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Review Article

A Review of Korean Medicine Treatment for Postherpetic Neuralgia

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ABSTRACT

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The purpose of this study was to analyze the Korean medicine treatment methods for Postherpetic Neuralgia (PHN) in Korea. There were 5 online databases searched (OASIS, NDSL, RISS, KISS and KMBASE) for studies which were related to PHN. A total of 12 studies were selected. Various treatments such as acupuncture, herbal medicine, and moxibustion were reported treatments for PHN, some of which included Western medicine and Korean medicine treatment. Korean herbal medicine was the most frequently used treatment method, followed by manual acupuncture. Sipjeondaebotanggami was the most frequently used prescription. Poria Sclerotium was the most frequently used principal herb, followed by Angelicae Gigantis Radix, Zingiberis Rhizoma, and Ginseng Radix. GB44, LI4, LR3 were the common acupoints used for the treatment of PHN. CV12 was the most frequently used moxibustion point, and gabapentin was the most frequently used concomitant Western drug. Additional research on Korean medicine treatment of PHN is expected in the future.

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Introduction

Herpes Zoster (HZ) also known as Shingles, is a disease whereby the Varicella zoster virus (VZV) which had been dormant in the dorsal root ganglion or trigeminal ganglion since the initial infection with VZV, is reactivated when the human body is weakened or compromised immune system [1]. It is a disease where small vesicles appear in a band shape alongside a rash, and usually accompanied by sharp pain [1]. HZ can cause various complications such as meningitis, pneumonia, secondary bacterial infection, and postherpetic neuralgia (PHN) during or after treatment. Among them, PHN is the most common complication and is one of the causes of intractable chronic pain syndrome [2]. PHN is a condition where pain can continue for more than 1 month after the skin rash caused by the acute HZ has healed [3]. PHN can be accompanied by intermittent lancinating pain, allodynia, and persistent deep burning pain. These symptoms tend to be more unpleasant than those of HZ. In some cases, alongside the pain, there is a decrease in sensation in the skin. Chronic

neuralgia can also lead to physical and emotional dysfunction, which significantly reduces the patient's quality of life [4]. It has been reported that when the intensity of the pain was severe in patients, the prodromal symptoms before the rash were severe, and people were older, with an increased probability of transition to PHN [5]. The annual worldwide incidence of PHN is 1.5 to 4 per 1,000 people, but among those in their 60s and older, the incidence rate is 7.2 to 11.8 per 1,000 people [6]. The number of patients treated for HZ in Korea increased from 480,000 in 2010 to about 720,000 in 2020 [7]. Considering that 4-70% of patients over the age of 60 with HZ experience PHN [8], the number of patients with PHN are expected to increase accordingly. Western medicine including antidepressants, anticonvulsants, nerve blocks by topical anesthetic, sympathectomy, and intrathecal drug pump insertion, have all been used to treat PHN, however, no successful treatment has been reported so far [9]. Besides, the effectiveness of pharmacological treatment is limited [10] with satisfactory analgesia reported in approximately 50% patients [11], and these treatments may increase the incidence of adverse effects, such as

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sedation, xerostomia, dizziness, fatigue, and weight gain [12-14]. Thus, an effective pain management for PHN is needed [15]. It has been reported that PHN could be relieved effectively by using traditional medicine such as acupuncture, moxibustion, Chinese medicine, and cupping with bleeding for patients with PHN [16,17].

In the Korea Health Insurance Review and Assessment Institute, HZ ranked 70th in the list for frequent diseases where Korean medicine treatment (KMT) was received as inpatient treatment and 127th in outpatient treatment for patients aged 60-69 years between 2017 and 2020 [18]. However, there was not much data on the type of KMT implemented for PHN, the most common complication of HZ. For this reason, we tried to determine the status and possibility of KMT for PHN in Korea.

In this study, we reviewed Korean Medicine journals published between 2000 and 2020 and analyzed clinical research where KMT was applied to PHN. Through this, we intend to provide practically effective data to support KMT for PHN clinical treatment.

Materials and Methods

Research participants

To review the clinical research related to this research topic, 5 databases were searched [Oriental Medicine Advanced Searching Integrated System (OASIS), National Discovery for Science Leader (NDSL), Research Information Sharing Service (RISS), Korean studies Information Service System (KISS), and Korean Medical Database (KMBASE)] for a time period ranging from January 1, 2000, to December 31, 2020. The search terms were as follows: “acupuncture” OR “moxibustion” OR “Korean medicine treatment” OR “pharmacopuncture” AND “PHN” OR “Postherpetic Neuralgia.”

