Ann Dermatol Vol. 23, No. 2, 2011 DOI: 10.5021/ad.2011.23.2.162

ORIGINAL ARTICLE

Efficacy of Piroxicam Patch Compared to Lidocaine Patch for the Treatment of Postherpetic Neuralgia

Jun Young Kim, M.D., Hyun Jung Lim, M.D., Weon Ju Lee, M.D., Seok-Jong Lee, M.D., Do Won Kim, M.D., Byung Soo Kim, M.D.[1,2]

Department of Dermatology, Kyungpook National University School of Medicine, Daegu, [1]Department of Dermatology, Pusan National University School of Medicine and [2]Medical Research Institute, Pusan National University Hospital, Busan, Korea

Background: The lidocaine patch has been effectively used as a first-line therapy to treat neuropathic pain such as postherpetic neuralgia (PHN). **Objective:** To evaluate the safety and efficacy of the topical piroxicam patch as a treatment option for the treatment of PHN. **Methods:** Eighteen patients completed a 3-session study, applying three different patches (lidocaine, piroxicam and control) in random order. A maximum of three patches were applied to the most painful area for three consecutive days (12 hours on followed by 12 hours off). Each session was conducted at least seven days apart. The changes in visual analog scale (VAS) scores based pain intensity, quality of sleep and adverse effects were recorded. **Results:** When compared to the control, both the lidocaine and piroxicam patches significantly reduced the mean VAS scores of pain intensity of all different types. However, the lidocaine patch was better at reducing allodynia, whereas the piroxicam patch was more effective for dull pain. The lidocaine patch worked faster than the piroxicam patch for the response to overall pain relief. **Conclusion:** The results of this study suggest the use of the piroxicam patch for dull pain and in patients where the lidocaine patch is contraindicated. **(Ann Dermatol 23(2) 162～169, 2011)**

-Keywords-
Allodynia, Dull pain, Lidocaine patch, Piroxicam patch, Postherpetic neuralgia

Received July 21, 2010, Revised December 20, 2010, Accepted for publication December 20, 2010
*This work was supported by clinical research grant from Pusan National University Hospital 2010.

Corresponding author: Byung Soo Kim, M.D., Department of Dermatology, Pusan National University School of Medicine, 305 Gudeok-ro, Seo-gu, Busan 602-739, Korea. Tel: 82-51-240-7338, Fax: 82-51-245-9467, E-mail: dockbs@pusan.ac.kr

INTRODUCTION

Pain causes significant discomfort in patients with herpes zoster, and postherpetic neuralgia (PHN) is a complication that causes the persistence of pain 1 to 6 months after the rash has healed[1-3]. Both the acute pain associated with herpes zoster and the chronic pain associated with PHN may interfere with quality of life including physical, emotional, and social functioning, as well as an increase in health care costs[4-7].

Oral medications such as opiates, tricyclic antidepressants and anticonvulsants are currently recommended for the treatment of PHN[8]. However, in clinical practice these agents frequently result in a poor therapeutic response and intolerable side-effects, especially in patients of advanced age. Thus, there is a need for more effective and better-tolerated therapies[8,9].

The topical administration of the local anesthetic lidocaine has been effective and extremely well tolerated for the treatment of PHN[10-13]. This formulation of topical lidocaine is applied directly to the painful skin in a patch vehicle, which has been shown to produce pain relief without significant elevation of serum levels[10,14]. However, the lidocaine patch cannot be used in patients with a history of neurosurgery or cardiovascular problems such as arrhythmias; it is also not recommended in patients that have hypersensitivity to topical amide anesthetics. Therefore, this randomized, controlled study was designed to assess the efficacy of the piroxicam patch as an alternative to the lidocaine patch in patients with PHN.

MATERIALS AND METHODS

Patients

Patients were eligible for this study if they had PHN,

defined as pain present for more than one month after the skin rash from herpes zoster had healed[1], a visual analogue scale (VAS, 0 mm=no pain, 100 mm=maximum pain) score of more than 40 mm, and a well-defined area of painfully sensitive skin on the trunk or extremities. Exclusion criteria included patients not in stable health, or patients that had medical contraindications to topical application of lidocaine and piroxicam. Patients that had received prior neurolytic or neurosurgical therapy for PHN were also excluded. Patients whose skin lesions were not completely healed and those that could not follow the study protocols were excluded. Any use of topical medications for herpes zoster, including capsaicin, steroids or antibiotics, had to be discontinued for at least one week prior to the first study session[15]. During the study, subjects were not permitted to use any topical agents on the area affected by PHN. However, they were allowed to continue oral medications previously used for the control of PHN at the same dosages that they had been using. However, patients could not change medications during the course of the study. All participants were enrolled after Institutional Review Board approval of the study, and all provided informed consent prior to participation.

