Submitted: 18 January, 2021 Accepted: 18 May, 2021 Published: 08 January, 2022 DOI:10.22514/sv.2021.114

Open Access
Signa Vitae

ORIGINAL RESEARCH

Topical 5% lidocaine patches for treating postherpetic neuralgia: a survey among nurses and patients

Joseph V. Pergolizzi Jr.[1], Sri Nalamachu[2], Kailyn Mitchell[1], Antonella Paladini[3], Robert Taylor Jr.[1,*], Giustino Varrassi[1,4]

[1]NEMA Research Inc., 868 106th Ave North, Naples, FL 34108, USA
[2]Mid-America Poly Clinic, 7100 College Boulevard, Overland Park, Overland Park, KS 66210, USA
[3]Department of MESVA, University of L'Aquila, 67100 L'Aquila, Italy
[4]Paolo Procacci Foundation, Via Tacito 7, 00193 Roma, Italy

***Correspondence**
rtaylor@nemaresearch.com;
robert.taylor.phd@gmail.com
(Robert Taylor Jr.)

Abstract

Introduction: Postherpetic neuralgia (PHN) is associated with moderate to severe pain with peripheral and central mechanisms. While there is no clear-cut first-line therapeutic approach to PHN pain control, lidocaine patches are frequently used as monotherapy or part of a multimodal pain regimen.

Methods: An online survey, the first of its kind, was conducted among PHN patients (n = 153) and nurses (n = 151) in order to determine clinical and patient knowledge, attitudes and practices toward the lidocaine patch and current unmet needs.

Results: Results of the survey indicated that PHN patients are prescribed a mean of 2.6 medications to control their PHN pain, including the lidocaine patch. There were negative responses related to the patches' ability to adhere to the skin. Patients reported the use of tape to hold the patches in place and/or patches that detached completely, truncating the therapeutic dose period. Most nurses (53%) found the biggest obstacle to PHN pain control was noncompliance and 98% stated that reliable patch adhesion for the intended 12-hour application was "somewhat important" or "very important" for PHN pain control. Forty-five percent of nurses said that poor patient adherence to PHN analgesic regimens was related to poor adhesion of the lidocaine patch.

Conclusion: A new bioequivalent lidocaine patch has been developed with better adhesive characteristics, nine-fold greater bioavailability, and improved form factor.

Keywords

Post-herpetic neuralgia; Lidocaine patch; Survey; Nurses; Pain; Quality of life; Daily living

1. Plain language summary

Post-herpetic neuralgia (PHN) occurs when pain persists following an episode of shingles. PHN can cause moderate to severe pain, which may be treated in several ways. One of the most frequent pain-control treatments is the use of a lidocaine patch. A survey was conducted to assess the knowledge, attitudes and practices of clinicians and patients about the lidocaine patch and uncover current unmet needs. Patients and nurses were surveyed about the use of the lidocaine patch and one of the drawbacks of an older version of the patch was the fact that it did not remain properly affixed for the 12 hours needed for treatment. Most patients and nurses found that the patch provided effective pain control. On average, patients refilled their lidocaine patch prescription three times and 26% of patients used more than three refills. Since the time of the survey, a new lidocaine transdermal system has been developed which has higher bioavailability, lighter in weight and designed for better, long-lasting adhesion. Since most patients (80%) and most nurses (88%) thought a lidocaine patch with longer-lasting ability to adhere to the body was needed, the introduction of this new product is timely.

2. Introduction

Postherpetic neuralgia (PHN) is the most frequently reported complication of varicella zoster (VZ) viral infection (shingles) with an estimated incidence of 9% to 19% [1–3]. PHN typically occurs among older people who have had chickenpox more than 20 years ago and is likely to become increasingly prevalent with the aging population [1]. Risk factors for PHN include advanced age, stress, suppressed immune system, the use of immunosuppressive drugs, autoimmune disorders, certain solid cancer, certain chronic diseases such as chronic obstructive pulmonary disease, depression, recent physical trauma, and recent exposure to the VZ virus [1].

PHN is associated with moderate to severe or very severe pain of varying characteristics (dull, throbbing, electric, shooting, stabbing) and an unpredictable manifestation. Thirty to 50% of those with PHN have pain that has persisted a year or more [4]. Pain typically follows the course of the nerve along the acute segmental rash of the VZ [5, 6]. Guidelines for

TABLE 1. First-line therapies for PHN based on guidelines for the European Federation of Neurological Societies (EFNS) [7], the American Academy of Neurology (ANN) [10], the Canadian Pain Society (CPS) [11], and the Neuropathic Pain Special Interest Group (NeuPSIG) of the International Association for the Study of Pain (IASP) [8]. It should be noted that the ANN guidance from 2004 appears in the table below but has since been retired. Not all of these guidelines addressed PHN specifically.

	AAN 2004 (ret)	EFNS 2010	CPS 2014	NeuPSIG of IASP 2015
1st Line	PHN	Neuropathic pain (PHN section)	Neuropathic pain	Neuropathic pain
	Gabapentin/pregabalin	Gabapentin/pregabalin	Gabapentin/pregabalin	Gabapentin/pregabalin
	Lidocaine patch	Lidocaine patch (in elderly)	SNRI*	Lidocaine patch (especially frail, elderly)
	Opioid*	TCA*	TCA*	SNRI*
	TCA*			TCA*
2nd Line	Aspirin in cream or ointment*	Opioid*	Lidocaine patch (for PHN)	For peripheral pain:
	IT methyl-prednisonlone*	Topical capsaicin	Opioid*	Capsaicin patch
	Topical capsaicin		Tramadol*	Lidocaine patch
				Tramadol*

AAN, American Academy of Neurology; CPS, Canadian Pain Society; EFNS, European Federation of Neurological Societies; IASP, International Association for the Study of Pain; IT, intrathecal; NeuoPSIG, Neurological Pain Special Interest Group; PHN, post herpetic neuralgia; SNRI, selective norepinephrine reuptake inhibitor; TCA, tricyclic antidepressant.
The asterisk (*) designates a therapy that is not approved by the U.S. Food and Drug Administration for post-herpetic neuralgia (PHN) pain.

the control of pain associated with PHN recommend lidocaine plasters as well as systemic agents such as anticonvulsants, tricyclic antidepressants, and opioids. Therapy may involve a single agent or combination. There is no clear optimal first-line course of treatment, but lidocaine plasters are among the first- or second-line medications recommended and are often an important part of multimodal pain therapy [7–9]. See Table 1 (Ref. [7, 8, 10, 11]).

