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# ORIGINAL RESEARCH Parameters associated with efficacy of epidural steroid injections in the management of postherpetic neuralgia: the Mayo Clinic experience

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Shirin Ghanavatian<sup>1</sup> Christopher S Wie<sup>2</sup> Rhonda S Low<sup>3</sup> Richard J Butterfield<sup>4</sup> Nan Zhang<sup>4</sup> Gurman Singh Dhaliwal<sup>5</sup> Jordan M Montoya<sup>6</sup> David L Swanson<sup>1</sup>

<sup>1</sup>Department of Dermatology, Mayo Clinic, Scottsdale, AZ, USA; <sup>2</sup>Department of Anesthesiology and Perioperative Medicine, Mayo Clinic Hospital, Phoenix, AZ, USA; <sup>3</sup>Division of Preventive, Occupational, and Aerospace Medicine, Mayo Clinic, Scottsdale, AZ, USA; <sup>4</sup>Biostatistics, Mayo Clinic, Scottsdale, AZ, USA; <sup>5</sup>University of Arizona College of Medicine-Phoenix, Phoenix, AZ, USA; <sup>6</sup>Mayo Clinic School of Medicine, Scottsdale, AZ, USA

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Purpose: Thirty percent of patients with postherpetic neuralgia (PHN) receiving conservative treatment report unsatisfactory pain relief. Epidural steroid injections (ESIs) are commonly used as a therapeutic intervention in these patients. In this study, we aimed to determine if there are variables that predict the efficacy of ESI in patients with PHN.

Patients and methods: We retrospectively identified patients seen at Mayo Clinic who had PHN and received ESI. From their medical records, we abstracted the demographic variables, concurrent medication use, anatomic approach and medication for ESI, and degree of pain relief at 2 and 12 weeks' postintervention.

Results: None of the studied variables were significantly associated with efficacy of ESI in patients with PHN. PHN that began <11 months before treatment was predictive of a response to ESI at 12 weeks postintervention (positive predictive value, 55%). Patients who reported poor ESI efficacy 2 weeks after the intervention had a 94% chance of still having pain at 12 weeks. **Conclusion:** For this cohort of patients with PHN being treated with ESI, no demographic characteristics, concurrently used medications, or type of ESI were associated with ESI treatment efficacy at 2 or 12 weeks after the intervention.

Keywords: herpes zoster, intervention, neuropathy

#### Introduction

Postherpetic neuralgia (PHN), the most common complication of varicella zoster virus reactivation, may cause serious clinical problems that severely impair quality of life to an extent comparable to cancer, chronic obstructive pulmonary disease, AIDS, and fibromyalgia.<sup>1-4</sup> The pain of PHN is severe and may result in anorexia, weight loss, fatigue, depression, and insomnia; taken together, these factors negatively impact work, quality of life, and social activities.<sup>5</sup> PHN is caused by nerve damage from a herpes zoster (HZ) infection; pathologically, patients may have primary afferent neural body and axon degeneration, spinal cord atrophy, scarring of the dorsal root ganglion, and loss of epidermal innervation.<sup>6,7</sup> These changes contribute to increased N-methyl-D-aspartate glutamate receptor-dependent excitability of spinal dorsal horn neurons,<sup>8–10</sup> which contribute to the neuropathic pain of PHN.

Noninvasive management practices, which are widely used for PHN, have not been consistently effective.<sup>11,12</sup> Invasive treatment options have been developed, including

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Correspondence: David L Swanson Department of Dermatology, Mayo Clinic, 13400 E Shea Blvd, Scottsdale, AZ 85259, USA Email swanson.david@mayo.edu

local infiltration, sympathetic nerve blocks, and intrathecal injections. However, the reported efficacy of the invasive methods also is inconsistent.<sup>13–17</sup>

Epidural steroid injection (ESI) with the transforaminal and interlaminar administration of steroids and local anesthetics is among the more common treatments for patients with refractory PHN. However, its effectiveness is controversial. To our knowledge, the only study investigating factors associated with improved efficacy of transforaminal ESI for PHN reported a symptom duration of <3 months as the only significant predictor of benefit.<sup>18</sup> The specific aims of the present study were to seek other factors associated with the efficacy of ESI in our patient population with PHN and to report our experience for therapeutic success with ESI.