Procedures

This study consisted of three sessions with different patches randomly applied to the area of the skin with greatest pain based on the patient reports. The three sessions included one session with the lidocaine patch (Lidotop®, Teikoku Seiyaku Co. Ltd., Higashikagawa, Japan, 700 mg/patch), another session with the piroxicam patch (Trast®, Life Science Research Center, Seoul, Korea, 48 mg/patch), and the last session with a control patch. The control patch (Mepilex Lite®, Mölnlycke Health Care, Göteborg, Sweden) was a soft silicone faced polyurethane foam material, widely used on wounds with exudates. A total of 20 patients were randomly divided into three groups of treatment in an 8:6:6 ratio and stratified by indication with treatment allocation via a centralized procedure. Each session was carried out for three consecutive days (12 hours on followed by 12 hours off) and typically included a drug wash-out period for at least one week. A maximum of three of the same patches were allowed for concurrent application. If a subject experienced prolonged relief during one session, the next session was delayed until pain returned to at least 70% of the average pain level prior to entering the study.

Efficacy and safety assessment

Daily telephone surveys of outpatients and face-to-face interviews of inpatients were carried out to assess the efficacy of each patch. Every participant was asked at baseline before every session of application and at least five additional points in time at each session (12 hours, 24 hours, 48 hours, 72 hours, and the seventh day after patch application) about the following information: verbal pain relief according to the nature of the pain, improvement of sleep quality, and any adverse events during the use of the patches. Different quality of the pain was categorized as overall pain, allodynia, dull pain, hypoesthesia, burning sensation, paresthesia, prickling sensation, stinging sensation, and tingling sensation. Overall pain was defined by a question of 'how painful in whole (including the combination of sensory discomfort, painful feelings, sensory change, sensory hypersensitivity, or others) do you feel from your herpes zoster?' Other categorized pains were also explained to patients by more understandable expressions, for example as an allodynia; a pain due to a thermal or mechanical stimulus which does not normally provoke pain, a dull pain; a pain which is generally described as blunt and a loss of keenness or sharpness, a hypoesthesia; a reduced sense of touch or sensation, or a partial loss of sensitivity to sensory stimuli, a burning sensation; a pain experienced in heat burns, a paresthesia; a pain characterized by sensory feelings of pins and needles, a prickling sensation; experiencing a painful shivering feeling as from many tiny pricks, a stinging sensation; a pain which is sudden and felt as a sting, and a tingling sensation; a pain to feel as if a lot of small sharp points are pushing into skin. Decrement of pain intensity was assessed using a horizontal 100 mm VAS by each patient. Patients indicated the severity of their pain with a mark along the line between 0 mm=no pain and 100 mm=the worst pain imaginable. Prior to a patch application, VAS scores were obtained three times over a 45 minute period. The quality of sleep was evaluated by asking the question, 'How did you sleep last night?' and was assessed using a category scale indicating that: 0=the sleep was 'very poor', 1=the sleep was 'poor', 2=the sleep was 'fair', 3=the sleep was 'good', 4=the sleep was 'very good'. The safety profile for local adverse reactions was assessed throughout the study.

Statistical analysis

The efficacy of the lidocaine and piroxicam patches compared to the control was assessed by changes in the mean VAS scores and the 4-item quality of sleep scales. The correlation between the efficacies of each patch was analyzed using the Mann-Whitney test. The efficacy of each treatment was analyzed using the Wilcoxon signed rank test. Statistical significance was assigned at the

$p=0.05$ level. The data is presented as the mean values±standard deviation, and all analyses were performed using the SPSS package 12.0 for Windows.

RESULTS

Patients

A total of 18 subjects, 10 men and 8 women, completed the study. Twenty subjects were initially recruited, but two patients dropped out due to severe burning sensation after lidocaine patch application. There was no subject who was freed from PHN during the study. Fig. 1 summarizes the overall process and patient disposition during the study. The age range was 41～87 years and the mean age was 64.4±12.50. The duration of PHN ranged from 4 to 152 weeks, with a mean duration of 54.4±48.90 weeks. The quality of pain in these 18 subjects was described as follows: 9 had a prickling sensation, 8 had allodynia, 6 had paresthesia, 5 had a burning sensation, and 4 had dull pain. In addition, 4 had hypoesthesia, 2 had a stinging sensation, and 2 had a tingling sensation (Table 1).