Search methods

From January 1, 2000, to December 31, 2020, articles were retrieved from the databases without duplication. The title and abstracts were checked to select studies containing information on the treatment of PHN. In this study, PHN was defined as described

by Dworkin’s work, where pain persists for more than 30 days after the rash has disappeared [5]. Articles that did not include PHN were excluded, such as those where the pain disappeared within 30 days of the disappearance of the rash. Of the 679 articles, 228 were selected (excluding 451 duplicate articles). Of 228 articles, 128 articles not associated with KMT, 87 articles that did not contain information about PHN, and 1 article whose original text could not be confirmed were excluded. For this reason, 12 articles were finally included in this review. Where the treatment period was long or there was only 1 study that reported multiple cases, only the treatment method of PHN was included in the analysis. Methods implemented to treat symptoms other than those caused by HZ were also excluded from the analysis. In the analysis of herbal medicine prescriptions, only prescriptions administered 30 days after the loss of the rash were included in the analysis. When analyzing the frequency of prescription prescribed for Korean medicine, if the same prescription was used multiple times in 1 case, it was not calculated as a duplicate. When multiple prescriptions were used in 1 case, only cases where the drug dose was specified were included. With regards to herbal medicine analysis, if the prescription’s herbal constituents were not accurately specified in the articles, it was excluded from the analysis (Fig. 1).

Results

Publication trends

A total of 12 case reports were selected for review. Publications were in the Journal of Korean Medicine ($n = 1$), Ophthalmology ($n = 1$), Otolaryngology ($n = 1$), Dermatology ($n = 1$), Korean Journal of Medicine ($n = 4$), Journal of Physiology and Pathology in Korean Medicine ($n = 1$), Research Institute of Korean Medicine ($n = 1$), Journal of East-West Medicines ($n = 1$), and the Journal of Korean Medical Association of Clinical Sanghan-Geumgwe ($n = 1$).

Year of publication

Case reports on PHN treated by KMT were published regularly between 2004 and 2018 (Fig. 2).

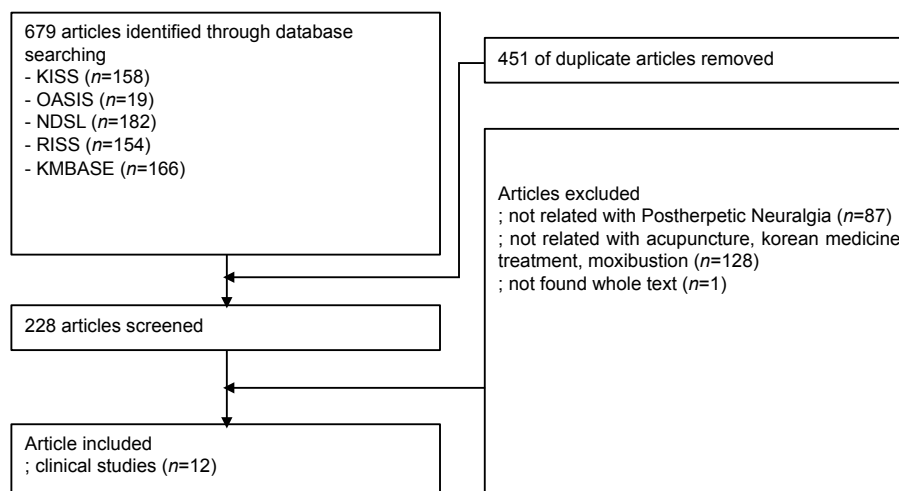


Fig. 1. Flow chart of the study selection process.

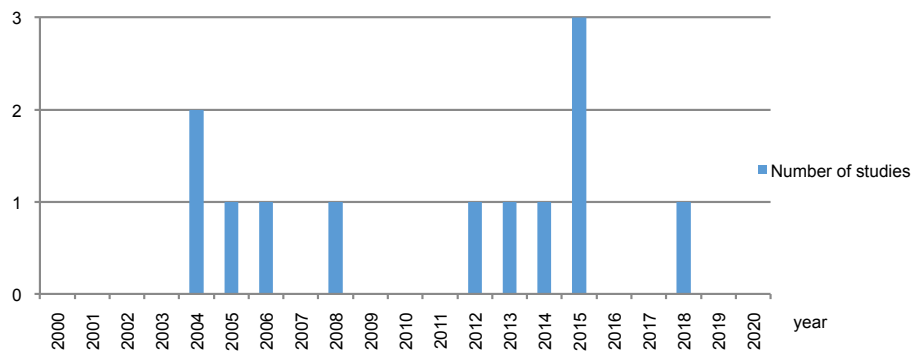


Fig. 2. Analysis of publication year.

Table 1. Age and Sex Distribution.

Age (y)	Total	Female	Male
0-9	-	-	-
10-19	-	-	-
20-29	-	-	-
30-39	-	-	-
40-49	1	-	1
50-59	5	4	1
60-69	7	3	4
70-79	4	1	3
Total	17	8	9

Analysis of sample data

As a result of analyzing the gender distribution of PHN, it was confirmed that there were 9 males and 8 females in the sample of 12 articles. As a result of distribution analysis by age, all 17 patients were between the ages of 40 and 79, with the most common age being between 60 to 69 (Table 1). When duplication was allowed, the site of pain was determined to be the face ($n = 2$), the thoracic region ($n = 14$), the head ($n = 2$), or the whole body ($n = 1$).