#### Methods

The Mayo Clinic Institutional Review Board approved this retrospective study.

We searched electronic health records to identify patients with PHN managed by ESI who were seen at Mayo Clinic (Arizona, Florida, and Rochester campuses) from January 1, 1997, through April 1, 2018. PHN was defined as pain in the area of the eruption that persisted for >90 days after the onset of the rash.<sup>19-22</sup> The following patient data were recorded: age, sex, comorbidities, concurrent medications, duration of PHN, anatomic approach of ESI, medication used for ESI, number of blocks, treatment date, and degree of pain relief at 2 and 12 weeks' postintervention. Pain relief was noted in the records in multiple ways: 1) as "good," "moderate," or "poor"; 2) as percent pain relief; or 3) as a point reduction on a pain scale (1-10, with 10 being severe pain). For records showing percent pain relief or pain scales, we considered up to 20% or a 2-point reduction as poor relief; 30-60% or a 3- to 6-point reduction as moderate relief; and >70% or at least a 7-point reduction as good relief. All patientspecific identifiers were removed from the data set before analysis.

Univariate logistic regression using the Firth penalized likelihood approach<sup>23</sup> was used to investigate the association between patient characteristics, concurrent medication use, type of intervention, and moderate-to-good pain relief outcomes at 2 and 12 weeks' postintervention. Receiver operating characteristic analysis and the Youden index were used to establish the optimum cutoff point for PHN duration that would be predictive of moderate-to-good pain relief at 12 weeks. The statistical analysis was

completed using SAS software, version 9.3 (SAS Institute Inc., Cary, NC, USA).

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#### Results

Our initial search of the electronic health records, using the terms "epidural steroid injection" and "postherpetic neuralgia," yielded 528 medical records. The records were reviewed, and we identified 42 patients meeting the definition of PHN from reactivation of HZ who were treated with ESI (54.8% male). Table 1 summarizes the demographic and clinical characteristics of the patients.

We did not identify any significant association between moderate-to-good pain relief (at 2 or 12 weeks post-ESI) and patient demographics, concurrent medication use, ESI approach, or medications injected for the intervention (Tables 2 and 3). Patients who reported poor ESI efficacy 2 weeks after the intervention had a 94% chance of still having pain at 12 weeks. Of the 24 patients who had a moderate-to-good pain relief 2 weeks after ESI, 19 (79%) had persistent relief after 12 weeks. PHN duration <11 months was predictive of moderate-to-good pain relief at 12 weeks' post-ESI, with a positive predictive value of 55.2% (Table 4).

#### Discussion

PHN is associated with an impaired quality of life, especially for elderly patients.<sup>24</sup> Current American Academy of Neurology guidelines<sup>13</sup> for reducing PHN-associated pain recommend TCA, anticonvulsants such as gabapentin and pregabalin, opioids, and topical lidocaine. However, at least 30% of patients with PHN have unsatisfactory relief of pain with these suggested treatments.<sup>25</sup> Hence, regional anesthetic procedures, including subcutaneous anesthetic and steroid injections, sympathetic and intrathecal nerve blocks, and ESI, are often used for management of PHN, even though these treatments are not strongly evidence based.

Mixed results have been reported with subcutaneous anesthetic plus steroid injections or sympathetic nerve blocks in the management of PHN.<sup>13,14</sup> Intrathecal injections have shown promise, but concerns regarding their safety remain.<sup>11,13,14,26–30</sup> The risk of arachnoiditis reported with intrathecal injections likely will prevent this treatment from becoming widely used.<sup>27,28,30</sup>

The role of ESI in established PHN is also controversial. Although ESI can induce short-term (1-month) pain relief for patients with acute HZ, it is not effective for preventing longterm PHN.<sup>15</sup>Two studies by Forrest<sup>16,17</sup> compared the effects