Despite numerous options for PHN pain control, there is no clear-cut first-line therapy and PHN analgesia remains suboptimal. In fact, less than half of all PHN patients report a >50% pain reduction with any type of therapy [12, 13]. This creates concern and frustration among both patients and healthcare professionals that is exacerbated by the fact that PHN pain is complex. Since PHN involves a reactivation of latent VZ virus that results in an inflammatory response, it is capable of destroying both peripheral and central neurons [14, 15]. Even when the rash of PHN resolves, neural damage and inflammation can lead to central sensitization and chronic pain, resulting in a complex pain syndrome with a neuropathic component [6, 13, 16, 17]. The lidocaine patch concept confers the apparent advantage over systemic pharmacological treatments in that there is low systemic absorption of the drug, associated with fewer and milder side effects [18, 19]. This can be of particular importance for patients on polypharmacy, which is more prevalent among geriatric than younger patients [20]. Furthermore, topical delivery systems are thought to be relatively easy to use and well accepted by patients.

The introduction of a 5% lidocaine plaster (Lidoderm®, Hind Health Care, Inc., San Jose, California) in 1999 provided topical delivery of lidocaine to PHN patients. Lidocaine patches were soon considered a first-line approach to PHN by many specialty societies and found resonance among patients and prescribers [7, 8, 10]. Early reports of inadequate patch adhesion occurred in the Food and Drug Administration (FDA) Adverse Events Reporting System (FAERS) [21]. Anecdotal reports of patient dissatisfaction and suboptimal compliance followed. A new topical lidocaine patch (ZTLIDO®, SCILEX, San Diego, California) was designed to overcome the adhesion problem. This new patch uses 1.8% lidocaine but is bioequivalent to the 5% patch, meaning both products are similarly efficacious.

Compliance with the older patch system has been suboptimal, which has resulted in the pain of PHN not being effectively controlled. Furthermore, there may be other unmet medical needs associated with pain control of PHN. In order to better understand the needs of PHN patients with respect to lidocaine plaster therapy and the attitudes of the nurses caring for such patients, a survey was conducted to determine the unmet medical needs in PHN and the potential role of lidocaine plasters. The objective of this survey was to better describe PHN therapy using lidocaine patches and the perceptions and opinions of patients and their nurses about lidocaine patches used to help manage PHN pain. Note that this survey predated the market release of this new and improved lidocaine patch and the views about lidocaine patches expressed in the survey refer exclusively to the older patch models.

The purpose of this survey was to assess the attitudes of nurses and patients using the lidocaine patch in terms of its safety, efficacy, and practicality.

3. Methods

Two companion internet anonymized surveys were conducted in May 2016. The “patient survey” was conducted among American adults >18 years with a PHN diagnosis within the

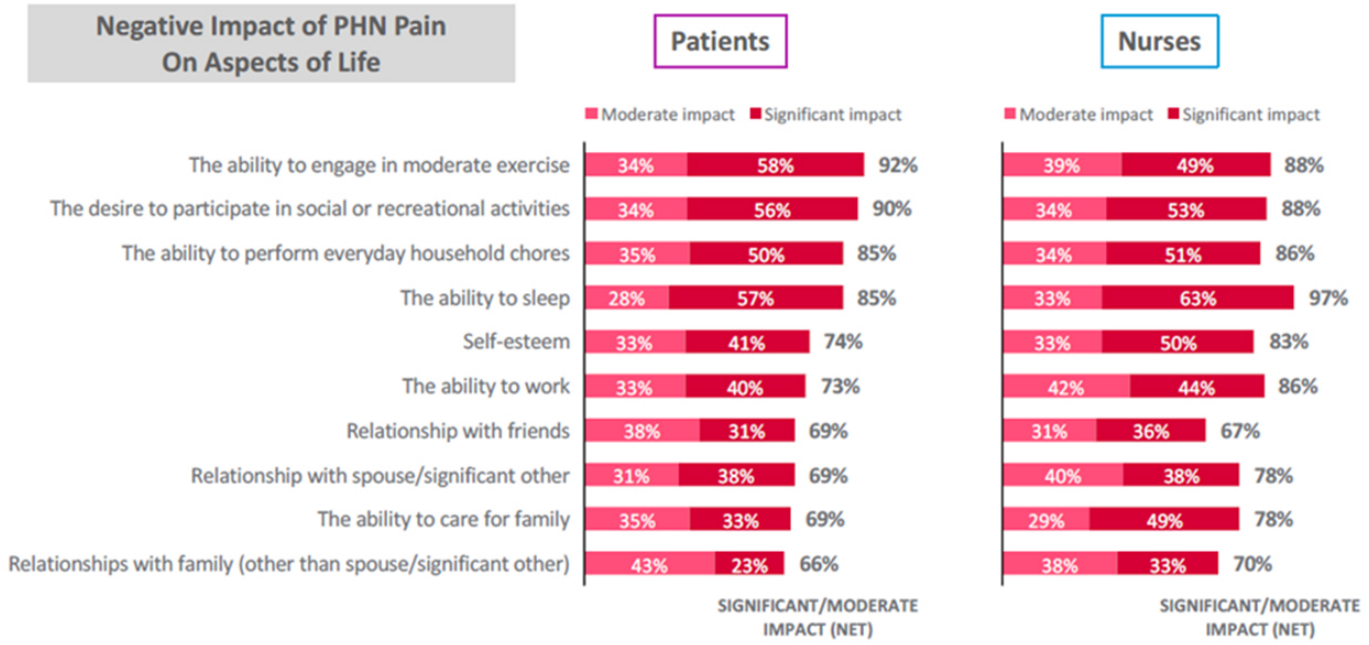

FIGURE 1. Patients and nurses were asked which areas of the patients' live have been negatively impacted by after-shingles pain. Respondents could give more than one answer.

past two years and who used lidocaine patches in that time for pain control. The "nurse survey" was conducted at the same time by the same investigators among American registered nurses and nurse practitioners who were >18 years or older, employed full-time in a non-pediatric healthcare practice and who consulted with at least five PHN patients in the past six months and who have used lidocaine patches to treat PHN in the past two years. Survey participants consented into the survey prior to answering any questions. No identifying information was obtained or recorded during the course of the survey. No identifying information was recorded to link a person with the data such that it could reasonably harm the individual's reputation, employability, financial standing, or place them at risk for criminal or civil liability. The surveys were not reviewed by an IRB.

Data from patients about their diagnoses, conditions, and prescription medications came from patients' responses to the survey and were not cross-checked against medical records.

4. Results

A total of 153 patients and 151 nurses participated in these surveys. Demographic data appears in Table 2. Surveys covered PHN pain and its impact on daily living, PHN treatments and unmet medical needs, and the evaluation of lidocaine patches for PHN treatment.

4.1 HN background and its impact on daily living

Patients (68%) stated that the after-shingles pain lasted 1 to 6 months, with a mean of 6.2 months. 5% of patients said their pain lasted ≥13 months. When asked to rate PHN pain intensity, 91% of patients and 74% of nurses said that PHN pain was moderate to severe. Nurses reported PHN pain in their patients as mild more frequently than patients did (26% vs. 9%, respectively). Key findings are summarized in Table 3.

