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Original Article

Early application of salvia miltiorrhiza at huatuojiaji points reduces incidence of post-herpetic neuralgia

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Abstract: Objective: This study aimed to investigate whether injection of salvia miltiorrhiza at huatuojiaji points in treating acute herpes zoster would reduce the intensity and duration of pain and incidence of post-herpetic neuralgia (PHN). Methods: A total of 104 patients, over 50 years old, were randomized to receive either saline (Arm 1) or salvia miltiorrhiza (Arm 2) injections at huatuojiaji points in addition to standard treatment. Visual analogue scale and total amount of analgesics (gabapentin and tramadol) were recorded during the initial visit, 1st, 3rd and 6th week after injection and 3rd and 6th month after rash onset, respectively. In the 3rd and 6th months after onset, PHN was assessed using Douleur Neuropathique 4 Questions. Patient satisfaction was evaluated using Medical Outcomes Study Questionnaire Short-Form 36. Results: Compared with Arm 1, Arm 2 had much lower scores of visual analogue scale at all follow up time points (P<0.001) and less incidence of PHN, after 3 and 6 months (both P<0.05). Additionally, there was a significant reduction in doses of gabapentin and tramadol in Arm 2 beginning the third week (P<0.001). Improvement experienced in Arm 2 was greater than in Arm 1, after 3 and 6 months (P<0.05). No serious adverse effects were reported during the study. Conclusion: Injection of salvia miltiorrhiza at huatuojiaji points can reduce incidence of PHN, decrease the intensity of pain, and shorten pain duration.

Keywords: Huatuojiaji points, salvia miltiorrhiza, herpes zoster, post-herpetic neuralgia, prevention

Introduction

Acute herpes zoster (AHZ) is a disease characterized by a painful skin rash with blisters in a dermatomal distribution, usually occurring when the latent varicella zoster virus within the dorsal root or cranial nerve ganglia is reactivated. The most common complication of AHZ is post-herpetic neuralgia (PHN), defined as pain persisting for over 3 months after rash onset [1, 2]. Incidence rate of PHN is about 20%-35% in individuals over 50 years old. PHN can severely affect quality of life (QoL). Unceasing pain can bring about serious physical, occupational, psychosocial, and social disabilities. Because of long-term suffering and limited efficacy of current medications, patients can develop drug dependency, sleep disturbance, hopelessness, depression, and even commit suicide [3, 4]. Families and the society are also affected by the financial burden due to medical costs and lost productivity.

Although PHN is a condition that has been known for decades, prevention of its development remains a challenge. Some studies have indicated that early intervention is crucial to reduce incidence of PHN [5, 6]. However, there have been no disease-modifying therapies available in this area. According to traditional Chinese medicine (TCM), causes of PHN include incomplete clearing of heat and dampness in the liver and spleen meridians, stagnation of qi and toxic pathogens, accumulation of yin, internal heat, and obstruction of meridians [7]. Acupuncture works by regulating qi and blood movement to dispel wind, clear heat, and dry dampness [8, 9]. A number of acupuncture points, including huatuojiaji points, have been used in the treatment of PHN [7, 10]. Salvia miltiorrhiza is a Chinese medicinal herb with various pharmacological properties for improving circulation and relieving stasis [11]. Lin et al. reported that short-term supplementation of salvia miltiorrhiza (250 mg per day for 7 days,

by oral administration) can relieve delayed onset muscle pain induced by acute downhill running exercise [12]. The authors believed that salvia miltiorrhiza supplementation could reduce systemic inflammation induced by eccentric exercise, thus, resulting in fast recovery from muscle injury. Persistent inflammation of peripheral nerves is associated with development of PHN [13]. However, there have been no studies on whether early application of salvia miltiorrhiza at huatuojiaji points can prevent PHN. Therefore, in this study, a randomized, double-blinded, and controlled trial was designed to evaluate the efficacy of early injection of salvia miltiorrhiza at huatuojiaji points in reducing acute pain and incidence of PHN.