Acupuncture

Of the 12 articles reviewed, 11 studies performed acupuncture treatment (6 employed manual acupuncture, 2 studies used sa-am acupuncture, 2 of which used various acupuncture methods simultaneously and 1 of which used warm acupuncture). Pharmacopuncture was used simultaneously in 5 of the 12 studies, and electroacupuncture was used in 1 of the 12 studies.

Ash-point was used the most, and Liver-tonification acupuncture was the most used sa-am acupuncture method. The most frequently used acupoints were GB44, LI4 and LR3 (Table 2). The Gallbladder Meridian was used the most in the Meridian system. In the cases using the non-acupoints, the treatment location was selected based on the acupoints and the sites of anatomical lesions.

Of the 16 cases, the average time the needle remained in the body was 17 minutes, with the exception of 4 cases that did not specify a time. There were 5 cases where the needle remained in the body for 20 minutes, 6 for 15 minutes, and 1 for 30 minutes. The duration of treatment varied from 7 days up to 34 days. Treatment from 11 to 20 days took the largest share, recording 7 cases respectively (Table 3). In 9 of the cases (from 5 articles), the patients were also treated with pharmacopuncture including bee venom. Bee venom was used in 4 of the studies, and Hwanglyeonhaedok injection was used in 1. In 5 studies, all the pharmacopuncture was injected into the ashi-point (Table 4).

Herbal medicine

In all 12 studies, herbal medicine was used as a treatment method, and in all of those cases, a complex prescription was used rather than a single herb. In the 12 studies there were 20 different prescriptions used in 17 of the cases, with Sipjeondaebotanggami being the most frequently used herbal medicine prescription (5 cases), followed by Yongdamsagatang (3 cases), and Sosihotang (2 cases; Table 5). There were 2 of the 12 studies that used an external therapy such as ointment treatments or fumigation treatments. In 1 study, gagamunhwangsang in powder form, was mixed in vinegar, and applied to the affected area, and then an ointment containing Olibanum, Myrrha decoction, and Vaseline was applied once a day. In the other study, Gardeniae Fructus, Alumen, Borneolum, Olibanum, and Myrrha powder were applied to the affected area, and fumigation treatment was performed with decoctions of medicinal herbs such as Artemisiae Annuae Herba, Gentianae Macrophyllae Radix, Glycyrrhizae Radix et Rhizoma, Olibanum, and Myrrha.

Herbs used in complex prescription

A total of 81 different herbs were used in the compound prescription (detailed pharmaceutical compositions can be found

Table 2. Acupoints Used.

Usage frequency	Acupoints
4	GB44, LI4, LR3
3	ST36, LU8, LR4, HT8, LR2, LI1
2	SP1, SI5, GB40, LI11, TE5, ST43, GB41
1	SP2, LR1, LU9, SP3, SP6, LR8, TE3, TE6, GB43, BL66, GB38, ST45, PC6, SP11, EX-B2

Table 3. Summary of 11 Case Reports Concerning Patients Treated with Acupuncture.

Author (y)	Sample size	Patient gender /Age	Acupuncture methods	Acupoints	Frequency/treatment period	Needle size (mm)	Time (min)
Kim (2005) [19]	1	M/66	Manual acupuncture	EX-B2	Unknown/34d	Unknown	Unknown
Yoon (2006) [20]	1	M/70	Manual acupuncture	LI4, LR3, ST36	1x/d/33d	0.25 x 30	20
			Sa-am acupuncture	LU8, LR4, HT8, LR2, SP2, HT8, SP1, LR1	1x/2d/33d		
Choi (2008) [21]	2	F/56 M/55	Sa-am acupuncture	LU8, LR4, HT8, LR2,	1x/d/7d 1x/d/10d	0.20 x 30	20
		Electroacupuncture	Ashi-point	1x/d/33d			
Chun (2004) [22]	1	M/61	Manual acupuncture	LI1, GB44, SP3, LU9, SI5, GB40, LI11, TE5, CV10, CV12, CV13, ST25, CV4	Unknown/23d	0.25 x 30	Unknown
Kim (2012) [23]	1	F/53	Manual acupuncture	LI4, LI11, LR3, TE5, SP6	2x/d/18d	0.25 x 30	20
Kweon (2018) [24]	5	F/69 F/60 M/70 M/74 M/45	Warm acupuncture	Ashi-point	1x/d/14 1x/d/22d 1x/d/9d 1x/d/25d 1x/d/12d	0.30 x 40	15
Lee (2015) [25]	1	F/77	Manual acupuncture	LI4, LR3, PC6, ST36	1x/d/11d	0.25 x 30	20
Jung (2015) [26]	1	F/52	Manual acupuncture	LI4, LR3, PC6, ST36, TE5, ST43, GB40, GB41, Ashi-point	2x/d/19d	0.25 x 30	unknown
Yang (2013) [27]	1	M/69	Manual acupuncture	LR14, LR8, GB44, TE3, TE6, Ashi-point	1x/d/28d	0.20 x 30	15
Lee (2004) [28]	1	F/60	Sa-am acupuncture	GB43, BL66, LI1, GB44, GB41, ST43, ST45, LI1	1x/d/14d	Unknown	Unknown
Park (2014) [29]	1	M/69	Sa-am acupuncture Manual acupuncture	LU8, LR4, HT8, LR2 GB43, BL66, LI1, GB44, Ashi-point	2x/d/15d	0.25 x 30	30

Table 4. Summary of 5 Case Reports Concerning Patients Treated with Pharmacopuncture.