Efficacy assessment

1) Overall pain intensity

The overall pain intensity compared to the pretreatment levels, after the application of lidocaine and piroxicam patches, showed highly significant decrements ($p<0.05$ in both), however, the control patch ($p\geq0.05$) did not. Compared to the piroxicam patch, the lidocaine patch was better for reducing the overall pain intensity for 12 to 48 hours after application ($p<0.05$). The mean pre-treatment VAS scores for overall pain intensity were 71.9 mm for the lidocaine patch sessions, 71.7 mm for the piroxicam patch sessions, and 67.5 mm for the control. Changes in the mean VAS scores based on the time after different patch applications are shown in Fig. 2. During the lidocaine

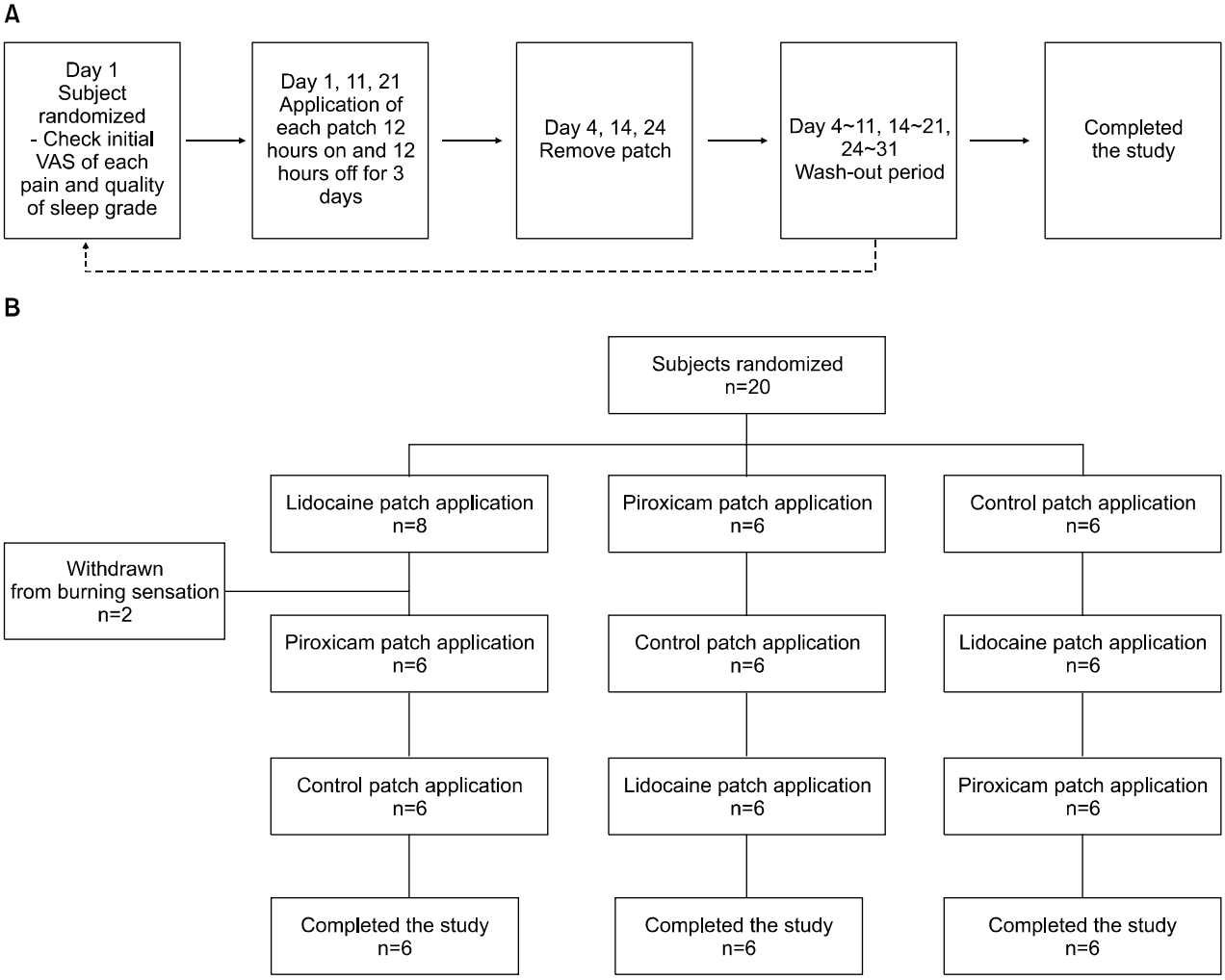

Fig. 1. Overall flow chart for the study procedure (A) and patient disposition (B).