Materials and methods

Participants

The study was approved by the Ethics Committee of Ruijin Hospital Luwan Branch, Shanghai Jiao Tong University School of Medicine. All cases were conducted in the same institute. A total of 104 adult patients, with pain associated with herpes zoster (HZ), were recruited from the Pain Clinic.

Inclusion criteria: (1) Patients had a herpetic eruption for less than one week; (2) Patients had a visual analog scale (VAS) score over 3; (3) Patients aged over 50 years; and (4) Patients had no other treatment except for appropriate antiviral therapy.

Exclusion criteria: (1) Rashes localized on face and head; (2) Eruption lasting for more than one week; (3) Infection at the site of injection; (4) Patients had a history of renal or hepatic disease, coagulopathy, diabetes, and malignancies; (5) Patients had immune dysfunction; and (6) Patients allergic to salvia miltiorrhiza.

Methods

During the first visit, medical histories were checked and clinical examinations conducted. Afterward, the study procedure (injections and follow up) was explained to patients and written informed consent was obtained.

Patients were assigned to different groups using computer-generated random numbers. Patients in Arm 1 received injection of saline as placebo at juatuojiaji points, while patients in Arm 2 received injection of salvia miltiorrhiza (manufacturer: Zhengda Qingchunbao Pharmaceutical Co. Ltd, State Food and Drug Administration Approval No. Z33020177) at huatuojiaji points. Syringes containing solutions of salvia miltiorrhiza or saline were prepared by a pain physician that did not participate in the study or data collection.

Huatuojiaji points are located half an inch (1.3 cm) away from the lower spinous process of spine at the vertebral level. Appropriate points must be selected corresponding to the location of the involved dermatome of HZ (plus 1-2 dermatomes above and below the vertebral level of lesion) [7, 14]. A No. 7 puncture tip was used to pierce the skin, vertically, until the needle reached lamina. Salvia miltiorrhiza (4 mL) was diluted to 20 mL with normal saline solution. A volume of 1-3 mL was injected at each point, while the total amount was no more than 20 mL. Treatment started from their first visit and was performed once every 7 days for 3 weeks.

All patients received 1,000 mg valacyclovir, three times a day, for 7 days (initially within 72 hours of onset of symptoms) and 300 mg gabapentin three times a day, later gradually increased to a maximum of 1,800 mg/day. Tramadol was available as needed. If a patient reported mild pain (VAS $\leq$ 3), the amount of gabapentin could be reduced every other day on the condition that pain scores remained less than 3 with each reduction.

Outcome measures

Main outcome measures were as follows: (1) VAS: VAS was used for evaluating severity of zoster associated pain. Scores were on a scale of 0-10: a score of 10 represented most severe pain, whereas 0 represented no pain; a score of 3 or less was defined as mild pain; a score of 4 to 6 was defined as moderate pain; and a score of 7 and higher was defined as severe pain. VAS evaluations were conducted at initial visit (basal), the 1st, 3rd and 6th week after injection, and 3rd and 6th month after rash onset (approximately at 8-10 AM each day); (2) Percentage of patients with neuropathic pain (incidence of PHN): Douleur Neuropathique in 4 Questions (DN4 questionnaire) served as a useful tool for diagnosing neuropathic pain [15-17]. The scale contained ten items. A “yes” response was scored as 1. The questionnaire was made up of

Table 1. Subscales in medical outcomes Study Questionnaire Short-Form 36

Subscale	Description
Physical functioning	Ten items measuring limitations in performance of various physical activities, ranging from vigorous activities to simple self-care functions
Role physical	Four items which measure functionality in work and other daily activities as a result of physical health
Bodily pain	Two items which measure degree of pain and pain-related functional limitations
General health	Five items which measure an individual's appraisal of their overall health
Vitality	Four items which measure energy level
Social functioning	Two items which measure functionality in work and other daily activities as a result of emotional health
Role emotional	Three items measuring functionality in work and other daily activities as a result of emotional health
Mental health	Five items which measure the presence and degree of depression and anxiety