When asked the extent to which PHN pain affected the patients' ability to engage in the activities of daily living, 37% of patients said their PHN pain had adversely affected daily living "a great deal" and 32% of nurses said the same. PHN patients specifically reported that PHN pain negatively affected their ability to exercise (58%), sleep (57%), participate in social or recreational activities (56%), and perform household tasks (50%). Only 4% of patients and 3% of nurses reported that PHN pain had no effect at all on their ability to go about ordinary daily activities. Patients reported that their PHN pain "moderately" or "significantly" affected their ability to work (33% and 40%, respectively) and 74% said it "moderately" or "significantly" impacted their self-esteem. PHN pain interfered with the patient's relationship with spouse/partner "moderately" or "significantly" for 69% of respondents. See Fig. 1.

4.2 PHN treatments and unmet medical needs

There is no standard course of treatment for PHN pain control, and there remain many gaps in treatments despite the fact that there are numerous treatment options. See Table 4. Patients who consult prescribers for PHN pain relief are prescribed a mean of 2.6 medications; only 11% said they got only one prescription, and 13% got four or five medications. In clinical practice, lidocaine is typically a first-line treatment [22] with about two-thirds of patient respondents (66%) in our survey saying they were prescribed a patch alone or as part of combination therapy as their initial treatment. The most commonly prescribed combination therapy reported was the lidocaine patch plus an NSAID (15%).

While 87% of nurses stated they believed their patients

TABLE 2. Demographics of nurse and patient study populations.

	Nurses	Patients
Population	151	153
Mean age	43.3 years	45.2 years
Sex (percentage males)	21%	50%
Educational background		
High school or less	3%	20%
Attended college and/or college degree	54%	51%
Graduate school and/or graduate degree	42%	25%
Race, ethnicity		
White	59%	51%
Hispanic	9%	38%
African-American, black	23%	8%
Asian	5%	2%
Native American or Alaskan Native	1%	0
Declined to answer	2%	0
Marital status		
Married or civil union	65%	55%
Divorced, widowed, separated	17%	13%
Living with partner	5%	10%
Never married	14%	23%
Nursing roles		
Registered nurse	71%	
Nurse practitioner	29%	
Hospital-based work setting	48%	Not applicable
Physician office work setting	23%	
Mean number of PHN patients treated in past six months	23.7 patients	
Mean number of patients with shingles treated in past six months	39.7 patients	
Patient employment		
Total employed in some capacity		79%
Full-time employment		65%
Part-time employment		4%
Self-employed, full-time		7%
Self-employed, part-time	Not applicable	3%
Not employed but seeking work		4%
Retired		9%
Not employed due to disability or illness		5%
Stay-at-home spouse or partner		3%
Student		0
Patient conditions		
Shingles		100%
Hypertension		63%
High cholesterol		60%
Anxiety		52%
Diabetes	Not applicable	46%
Depression		42%
Stomach ulcers or bleeding		27%
Liver disease or cirrhosis		26%
History of myocardial infarction		24%
Medicines prescribed in past two years for PHN		
Lidocaine patch (inclusion criterion)	100%	100%
Opioids	56%	49%
NSAIDs	65%	48%
Gabapentin or pregabalin	65%	45%
Tricyclic antidepressants	43%	37%
Geographical region		
South	48%	43%
Midwest	23%	11%
West	16%	28%
East	14%	19%

TABLE 3. Key points about PHN pain and its impact on daily living.

Finding	Key data	Comments
After-shingles pain persists for an average of 6.2 months in survey respondents	1–6 months (68% of respondents) 7–12 months (22% of respondents) 13+ months (5% of respondents)	32% of patients had pain for >6 months
Most patients and nurses describe PHN as moderate to severe	Patients: 91%, Nurses 74%	Only 9% of patients said pain was mild compared to 26% of nurses
The ability to engage in daily activities is negatively impacted by PHN pain	Moderate to severe adverse impact reported by 85% of patients and 88% of nurses	
PHN pain has negative impact on various aspects of patients' lives	Most affected areas: sleep, exercise, social activities, chores, work	

were satisfied with pain relief offered by their first-line approaches to PHN pain (including but not limited to lidocaine patches), fewer patients (54%) reported satisfaction with first-line approaches. Patients dissatisfied with their PHN treatment almost always chose to speak with their physician (97%) with 33% addressing their concerns to a nurse and 28% to a pharmacist. Only 1% of patient respondents said they did not express therapeutic dissatisfaction to anyone. When patients on opioid monotherapy complained of inadequate analgesia, 67% of nurses reported the physician would add the lidocaine patch, 53% added an anticonvulsant, 44% added NSAIDs, and 36% added tricyclic antidepressants. Nurses stated that about half of their patients required a second analgesic to get effective pain relief and 38% of them said in such cases a lidocaine patch was added compared to 17% getting an add-on anticonvulsant and 15% an opioid. Multimodal therapy is common in PHN patients and 95% of nurses stated that patients were "very" or "somewhat" satisfied with such combination regimens.

When patients had questions about PHN pain or wanted to know about ways to treat it, 42% of patients said they were "always" satisfied with what they learned from the physician, 20% were "always" satisfied with answers from their pharmacists, and 18% were "always" satisfied with the answers provided by nurses. Patients reported they were most comfortable speaking to physicians (61%) compared to nurses (44%) and pharmacists (32%).

Only 22% of patients reported they had "complete understanding" of their PHN pain and 26% said they had "full confidence" in their treatment plans to manage this pain. About half of patients (54%) said that they needed more than one medication to control PHN pain and 51% reported that their PHN pain was more bearable after taking their prescribed medication(s).

The barriers to better analgesia for PHN were described by nurses, with the most-reported obstacle being noncompliance (named by 53% of nurses). In fact, 12% of nurses rated noncompliance as the single "biggest challenge" in PHN patient care. Other barriers to optimal care were lack of patient understanding about when and how to take their medications, difficulties with comorbidity management, lack of specific PHN pain control guidelines, drug-drug interactions, and adverse events. Patient compliance must be considered one of the main barriers to optimal PHN pain control for all types of treatments. Nurses reported that poor compliance for all PHN treatment regimens had to do with managing multiple medications (57%) and a lack of patient understanding how and when to take or use their medications (51%). For lidocaine patches specifically, poor adhesion of the patch (45%), inconvenience (34%), and messiness of using a patch (34%) were reported. With respect to systemic agents, noncompliance was thought by nurses to be associated with adverse events (29%) or poor efficacy (23%). When the nurses were asked to name the major factors contributing to patient noncompliance in general, they named lack of understanding of how and when to take or use the medications (23%), the difficulties in managing multiple medications (22%), poor adhesion offered by lidocaine patches (15%), inconveniences associated with both patches and gels (11%), and inadequate efficacy (11%).

Despite the wealth of pain medications in the PHN armamentarium, 18% of nurses were not aware that the American Academy of Neurology (AAN) recommends lidocaine patches for treating PHN pain.