Table   Demogra	phics and o	clinical charac	teristics (N=42)
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Characteristic	Value
Age at the time of first ESI, years Mean (SD) Median (range)	70.3 (15.4) 74 (16.0–91.0)
Female sex, n (%) Diabetes mellitus, n (%) Inflammatory disease, n (%) Malignant disease, n (%)	19 (45.2) 5 (11.9) 12 (28.6) 8 (19.0)
Concurrent medication, n (%) <sup>a</sup> Aspirin Acetaminophen Gabapentin Local anesthetic Opioid SSRI or SNRI Steroid Tricyclic antidepressant Location of cutaneous rash	3 (7.1) 2 (4.8) 24 (57.1) 5 (11.9) 13 (31.0) 2 (4.8) 1 (2.4) 6 (14.3)
Cocation of cutaneous rash Cervical Extremity Lumbar Thoracic Duration of postherpetic neuralgia, median (range), months	I (2.4) 2 (4.8) 5 (11.9) 34 (81.0) 4 (0–217)
ESI medication Steroid only Steroid + local anesthetic No data	15 (40.5) 22 (59.5) 5
Approach of ESI Interlaminar Transforaminal No data	37 (97.4) I (2.6) 4
Number of ESI treatments Mean (SD) Median (range)	1.2 (0.5) I (1–3)
Moderate-to-good pain relief after ESI 2 weeks 12 weeks	24 (57.1) 19 (45.2)

**Note:** <sup>a</sup>No patient concurrently used a nonsteroidal anti-inflammatory drug. **Abbreviations:** ESI, epidural steroid injection; SNRI, serotonin–norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

of ESI in patients with 1) PHN lasting >6 months or 2) posttraumatic neuralgia. He reported that the pain of PHN was significantly reduced by ESI with local anesthetics, but the treatment was not as effective for patients with posttraumatic neuralgia. However, it is unclear whether an interlaminar or transforaminal approach was applied.

A case report by Mehta et al <sup>5</sup> described a 64-year-
old man with refractory thoracic dermatome PHN, 1.5
years after HZ onset; 12 weeks after transforaminal ESI,
he had complete resolution of symptoms. Kwak et al <sup>18</sup>
suggested that the only factor positively associated with
the effectiveness of transforaminal ESI was a symptom
duration shorter than 12 weeks; factors such as patient
age, sex, severity of initial pain, number of nerve
blocks, or comorbidities such as diabetes mellitus or
malignancy were not associated with the effectiveness
of transforaminal ESI. Mixed reports have been pub-
lished describing the application of interlaminar ESI in
HZ and PHN. <sup>15,31,32</sup>

In our study, 97% of patients were treated with interlaminar ESI. We did not identify any factor that predicted an increased likelihood of moderate-to-good pain relief with interlaminar ESI at 2 and 12 weeks' postintervention. However, we verified the overall effectiveness of the intervention with ESI and noted a sustained benefit when the therapy was given to patients with PHN duration <11 months.

A limitation of our study was that we had only 1 patient for whom a transforaminal approach was confirmed. The transforaminal approach delivers therapy close to the site of inflammation of the targeted dorsal root ganglion and spinal nerve, thereby possibly providing the greatest potential for benefit with limited systemic impact.<sup>33,34</sup> We are aware of no published studies that have compared the effect of interlaminar and transforaminal ESI for PHN.

Our study was also limited by its retrospective design; therefore, some aspects of data collection may have been incomplete. A high number of our patients presented to their primary care physicians at the time of HZ, and data such as pain severity and antiviral and adjuvant treatment determined at those consultations were not available for review. Our sample size was small and the study may have been underpowered.

Inherent risks of ESI include infection, bleeding, and minor trauma along the course of the needle; such risks must be acknowledged when considering this treatment.<sup>35</sup>

In conclusion, this study is the first to investigate predictive factors associated with the efficacy of interlaminar ESI in patients with PHN. PHN duration <11 months was predictive of moderate-to-good pain relief 12 weeks after ESI. Additionally, 80% of patients Journal of Pain Research downloaded from https://www.dovepress.com/ by 150.135.118.70 on 20-Aug-2019 For personal use only. Table 2 Variables associated with moderate-to-good pain relief, 2 weeks after ESI