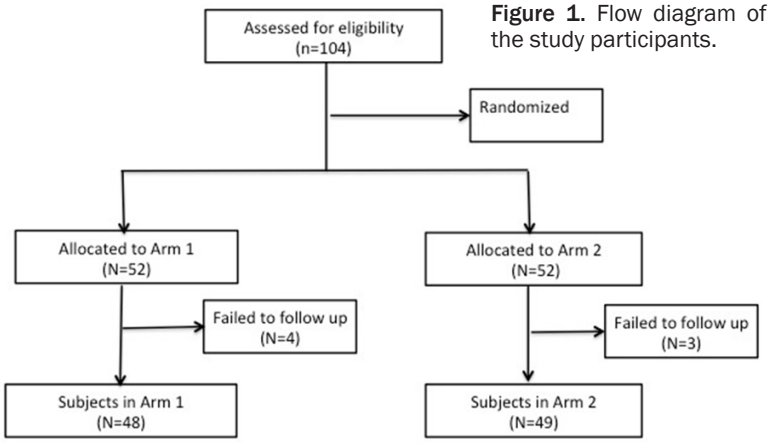

Figure 1. Flow diagram of the study participants.

Table 2. Clinical characteristics of patients

	Arm 1 (n=48)	Arm 2 (n=49)
Age (year, mean ± SE)	63±2.45	66±1.57
Sex (male/female)	22/26	24/25
Duration of pain after rash onset (day; mean ± SE)	3.3±0.25	3.5±0.23
VAS (min, mean ± SE)	7.3±0.11	7.6±0.14
Area		
Cervical region	5 (10%)	6 (12%)
Thoracic region	17 (35%)	15 (31%)
Lumbar region	26 (55%)	28 (57%)

Note: VAS, visual analog scale; Arm 1: injection of saline at huatuojiaji points; Arm 2: injection of salvia miltiorrhiza at huatuojiaji points.

descriptors (seven items) and signs related to sensory test (three items). A score over 4 suggested an existence of neuropathic pain [18]. Evaluations using DN4 questionnaire were performed during initial visit (basal) and 3rd and 6th month after rash onset.

Secondary outcome measures were as follows: (1) Total dosage of medication: at each assessment visit, the amount of analgesia on-request and amount of gabapentin used were recorded; (2) QoL: Medical Outcomes Study Questionnaire Short-Form 36 (SF-36), a 36-item self-report survey containing eight sections, was used to assess the QoL. The system included the following items: physical functioning (PF: 10 items), role physical (RP: 4 items), general health (GH: 5 items), mental health (MH, 5 items), vitality (VT, 4 items), role emotional (RE, 3 items), bodily pain (BP; 2 items) and social functioning (SF, 2 items). Scores for the 8 scales ranged from 0 (worst QoL) to 100 (best QoL) [19]. Remaining categories were associated with experience of change in general health in the past few years. SF-36 scores were assessed prior to the treatment and in the 3rd and 6th month after rash onset (**Table 1**); (3) Side effects: any reported adverse event would be recorded, including time of onset, type of event, duration, and severity.

Statistical analysis

According to a study by Lapolla et al., sample size was determined based on the assumption that expected incidence of PHN in patients above 50 years old in the control group was 20% [20]. With an aim of lowering incidence to 5%, a sample size of 47 was calculated to detect an incidence reduction of 15% with 92% power and significance level of 0.05.

Table 3. VAS before and after treatment in the two groups (mean ± SE)

Time	VAS		t, P	Group effect	Time effect	Group * time interaction
	Arm 1	Arm 2		F, P	F, P	F, P
Basal	7.3±0.10	7.6±0.13	1.824, 0.071	10.22, 0.002**	2.96, 0.012***	2.05, 0.071
1st week	4.5±0.17	3.1±0.10	7.134, <0.001*			
3rd week	3.6±0.17	2.3±0.10	6.624, <0.001*			
6th week	2.3±0.16	0.3±0.10	10.658, <0.001*			
3rd month	1.3±0.13	0.15±0.07	6.994, <0.001*			
6th month	1.1±0.10	0.08±0.01	10.254, <0.001*			

Note: VAS, visual analog scale; Arm 1: injection of saline at huatuojiaji points; Arm 2: injection of salvia miltiorrhiza at huatuojiaji points; *P<0.0083, **P<0.01, ***P<0.05.