Author	Gender/sex	Type/amount	Acupoints	Frequency/treatment period
Kim (2005) [19]	M/66	BV (1:2,000) 1.5 cc	Ashi-point	1x/d/5d
Chun (2004) [22]	M/61	BV (1:10,000) 0.8 cc BV (1:4,000) 0.3 cc	Ashi-point	3x/wk/52d
Kweon (2018) [24]	F/69 F/60 M/70 M/74 M/45	Allergy Free Bee Venom 10% 1 cc	Ashi-point	Unknown
Lee (2015) [25]	F/77	Hwanglyeonhaedok injection 1 cc	Ashi-point	1x/d/8d
Yang (2013) [27]	M/69	Sweet BV (1:10,000) 1 cc	Ashi-point	1x/d/19d

Table 5. Summary of 12 Case Reports Concerning Patients Treated with Herbal Medicine.

Author (y)	Sample size	Patient gender /Age	Herbal medicine formula	Dosing period (d)	Frequency	Volume of each pack (cc)	Dosing time	Total dosing period (d)
Kim (2005) [40]	1	M/66	Yongdamsagantang Yukmijihwangtang	16 18	2x/d	Unknown	2 h after meal	34
Yoon (2006) [20]	1	M/70	Yongdamsagan-tang Boyanghwanotanggagam Siryengtang	3 2 27	3x/d	Unknown	2 h after meal	32
Choi (2008) [21]	2	F/56 M/55	Soyosangami Bunsingieumgami	7 10	3x/d	Unknown	Unknown	7 10
Chun (2004) [22]	1	M/61	Daeshihotang gami	52	Unknown	Unknown	Unknown	52
Kim (2012) [23]	1	F/53	GamiGuibitang Sosihotang Gamchobujatang Gamisoyosan	2 4 4 8	3x/d	Unknown	1 h after meal	18
Kweon (2018) [24]	5	F/69 F/60 M/70 M/74 M/45	Sipjeondaebotanggami	30 22 10 10 10	3x/d	120	30 min after meal	30 22 10 10 10
Lee (2015) [25]	1	F/77	Gyejibanhasaenggangtang Lizhongtang	2 9	3x/d	120	2 h after meal	11
Jung (2015) [26]	1	F/52	Bogijetongtang	19	3x/d	100	Unknown	19
Yang (2013) [27]	1	M/69	Dokhwajihwangtang Sosihotanggami	2 26	3x/d	120	30 min after meal	28
Lee (2004) [28]	1	F/60	Yongdamsagantang Sunbanghapsipmipaedoktang Sungmagalguntanggami	2 3 9	3x/d	Unknown	Unknown	14
Lee (2015) [30]	1	F/52	Bujatang	30	3x/d	120	Unknown	30
Park (2014) [29]	1	M/69	Samguiyangyoungtanghaposihotang Yeoldahansotang	4 10	3x/d	Unknown	Unknown	13

in the original publications). When prescription herbs were listed by frequency, Glycyrrhizae Radix et Rhizoma was the most frequently used (21 times in total), followed by Poria Sclerotium (18 times), Angelicae Gigantis Radix (16 times), Zingiberis Rhizoma and Gingseng Radix (14 times), and Atractylodis Rhizoma alba (13 times; Table 6).

Western medicine treatment

In 5 articles, Western medicine treatment was implemented simultaneously with Korean medicine for the treatment of PHN. The most commonly used drug was gabapentin, which was used in 4 of the 5 studies. Next, acetaminophen and tramadol mixed drugs were used in 2 studies. Additionally, hydrocobalamin,

Table 6. The Frequency of Commonly Used Herbs and Classification of Herbs in Categories.