4.3 Evaluation of PHN treatment using lidocaine patches

Most patients and nurses (79% and 84%, respectively) reported that the lidocaine patch was prescribed as first- or second-line treatment for PHN pain and 16% of both patients and nurses said it was first prescribed as third-line treatment. Patients and nurses expressed strong opinions about current patches; see Table 5. On average, patients refilled their prescription for the lidocaine patch 3.0 times and 26% refilled it $\geq$4 times. When nurses were asked the key factors of importance to them in selecting a lidocaine patch, they said it was "very" or "somewhat" important that the patch maintain skin contact over 12 hours (98%), maintain skin contact even during heat or during exercise (94%), and that data on patch adhesion be available (87%). About a third of nurses (36%) reported they found the lidocaine patch "very effective" in treating PHN pain while 91% found the patch "very" or "somewhat" effective. A variety of factors were reported by nurses as to why they found patches less than efficacious. See Fig. 2.

Only a subset of patients (30%) report being "very" satisfied with the lidocaine patch with 50% more reporting being "somewhat" satisfied. In contrast, 58% of nurses thought patients were "somewhat satisfied" with the lidocaine patch. Nurses

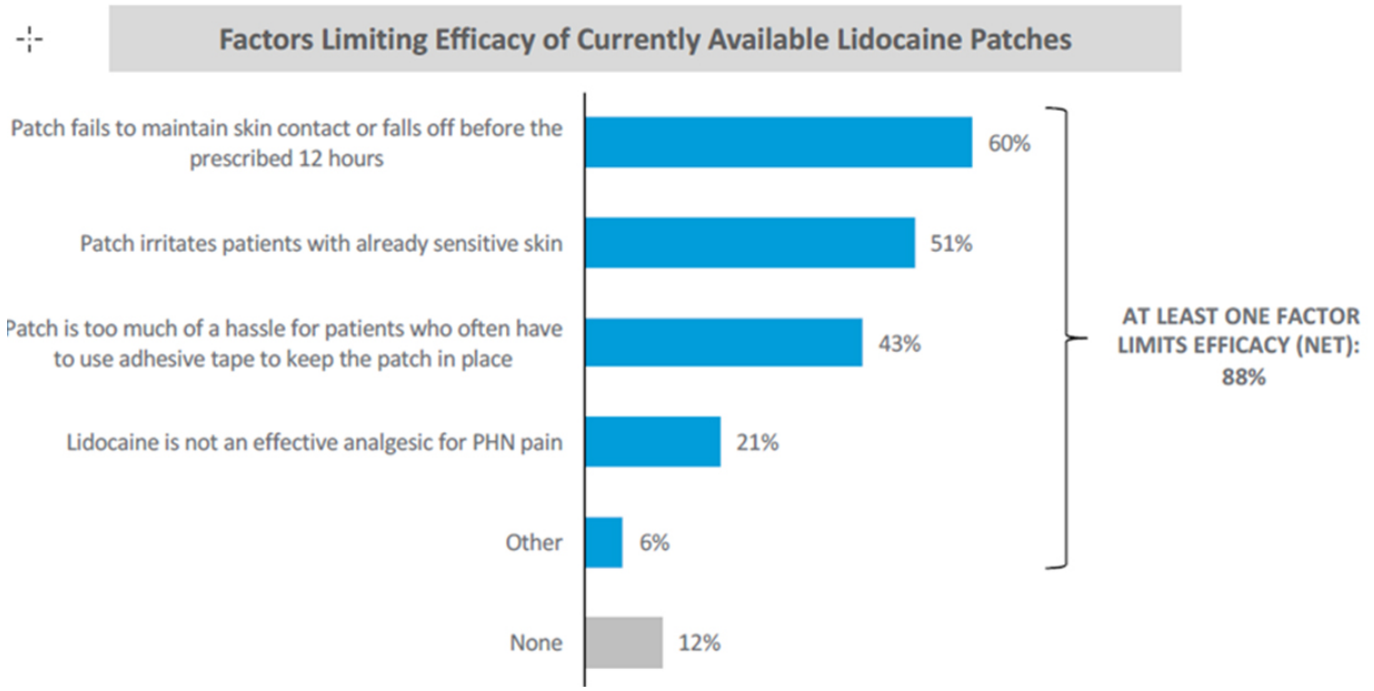

FIGURE 2. Asked of nurses (n = 151): "Which of the following factors, if any, do you believe limit the efficacy of the lidocaine patches that are currently available?" Respondents were permitted to select more than one answer.

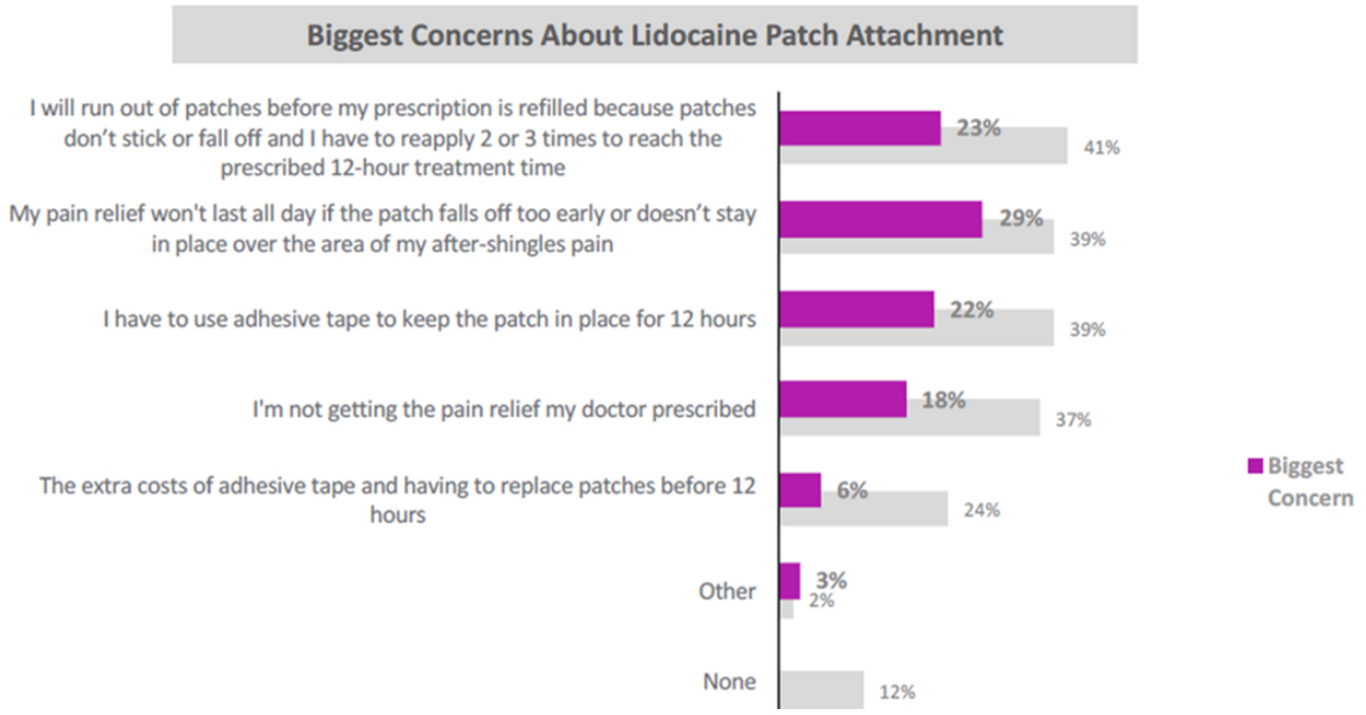

FIGURE 3. Asked of all patients (n = 153), "Which of the following, if any, are you biggest concerns about the lidocaine patch not staying attached to your skin and/or not staying in place over the area of after-shingles pain?" Respondents were permitted to give more than one answer.