Table 4. Incidence of PHN at various time points

	3 months	6 months
Arm 1 (48)	10/48 (20.83%)	7/48 (14.58%)
Arm 2 (49)	3/49 (6.12%)*	1/49 (2.04%)*

Note: PHN, post-herpetic neuralgia; Arm 1: injection of saline at huatuojiaji points; Arm 2: injection of salvia miltiorrhiza at huatuojiaji points; *P<0.05 vs. Arm 1.

Allowing for 10% loss to follow up, 104 patients were included. Quantitative data are expressed as mean ± standard error and categorical data as percentages. For demographic data, Student's t-test was used to compare quantitative variables, while Fisher's exact test and Chi-square test were used for categorical variables. Repeated measures analysis of variance (ANOVA) was conducted for analyzing inter-groups (Arm 1 vs. Arm 2) effects, intra-groups (different time points) effects, and interaction (group * time) effects related to VAS score, dose of tramadol, dose of gabapentin on-request, and SF-36 score. Inter-group differences, at each time point, were examined by t-test with Bonferroni's correction (two-sided alpha level of 0.05/number of time point). A two-sided alpha level of 0.05 was considered statistically significant, except for Bonferroni's t-test. Statistical analysis was performed by SPSS version 16 (SPSS Inc., Chicago, IL) [14].

Results

A total of 104 adult patients, above 50 years old, were randomly assigned into two groups (with 52 in each). Four patients in Arm 1 and three patients in Arm 2 were excluded from the study because they were unavailable for follow up (**Figure 1**). Baseline demographic characteristics were similar between the two groups (**Table 2**).

Comparison of VAS scores between the two groups at basal, 1st, 3rd, 6th week, and 3rd and 6th month after treatment are shown in **Table 3**. There were no significant intergroup differences in VAS scores at basal. Results of repeated measures ANOVA showed that VAS scores decreased in both groups during the study period (time effect, P=0.012) and significant differences in VAS existed between the two groups (P=0.002). Besides, VAS scores at each time point after treatment in Arm 2 were much lower than those in Arm 1 (all P<0.001). No significant effects of group-time interaction were observed (P=0.071).

Incidence of PHN was lower in Arm 2 than in Arm 1, after 3 months (6.12% vs. 20.3%, P< 0.05) and 6 months (2.04% vs. 14.58%, P< 0.05). See **Table 4**.

By performing the same analytical procedure, it was found that use of gabapentin and tramadol decreased significantly in both groups (all P< 0.001), while reduction in the doses of these two drugs in Arm 2 were even greater compared with those in Arm 1 after the third week (all P<0.001). See **Tables 5** and **6**.

It can be seen in **Figure 2** that Arm 2 experienced more improvement than Arm 1 in terms of SF-36 index scores in the 3rd and 6th month after treatment (all P<0.017).

No serious adverse effects were reported during the study period. Drowsiness occurred in 5 patients in Arm 1 and 6 patients in Arm 2, in the first week. However, this symptom was much improved during the second week. No patients required any additional treatment.

Discussion

Results of the present study demonstrated that injection of salvia miltiorrhiza at huatuojiaji

Table 5. Gabapentin dosage (mg/week) in the two groups (mean ± SE)

Time	Gabapentin dosage		t, P	Group effect	Time effect	Group * time interaction
	Arm 1	Arm 2		F, P	F, P	F, P
1st week	5431±201	5249±217	0.612, 0.542	10.78, 0.001*	3.49, 0.008*	2.35, 0.054
3rd week	3645±178	1960±41*	9.494, <0.001*			
6th week	2310±93	907±76*	11.63, <0.001*			
3rd month	1960±41	392±68*	19.60, <0.001*			
6th month	945±55	56±21*	17.87, <0.001*			

Note: Arm 1: injection of saline at huatuojiaji points; Arm 2: injection of salvia miltiorrhiza at huatuojiaji points; *P<0.01.