Table 1. Characteristics and nature of pain in postherpetic neuralgia patients

Patient	Sex/Age	Disease duration (weeks)	Nature of pain	Order of applying patches
1	M/60	8	Burning, stinging, tingling	L - P - C
2	M/76	11	Stinging, tingling	P - L - C
3	F/70	22	Allodynia, dull pain	C - P - L
4	M/63	6	Paresthesia, prickling	C - L - P
5	F/87	10	Paresthesia, prickling	L - C - P
6	F/53	15	Allodynia, paresthesia, prickling	P - C - L
7	F/42	4	Allodynia, burning, dull pain	L - P - C
8	M/83	152	Paresthesia	P - L - C
9	F/59	81	Allodynia, prickling, burning	C - P - L
10	F/41	70	Paresthesia, prickling	C - L - P
11	M/71	66	Allodynia, burning	L - C - P
12	M/68	110	Allodynia, paresthesia	P - C - L
13	M/68	14	Allodynia, prickling	L - P - C
14	F/77	120	Prickling, hypoesthesia	P - L - C
15	M/65	35	Burning, dull pain	C - P - L
16	F/49	42	Prickling, hypoesthesia	C - L - P
17	M/71	80	Allodynia, dull pain, hypoesthesia	L - C - P
18	M/60	134	Prickling, hypoesthesia	P - C - L
Drop out	M/61	17	Due to intolerable severe burning sensation	L - stop
Drop out	F/54	8	after lidocaine patch application	L - stop

L: lidocaine patch, P: piroxicam patch, C: control patch.

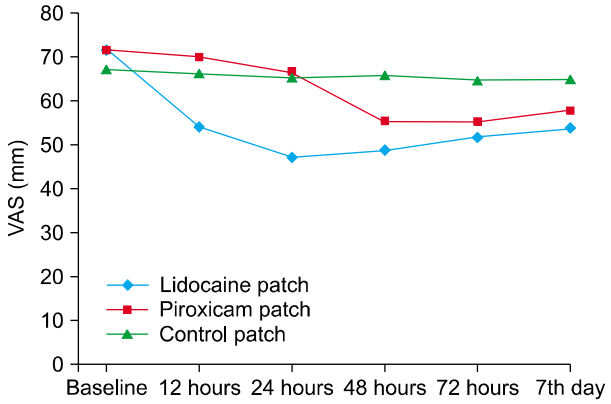

Fig. 2. Reduction of overall pain intensity assessed by visual analog scale.

sessions, the greatest reduction in the mean VAS score for overall pain intensity was 17.8 mm after a 12 hour application. However, the piroxicam patch had the greatest reduction in the VAS score, 11.6 mm, after 48 hours. Compared to the control, application of both lidocaine ($p<0.05$) and piroxicam ($p<0.05$) patches significantly reduced the overall pain intensity at all points in time from 12 to 48 hours (Table 2).

2) Other different categorized pain intensities

Although the effects at different time points varied significantly based on the quality of pain, the application of both lidocaine and piroxicam patches showed significant responses in the reduction of pain for all types of pain ($p<0.05$). For allodynic pain (Fig. 3), lidocaine was effective after 12 hours of application ($p<0.05$), whereas piroxicam was effective after 48 hours of application ($p<0.05$). For dull pain (Fig. 4), lidocaine was effective after 48 hours of application ($p<0.05$), whereas the piroxicam patch was effective after 12 hours of application ($p<0.05$). For hypoesthesia, the lidocaine patch showed a significant response after 12 hours of application ($p<0.05$) and the piroxicam patch after 24 hours of application ($p<0.05$). For a burning sensation, both lidocaine and piroxicam patches were effective after 24 hours of application ($p<0.05$). For paresthesia, the lidocaine patch and the piroxicam patch were effective after 24 hours ($p<0.05$) and 48 hours ($p<0.05$) of application, respectively. For a prickling sensation, both the lidocaine and piroxicam patches were effective after 24 hours of application ($p<0.05$).

When comparing the efficacy of the lidocaine and piroxicam patches for reducing the intensity of different types of pain, the lidocaine patch was superior for allodynia after 12 hours ($p<0.05$), hypoesthesia after 24 hours ($p<0.05$), and paresthesia after 48 hours ($p<0.05$) of application. However, for dull pain the piroxicam patch was more effective than the lidocaine patch after 12 hours of application ($p<0.05$). Although both patches showed a significant reduction in a burning and prickling sensation, there were no significant differences between the two patches for these types of pain ($p>0.05$). The results of the comparisons for the stinging and tingling sensations

Table 2. Visual analog scale scores and the 4-item quality of sleep scales on 6 point from patients after using the patches (mean±standard deviation)

