An episode of shingles will normally last for 2 to 4 weeks and the afflicted area is extremely sensitive and painful. But once the rash resolved, as mentioned earlier especially in the older people the pain becomes chronic leading PHN. The diagnosis of herpes zoster and PHN is primarily based on the clinical history and physical examination. However, laboratory tests can be performed to confirm the diagnosis [7].

II.2. Immunity Aspect of *Herpes zoster*

There are 2 main focuses to treat this disease effectively. Besides controlling pain, the other is to address the issue of immunity. As we age our cell-mediated immunity (CMI) declines naturally over time in which the T-cells responsible for controlling the viral replication of the disease are lacking. This phenomenon is called immune senescence which is similar to a weak constitution in TCM theory. And this is the reason why the lack of CMI has been associated with higher risks of developing post-herpetic neuralgia (PHN) which is most commonly seen and more severe in the elderly [8].

II.3. Western Medicine Treatment for HZ Pain

Western medicine treatment of acute herpes zoster mainly involves antiviral and pain relief medications. A comprehensive list of medications can be found in Appendix A, B, and C. Antiviral drugs including Acyclovir, Famciclovir, Valacyclovir, are the first line management of acute HZ and should be initiated within 72 hours in order to reach their optimal effectiveness [9]. In conjunction with antiviral medications, oral corticosteroids such as Prednisone are commonly used to reduce HZ pain [10]. Patients with mild to moderate pain may respond to over-the-counter analgesics such as Tylenol or Advil, tricyclic antidepressant (TCA) such as nortriptyline and anticonvulsives such as Gabapentin or Pregabalin have been used as well. Neurolytic blocks, local anesthetic and intrathecal corticoid-steroid injection are also recommended for advanced HZ pain, but often times patients with more severe pain as seen in PHN require the addition of opioids — Vicodin, Oxycontin, Norco — that can lead to abuse, dependency and addiction [11].

Appendix B has extensive information on drug therapy regarding the management of PHN.

II.4. Acupuncture for Treating HZ Pain

In China, different kinds of acupuncture methods are deployed for treating HZ such as fire needling, electro-acupuncture, surrounding needling, pricking blood and cupping [12]. Traditional Chinese Medicine (TCM) theory for the acupuncture treatment of herpes zoster is mainly categorized into four patterns according to how the disease is presented. They are as follows: **(1) Blazing Fire in the Liver & GB Channel** — use acupoints SJ6, GB34 ; **(2) Damp-Heat in the Spleen Channel** — use acupoints SP9, LV5 ; **(3) Qi and Blood Stagnation** — use acupoints LV3, PC6, UB 40, SP10; **(4) Yin Deficiency and Qi and Blood Deficiency** — use acupoints LV2, KD 7, KD6 [13]. For advanced pain, ashi points, extrapoints HuaTuoJiaJi are inserted corresponding to the vertebrae above and below for each nerve root that is affected as well as scalp acupuncture has been used for pain involving the face and head [14].

III. MATERIALS AND METHODS

III.1. Literature Search

In August 2018, literature selection was performed using the following electronic databases: PubMed, EBSCO Host, the Cochrane Central Register of Controlled Trials, EMBASE, and WHO ICTRP (International Clinical Trials Registry Platform). A comprehensive search of abstract database was carried out using the keyword “acupuncture”, “herpes zoster”, “acupuncture”, and “immunity”. Initially 537 published articles were identified through the databases specified above. Only articles in the period from July 1998 to July 2018 were filtered out, and the record was narrowed down to 187 articles. Then the articles were screened for duplications which were filtered down to 96. After further screening based on the predetermined inclusion and exclusion criteria and for eligibility, 20 full-text articles relevant articles were identified from full-text articles. Finally, a total of 12 free full-text articles that met inclusion criteria were collected for analysis of treatment approaches. Two articles were additional selected by manual search or internet search through the electronic databases stated above to synthesize for this review.

III.2. Inclusion and Exclusion

This study included studies published in the past 20 years that met the following criteria: (1) randomized controlled trials (RCTs) that adopted a double-blind, single blind, or non-blind, (2) not randomized but well-designed clinical trial which have experimental

group and control group, (3) qualitative clinical trial which doesn't have control group, and (4) studies on benefiting on immunity or effectiveness on HZ pain.

Exclusion criteria included (1) non-English language materials, (2) animal study, (3) case studies, and (4) non-scholarly articles such as comments, letters, media reviews, and magazines.

III.3. Data Extraction and Analysis

The following key information was extracted from each study: first author, publication year, and sample size, type of intervention: acupuncture method, type of control, treated acupoints/sites selected, outcome measures, and results reported and summarized into a table. The quality of the selected clinical studies was assessed using the Jadad Scale [16]. Pain intensity was the primary outcome assessed following by secondary outcomes which are global impression, quality of life, and safety. The findings of all the extracted data were comparatively analyzed and synthesized for the review. The literature selection process is illustrated in Figure III-1.