Table 6. Tramadol dosage (mg/week) in the two groups (mean ± SE)

Time	Tramadol dosage		t, P	Group effect	Time effect	Group * time interaction
	Arm 1	Arm 2		F, P	F, P	F, P
1st week	875±45	840±41	0.575, 0.567	11.13, 0.001*	3.71, 0.006*	2.37, 0.052
3rd week	210±47	18±11	4.010, <0.001*			
6th week	175±45	11±4	3.665, <0.001*			
3rd month	52±12	5±2	3.907, <0.001*			
6th month	35±7	1±1	4.856, <0.001*			

Note: Arm 1: injection of saline at huatuojiaji points; Arm 2: injection of salvia miltiorrhiza at huatuojiaji points; *P<0.01.

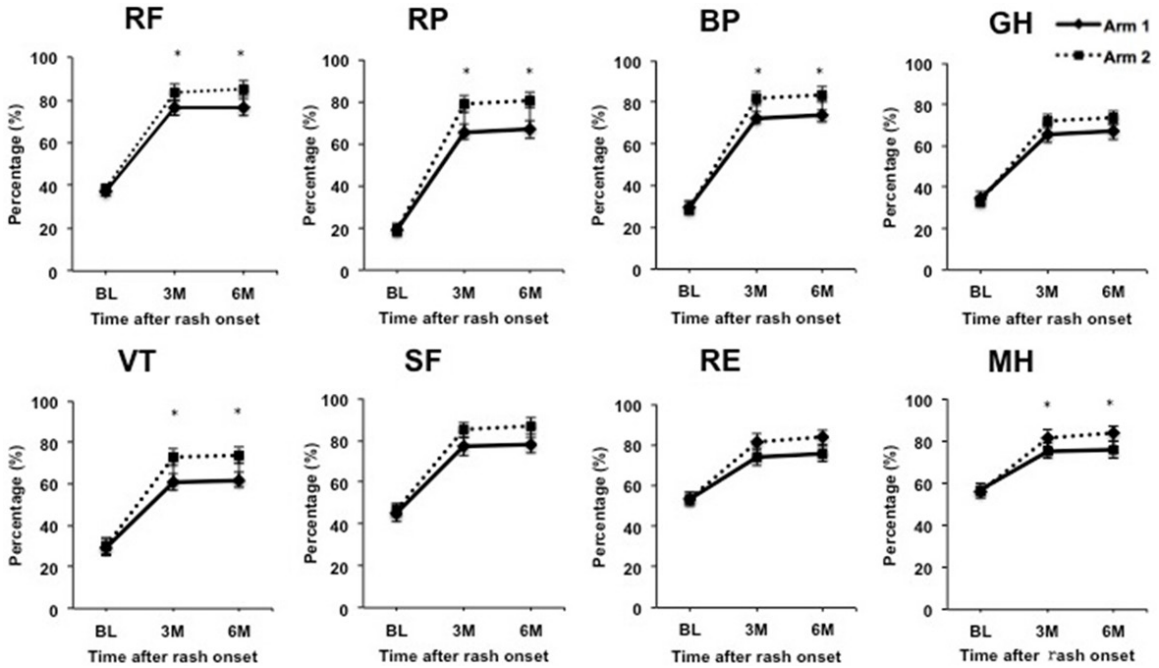

Figure 2. Quality of life (SF-36) before and after intervention between the two arms. PF, physical functioning; RP, role physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role emotional; MH, mental health; in all panels, higher scores indicate improvement; error bar is represented by standard error; *P<0.05.

points, within first week of rash onset, could help reduce pain intensity and shorten pain duration. Furthermore, if patients received this injection every 7 days for 3 weeks, they experienced much lower incidence of PHN after 3 and 6 months, a marked reduction in doses of gabapentin and tramadol, and a great improvement in QoL as measured by SF-36.