		Baseline	12 hours	24 hours	48 hours	72 hours	7 days
Overall pain	Lidocaine patch	71.94±14.28	54.11±10.58	47.22±8.67	48.94±9.12	51.83±11.83	53.50±10.97
	Piroxicam patch	71.72±14.08	70.00±13.84	66.94±13.91	55.39±11.52	55.22±11.24	57.89±11.84
	Control patch	67.50±15.93	66.22±12.76	65.44±12.17	65.67±11.11	64.89±10.98	64.94±10.81
Allodynia	Lidocaine patch	89.13±8.36	52.25±6.56	50.50±4.90	55.13±6.79	57.00±7.33	56.88±6.29
	Piroxicam patch	89.38±9.04	85.88±8.94	82.13±9.11	79.25±9.24	77.13±9.95	75.88±10.34
	Control patch	89.00±9.50	87.63±9.18	87.13±9.30	87.50±9.13	87.50±8.38	86.88±9.28
Dull pain	Lidocaine patch	95.25±5.91	88.25±7.68	83.00±9.63	81.00±10.68	77.25±11.70	75.00±9.13
	Piroxicam patch	95.25±5.91	73.00±6.00	53.75±4.79	43.75±4.79	46.75±4.27	49.00±4.55
	Control patch	96.50±2.65	94.75±3.20	94.50±2.38	94.50±1.91	94.00±1.63	94.00±2.58
Hypothesia	Lidocaine patch	90.00±9.63	77.50±9.57	68.50±7.51	62.75±9.29	59.00±8.83	57.75±7.37
	Piroxicam patch	95.25±5.91	88.75±6.40	82.50±6.45	77.75±5.62	73.25±4.27	71.50±4.36
	Control patch	96.50±2.65	94.75±3.20	94.50±2.38	94.50±1.91	94.00±1.63	94.00±2.58
Burning sensation	Lidocaine patch	91.80±9.26	84.00±8.34	78.00±7.71	73.80±6.30	70.00±6.67	69.00±6.52
	Piroxicam patch	90.80±9.71	83.00±9.00	76.60±8.05	72.40±6.99	68.80±6.87	67.80±6.50
	Control patch	93.00±8.15	91.40±7.99	90.80±8.53	91.00±8.00	90.80±7.29	90.40±8.35
Paresthesia	Lidocaine patch	88.67±8.62	77.17±8.50	68.17±7.52	61.83±7.99	57.17±7.73	56.00±6.51
	Piroxicam patch	89.83±9.58	84.17±8.86	78.83±7.88	74.67±7.52	70.83±5.60	69.00±5.73
	Control patch	90.00±10.35	88.67±9.79	88.00±10.26	88.33±9.69	88.17±9.17	87.67±10.03
Prickling sensation	Lidocaine patch	89.44±7.88	82.56±6.75	77.22±6.44	72.56±5.46	69.44±5.22	67.78±5.07
	Piroxicam patch	90.00±8.66	85.56±8.56	81.22±7.46	77.22±6.53	74.22±6.42	72.56±6.29
	Control patch	89.67±9.11	88.44±8.93	87.67±8.85	88.22±8.81	88.11±8.05	87.33±8.79
Quality of sleep	Lidocaine patch	1.61±1.20	2.06±1.35	2.44±1.34	2.72±1.13	3.11±0.90	2.83±0.92
	Piroxicam patch	1.61±1.20	1.83±0.99	2.22±1.00	2.78±0.88	3.00±0.84	2.83±0.92
	Control patch	1.56±1.25	1.56±1.25	1.61±1.20	1.72±1.18	2.11±1.08	2.33±0.97

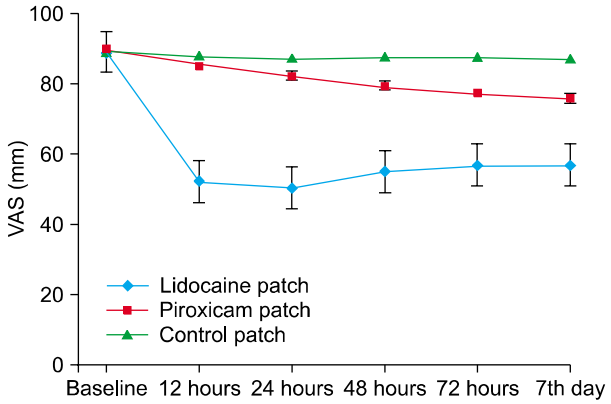

Fig. 3. Reduction of allodynic pain intensity assessed by visual analog scale.