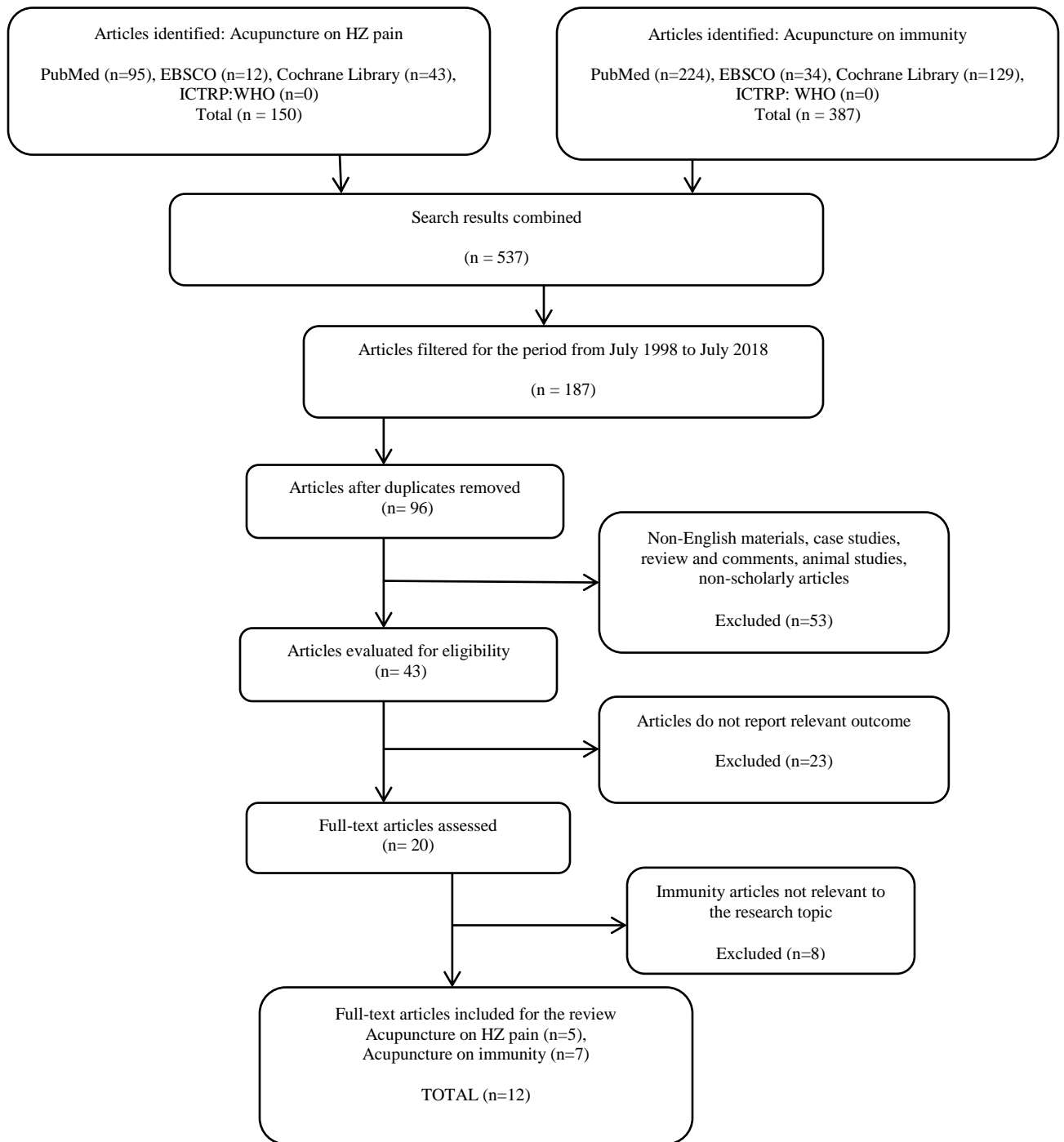


Figure III-1. Flow Chart of Literature Selection for the Review

IV. RESULTS

IV.1. Effectiveness of Acupuncture vs. Drug Therapy on HZ Pain

Acupuncture treatment approaches for HZ pain in the studies were mainly based on indications according to TCM theory. Recent studies [17-21] indicated that acupuncture was an effective means of alleviating HZ pain. When acupuncture combined with drug therapy showed better outcomes than drug therapy only [18]. Similarly in Ursini et al's study, which compared acupuncture with standard drug treatment for chronic HZ pain, concluded that acupuncture provided pain relief equivalent to the standard analgesic therapy. It showed that the effectiveness for both treatment methods were about the same and no statistically significance [20]. Furthermore one study from Coyle et al's review had shown that when patients received both acupuncture plus moxabustion therapy had better results compared to only drug therapy [21]. Almost all of the five studies [18-21] except for the study by Hui et al [17] had shown that patients were best served with an integrated treatment protocol of acupuncture, herbal medicine, and drug therapy. Therefore based on the findings from these studies, it is reasonably to conclude that acupuncture is best practiced when combining with drug therapy.

IV.1.1. Outcome Measures and Assessment

The primary outcome of the studies were measured by pain intensity using pain scale such as visual analogue scale (VAS) or time it takes for pain relief measured by number of days. [17-21]. The secondary outcomes were the assessment on the quality of life and safety as measured by the incidence, severity of the adverse effects. The benefit

of the treatment group was reported in all of the five studies [17-21]. These studies have shown that acupuncture alone or combined with other modalities could reduce pain and discomfort in most patients. Since stress and anxiety are often present among these patients and that these symptoms exacerbate pain, thus acupuncture treatment in addition to the standard drug therapy may serve as a safe adjuvant therapy along with analgesic regimen. The details of the acupuncture intervention and control are summarized. Standard acupuncture with different manual techniques such as the surrounding acupuncture technique and ashi points, laser acupuncture, electro-acupuncture, warm needling with or without moxibustion, and acupoint stimulation with herbs were deployed for the studies. The modalities used for control were placebo, sham acupuncture, delayed treatment and combined therapy of western drug. The treatment duration and follow-up period of each research are also summarized. The details of the acupuncture outcome measures and assessment are summarized in Table IV-1.