Neuronal injury and skin damage are believed to be the causes of acute pain in patients with HZ [21]. Pain can be exacerbated by movement

or contact and level of pain is related to the location of the affected area. Antiviral agents and analgesics are, currently, part of the standard treatment modality for HZ [22, 23]. In the present study, all patients received valacyclovir (1,000 mg, three times a day for 7 days), gabapentin (up to 1,800 mg per day), and tramadol as needed. In TCM, perpendicular punctures at huatuojiaji points have been demonstrated to have therapeutic effects on relieving pain during the acute stage of HZ [24]. Possible mechanisms behind this are that the treatment can help release endogenous opioid peptides, inhibit secretion of inflammatory factors, and enhance barrier function [25].

Salvia miltiorrhiza, a Chinese medicinal herb, has been widely used in the treatment of ischemic diseases due to its pharmacological effects of dilating arteries, increasing blood flow, and scavenging free radicals. Other studies have found that salvia miltiorrhiza, combined with valacyclovir, could effectively relieve neuralgia and shorten the recovery from AHZ, consistent with our findings [26]. Results of the present study showed that pain scores and use of analgesics were much lower in the treatment group than in control group.

PHN is known to have severely negative effects on QoL [27, 28]. Reducing incidence of PHN is one of the primary goals in treating HZ [29]. Early intervention during AHZ is recommended [29, 30]. However, standard therapy, with oral administration of antiviral agents and gabapentin, can't reduce incidence of PHN and methods of preventing its development remain controversial.

Increase in local cytokines related to neuralgia might be the potential mechanism for inducing PHN. Zhu et al. found that incidence of PHN was correlated with levels of interleukin (IL)-1β, IL-6, IL-8, tumor necrosis factor (TNF), and IL-10 [31]. Interventions with anti-inflammatory effects have been applied clinically for preventing development of PHN. In the single treatment mode, neither epidural nor paravertebral block can reduce incidence of PHN, whereas repetitive interventional treatments, including paravertebral block and low-level laser therapy, have the potential to prevent development of the disease. The present study adopted the repetitive mode, in which salvia miltiorrhiza was injected at huatuojiaji points every 7 days for 3 weeks. Study results found that incidence rates of PHN in patients treated with salvia miltiorrhiza and placebo were 6.12% and 20.83% in the 3rd month ($P<0.05$) and 2.04% and 14.58% in the 6th month, respectively ($P<0.05$). This finding indicates that repetitive injections of salvia miltiorrhiza at huatuojiaji points could significantly reduce incidence of PHN. The effectiveness of this repetitive intervention might be due to persistent inhibition of inflammatory factors.

This present study was the first study to demonstrate that repetitive injections of salvia miltiorrhiza at huatuojiaji points can prevent development of PHN. As major components of salvia miltiorrhiza, tanshinone IIA and salvianolic acid B have been found to suppress the production of vasoconstrictor endothelin-1 and lower expression of vascular adhesion molecules *in vitro* [32]. Modern pharmacological studies have proven that salvia miltiorrhiza can prevent calcium overload, eliminate oxygen free radicals, combat inflammation, and improve microcirculation with significant antinociceptive effects on somatic and visceral pain [33]. More recently, in a randomized, double blind, and controlled animal trial, Hao et al. found that tanshinone IIA could suppress expression of inflammatory factors (IL-1β, TNF-α and IL-6) and attenuate cancer-induced ongoing pain and breakthrough pain in a dose-dependent manner [34]. Since elevated cytokine levels in AHZ are assumed to induce PHN, it may explain why early suppression of these cytokines by salvia miltiorrhiza can prevent development of PHN.

There were some limitations to the present study. For example, it was unclear which component of salvia miltiorrhiza played the effective role during treatment, even though pharmacological compounds of the herb have all been identified. Additionally, cytokines levels were not monitored in patients, although the anti-inflammatory effects in salvia miltiorrhiza were assumed to reduce incidence of PHN.

In conclusion, injection of salvia miltiorrhiza at huatuojiaji points during early stage, in combination with antiviral agents, can be a safe and effective method for treatment of AHZ. It can decrease the intensity of acute pain, shorten pain duration, reduce incidence of PHN, and improve patient QoL.