Main category	Herbs (scientific name)	Frequency
Exterior-releasing medicinal	Zingiberis Rhizoma Recens (14)	47
	Perillae Folium (1)	
	Saposhnikoviae Radix (3)	
	Schizonepetae Spica (1)	
	Osterici Radix (1)	
	Cinnamomi Ramulus (2)	
	Angelicae Dahuricae Radix (3)	
	Angelicae Tenuissimae Radix et Rhizoma (1)	
	Bupleuri Radix (12)	
	Menthae Herba (2)	
	Puerariae Radix (3)	
	Cicadidae Periostracum (1)	
	Vitici Fructus (1)	
Cimicifugae Rhizoma (2)		
Heat-clearing medicinal	Gardeniae Fructus (4)	44
	Gypsum Fibrosum (1)	
	Anemarrhenae Rhizoma (3)	
	Trichosanthis Radix (1)	
	Genianae Scabrae Radix (4)	
	Scutellariae Radix (9)	
	Phellodendri Cortex (1)	
	Coptidis Rhizoma (1)	
	Rehmanniae Radix (6)	
	Moutan Radicis Cortex (5)	
	Scrophulariae Radix (2)	
	Paeoniae Radix Rubra (3)	
	Lonicerae Flos (2)	
Forsythiae Fructus (1)		
Lycii Radicis Cortex (1)		
Wind-dampness-dispelling medicinal	Angelicae Pubescentis Radix (2)	3
	Chaenomelis Fructus (1)	
Dampness-resolving medicinal	Amomi Cardamomi Fructus (1)	8
	Agastachis Herba (1)	
	Atractylodis Rhizoma (1)	
	Amomi Fructus (5)	
Dampness draining Diuretic medicinal	Alismatis Rhizoma (6)	35
	Poria Sclerotium (18)	
	Polyporus (1)	
	Hoelen cum Pini Radix (2)	
	Akebiae Caulis (4)	
	Plantaginis Semen (3)	
Junci Medulla (1)		
Interior-warming medicinal	Aconiti Lateralis Radix Preparata (2)	10
	Zingiberis Rhizoma (2)	
	Cinnamomi Cortex (6)	
Digestant medicinal	Crataegi Fructus (6)	17
	Hordei Fructus Germinatus (5)	
	Massa Medicata Fermentata (5)	
	Raphani Semen (1)	
Qi-regulating medicinal	Aurantii Fructus Immaturus (2)	12
	Citri Unshius Pericarpium Immaturus (2)	
	Citri Unshius Pericarpium (3)	
	Aucklandiae Radix (2)	
	Aurantii Fructus Immaturus (2)	
Cyperii Rhizoma (1)		

amitriptyline, azelastine, hydrochlorid, and amitriptyline were used in 1 study each. Finally, ketoprofen was used for external application in 1 study (Table 7).

Moxibustion

Moxibustion treatment was used in 6 studies, all of which used indirect moxibustion. With regards to the acupoints used for moxibustion, CV12 was used in 4 studies, CV4 in 3, CV8 in 2 studies, and CV14 in 1 study. The frequency of treatment was once a day in all 6 cases, and the total treatment period varied from 7 days to 39 days (Table 8).

Physical therapy

Only 1 study applied physical therapy which was over a 4-week period, using carbon 2 times/day, and Interferential Current Therapy (ICT) 1 time/day (Table 9).

Assessment tools

Of the 12 articles, when the evaluation scale was analyzed, the Visual Analog Scale (VAS) was the most frequently used method (7 studies) for evaluating pain, followed by the Numerical Rating Scale (NRS) in 3 studies, the Verbal Rating Scale in 1 study, the Pain Rating Scale (PRS) in 1 study, Quality of Sleep in 1 study, and Inconvenience Degree in 1 study. Two of the studies used an arbitrary designed evaluation scale without using a general evaluation scale for evaluating pain (Table 10).

Table 6. (Continued).

Main category	Herbs (scientific name)	Frequency
Blood-activating and stasis-dispelling medicinal	Persicae Semen(2) Cnidii Rhizoma (9) Carthami Flos (3) Corydalis Rhizoma (2) Trogopterorum Faeces (1) Myrrha (8) Salviae Miltiorrhizae Radix (3) Olibanum (7) Spatholobi Caulis (1) Gleditsiae Spina (1) Manitis Squama (1)	38
Phlegm-resolving, cough-suppressing and panting-calming medicinal	Pinelliae Rhizoma (7) Platycodonis Radix (5) Trichosanthis Fructus (1) Peucedani Radix (1) Fritillariae Bulbus (1)	15
Tranquillizing medicinal	Zizyphi Spinosae Semen (3) Fossilia Osis Mastodi (1) Polygalae Radix (1) Albiziae Cortex (1)	6
Liver pacifying medicinal	Ostreae Concha (3) Uncariae Ramulus et Uncus (1) Lumbricus (2)	6
Tonifying and replenishing medicinal	Glycyrrhizae Radix et Rhizoma (21) Dioscoreae Rhizoma (1) Astragali Radix (9) Atractylodis Rhizoma Alba (13) Ginseng Radix (14) Zizyphi Fructus (10) Alpiniae Oxyphyllae Fructus (1) Cervi Cornu Colla (5) Epimedii Herba (1) Cibotii Rhizoma (1) Angelicae Gigantis Radix (16) Rehmanniae Radix Preparata (10) Cistanchis Herba (1) Polygoni Multiflori Radix (1) Liriopis Radix (2) Paeoniae Radix Alba (8)	116
Astringent medicinal	Corni Fructus (1)	1
Purgative medicinal	Rhei Rhizoma (1)	1

Analysis of effects

In all studies, it was reported that KMT was effective in relieving PHN. In 10 out of 12 studies, patients commonly complained of sleep disorders due to severe pain caused by PHN, all of which were alleviated by reduced night pain. On average, in the 10 studies using the NRS or VAS scale, the patient's pain was reduced by about 70%. The other 2 studies using arbitrarily designed evaluation measures also reported reduction in patient's pain (Table 10 [19-30]). The most effective treatment case was reported by Kim et al [19], which reported thoracic region allodynia causing the most imaginable pain which was completely resolved after

treatment (VAS score 10 to 0). The least effective treatment case was the 4th case reported by Kweon et al [24], which reported pantalga which caused pain which the patient rated as a VAS score 9, which after treatment was only reduced to 7. There were no side effects reported in any of the 12 studies.