felt that patients were dissatisfied with the patch because of poor adhesion (57%), lack of efficacy (55%), the need to use tape or other means to keep the patch in place (46%), and difficulty applying the patch (23%). About two-thirds of patients (62%) agreed that they were frustrated with patch adhesion or that it did not stay in place over the affected site. In fact, 14% stated they were "very" frustrated about patch adherence. The patch is to remain in place for 12 hours for the recommended treatment, but 85% of patients said the patch did not always remain properly affixed for the duration of treatment. More than half of patients (51%) said the patch moved or became detached ≥3 times. Most patients (80%)

TABLE 4. Key findings about PHN treatments, pain control, and barriers to optimal therapy.

Finding	Key data	Comments
The average number of pain medications prescribed as front-line treatment is 2.6	78% of patients were prescribed 2 or more medications during first pain experience	Most patients report multimodal therapy is more effective than monotherapy
First-line treatment typically includes lidocaine patches	66% of patients were prescribed the lidocaine patch alone or with other medicines as first treatment	When combined, lidocaine patches were most often used with an NSAID
		When second-line therapy was prescribed, lidocaine patches were also the most frequent choice
Moderate satisfaction with first-line pain relief	54% of patients and 87% of nurses were very or somewhat satisfied with pain control	Almost half of patients (46%) were very or somewhat dissatisfied while most nurses were very or somewhat satisfied
Nearly all who were dissatisfied spoke to the doctor	Only 1% did not speak to anyone; 97% talked to the physician	Patients seemed most comfortable speaking to a physician
Lidocaine patches used to augment opioid-only therapy in many	When PHN pain is not controlled by opioid monotherapy, 67% of the time a lidocaine patch is added	Lidocaine patches are frequently used as part of multimodal therapy
Patches are also prescribed most often second-line	When any therapy must be augmented with another pain reliever, 38% of the time, lidocaine patches are used	47% of PHN patients who are not prescribed patches as first-line treatment require two analgesics to control pain
Nurses believe that patient satisfaction is higher with multimodal therapy	Nearly all nurses (95%) report that patients are very or somewhat satisfied when 2 or more analgesics are used	Fewer patients (66%) than nurses say they are satisfied or very satisfied with two or more analgesics
Most patients say that healthcare providers are not always able to provide the answers they need	According to patients, nurses have the answers 40% of the time compared to pharmacists at 47% and physicians at 70%	61% of patients say they are very comfortable asking questions of their physician compared to 44% who are very comfortable asking nurses and 32% are very comfortable asking pharmacists
Complete understanding of pain is low	Only 22% of patients report that they have complete understanding of pain and their medications	23% of patients said they "don't fully understand" or have no understanding of pain and their medications
Complete confidence in treatment plan is low	26% of patients report being "very confident" about their treatment plan for PHN pain	Most patients were less than fully confident in their treatment strategy
Few patients say medicine offered complete pain relief	16% reported complete pain relief and 51% said PHN pain was more bearable after taking medications	54% of patients overall said they needed more than one medication to control their PHN pain
Patient noncompliance seen as challenge to treatment efficiency	53% of nurses saw patient noncompliance as a challenge with PHN treatment and 12% said it was the single "biggest challenge"	Other challenges were patients not understanding how to take their medicine, comorbidities, lack of PHN guidelines, drug-drug interactions, adverse events, and poor efficacy
Nurses report patch-related factors as contributing to noncompliance	45% of nurses say that poor adhesion led to poor compliance	Poor adhesion can cause the patch to move off the pain site, detach, or require tape to hold in place; patients and nurses view this as an inconvenience
One in five not aware the American Academy of Neurology recommends patches for PHN treatment	18% of nurses did not know that the American Academy of Neurology recommended lidocaine patches	There are few guidelines specific to PHN pain control

TABLE 5. Nurses' and patients' evaluations of the lidocaine patch as PHN pain treatment.

Finding	Key data	Comments
Most patients and nurses say lidocaine patches are prescribed first- or second-line	80% of patients reported the patch was first- or second-line therapy, similar to nurses where 84% said the patch was first or second line	Only 16% of both patients and nurses reported the patch was used as a third-line treatment
The patch prescription is typically refilled three times	Mean refill is 3.0 and 26% of patients refill their prescription >3 times	10% of patients filled their lidocaine patch prescription only once
Patch adhesion considered very important in treatment choice for nurses	Nearly all nurses (98%) said it was very or somewhat important that the patch adhere to skin during normal activities for 12 hours, 94% said it was important or very important that adhesion was maintained during heat or exercise	87% of nurses said that the availability of data on patch adhesion was very or somewhat important
Not all nurses think patches are "very effective"	91% of nurses said patches were "effective" but only 36% rated them as "very effective"	Most nurses did not find the lidocaine patch "very effective"
Nurses say patch efficacy is limited by lack of adhesion	60% said the main factor limiting efficacy of the patch was that the patch could not maintain contact with the skin over the prescribed 12 hours	About half of nurses (51%) said the patch irritated patients with sensitive skin
Few patients are "very satisfied" with their patch	30% of patients are "very satisfied" with the lidocaine patch and another 50% are "somewhat satisfied"	Most nurses (58%) report they think patients are "satisfied" with the patch
Nurses say patient dissatisfaction with the patch is due to adhesion and efficacy	57% of nurses thought that if patients were not satisfied with the patch, it was because of adhesion problems, 55% said it provided inadequate pain control, and 46% said the patch had to be taped in place	23% of nurses said they thought patients found the patches difficult to apply
Many patients frustrated with patch adhesion	62% of patients say they are "frustrated" with the patch staying appropriately adhered; 14% were "very frustrated"	Lack of adhesion limits therapeutic efficacy and is inconvenient
Very few patients say the patch always stays attached for the full treatment time	13% said the patch rarely stayed attached for the full treatment time and 51% of patients said the patch became detached or moved off the application site ≥3 times in the 12-hour treatment period	11% of patients said the patch did not move or become detached in 12 hours
Patients say adhesion issues hinder exercise	80% said they "agreed" or "strongly agreed" that the patch impeded their ability to exercise	
Nurses say more than one in three patients report problems with patch adhesion	Nurses say about a third of patients (35%) report the patch becomes detached and 35% of patients require patch re-attachment after the initial application	
Patients unable to wear patch because of need for tape, adhesion issues	41% of patients said they had to tape the patch in place, 39% said the patch moved off the application site, and 37% said the patch fell off	21% of lidocaine patch patients reported they were not able to wear the patch for 12 hours

TABLE 5. Continued.