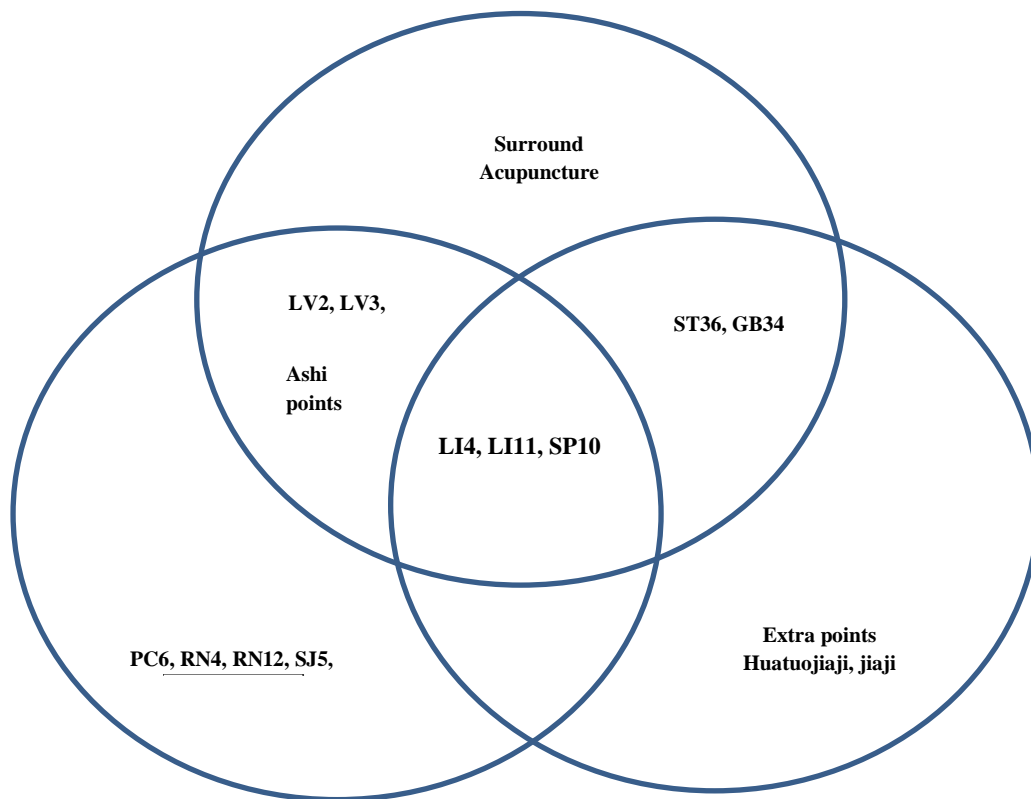
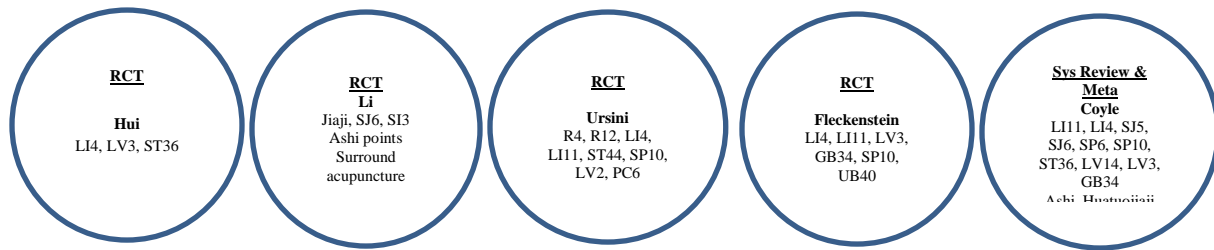
Table IV-1. Summary of Studies Selected and Analyzed: Acupuncture and Related Modalities for *Herpes zoster* Pain

Primary Research: Effectiveness of Acupuncture and related modalities for Herpes zoster Pain									
First Author (year)	Study Design & Origin	Duration of Pain or Intensity	Intervention Group	Control Group	Treatment Duration, Follow-up	Outcome Pain Relief Intensity	Other Outcomes Reported	Adverse Reaction	Acupuncture Points
Hui (2012)	RCT (Toronto, Ontario) Divided into 2 groups 1. Immediate treatment (n=32) 2. Delayed treatment (n=27)	1 month to 15 years, 4.8 months median	• Acupuncture + anesthesia injection + cupping and bleeding + TCM herbs	• Delayed treatment group (received same treatment 3 weeks after)	3, 6, 9 weeks f/u up to 2 years	Before treatment: Ave 7.5/7.8 After treatment: Ave 2.3/2.3 Greatest pain relief within 3 weeks and up to 2 years	• Quality of life assessment improved (social functioning, emotional and mental health) • Depression assessment improved	Pain from anesthesia injection site, mild bleeding from cupping. No significant adverse event from acupuncture	• LI4, LV3, ST36
Li (2012)	RCT (China) n=500 Divided in 5 groups (A, B, C, D, E)	Acute HZ pain 10 days	A. Acupuncture + EA B. Acupuncture + Moxa C. Hot needles puncture D. Tapping + cupping E. Western medicine (antiviral therapy with Valacyclovir)	• E group (Western medicine antiviral therapy with Valacyclovir)	10 days	Ave days pain relief A. 6.63 B. 7.07 C. 6.16 D. 6.21 E. 7.69 Acupuncture modalities alleviated pain faster compared to drug therapy	• Some money saving since treatment groups A, B, C, D alleviated pain one day faster than in group E	Not mentioned	• Ex-B2 (Jiaji), SJ6, SI3 • Surround acupuncture • Ashi points
Ursini (2011)	RCT (Italy) Divided into 2 groups 1. Acupuncture (n=52) 2. Drug therapy (n=50)	HZ pain more than 3 months and pain intensity at presentation VAS>7 (0-10)	• Acupuncture	• Drug therapy (Pregabalin, transdermal buprenorphine or oral oxycodone)	4 weeks and f/u over 1 year	Before treatment: Acupuncture Ave 7.81 Drug therapy Ave 8.02 After treatment: Acupuncture Ave 2.89 Drug therapy Ave 3.89 The effectiveness for both treatments acupuncture and drug therapy were about the same. No significance statistically.	NA	No serious treatment related adverse event was observed in both groups	• RN4, RN12, LI4, LI11, ST44, SP10, LV2, PC6