Discussion

In this study, clinical research on PHN that were published between January 1, 2000, and December 31, 2020, in 5 Korean databases were analyzed. A total of 17 cases were reported in 12 studies. The studies covered 8 female cases and 9 male cases.

Table 7. Summary of 5 Case Reports Concerning Treated with Western Medicine.

Author (y)	Sample size	Patient gender /age	Western medicine	Frequency	Treatment period
Yoon (2006) [20]	1	M/70	Neurontin cap. 300 mg 1 C Tramadol hydrochloride 1 ampule	2x/d Prn Inj.	unknown
Kim (2012) [23]	1	F/53	Gabapentin 100 mg 1 C Paramacetamol tab. 1 T Tizalead tab. 1 mg 1 T	3x/d 3x/d 3x/d	8 d
Lee (2015) [25]	1	F/77	Neurontin cap. 300 mg 1 C	2x/d	Unknown
Lee (2004) [28]	1	F/60	Neurotin 1 T Hydrocobalamin 1 T Amitriptyline 1 T Azeptin 1 T Trodon 1 ampule	3x/d 3x/d 3x/d 2x/d 1x/d	Unknown Unknown Unknown Unknown 5 d
Park (2014) [29]	1	M/69	Neurontin cap 300 mg 1 C Etravil 10 mg 0.5 C Ketoprofen 30mg 1EA	Prn/d	7 d

Table 8. Summary of 6 Case Reports Concerning Patients Treated with Moxibustion.

Author (y)	Gender/age	Used acupoints	Indirect or direct	Frequency/treatment period	Time (min)
Yoon (2006) [20]	M/70	CV4, CV12	Indirect	1x/d/33d	Unknown
Choi (2008) [21]	1) F/56 2) M/55	1) CV4, CV12, ST36, PC6 2) CV4, CV12	Indirect	1x/d/7d	Unknown
Lee (2015) [25]	F/77	CV12, CV14	Indirect	1x/d/11d	3-40
Jung (2015) [26]	F/52	CV8	Indirect	1x/d/19d	Unknown
Yang (2013) [27]	M/69	CV4, CV12	Indirect	1x/d/28d	30
Park (2014) [29]	M/69	CV8	Indirect	1x/d/15d	Unknown

Table 9. Summary of 1 Case Report Concerning Patients Treated with Physical Therapy.

Author (y)	Sample size	Patient gender /Age	Physical therapy	Frequency/Treatment period	Time (min)
Yang (2013) [27]	1	M/69	Carbon ICT	2x/d/28d 1x/d/28d	15

Table 10. Summary of 12 Case Reports Concerning Patients Assessment Tool.

Author (y)	Sample size	Patient gender /age	Intervention	Evaluation	Result/score
Kim (2005) [19]	1	M/66	A-Tx, H-med, BV, cupping with bleeding	Pain sleeping clothing	Pain: +++ -> - Sleeping: +++ -> - Clothing: +++ -> +
Yoon (2006) [20]	1	M/70	A-Tx, H-med, Moxi-Tx, cupping with bleeding, Electroacupuncture	VAS	VAS 9->1
Choi (2008) [21]	2	1) F/56 2) M/55	A-Tx, H-med, Moxi-Tx	VAS	1) VAS 10->1-2 2) VAS 10->2
Chun (2004) [22]	1	M/61	A-Tx, H-med, BV	VAS	VAS 10-> VAS 1->2-6
Kim (2012) [23]	1	F/53	A-Tx, H-med, cupping with bleeding	VAS	VAS 10->0
Kweon (2018) [24]	5	1) F/69 2) F/60 3) M/70 4) M/74 5) M/45	Warm acupuncture, H-med, BV, cupping with bleeding	VAS PRS QSP	1) VAS 7, PRS 70, QSP 3->VAS 2, PRS 10, QSP 0 2) VAS 8, PRS 88, QSP 3->VAS 4, PRS 32, QSP 1 3) VAS 5, PRS 30, QSP 1-> VAS 1, PRS 4, QSP 0 4) VAS 9, PRS 72, QSP 3->VAS 7, PRS 56, QSP 2 5) VAS 7, PRS 49-> VAS 3, PRS 15
Lee (2015) [25]	1	F/77	A-Tx, Pharmacopuncture, Moxi-Tx, H-med	NRS	NRS 7->3
Jung (2015) [26]	1	F/52	A-Tx, Moxi-Tx, H-med	NRS	NRS 8->3
Yang (2013) [27]	1	M/69	A-Tx, H-med, BV, Moxi-Tx, cupping, P-Tx	VAS ICD	VAS 10->3 ICD 3->1
Lee (2004) [28]	1	F/60	A-Tx, H-med, ointment, cupping with bleeding, Venesection	Headache	100 -> 20
Lee (2015) [50]	1	F/52	H-med	NRS VAS	VAS 7->0 NRS 8->3
Park (2014) [29]	1	M/69	A-Tx, H-med, Moxi-Tx, ointment, Fumigation, Qigong therapy	NRS	NRS 10->1-2

A-Tx, acupuncture treatment; H-med, herbal medicine; Moxi-Tx, moxibustion treatment; P-Tx, physical therapy; Cupping-Tx, cupping treatment; BV, bee venom, VAS, visual analogue scale, ICD, inconvenience degree, PRS, pain rating scale, QSP, quality of sleep; NRS, numeral rating scale.