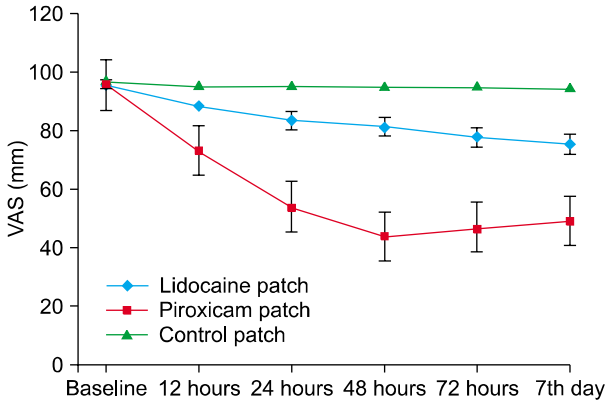

Fig. 4. Reduction of dull pain intensity assessed by visual analog scale.

were not significant but the number of patients with these symptoms was too small to reach accurate conclusions.

3) Quality of sleep

The quality of sleep was significantly better when one of the study patches were used compared to the control ($p<0.05$), but there was no significant difference between the two study patches ($p>0.05$) (Fig. 5).

Safety assessment

No serious adverse events were reported that may be looked as 'possibly' or 'probably' related to the study medication. The patients reported a burning sensation, erythema, pruritus, a tingling sensation and gastrointestinal (GI) discomfort. However, these events were usually 'mild' or 'moderate' in severity except for two patients who dropped out from severe burning sensation after applying a lidocaine patch. No significant difference was observed in the frequency of adverse events other than the burning sensation between the lidocaine and piroxicam patches (Table 3).

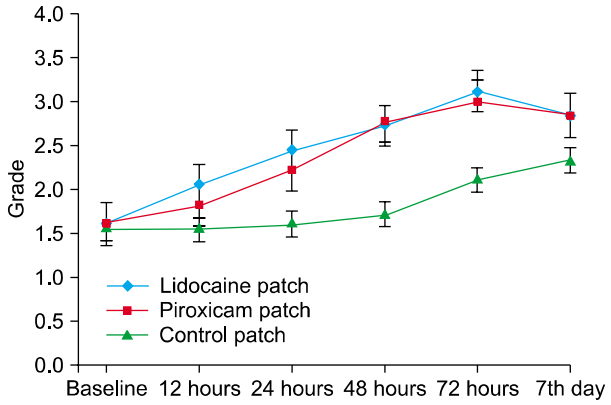

Fig. 5. Changes in the quality of sleep assessed by a 5-point-score.

DISCUSSION

PHN is a neuropathic pain syndrome occurring after the reactivation of varicella zoster virus. The acute outbreak of zoster may damage the peripheral nerve apparatus from the dorsal root to cutaneous nerve endings[16-18]. Surviving but damaged cutaneous nociceptor fibers in the area of pain may have abnormal spontaneous activity and be sensitized to mechanical or other stimuli[19-23]. These changes may in part be due to accumulation of sodium channels at the injury sites[23-25].

Similar to other types of neuropathic pain, PHN can be resistant to many types of pharmacological and interventional therapies. Pharmacological therapies include anticonvulsants, gabapentin and pregabalin, lidocaine patch, capsaicin cream, opioid analgesics and tricyclic antidepressants, which have been used and resulted in various outcomes[26]. In addition, interventional strategies such as sympathetic nerve blocks, spinal cord stimulation and surgical treatments have been used for treatment.

Oral medications are generally effective and are commonly used methods for the treatment of PHN, but they have some limitations. PHN is common in the elderly, and may be accompanied by underlying systemic disorders especially of the kidneys or liver. Therefore, their use can be restricted. In such cases, topical treatments can provide an alternative treatment with demonstrated safety. The lidocaine patch contains an adhesive with 5% lidocaine base (700 mg/patch), water, glycerin, D-sorbitol, sodium polyacrylate, sodium carboxymethylcellulose, propylene glycol and other ingredients on a non-woven polyester backing. The effect of the lidocaine patch on PHN has been shown in several reports[10-13] but several limitations have also been reported[27]. The lidocaine patch cannot be used in patients that have hypersensitivity to lidocaine or amide type compounds. In addition, patients with cardiovascular abnormalities, especially of the conductive system, are not candidates for the lidocaine patch (i.e., arrhythmia). Furthermore, some reports have demonstrated that the lidocaine patch may be ineffective in 19% of PHN patients[27].