Fleckenstein (2009)	RCT (Germany) Divided into 3 groups 1. Acupuncture (n=168) 2. Drug therapy Gabapentin (n=84) 3. Sham laser acupuncture (n=84) * No results yet from this study since investigating is ongoing	Acute herpes zoster pain VAS>30mm (0-100)	<ul style="list-style-type: none"> • Acupuncture • Drug therapy (Gabapentin) 	<ul style="list-style-type: none"> • Sham laser acupuncture (Placebo Control) 	6 months, 4 weeks	VAS pain scores Use of acupuncture reported being promising but no enough evidence to recommend acupuncture as standard regimen	<ul style="list-style-type: none"> • Quality of life assessed (Data not yet available as investigation is ongoing) 	<ul style="list-style-type: none"> • Dizziness and sedation are reported from drug therapy Gabapentin use 	<ul style="list-style-type: none"> • LI 4, LI 11, LV 3, GB 34, SP 10, UB 40
Coyle (2017)	Systematic review and meta-analysis (China-Australia) 9 studies from English and Chinese databases from inception to 2016 This review examined the efficacy and safety of the combination of acupuncture with moxibustion in the acute stages of herpes zoster Pain effectiveness were assessed based on 2 parameters (1) pain relief scale and (2) time to resolution of pain	Acute HZ pain 10 days	<ul style="list-style-type: none"> • Acupuncture modalities + Moxa • Acupuncture + drug therapy <p>Acupuncture modalities which include (standard acupuncture, electro-acupuncture, surrounding acupuncture technique)</p>	<ul style="list-style-type: none"> • Drug therapy (Acyclovir, Valacyclovir, gabapentin, prednisone) 	90 days, 10 days, 14 days, 30 days, 60 days	<ul style="list-style-type: none"> • Pain relief acupuncture + moxa > drug therapy (Li, 2011)VAS pain scores at the end of treatment 8.25 lower compared to antiviral drug • Acupuncture + moxa resolution of pain was achieved 6.59 days earlier compared to antiviral drug (Lin & Zhao, 2012) • Pain relief Acupuncture + drug therapy > drug therapy alone (Wang, 2016) 	NA	<ul style="list-style-type: none"> • Mild adverse events were mild and the symptoms were relieved by local pressing or massage (2 cases reported hematoma , 5 cases reported bleeding • 7 studies reported no adverse events 	<ul style="list-style-type: none"> • LI 11, LI 4, SJ 5, SJ 6, SP 6, SP 10, ST 36, LV 14, LV 3, GB 34 • Ashi points • Huatuojiaji • Surrounding acupuncture

IV.1.2. Acupuncture Points Selected for Treatment on HZ Pain

The most commonly acupuncture approach used for treating acute HZ pain was using ashi points and surrounding acupuncture technique. Huatuojiuji points were selected corresponding to the location of the involved dermatomal of HZ pain. However the most common acupoints selected for HZ pain were LI4, LI11 and SP10 [17, 19, 20 and 21], followed by LV2, LV3, ST44, ST36 and GB34. For extensive details please refer to Figure IV-1.



Primarv: LI4, LI11, SP10 **Secundarv:** LV2, LV3, ST44, ST36, GB34 **Tertiarv:** Ashi points, surround acupuncture

Figure IV-1. Acupuncture Points used on *Herpes zoster* Pain

IV.2. Benefits of Acupuncture on the Immune System

The studies have shown that acupuncture has a positive impact on immune function. Acupuncture aids the immune system in fighting infections by increasing white blood cells, red blood cells and platelet count and promotes the synthesis of various kinds of cytokines and antibodies. It is postulated by most researchers that acupuncture has both regulatory and anti-inflammatory effects on the immune system. The study by Yang et al examined the immune effects of acupuncture in patients with allergic asthma found that the total efficacy was 85% improved after one course of treatment, and the number of CD3, CD4, CD8 T lymphocytes in the peripheral blood were significantly increased [24]. And similar results were found in the pilot study using saam acupuncture to treat cancer patients done by Kim et al., which showed that acupuncture not only increased the number of immune cells, but also significantly relieved fatigue in cancer patients [23]. In the study by Yamaguchi et al, they found after acupuncture treatment, the measurement of certain immune cells and various cytokines in the blood were significantly increased. There was a statistically significant increase in the number of CD2+, CD4+, CD8+, CD11b+, CD16+, CD19+, CD56+ cells as well as IL-4, IL-1b and IFN- γ levels in the cells [28]. In Ye Fang et al's study, it found that electro-acupuncture may improve immune function caused by the harm from chemotherapy. In addition, it found that electro-acupuncture can help decrease fatigue, stress and improve sleep and general wellness of cancer patients [27].

IV.2.1. Outcome Measures and Assessment

Outcome measures from the seven studies [22-28] on immunity are based on the samples taken from the blood and tissues of the participants, which are thought to have

anti-inflammatory effects and regulating immune function. In Karatay et al study, anti-inflammatory markers both C-reactive protein (hsCRP) and tumor necrosis factor alpha (TNF-a) were measured. Surprisingly it showed no increase in the intervention group, but it found that hsCRP levels were significantly reduced in the sham acupuncture group [25]. In respect to the effects of acupuncture on immune system, several studies have shown that acupuncture has certain regulating effect on both cellular immunity and humoral immunity [22, 23, 24, 26, and 28]. Acupuncture influences the immune system in the aspects that it can increase the number and activity of natural killer (NK) cells, promote the proliferation of T cells, improve the ratio of CD4 T cells and CD8 T cells, and stimulate the release of inflammatory cytokines in the immune response. The details of the acupuncture intervention and control are summarized. Traditional acupuncture with different manual technique such as Saam acupuncture and electro-acupuncture are deployed for the studies. The modalities used for control were placebo, sham acupuncture and combined therapy of western drug and chemotherapy. The treatment duration and follow-up period of each research are also summarized. Further details are described in Table IV-2.