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Disclosure of conflict of interest

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References

[1] Schutzer-Weissmann J and Farquhar-Smith P. Post-herpetic neuralgia-a review of current management and future directions. Expert Opin Pharmacother 2017; 18: 1739-1750.

[2] Hadley GR, Gayle JA, Ripoll J, Jones MR, Argoff CE, Kaye RJ and Kaye AD. Post-herpetic neuralgia: a review. Curr Pain Headache Rep 2016; 20: 17.

[3] Weinke T, Glogger A, Bertrand I and Lukas K. The societal impact of herpes zoster and postherpetic neuralgia on patients, life partners, and children of patients in Germany. ScientificWorldJournal 2014; 2014: 749698.

[4] Drolet M, Brisson M, Schmader KE, Levin MJ, Johnson R, Oxman MN, Patrick D, Blanchette C and Mansi JA. The impact of herpes zoster and postherpetic neuralgia on health-related quality of life: a prospective study. CMAJ 2010; 182: 1731-1736.

[5] Kim YN, Kim DW and Kim ED. Efficacy of continuous epidural block in acute herpes zoster: incidence and predictive factors of postherpetic neuralgia, a retrospective single-center study. Medicine (Baltimore) 2016; 95: e4577.

[6] Makharita MY, Amr YM and El-Bayoumy Y. Effect of early stellate ganglion blockade for facial pain from acute herpes zoster and incidence of postherpetic neuralgia. Pain Physician 2012; 15: 467-474.

[7] Avijgan M, Hajzargarbashi ST, Kamran A and Avijgan M. Postherpetic neuralgia: practical experiences return to traditional Chinese medicine. J Acupunct Meridian Stud 2017; 10: 157-164.

[8] Tang JL, Liu BY and Ma KW. Traditional Chinese medicine. Lancet 2008; 372: 1938-1940.

[9] Han JS. Acupuncture research is part of my life. Pain Med 2009; 10: 611-618.

[10] Serres G. Comments on the technique of the treatment of herpes zoster. Zhen Ci Yan Jiu 1988; 13: 6-9, 5.

[11] Han JY, Fan JY, Horie Y, Miura S, Cui DH, Ishii H, Hibi T, Tsuneki H and Kimura I. Ameliorating effects of compounds derived from Salvia miltiorrhiza root extract on microcirculatory disturbance and target organ injury by ischemia and reperfusion. Pharmacol Ther 2008; 117: 280-295.

[12] Lin HF, Tung K, Chou CC, Lin CC, Lin JG and Tanaka H. Panax ginseng and salvia miltiorrhiza supplementation abolishes eccentric exercise-induced vascular stiffening: a double-blind randomized control trial. BMC Complement Altern Med 2016; 16: 168.

[13] Mallick-Searle T, Snodgrass B and Brant JM. Postherpetic neuralgia: epidemiology, pathophysiology, and pain management pharmacology. J Multidiscip Healthc 2016; 9: 447-454.

[14] Ni J, Wang X, Tang Y, Yang L, Zeng Y and Guo Y. Subcutaneous injection of triamcinolone and lidocaine to prevent postherpetic neuralgia. Pain Physician 2017; 20: 397-403.

[15] Bouhassira D, Attal N, Alchaar H, Boureau F, Brochet B, Bruxelle J, Cunin G, Fermanian J, Ginies P, Grun-Overdyking A, Jafari-Schluep H, Lanteri-Minet M, Laurent B, Mick G, Serrie A, Valade D and Vicaut E. Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain diagnostic questionnaire (DN4). Pain 2005; 114: 29-36.

[16] Chatila N, Pereira B, Maarrawi J and Dallel R. Validation of a new arabic version of the neuropathic pain diagnostic questionnaire (DN4). Pain Pract 2017; 17: 78-87.

[17] Kim HJ, Park JH, Bouhassira D, Shin JH, Chang BS, Lee CK, Baek CH and Yeom JS. Validation of the korean version of the DN4 diagnostic questionnaire for neuropathic pain in patients with lumbar or lumbar-radicular pain. Yonsei Med J 2016; 57: 449-454.