Finding	Key data	Comments
Few patients are very satisfied with patch adhesion	26% of patients are "very satisfied" with patch adhesion and 50% more were "somewhat satisfied" compared to 54% of nurses who thought patients were "satisfied"	
Some patients speak with their nurse about patch adhesion	73% of patients said they told a healthcare professional (58% physician, 38% nurses, 31% other) about adhesion problems	On average, about a third (37%) of patients complain to their healthcare team that the patch does not adhere properly
Patch adhesion is critical to pain relief	86% of patients and 94% of nurses thought that adequate patch adhesion for the full 12 hours was critical to pain relief	Nearly all nurses and most patients understand the importance of adhesion to therapeutic efficacy
Pain relief top concerns regarding patch adhesion	The concerns reported by patients were: inadequate patch adhesion: running out of patches (41%), inadequate duration of therapy (39%), having to tape the patch (39%), not getting adequate analgesia (37%), costs (24%)	The biggest concern was that with poor adhesion, pain control would not last all day (29% said this was their "biggest concern")
Half of patients use tape to assist with patch adhesion	46% said they used tape to hold the patch in place and of those patients 65% found this inconvenient and 41% said it was uncomfortable on their skin	24% of patients who had trouble with patch adhesion said they requested a different patch
Additional adherence measures lessen the likelihood of receiving full treatment	72% of patients said that if the patch adhered better and they did not have to use tape, they would have been more likely to get the full 12 hours of pain relief	Patients recognize that adhesion problems decrease the therapeutic efficacy of the patch
Half of patients switch patches because of adhesion issues	37% of patients have asked for a different brand of patch because of adhesion issues but only 49% actually switched. The mean number of times patients switched patches was 1.2 times	26% of patients switched patch brands $\geq$2 times
Patient likelihood to try patch is higher if no tape is needed	80% of patch patients said they would be "very" or "somewhat" likely to try the patch again if PHN pain recurred. If they could be sure tape was not needed, 90% said they were "very" or "somewhat" likely to try the patch again	Overall, 20% of patients said they were "not very" or "not at all" likely to use the patch again but if they could be assured tape would not be necessary, only 10% were "not very" or "not at all" likely to use the patch again
Nurses say available patches don't provide adequate adhesion	69% of nurses agree or strongly agree that patches do not provide adequate adhesion	This was a source of concern for nurses and a common complaint of patients
Patients and nurses agree that better patch options are needed	80% of patients and 88% of nurses wish there were better patch options	This represents an unmet medical need

agreed that the patch would lift or detach when they exercised. About a third of patients (35%) reported the patch did not stay attached during the 12-hour treatment regimen and 35% said the patch required reattachment after the initial application. Of those who could not keep the patch properly adhered over the 12-hour treatment, 41% said they had to use tape to hold the patch in place. While 54% of nurses reported being "somewhat" satisfied with patch adhesion, 50% of patients said the same. Only 26% of patients agreed that they were "very satisfied" with the patch's ability to adhere properly in place over the 12-hour treatment. Patients reported that they discussed poor patch adhesion with the physician (58%), nurses (38%), or another healthcare provider (31%). Both patients (86%) and nurses (94%) agreed that the ability of the patch to stay in place over the 12-hour course of therapy was crucial to analgesic efficacy. Patients were concerned about lack of therapeutic benefit, costs, and inconvenience due to adhesion problems. See Fig. 3.

Almost half of patients (46%) reported that when they had problems with patch adhesion thus used tape to hold the patch in place, something they reported inconvenient (65%), uncomfortable (41%), caused them to lose faith in the quality of the patch (35%), cost (32%), extra trips to the pharmacy (30%), and difficult (29%). Adhesion issues caused 24% of respondents to request a different brand of patch and 16% discontinued patch therapy for this reason. Most patients (72%) "strongly" or "somewhat" agreed that if they did not have to take extra measures like using tape to affix the patch, they would have been more likely to get the benefits from 12 hours of pain relief. A third of patients (37%) asked to switch patches and the mean number of times a patient changed patch brands was 1.2 times. About a quarter of patients (26%) switched brands $\geq$2 times.

When asked if they would use the lidocaine patch again if PHN pain recurred, 42% of patients said they would be "very likely" to use a patch again. If that patch did not require tape to affix it in place, 54% said they would be "very likely" to use a patch again. More than two-thirds of nurses (69%) agreed "strongly" or "somewhat" that the currently available lidocaine patches do not offer patients the adhesion they need to get the full treatment. Nearly all nurses (88%) and most patients (80%) agreed with the statement that better lidocaine patch options would better meet treatment needs.

5. Discussion

This is the only survey of patients and nurses about their direct experiences with PHN of which the authors are aware. Our results are congruent with other findings about PHN. The literature has reported that PHN is associated with moderate to severe pain in many patients [23, 24] and functional deficits [25, 26]. As many as 40% of PHN patients may suffer long-term pain [27]. The lidocaine patch has been recognized as an important treatment modality [26, 27]. In a clinical study of 77 PHN patients, the 5% lidocaine patch was found in two weeks to significantly reduce pain [28].

This is not a trivial problem; PHN has a prevalence of 2.7% in patients referred to general practitioner, in a population of over 1000 patients [29]. Their quality of life is generally poor [30, 31]. No guidelines offer advice specific to PHN treatment (See Table 1), but there are suggestions on pharmacological [9] or non-pharmacological managements [32]. Experimental data suggest that the antagonism of the complement may become an efficacious therapy, in the future [33]. At the moment, as shown in this study, it is frequently considered a pain that may benefit of the use of anti-inflammatories, especially the ones suggested as more safe [34, 35]. Multimodal analgesia has resulted very frequently used in this study, and it represents always a better choice than a monotherapy [36, 37].

Our survey provided patients the opportunity to self-report pain symptoms and these results align with previous studies. Our study did find that although the American Academy of Neurology recommends lidocaine patches for treating PHN pain, one out of five nurses surveyed were not aware of this. First-line treatments typically include one or more of the following: the lidocaine patch, gabapentin, pregabalin, systemic NSAIDs, or tricyclic antidepressants. Opioids and the capsaicin patch are recognized treatment modalities, but they are not usually used as first line therapy [7–9]. While there are many therapeutic options, there is no clear-cut first therapy choice. Patients may be treated first with monotherapy or a multimodal approach, but it is estimated that fewer than half of all PHN patients achieve a 50% or greater reduction in their pain [12, 13].