Table IV-2. Summary of Studies Selected and Analyzed: Effects of Acupuncture and Related Modalities on Immunity

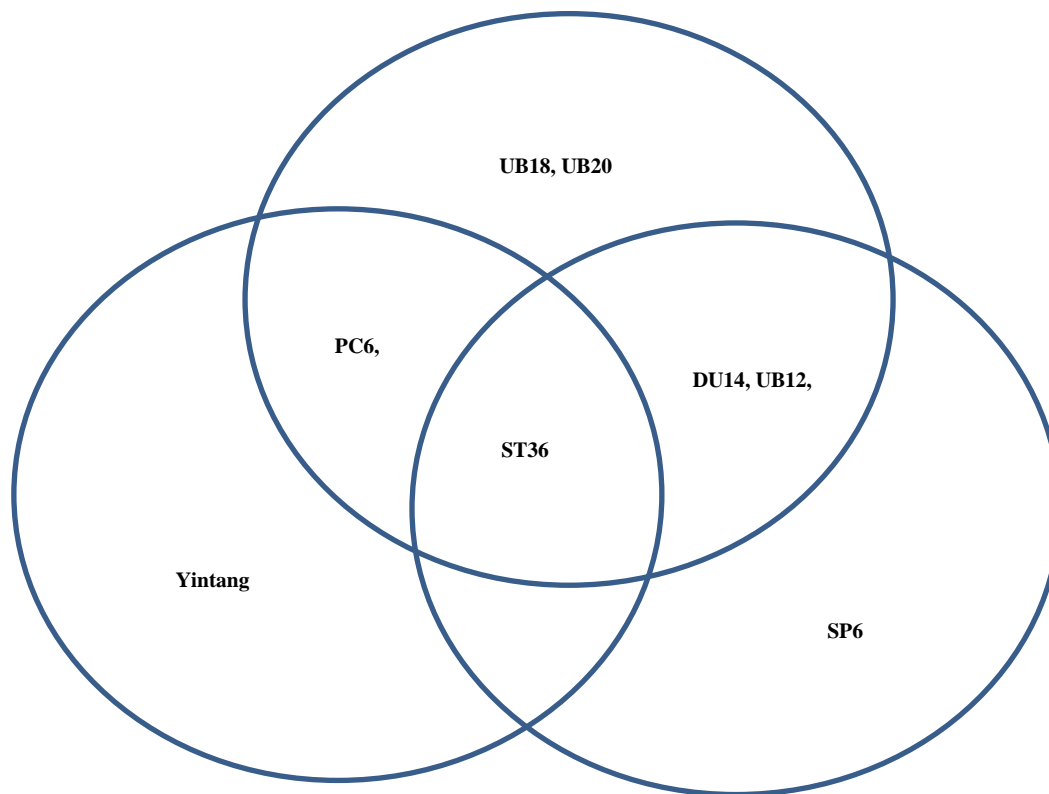
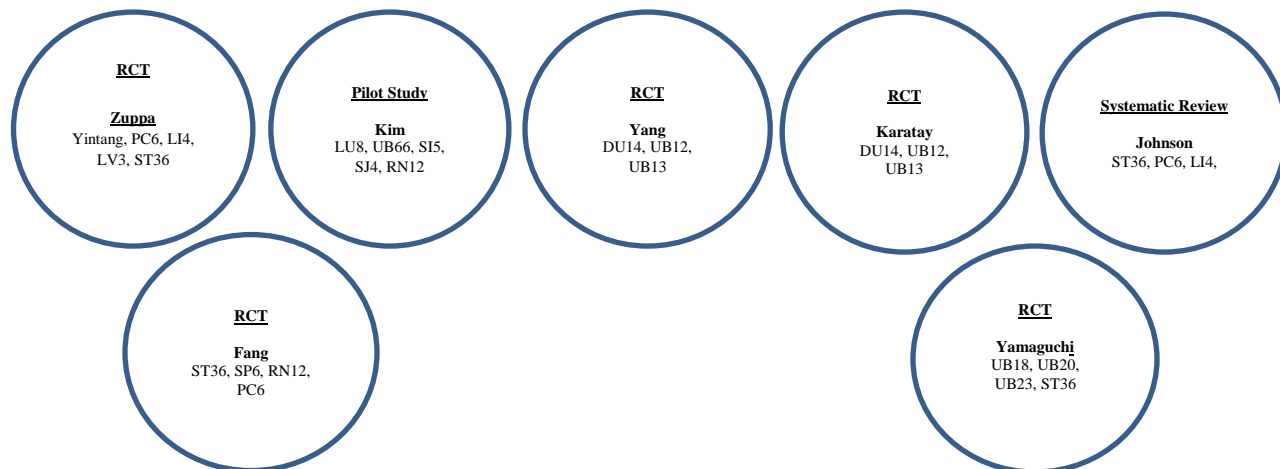
Research: Effects of Acupuncture and related modalities on Immunity							
First Author (year)	Study Design & Origin	Intervention Group	Control Group	Treatment Duration, Follow-up	Outcome Measures	Adverse Reaction	Acupuncture Points
Zuppa (2015)	RCT (Brazil) Examine the effects of acupuncture on sleep quality, psychological stress and immunity function in elderly. Divided into 2 groups 1. Manual acupuncture 2. Sham acupuncture	• Manual Acupuncture (n=24)	• Sham acupuncture (n=24)	• 5 weeks • 2x/wk in a total of 10 sessions	• Scores for sleep quality, stress, and depression statistically significant $p < 0.01$ • Blood immune cells measurement before and after treatment statistically no difference	Not mentioned	Yintang, PC 6, LI 4, LV 3, ST 36
Kim (2014)	Pilot Study (South Korea) Examine the effects of Saam acupuncture on immune cell numbers in cancer patients n= 10	• Saam acupuncture	• Non-controlled	• 2 weeks 4 sessions	• Increase T-cells statistically significant CD3+ $p = 0.023$, CD8+ cells $p < 0.001$, • Decrease fatigue after acupuncture	Not mentioned	LU 8, UB 66, SI 5, SJ 4, RN 12
Yang (2013)	RCT (China) Examines the clinical and immune effects of acupuncture in the treatment of patients with allergic asthma	• Standard acupuncture	• Placebo-controlled	• 5 weeks • 3 times per week	• After treatment, numbers of eosinophils were significantly decreased ($p < 0.01$) • The numbers of CD3, CD4, CD8 T lymphocytes were significantly increased. ($p < 0.001$, $p < 0.01$, and $p < 0.001$,	Not mentioned	DU 14, UB 12, UB 13