Among all the cases, those in their 50s or older accounted for the majority with 8 female cases (100% of female cases) and 8 male cases (88.8% of total male cases). This was consistent with a previous study, which reported that 40.6% (13 men) and 39.1% (25 women) of cases had no significant gender difference in PHN outbreaks [2]. With regards to the type of PHN (according to the classification by the site of pain), thoracic pain was the most frequently observed with 13 cases (72.2%), and among them, left thoracic pain was dominant with 9 cases (52.9%). This result was also consistent with a previous study showing that the thoracic innervation area is the most commonly PHN-affected site [2].

KMT was conducted including acupuncture, herbal medicine, moxibustion, physical therapy, and together with Western medicine in some cases. Acupuncture and herbal medicine were used as the main methods for the KMT of PHN. The most frequently mentioned acupoints were GB44, LI4 and LR3. GB44 was frequently used when the pain was located in the thoracic region. In previous studies, LI4 was frequently used for acupuncture anesthesia due to its excellent pain control [31,32]. LR3 has been reported to have pain control and nerve regeneration effects [33]. In a study by Choi et al, the overseas, randomized clinical study included acupuncture treatment for acute stage HZ which reported

similar results to this study, as the LI11, LR3, and ST36 acupoints were the most frequently used after the Ashi-point [34]. It can be concluded that these acupoints were also chosen to control pain in PHN.

When using pharmacopuncture, Bee venom was most frequently used, and has been reported to improve neurological disorders through anti-inflammatory, analgetic, immunomodulatory, antimicrobial, antiviral, vascular permeability, and nervous system excitatory effects of the nervous system [35,36]. In addition, Hwanglyeonhaedok injection was also used to treat PHN symptoms due to its anti-inflammatory and analgesic properties [37]. In addition, Kweon et al [24] reported the results of 5 patients who were treated with warm acupuncture [24]. It is said that the condition in which the nervous system is damaged and does not function properly due to the sequelae of HZ is similar to that of a stagnant meridian therefore, warm acupuncture treatment was applied [24]. In addition to the analgesic effect, warm acupuncture is widely used for musculoskeletal pain conditions/diseases and has been applied to various conditions/diseases because of its effect on enhancing immunity [38].

Sipjeondaebotanggami was the most frequently used herbal medicine prescription in 5 cases. It is a prescription made by

adding Cinnamomi Cortex Spissus and Astragali Radix to Sagunjatang, which is mainly used for invigorating the body, and adding Samultang, which is mainly used for tonifying blood. Sipjeondaebotang has been reported to be involved with the immune response of organs of the immune system such as the bone marrow, spleen, thymus, and liver [39]. Sipjeondaebotang not only improves immune function in the body through increased activity of the bone marrow, spleen, thymus and immunoglobulin, but also possesses antioxidant, antibacterial and anti-inflammatory properties [39]. Since all 5 patients who received Sipjeondaebotang treatment were elderly and frail, it seems that pain control was performed by adding herbal medicines (such as Olibanum and Myrrha which activate blood flow, and remove blood stasis) to Sipjeondaebotang, which has been shown to improve immune function in the body.

Yongdamsagantang was used in 3 cases. Yongdamsagantang has been reported to have antiallergic, anti-inflammatory, and antiviral properties [40]. Furthermore, it is known to have a cellular immunomodulatory effect, which is reported to alleviate inflammatory responses of HZ to control pain and rash [41]. In all 3 studies, Yongdamsagantang was prescribed at the beginning of PHN treatment. While Sipjeondaebotang was primarily used for elderly and feeble patients, Yongdamsagantang was used in robust patients for a relatively short period of time to relieve severe pain. It is likely that when prescribing herbal medicine for PHN, the patient's symptoms and physical conditions are taken into consideration.

Glycyrrhizae Radix et Rhizoma was most frequently used compositional drug with a total of 21 cases of usage. Next was Poria Sclerotium, which was used 18 times, followed by Angelicae Gigantis Radix, which was used 16 times. Since Glycyrrhizae Radix (being used as the harmonizer for all medicines), the most used medicine as the principal herb was Poria Sclerotium. Poria Sclerotium is an important herbal medicine that has been reported to have anti-inflammatory, antioxidant, ulcer preventing, immune-enhancing, and anti-cancerous properties [42].