Table 3. Side effects of lidocaine patch and piroxicam patch

Side effects	Lidocaine patch (n = 20)	Piroxicam patch (n = 18)	*p*-value
Burning sensation	13 (65.0%)	10 (55.5%)	0.0327
Erythema	3 (15.0%)	1 (5.6%)	0.7831
Pruritus	2 (10.0%)	2 (11.1%)	0.9989
Tingling sensation	2 (10.0%)	0 (0.0%)	0.0795
Gastrointestinal discomfort	0 (0.0%)	1 (5.6%)	0.9999

Therefore, other types of topical analgesics that can be applied for the treatment of PHN are under investigation. The piroxicam patch (Trast®, Life Science Research Center) is widely used as a topical analgesic that contains piroxicam (48 mg/patch) as well as additional ingredients. Arachidonic acid produces prostaglandin (PG) D2, PGE2, PGF2a, PGI, and thromboxane (Tx) A2 by the cyclooxygenase pathway, and the generated cytokines activate peripheral nociceptors. Piroxicams are known to inhibit cyclooxygenase non-selectively and therefore have analgesic and anti-inflammatory effects[28]. However, no prior study has shown the effects of the piroxicam patch on PHN. The results of this study support the assertion that low doses of lidocaine delivered through an intact stratum corneum to abnormally functioning afferents can relieve pain by reducing abnormal spontaneous and evoked activity. Likewise, topical piroxicam can also inhibit cyclooxygenase non selectivity, leading to inflammatory cytokines like prostaglandins (PGD2, PGE2, PGF2a, PGI2, TxA2) that activate peripheral nociceptors[16,17].

It is well known that there are several different types of pain associated with PHN. The efficacy and time of onset for reducing pain intensity can be different according to the type of pain and treatment modality. The results of this study showed that both the lidocaine and piroxicam patch showed significant effects in reducing the overall pain intensity of PHN. However, the lidocaine patch had a better, more rapid response than the piroxicam patch (Fig. 2). The reduction of overall pain intensity was greatest after 24 hours of application of the lidocaine patch, and after 48 hours of application of the piroxicam patch. According to the different types of pain, both the lidocaine and piroxicam patches continuously showed a significant reduction in the intensity of the pain but the degree of pain relief differed. For allodynia, hypoesthesia and

paresthesia, the lidocaine patch showed faster and better effects than the piroxicam patch (Fig. 3). However, for dull pain, the piroxicam patch had faster and better effects than the lidocaine patch (Fig. 4). There were no significant differences between the two patches for burning sensation and prickling sensation. The quality of sleep and degree of pain on baseline analysis, was reported as mostly poor to fair in the patients with PHN in this study. However, all participants achieved good grades after 72 hours of lidocaine or piroxicam patch application (Fig. 5). There was no significant difference in efficacy between the two patches ($p>0.05$). Compared to other modalities used for the management of PHN, both the lidocaine patch and the piroxicam patch have many advantages[9,11,26]. They are easy to apply and remove, and comfortable to wear under clothing for a long duration of time with a low frequency of skin irritation[9,11,26]. In addition, by padding and protecting the painful areas from contact, patients with PHN were able to wear clothes more comfortably with these patches. Patients with large affected areas of PHN have been treated with these patches fit specifically for the desired areas[9,11,12]. Systemic side effects are not a concern, which is a major drawback of opioids, anticonvulsants and antidepressants[9,11,12]. Even though there were some 'application site reactions', such as a burning sensation, skin redness or rash, local pruritus, and a tingling sensation after the application of the lidocaine or piroxicam patch, in this study, both patches were well tolerated and easily used with no significant differences. We excluded two patients with a severe burning sensation with the lidocaine patch. One patient that used the piroxicam patch had GI symptoms but it was unclear whether the symptoms were due to the patch or the use of other oral medications. Further studies using a large sample size are needed to confirm the efficacy and safety of topical patches used for the treatment of PHN since the number of people evaluated in the current study was relatively small.

In conclusion, the findings of the present study support the use of both the lidocaine patch and the piroxicam patch for the treatment of PHN, especially for patients that cannot take oral medications due to underlying systemic disease. When choosing the primary treatment modality for patients with PHN, the lidocaine patch would be preferred in patients that complain of allodynia, hypoesthesia, or paresthesia, whereas the piroxicam patch would be preferred for dull pain. In addition, the piroxicam patch could be preferred as an alternative in patients who have limitations in using of lidocaine patch.