					respectively) • The concentration of cortisol did not change significantly		
Karatay (2011)	RCT (Turkey) Investigate the effect of immune-related acupuncture points on serum Tumor Necrosis Factor (TNF) and C-reactive protein (CRP) levels Divided into 5 groups 1. Manual acupuncture 2. Sham acupuncture	• Acupuncture DU14 (n=18) • Acupuncture LI 11 (n=16) • Acupuncture ST 36 (n=18) • Acupuncture SP 6 (n=17)	• Sham acupuncture (n=17)	• 2 weeks	• No significant difference between acupuncture and sham groups in terms of TNF and CRP values (p > 0.05)	Not mentioned	DU 14, LI 11, ST 36, SP 6
Johnson (2011)	Systematic Review (USA) Reviews evidence that acupuncture is associated with increases in NK cell quantity and function in both animals and humans Examined various studies design and outcomes	• Acupuncture and or electro-acupuncture	• Placebo control • Non-placebo control group	Varies	• Limited published studies provide suggestive evidence that acupuncture induces an increase of NK cells activity both in animals and humans	Not mentioned	ST 36, PC 6, LI 4
Ye Fang (2007)	RCT (China) To observe the effects of Electroacupuncture on T cells, NK cell activity,	• Electro-acupuncture + chemotherapy (n=48/21)	• Chemotherapy + leukopenic drugs given no acupuncture (n=49/20)	• 4 weeks • Electroacupuncture daily for 30 minutes	• Patients undergoing chemotherapy combined with EA showed higher leukocyte count than that of the control group statistically significant p < 0.01	Not mentioned	ST36, SP62, PC 6

	humoral activity and leukocyte count in patients undergoing chemotherapy 2 groups 1. Comparison of T cells and NK activity 2. Comparison of humoral immunity				<ul style="list-style-type: none"> • Electro-acupuncture may improve the patient's appetite and sleep, reduce the tumor pain and alleviate the gastrointestinal reactions caused by chemotherapy 		
Yamaguchi (2007)	RCT (Japan) Examine effects of acupuncture by measuring immunity cells counts on healthy adults Healthy adults n= 17 Male = 2 Female = 15	• Standard Acupuncture	• Placebo-controlled	• Blood drawn for analysis 1 hr before acupuncture treatment, 1,2 and 8 days thereafter and various WBCs counts were recorded	<ul style="list-style-type: none"> • Data are expressed as means +- SD and results statistically significant P value <0.05. • There's evidence to suggest acupuncture increases leukocyte counts and cytokine levels • Benefits of acupuncture lasted for 30 days after treatment 	Not mentioned	UB 18, UB 20, UB 23, ST 36

IV.2.2. Acupuncture Points Selected for Treatment on Immunity

The selection of acupoints has not been very unanimous according to the authors' clinical experience and TCM theory they applied. Some studies used a few acupoints [24, 26 and 27] while some used more than 5 acupoints [22, 23 and 28]. However ST 36 has been the most frequently used acupoint and was selected in almost every study, followed by DU 14, UB 12, UB 13, PC 6, LI4, and Yintang, SP 6, UB 18, UB 20 so forth. For extensive details refer to Figure IV-2.



Primary: ST36 **Secondary:** DU14,UB12, UB13, PC6, LI4 **Tertiary:** Yintang, SP6, UB18, UB20

Figure IV-2. Acupuncture Points used For Immunity

IV.3. Adverse Events of Acupuncture on HZ Pain and Immunity

All the studies concluded that acupuncture was safe with minimal to no adverse events for both HZ pain and immunity [18-29]. In the clinical study by Hui et al, only mild bleeding from cupping reported which was not directly related to acupuncture but to its modalities [18]. In the systematic review and meta-analysis by Coyle et al, two cases of hematoma and five cases of bleeding were reported in the intervention group of one study, which were mild and was relieved by local pressing or massage [22]. No mentioning of any adverse events for acupuncture treatments on immunity.

V. DISCUSSION

V.1. Acupuncture Combining with Immunity on Treating HZ Pain

The concept of combining immunity with acupuncture on treating HZ pain in the treatment approaches has been explored in this literature review. The studies presented in this review showed that acupuncture could reduce pain and discomfort for both acute and chronic HZ pain. The results in this review revealed that there was no single treatment both in acupuncture or drug therapy to be completely effective for all those suffering from HZ pain. Current clinical research has shown that antiviral drug combined with an analgesic is the better treatment over acupuncture for alleviating acute HZ pain, and it should be started within 72 hours of onset for the best result [30]. However in clinical practice the combinations of acupuncture and analgesic drugs might be the best means to achieve maximum benefits on alleviating HZ pain. Even as the use of acupuncture has been reported being promising in some of these studies, however there was not enough evidence to recommend acupuncture as standard regimen in the United States. Nevertheless, acupuncture does offer one major advantage over western drug therapy for which virtually has no harmful side-effects compared to medications.