The 5% lidocaine patch, first cleared for market release in 1999, offered some apparent advantages over systemic pharmacological therapy: as a topical system, it provided low systemic absorption, which theoretically may translate into fewer and milder adverse effects. The most commonly reported adverse event for the lidocaine patch is a mild application-site skin reaction [18, 19]. Since many patients with PHN are elderly and may be on polypharmacy, the benefits of a topical formulation seem particularly relevant. However, the FAERS database and anecdotal evidence from healthcare professionals revealed that patients were experiencing difficulties with patch adhesion.

The introduction of a new lidocaine topical system was intended to offer equivalent analgesic efficacy but better adhesion; the 1.8% lidocaine patch (ZTlido®, SCILEX, San Diego, California) was developed to be bioequivalent to the 5% lidocaine patch (Lidoderm®, Hind Health Care, Inc., San Jose, California.) meaning that these two products are similarly efficacious. The 1.8% topical system was specifically designed to solve the sticky problem of patch adherence by using a lower amount of lidocaine (reducing patch weight and bulkiness) but maintaining the same surface area for treatment with a superior adhesive and an easy-peel backing. This new patch system can offer nine times the lidocaine bioavailability as earlier patches because of its proprietary zero-water adhesive system and it was redesigned to offer an improved form factor, being much lighter in weight and 50% thinner. By comparison, the older 5% lidocaine patch contained more lidocaine (700 mg vs. 35 mg), is correspondingly heavier and thicker, and has a backing that must be peeled off from an edge. It must be noted that the survey preceded the introduction of this new patch and reflects viewpoints on the older patch systems. The new 1.8% plaster more efficiently utilizes residual drug in the system, allowing for a lighter, more flexible design. In studies by

the manufacturer, these 1.8% topical systems achieved >90% patch adhesion at the end of a 12-hour treatment in >90% of subjects, and patches were able to adhere effectively to patients even during moderate levels of exercise.

Proper and reliable adhesion is crucial to transdermal drug delivery, therapeutic efficacy, and patient compliance [22, 23]. Therapeutic efficacy requires the entire delivery area of the patch must maintain reliable skin contact throughout the prescribed therapeutic time [22]. If the patch does not have or maintain this full therapeutic contact or if the patch becomes displaced or detaches, an inadequate dose of medication may be delivered, providing subtherapeutic benefits [22].

To better measure patch adhesion characteristics, the FDA developed a five-point adhesion scale to evaluate patches where a score of 0 means ≥90% of the patch adhered to the skin and a score of 4 means the patch completely detached. In two open-label, single-dose studies conducted by SCILEX comparing the 1.8% patch to the 5% plaster, the 1.8% transdermal system demonstrated superior adhesion properties [38].

Thus, the new 1.8% lidocaine plaster meets a previously unmet medical need for safe, effective, and reliable PHN analgesia by responding to reports from patients and healthcare professionals about the need for a safe, effective, but more reliably adhesive lidocaine patch. This may improve compliance and, in that way, offer more effective pain control.

Our survey has several limitations. It was an anonymous survey using a convenience sample from the internet. Patients self-reported their pain, functional limitations, and other aspects of their condition. Nurses also self-reported their impressions. The nurse sample was derived independently from the patient sample meaning that the nurses in our study were not the same nurses who cared for the patients in our study. We surveyed only nurses, not physicians, as nurses have more direct experience with patch application and use than physician-prescribers. Any survey is subject to survey bias in that the type of person who responds to a survey may be inherently different from the sample population, particularly from those who do not respond to surveys. The survey offered multiple-choice answers meaning that respondents selected answers rather than provided original narrative comments. The survey was anonymous and therefore no medical records were used and diagnostic criteria and other aspects of care could not be independently confirmed.

6. Conclusions

PHN is associated with moderate to severe peripheral and central pain with no clear-cut first-line treatment. Lidocaine patches are a frequently used first-line therapy but were not as effective or frequently used as they might have been because of poor patch adhesion. Patients and nurses generally found lidocaine patches to be effective but greatly limited by their lack of reliable adherence to the skin. The bioequivalent 1.8% lidocaine transdermal delivery system overcomes this problem with a better-adhering patch.

AUTHOR CONTRIBUTIONS

JP, SN, KM, AP, RT, GV provided substantial contribution to the design of the work and interpretation of data; revised it critically; provided final approval and agreed to be accountable for all aspects of the written work. JP, SN, KM, AP, RT, GV did not design or conduct the survey.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This article is based on an anonymized online survey and does not contain any studies with human participants or animal performed by the authors without a previous Ethics Committee approval.

ACKNOWLEDGMENT

The authors are grateful to patients and nurses that voluntarily participated in the survey. They also acknowledge medical writing services from Jo Ann LeQuang of Angleton, TX, USA. Moreover, they thank NEMA Research Inc., Naples, FL, USA, and Paolo Procacci Foundation, Roma, Italy, for the support on editing and publishing the results of the research.

FUNDING

NEMA Research received funding for the editorial and medical writing services from Scilex Pharmaceuticals. NEMA Research did not receive funding to conduct the survey.

CONFLICT OF INTEREST

JP and GV are members of the editorial board of this journal. JP is also a Consultant/ Speaker, Owner, and Researcher for Spirify, US World Meds, Salix, Enalare, Scilex, Pfizer, Lilly, Teva, Taketa, Regeneron, Grunenthal, Neumentum, NEMA Research, BDSI and Bridge Therapeutics. The other authors have no potential conflict of interests.

AUTHORSHIP

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

REFERENCES

[1] Jianbo W, Koshy E, Mengting L, Kumar H. Epidemiology, treatment and prevention of herpes zoster: a comprehensive review. Indian Journal of Dermatology, Venereology and Leprology. 2018; 84: 251–262.

[2] Gialloreti LE, Merito M, Pezzotti P, Naldi L, Gatti A, Beillat M, *et al*. Epidemiology and economic burden of herpes zoster and post-herpetic neuralgia in Italy: a retrospective, population-based study. BMC Infectious Diseases. 2010; 10: 230.

[3] Gauthier A, Breuer J, Carrington D, Martin M, Rémy V. Epidemiology and cost of herpes zoster and post-herpetic neuralgia in the United Kingdom. Epidemiology and Infection. 2009; 137: 38–47.