REFERENCES

1. Rowbotham MC. Treatment of postherpetic neuralgia. Semin Dermatol 1992;11:218-225.
2. Eaglstein WH, Katz R, Brown JA. The effects of early corticosteroid therapy on the skin eruption and pain of herpes zoster. JAMA 1970;211:1681-1683.
3. Park SY, Kim JY, Kim CD, Kim CW, Lee KS. A clinical study on herpes zoster during the last 10-year-period (1994～2003). Korean J Dermatol 2004;42:1531-1535.
4. Coplan PM, Schmader K, Nikas A, Chan IS, Choo P, Levin MJ, et al. Development of a measure of the burden of pain due to herpes zoster and postherpetic neuralgia for prevention trials: adaptation of the brief pain inventory. J Pain 2004;5:344-356.
5. Katz J, Cooper EM, Walther RR, Sweeney EW, Dworkin RH. Acute pain in herpes zoster and its impact on health-related quality of life. Clin Infect Dis 2004;39:342-348.
6. Berger A, Dukes EM, Oster G. Clinical characteristics and economic costs of patients with painful neuropathic disorders. J Pain 2004;5:143-149.
7. Dworkin RH, White R, O'Connor AB, Baser O, Hawkins K. Healthcare costs of acute and chronic pain associated with a diagnosis of herpes zoster. J Am Geriatr Soc 2007;55:1168-1175.
8. Watson CP. Medical treatment of postherpetic neuralgia. In: Watson CP, editor. Herpes zoster and postherpetic neuralgia. 1st ed. Amsterdam: Elsevier, 1993:205-219.
9. Alakloby OM, AlJabre SH, Randhawa MA, Alzahrani AJ, AlWunais KM, Bukhari IA. Herpes zoster in eastern Saudi Arabia: clinical presentation and management. J Drugs Dermatol 2008;7:457-462.
10. Rowbotham MC, Davies PS, Verkempinck C, Galer BS. Lidocaine patch: double-blind controlled study of a new treatment method for post-herpetic neuralgia. Pain 1996;65:39-44.
11. Kissin I, McDanal J, Xavier AV. Topical lidocaine for relief of superficial pain in postherpetic neuralgia. Neurology 1989;39:1132-1133.
12. Rowbotham MC, Fields HL. Topical lidocaine reduces pain in post-herpetic neuralgia. Pain 1989;38:297-301.
13. Meier T, Faust M, Hüppe M, Schmucker P. Reduction of chronic pain for non-postherpetic peripheral neuropathies after topical treatment with a lidocaine patch. Schmerz 2004;18:172-178.
14. Rowbotham MC, Davies PS, Galer BS. Multicenter, double-blind, vehicle-controlled trial of long term use of lidocaine patches for postherpetic neuralgia [abstract]. Proceedings of the 8th World Congress on Pain. Seattle: IASP Press, 1996:274.
15. Kanai A, Kumaki C, Niki Y, Suzuki A, Tazawa T, Okamoto H. Efficacy of a metered-dose 8% lidocaine pump spray for patients with post-herpetic neuralgia. Pain Med 2009;10:902-909.
16. Csóka G, Balogh E, Marton S, Farkas E, Rácz I. Examination of the polymorphism of piroxicam in connection with the preparation of a new "soft-patch" type pharmaceutical

dosage form. Drug Dev Ind Pharm 1999;25:813-816.
17. Nicholls DS. Treatment of postherpetic neuralgia with topical piroxicam gel. N Z Med J 1993;106:233-234.
18. Dainty P. Prevention and medical management of postherpetic neuralgia. Br J Hosp Med (Lond) 2008;69:275-278.
19. Cline MA, Ochoa J, Torebjörk HE. Chronic hyperalgesia and skin warming caused by sensitized C nociceptors. Brain 1989;112:621-647.
20. Tanelian DL, MacIver MB. Analgesic concentrations of lidocaine suppress tonic A-delta and C fiber discharges produced by acute injury. Anesthesiology 1991;74:934-936.
21. Bowsher D. Sensory change in postherpetic neuralgia. In: Watson CP, editor. Herpes zoster and postherpetic neuralgia. 1st ed. Amsterdam: Elsevier, 1993:97-107.
22. Haanpää M, Laippala P, Nurmikko T. Pain and somatosensory dysfunction in acute herpes zoster. Clin J Pain 1999; 15:78-84.
23. Pappagallo M, Oaklander AL, Quatrano-Piacentini AL, Clark MR, Raja SN. Heterogenous patterns of sensory dysfunction in postherpetic neuralgia suggest multiple pathophysiologic mechanisms. Anesthesiology 2000;92:691-698.
24. Devor M, Govrin-Lippmann R, Angelides K. Na+ channel immunolocalization in peripheral mammalian axons and changes following nerve injury and neuroma formation. J Neurosci 1993;13:1976-1992.
25. Oaklander AL. Mechanisms of pain and itch caused by herpes zoster (shingles). J Pain 2008;9:S10-S18.
26. Tyring SK. Management of herpes zoster and postherpetic neuralgia. J Am Acad Dermatol 2007;57:S136-S142.
27. Devers A, Galer BS. Topical lidocaine patch relieves a variety of neuropathic pain conditions: an open-label study. Clin J Pain 2000;16:205-208.
28. Furst DE, Munster T. Nonsteroidal anti-inflammatory drugs, disease-modifying antirheumatic drugs, nonopioid analgesics, & drugs used in gout. In: Katzung BG, editor. Basic and clinical pharmacology. 8th ed. New York: McGraw-Hill, 2001:596-623.