[18] Rullan M, Bulilete O, Leiva A, Soler A, Roca A, Gonzalez-Bals MJ, Lorente P and Llobera J. Efficacy of gabapentin for prevention of postherpetic neuralgia: study protocol for a randomized controlled clinical trial. Trials 2017; 18: 24.

[19] Ruta D, Garratt A, Abdalla M, Buckingham K and Russell I. The SF 36 health survey questionnaire. A valid measure of health status. BMJ 1993; 307: 448-449.
[20] Lapolla W, Digiorgio C, Haitz K, Magel G, Mendoza N, Grady J, Lu W and Tyring S. Incidence of postherpetic neuralgia after combination treatment with gabapentin and valacyclovir in patients with acute herpes zoster: open-label study. Arch Dermatol 2011; 147: 901-907.
[21] Haanpaa M, Dastidar P, Weinberg A, Levin M, Miettinen A, Lapinlampi A, Laippala P and Nurmikko T. CSF and MRI findings in patients with acute herpes zoster. Neurology 1998; 51: 1405-1411.
[22] Jackson JL, Gibbons R, Meyer G and Inouye L. The effect of treating herpes zoster with oral acyclovir in preventing postherpetic neuralgia. A meta-analysis. Arch Intern Med 1997; 157: 909-912.
[23] Argoff CE, Chen C and Cowles VE. Clinical development of a once-daily gastroretentive formulation of gabapentin for treatment of postherpetic neuralgia: an overview. Expert Opin Drug Deliv 2012; 9: 1147-1160.
[24] Juan-Hong LI, Gui-Ying LI and Cheng B. Efficacy observation of acute herpetic neuralgia treated with perpendicular puncture at Jiaji points and ozone acupoint injection. World Journal of Integrated Traditional and Western Medicine 2013.
[25] Fu JL and Dong WY. Treatment of 36 cases of herpes zoster by electroacupuncture and moxibustion. Chinese Acupuncture and Moxibustion 2002; 22: 314.
[26] Chen XY. The clinical observation of Tan combined valacyclovir hydrochloride tablets in the treatment of herpetic neuralgia. Journal of Hunan Normal University 2016.
[27] Chidiac C, Bruxelle J, Daures JP, Hoang-Xuan T, Morel P, Leplege A, El Hasnaoui A and de Labareyre C. Characteristics of patients with herpes zoster on presentation to practitioners in France. Clin Infect Dis 2001; 33: 62-69.
[28] Dworkin RH and Portenoy RK. Pain and its persistence in herpes zoster. Pain 1996; 67: 241-251.
[29] Makharita MY. Prevention of post-herpetic neuralgia from dream to reality: a ten-step model. Pain Physician 2017; 20: E209-E220.
[30] Chen N, Li Q, Yang J, Zhou M, Zhou D and He L. Antiviral treatment for preventing postherpetic neuralgia. Cochrane Database Syst Rev 2014; Cd006866.
[31] Zhu SM, Liu YM, An ED and Chen QL. Influence of systemic immune and cytokine responses during the acute phase of zoster on the development of postherpetic neuralgia. J Zhejiang Univ Sci B 2009; 10: 625-630.
[32] Tang C, Xue HL, Bai CL and Fu R. Regulation of adhesion molecules expression in TNF-alpha-stimulated brain microvascular endothelial cells by tanshinone IIA: involvement of NF-kappaB and ROS generation. Phytother Res 2011; 25: 376-380.
[33] Zhang XP, Li ZJ and Liu DR. Progress in research into the mechanism of Radix salviae miltiorrhizae in treatment of acute pancreatitis. Hepatobiliary Pancreat Dis Int 2006; 5: 501-504.
[34] Hao W, Chen L, Wu LF, Yang F, Niu JX, Kaye AD and Xu SY. Tanshinone IIA exerts an antinociceptive effect in rats with cancer-induced bone pain. Pain Physician 2016; 19: 465-476.