V.2. Concerning Benefits of Acupuncture on Immunity

In this review there were scientific evidences suggesting that acupuncture may have a positive impact on the immune function. Numerous studies in this review had shown that acupuncture has both regulatory and anti-inflammatory effects on the immune system. It demonstrated that acupuncture on one hand has certain regulating effect on immunity mainly by promoting the proliferation of certain immune cells, and on the other

hand it had anti-inflammatory effects, activating inflammatory cytokines which aided in fighting infections. Interestingly when acupuncture combined with related modalities such as electro-acupuncture in Ye F et al's study, it showed that electro-acupuncture not only improved immune function but also alleviated some of the side-effects in cancer patients undergoing chemotherapy [27]. Similarly in the study by Kim et al, it showed that acupuncture may increase immune cells count as well as relieve fatigue in cancer patients [23]. This review also found that in almost all the studies concerning immunity, ST 36 was the most chosen acupoint followed by DU 14, UB 12, UB 13, PC 6 and LI 4. According to TCM theory, ST 36 was selected by most authors in the study of immunity because it is the most important point to tonify qi and blood; therefore ST 36 was widely recognized to strengthen the immunity. In treating older patients with PHN, it would be beneficial to include ST 36 in conjunction with LI 4, LI 11, SP 10, the most commonly used acupoints for HZ pain. Along with the reduction in pain, there would be also improvement in physical and mental health by relieving fatigue, improving appetite and sleep. Therefore the use of acupuncture treatment for older patients with PHN would be more suitable. Based on these reasons, acupuncture may be best served for this patient population.

V.3. Strength and Limitations of this Review

The strength of this review is that all the studies collected are the most current, and the findings are also the most recent. However, one major limitation is the concern with the reliability of the data collected in these studies because all the studies used for this review varies greatly in quality. It should be noted that all the clinical trials in these studies were conducted outside of the United States, which partly could have affected the

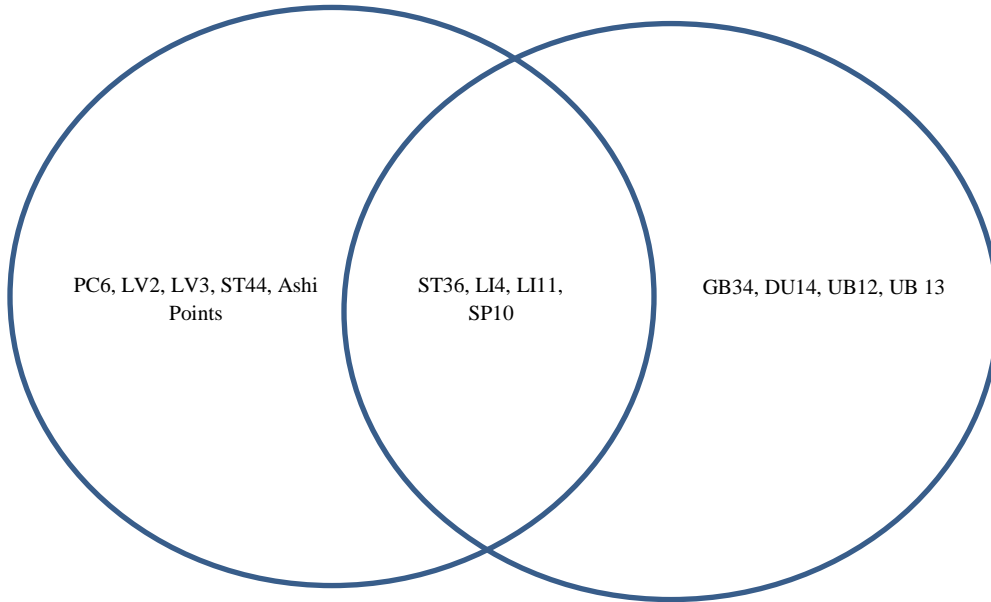
quality of their results. As mentioned in the systematic review and meta-analysis by Coyle et al, many of the studies had methodological flaws which limited the interpretation of the results. There was a lack of detail about the randomization process, blinding and outcome assessment [22]. In the study by Fleckenstein et al, the data is incomplete because the investigation is still ongoing. Another example in Zuppa et al's study, its main weakness was the relatively small sample size, which consisted of only 48 participants for both the intervention and control groups [23]. In Li et al's study, their secondary outcome in calculating the cost effectiveness comparing acupuncture versus drug therapy was not reasonable because the study was done in China and the prices for acupuncture treatment and drug therapy were different from that of United States [19]. Since this is a narrative review so there is no statistical analysis and the findings are purely descriptive without statistic values such as confidence interval (CI), weighted mean difference (WMD), standardized mean difference (SMD), standard deviation (SD) or relative risk (RR). Special acu punctures such as auricular acupuncture and scalp acupuncture are not mentioned in this review simply because these special acu punctures are not found in the clinical trials for this review topic. Further in-depths clinical studies of higher quality on this subject matter are needed to be conducted here in the United States.

VI. CONCLUSION

Through a comprehensive study on the literature review, this research not only has provided the fundamental understanding of the disease process of *Herpes zoster*, but also has showed that acupuncture treatment is effective for treating HZ pain along with the benefits in strengthening the immune system. Despite some limitations on the qualities of the data, this review also revealed treating HZ pain with acupuncture is comparable to drug therapy. The findings in this review have shown that the best acupuncture points for treating HZ pain are LI 4, LI 11 and SP 10, and the most significant points for immunity is ST 36. The treatment approaches using acupuncture points LI 4, LI 11, SP 10 and ST 36 are best served for treating PHN in the elderly. See Figure VI-1. The treatment approaches presented in the review hopefully would be accepted into the mainstream America.