According to the classification of herbal medicine [43], tonifying and replenishing medicines (16 types), heat-clearing medicines (15 types), exterior-releasing medicines (14 types), dampness draining diuretic medicines (8 types), and blood-activating and stasis-dispelling medicines (11 types) were used frequently. It is thought that the purpose of using herbal medicines such as tonifying and replenishing medicines was to strengthen the body's immunity as HZ occurred due to the recurrence of the latent VZV and PHN appeared as a complication. Seeing that many dampness draining diuretic medicines and heat-clearing and dampness-drying medicines were used, it is probable that the etiology of PHN was regarded as dampness-phlegm and herbal medicines were used to remove it. Herbal medicines that activate blood flow and remove blood stasis are used to promote blood circulation by removing the narrowing and occlusion of blood vessels caused by peripheral circulation disorders [44]. It can be inferred that the 2 external treatments were mainly used for this effect. In terms of the dosing period, the effect of the dosing period was seen as the number of cases that had periods of less than 10 days, 11-20 days, 21-30 days, and 31-40 days which were almost the same.

For the treatment of PHN using Western medicine combined with KMT, gabapentin was most frequently used alongside acetaminophen, tramadol, and hydrocobalamin. This was the same as the most frequently used medication in the guidelines for the treatment of PHN [1]. In the treatment medication guidelines for PHN, tricyclic antidepressants, anticonvulsants and topical lidocaine are recommended as primary medications, and opioids and tramadol were recommended as secondary medications [45].

Gabapentin is recommended as the primary choice for neuropathy pain because it has no serious complications compared with other anticonvulsants or antidepressants, and it has no interactions with other drugs. It is frequently administered in patients taking multiple medications [46].

Through various studies, moxibustion treatment has been reported to have analgesic effects, neural inhibition or excitatory effects, blood circulation promoting effects, nutritional status enhancement, absorption capacity activation, functional control of various glands, and the ability to increase natural healing [47]. CV12, the most frequently selected point in moxibustion, is the 12th acupoint of conception vessel meridian and is used for various digestive, neurological, and circulatory conditions/diseases [48]. In the cases in this review, it was used to treat pain, indigestion, and insomnia in PHN patients.

The VAS, the most commonly used method for pain assessment due to PHN, and is easy to apply. It is one of the most widely used methods for objectifying a patient's subjective pain and is relatively reliable when short-term changes are applied to the patient which can alter the level of pain a patient experiences [49]. However, there is a tendency to only report the intensity of pain [49]. In order to supplement this aspect, Kweon et al [24] evaluated pain using VAS alongside other methods such as PRS, QSP, etc. The symptoms were classified according to the pattern of pain the patients experienced and the degree to which sleep was disturbed due to pain. The NRS is a method where the patient selects a number corresponding to their degree of pain, and is mainly used to assess the overall pain intensity and can be evaluated simply and quickly. Both the VAS and NRS have the advantage of simplicity, however, both have the disadvantage of being a single-dimensional measurement method that measures only the intensity of pain [50]. Therefore, other methods of assessing different aspects of pain in PHN such as intermittent fulminant pain, lancinating pain, and allodynia did not lead to satisfactory results.

This review was conducted to report the current evidence for KMT of PHN. However, the quality of evidence for the treatment with Korean medicine in Korea was insufficient because only case reports existed. In addition to this, the number of research studies was small, and the number of cases in each article was also small (1-2 cases in most of the studies). Moreover, it was difficult to determine the effect of a single treatment because several treatments were often used concurrently.

Nevertheless, this study is significant in that it is a comprehensive analysis of the relatively recent case studies in Korea where KMT is used for PHN. It is also meaningful as this review suggests the possibility that KMT would be effective for PHN symptoms because patients who received KMT improved with no serious side effects. It is believed that well-designed studies that can raise the level of evidence for KMT for PHN and should be conducted in the future. Furthermore, we expect to see KMT in clinical practice guidelines for PHN.

Conclusion

This study analyzed 12 case studies that were selected by searching for clinical research on the topic of PHN published from January 1, 2000, to December 31, 2020 in Korean databases (OASIS, RISS, NDSL, KISS, KMBASE). The following conclusions were reached:

1. Twelve research articles were reviewed, with a total of 17 cases included. The pain sites were in the thoracic region for 13 cases, the facial region for 3 cases, and the whole body for 1 case.
2. The most frequently used treatments for PHN were acupuncture and herbal medicine.

3. A total of 30 acupoints were used for the treatment of PHN, the most frequently used acupoints being LI4, LR3, and GB44.

4. Herbal medicine prescriptions were used in all 17 cases, with Sipjeondaebotanggami being used the most frequently (5 cases).

5. In total, 81 herbs were used in 20 prescriptions. Glycyrrhizae Radix et Rhizoma was used the most, and Poria Sclerotium was used the most as a principal herb.

6. For Western medicine treatment, gabapentin was used the most.

7. The evaluation of the treatment was mainly performed through pain assessment tools, and the VAS was the most frequently used (7 of the 12 articles).

Conflicts of Interest

The authors have no conflicts of interest to declare.

Ethical Statement

This research did not involve any human or animal experiment.

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