[4] Kawai K, Gebremeskel BG, Acosta CJ. Systematic review of incidence and complications of herpes zoster: towards a global perspective. BMJ Open. 2014; 4: e004833.
[5] Ragozzino MW, Melton LJ, Kurland LT, Chu CP, Perry HO. Population-based study of herpes zoster and its sequelae. Medicine. 1982; 61: 310–316.
[6] Sacks GM. Unmet need in the treatment of postherpetic neuralgia. American Journal of Managed Care. 2013; 19: S207–S213.
[7] Attal N, Cruccu G, Baron R, Haanpää M, Hansson P, Jensen TS, *et al*. EFNS guidelines on the pharmacological treatment of neuropathic pain: 2010 revision. European Journal of Neurology. 2011; 17: 1113–e1188.
[8] Finnerup NB, Attal N, Haroutounian S. Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. Journal of Vascular Surgery. 2015; 14: 162–173.
[9] Liampas A, Rekatsina M, Vadalouca A, Paladini A, Varrassi G, Zis P. Pharmacological management of painful peripheral neuropathies: a systematic review. Pain and Therapy. 2021; 10: 55–68.
[10] Dubinsky RM, Kabbani H, El-Chami Z, Boutwell C, Ali H. Practice parameter: treatment of postherpetic neuralgia: an evidence-based report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2004; 63: 959–965.
[11] Moulin D, Boulanger A, Clark AJ, Clarke H, Dao T, Finley GA, *et al*. Pharmacological management of chronic neuropathic pain: revised consensus statement from the Canadian Pain Society. Pain Research & Management. 2015; 19: 328–335.
[12] Johnson RW. Herpes zoster and postherpetic neuralgia. Expert Review of Vaccines. 2010; 9: 21–26.
[13] Johnson RW, Rice ASC. Clinical practice. Postherpetic neuralgia. The New England Journal of Medicine. 2014; 371: 1526–1533.
[14] Argoff CE, Katz N, Backonja M. Treatment of postherpetic neuralgia: a review of therapeutic options. Journal of Pain and Symptom Management. 2004; 28: 396–411.
[15] Hadley GR, Gayle JA, Ripoll J, Jones MR, Argoff CE, Kaye RJ, *et al*. Post-herpetic neuralgia: a review. Current Pain and Headache Reports. 2016; 20: 17.
[16] John AR, Canaday DH. Herpes zoster in the older adult. Infectious Disease Clinics of North America. 2018; 31: 811–826.
[17] Schmader K. Herpes zoster. Clinics in Geriatric Medicine. 2016; 32: 539–553.
[18] Baron R, Allegri M, Correa-Illanes G, Hans G, Serpell M, Mick G, *et al*. The 5% lidocaine-medicated plaster: its inclusion in international treatment guidelines for treating localized neuropathic pain, and clinical evidence supporting its use. Pain and Therapy. 2019; 5: 149–169.
[19] Navez ML, Monella C, Bösl I, Sommer D, Delorme C. 5% lidocaine medicated plaster for the treatment of postherpetic neuralgia: a review of the clinical safety and tolerability. Pain and Therapy. 2015; 4: 1–15.
[20] Dagli RJ, Sharma A. Polypharmacy: a global risk factor for elderly people. Journal of International Oral Health. 2015; 6: i–ii.
[21] Food and Drug Administration. FDA adverse event reporting system. Food and Drug Administration. 2020; Available ta: https://open.fda.gov/data/faers/ (Accessed: 11 April 2020).
[22] Davies PS, Galer BS. Review of lidocaine 0atch 5
[23] Hadley GR, Gayle JA, Ripoll J, Jones MR, Argoff CE, Kaye RJ, *et al*. Post-herpetic neuralgia: a review. Current Pain and Headache Reports. 2016; 20: 17.
[24] Gruver C, Guthmiller KB. Postherpetic neuralgia. In: StatPearls. Treasure Island (FL): StatPearls Publishing. 2021.
[25] Baron R. Post-herpetic neuralgia case study: optimizing pain control. European Journal of Neurology. 2004; 11: 3–11.
[26] Shrestha M, Chen A. Modalities in managing postherpetic neuralgia. The Korean Journal of Pain. 2018; 31: 235–243.
[27] Dworkin RH, Schmader KE. Treatment and prevention of postherpetic neuralgia. Clinical Infectious Diseases. 2003; 36: 877–882.
[28] Argoff CE, Galer BS, Jensen MP, Oleka N, Gammaitoni AR. Effectiveness of the lidocaine patch 5
[29] Camilloni A, Nati G, Maggiolini P, Romanelli A, Carbone G, Giannarelli D, *et al*. Chronic non-cancer pain in primary care: an Italian cross-sectional study. Signa Vitae. 2020; 17: 54–62.
[30] Paterniani A, Sperati F, Esposito G, Cognetti G, Pulimeno AML, Rocco G, *et al*. Quality of life and disability of chronic non-cancer pain in adults patients attending pain clinics: a prospective, multicenter, observational study. Applied Nursing Research. 2020; 56: 151332.
[31] Girach A, Julian TH, Varrassi G, Paladini A, Vadalouka A, Zis P. Quality of life in painful peripheral neuropathies: a systematic review. Pain Research and Management. 2019; 2019: 1–9.
[32] Liampas A, Rekatsina M, Vadalouca A, Paladini A, Varrassi G, Zis P. Non-pharmacological management of painful peripheral neuropathies: a systematic review. Advances in Therapy. 2020; 37: 4096–4106.
[33] Brandolini L, Grannonico M, Bianchini G, Colanardi A, Sebastiani P, Paladini A, *et al*. The Novel C5aR antagonist DF3016a protects neurons against ischemic neuroinflammatory injury. Neurotoxicity Research. 2019; 36: 163–174.
[34] Varrassi G, Alon E, Bagnasco M, Lanata L, Mayoral-Rojals V, Paladini A, *et al*. Towards an effective and safe treatment of inflammatory pain: a delphi-guided expert consensus. Advances in Therapy. 2019; 36: 2618–2637.
[35] Varrassi G, Pergolizzi JV, Dowling P, Paladini A. Ibuprofen safety at the golden anniversary: are all NSAIDs the same? A narrative review. Advances in Therapy. 2020; 37: 61–82.
[36] Varrassi G, Hanna M, Macheras G, Montero A, Montes Perez A, Meissner W, *et al*. Multimodal analgesia in moderate-to-severe pain: a role for a new fixed combination of dexketoprofen and tramadol. Current Medical Research and Opinion. 2017; 33: 1165–1173.
[37] Gay-Escoda C, Hanna M, Montero A, Dietrich T, Milleri S, Giergiel E, *et al*. Tramadol/dexketoprofen (TRAM/DKP) compared with tramadolparacetamol in moderate to severe acute pain: results of a randomised, double-blind, placebo and active-controlled, parallel group trial in the impacted third molar extraction pain model (DAVID study). BMJ Open. 2019; 9: e023715.
[38] Pergolizzi JV, LeQuang J. Lidocaine topical systems in the treatment of postherpetic neuralgia. EC Anaesthesia. 2019; 5.8: 239–251.

How to cite this article: Joseph V. Pergolizzi Jr., Sri Nalamachu, Kailyn Mitchell, Antonella Paladini, Robert Taylor Jr., Giustino Varrassi. Topical 5% lidocaine patches for treating postherpetic neuralgia: a survey among nurses and patients. Signa Vitae. 2022;18(1):84-95. doi:10.22514/sv.2021.114.