Acute Phase

Chronic Phase



Common Points: ST36, LI4, LI11, SP10 **Acute Phase:** add PC6, LV2, LV3, ST44 **Chronic Phase:** add GB34, DU14, UB12, UB13

Figure VI-1. Conclusion: Acupuncture Points for Treating *Herpes zoster* Pain with Immunity

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APPENDIX

Appendix A: Antiviral Therapy for *Herpes zoster*

Medication	Typical Dosing	Side Effects
Acyclovir (Zovirax)	800 mg 5x/day, 7-10 days	Malaise
Famciclovir (Famvir)	500 mg 3x/day, 7 days	Headache, nausea
Valcyclovir (Valtrex)	1000 mg 3x/day, 7 day	Headache, nausea

Source: Shingles: a complete guide for clinicians. *Clinical Advisor*. January 2017.

Appendix B: Medication Therapy in the Pain Management of Postherpetic Neuralgia

Medication	Dose	Dose Adjustment	Maximum Dose	Side Effects
Opioid and nonopioid analgesics				
Oxycodone	5 mg every 4 hr as needed	Increase by 5 mg four times daily every 2 days as tolerated	None specified, but should not exceed 120mg daily except in consultation with a pain specialist	Drowsiness, dizziness, constipation, nausea, vomiting
Tramadol	50 mg once or twice daily	Increase by 50-100 mg daily in divided doses every 2 days as tolerated	400 mg daily; 300 mg daily if patient is > 75 years of age	Drowsiness, dizziness, constipation, nausea, vomiting
Glucocorticoid steroids				
Prednisone	60 mg daily for 7 days, then decrease to 30 mg daily for 7 days, then decrease to 15 mg daily for 7 days	none	60 mg daily	Gastrointestinal distress, nausea, vomiting, mood changes, edema, glucose intolerance, increased blood pressure
Anticonvulsants				
Gabapentin	300 mg at bedtime or 100-300 mg three times daily	Increase by 100-300 mg three times daily every 2 days as tolerated	3600 mg daily	Drowsiness, dizziness, ataxia, peripheral edema
Pregabalin	75 mg at bedtime or 75 mg twice daily	Increase by 75 mg twice daily every 3 days as tolerated	600 mg daily	Drowsiness, dizziness, ataxia, peripheral edema
Tricyclic antidepressants				
Nortriptyline	25 mg at bedtime	Increase by 25 mg daily every 2-3 days as tolerated	150 mg daily	Drowsiness, dry mouth, blurred vision, weight gain, urinary retention
Topical therapy				
Lidocaine patch (5%)	One patch, applied to intact skin only, for up to 12 hr per day	None	One patch for up to 12 hr per day	Local irritation; if systemic, absorption can cause drowsiness, dizziness

Source: Postherpetic Neuralgia. Seniors at Risk. *Geriatrics*. May 2011. [29]

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Appendix C: Drugs Therapy Treatment Options and Recommendations for *Herpes zoster*

Treatment Options	Recommendations	Limitations
Oral antiviral agents	Herpes zoster rash	Use within 72 h of rash onset
Intravenous acyclovir	<ul style="list-style-type: none"> ▪ Central nervous system ▪ Immunosuppressed 	May use after 72 h in immunosuppressed patients
Oral corticosteroids	Mild to moderate pain	May not be effective and use with caution in patients who have comorbid conditions
Aspirin, nonsteroidal anti-inflammatory drugs, antihistamines, calamine, silver sulfadiazine	Minor pain or itching	May not provide adequate pain relief
Opioids and opioid-like drugs	Moderate to severe pain	<ul style="list-style-type: none"> ▪ High potential for adverse effects ▪ Some potential for addiction

Source: Managing Herpes Zoster and Postherpetic Neuralgia. *Journal of the American Osteopathic Association*. June 2018. [30]

Appendix D: Details of the Articles used for this Narrative Review

Primary Research: Effectiveness of Acupuncture and related modalities for <i>Herpes zoster</i> Pain				
1st Author	Year	Title	Study Type & Origin	Jadad Score
Hui	2012	A randomized controlled trial of a multifaceted integrated complementary-alternative therapy for chronic herpes zoster-related pain	RCT (Canada)	3
Li	2012	Economic evaluation of treating herpes zoster with various methods of acupuncture and moxibustion	RCT (China)	2
Fleckenstein	2009	Acupuncture in acute herpes zoster pain therapy (ACUZoster)-design and protocol of a randomized controlled trial	RCT (Germany)	4
Ursini	2011	Acupuncture for the treatment of severe acute pain in herpes zoster: results of a nested, open-label, randomized trial in the VZV Pain Study	RCT (Italy)	3
Coyle	2017	Acupuncture plus moxibustion for herpes zoster: A systemic review and meta-analysis of randomized controlled trials	Systematic Review and Meta-Analysis (China & Australia)	NA
Research: Benefits of Acupuncture and related modalities on Immunity				
1st Author	Year	Title	Study Type & Origin	Jadad Score
Zuppa	2015	Acupuncture for sleep quality, BDNF levels and immunosenescence: A randomized controlled study	RCT (Brazil)	2
Kim	2014	Efficacy of Saam acupuncture treatment on improvement of immune cell numbers in cancer patients: a pilot study	Pilot Study (S. Korea)	1
Yang	2013	Considerations for use of acupuncture as supplemental therapy for patients with allergic asthma	RCT (China)	2
Karatay	2011	Effects of some acupoints (Du-14, LI-11, ST-36 and SP-6) on Serum TNP and hsCRP levels in Healthy Young Subjects	RCT (Turkey)	2
Johnston	2011	Acupuncture May Stimulate Anticancer Immunity via Activation of Natural Killer Cells	Systematic Review (USA)	NA
Ye Fang	2014	Effects of electro-acupuncture on T cell subpopulations, NK Activity, humoral immunity and leukocyte count	RCT (China)	2
Yamaguchi	2007	Acupuncture regulates leukocyte subpopulations in human peripheral blood	RCT (Japan)	2