Variable Number of patients (%)		Odds ratio (95% CI)	P-value	
Demographic variables				
Age at first intervention, years				
≤60	4/9 (44)	Reference		
>60	20/33 (61)	1.86 (0.42-8.21)	0.38	
Sex				
Male	14/23 (61)	Reference		
Female	10/19 (53)	0.72 (0.21–2.47)	0.60	
Diabetes mellitus				
No	19/37 (51)	Reference		
Yes	5/5 (100)	10.44 (0.41–265.7)	0.15	
Inflammatory disease				
No	17/30 (57)	Reference		
Yes	7/12 (58)	1.05 (0.27–4.07)	0.94	
Malignant disease				
No	20/34 (59)	Reference		
Yes	4/8 (50)	0.71 (0.15–3.32)	0.66	
Concurrent medications <sup>a</sup>				
Aspirin				
No	23/39 (59)	Reference		
Yes	1/3 (33)	0.42 (0.04-4.75)	0.48	
Acetaminophen				
No	23/40 (58)	Reference		
Yes	1/2 (50)	0.75 (0.04–12.77)	0.83	
Gabapentin				
No	10/18 (56)	Reference		
Yes	14/24 (58)	1.12 (0.33–3.84)	0.86	
Local anesthetic				
No	21/37 (57)	Reference		
Yes	3/5 (60)	1.07 (0.16–7.13)	0.94	
Opioid				
No	19/29 (66)	Reference		
Yes	5/13 (38)	0.35 (0.09–1.34)	0.12	
SSRI or SNRI				
No	24/40 (60)	Reference		
Yes	0/2 (0)	0.14 (0–5.86)	0.29	
Steroid				
No	24/41 (59)	Reference		
Yes	0/1 (0)	0.23 (0–23.01)	0.53	
Tricyclic antidepressant				
No	20/36 (56)	Reference		
Yes	4/6 (67)	1.45 (0.24-8.72)	0.68	

(Continued)

Variable	Number of patients (%)	Odds ratio (95% CI)	P-value			
Symptoms and interventions						
Level of ESI						
Thoracal	19/29 (66)	Reference				
Cervical	1/2 (50)	0.54 (0.03–9.54)	0.76			
Lumbar	4/7 (57)	0.69 (0.13–3.7)	0.95			
ESI medication						
Steroid only	/ 5 (73)	Reference				
Steroid + local anesthetic	13/22 (59)	0.56 (0.14–2.28)	0.41			
Approach of ESI						
Interlaminar	23/37 (62)	Reference				
Transforaminal	1/1 (100)	1.87 (0.02–184.23)	0.78			
Location of cutaneous rash						
Thoracic	21/34 (62)	Reference				
Cervical	1/1 (100)	1.89 (0.01–183.7)	0.58			
Extremity	1/2 (50)	0.63 (0.04–10.93)	0.92			
Lumbar	1/5 (20)	0.21 (0.03–1.78)	0.23			

Note: <sup>a</sup>No patients concurrently used nonsteroidal anti-inflammatory drugs.

Abbreviations: ESI, epidural steroid injection; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

Table 3 Variables associated with moderate-to-good pain relief, 12 weeks after ESI

Variable	Number of patients (%)	Odds ratio (95% CI)	P-value	
Demographic variables	·		•	
Age at first intervention, years				
≤60	4/9 (44)	Reference		
>60	15/33 (45)	1.02 (0.23-4.50)	0.98	
Sex				
Male	10/23 (43)	Reference		
male 9/19 (47) 1.16 (0.34–3.94)				
Diabetes mellitus				
No	16/37 (43)	Reference		
Yes 3/5 (60) 1.83 (0.28-		1.83 (0.28–12.11)	0.53	
Inflammatory disease				
No	14/30 (47)	Reference		
Yes	5/12 (42)	0.83 (0.22–3.22)	0.79	
Malignant disease				
No	15/34 (44)	Reference		
Yes	4/8 (50)	1.26 (0.27–5.88)	0.77	
Concurrent medications <sup>a</sup>				
Aspirin				
No	18/39 (46)	Reference		
Yes	1/3 (33)	0.7 (0.06–7.85)	0.77	
Acetaminophen				
No	18/40 (45)	Reference		

(Continued)

	Variable
	Demographic variables
	Yes
	Gabapentin No
	Yes
	Local anesthetic No Yes
	Opioid No Yes
	SSRI or SNRI No Yes
	Steroid No Yes
	Tricyclic antidepressant No Yes
	Symptoms and interventions
	Level of ESI Thoracal Cervical Lumbar
	ESI medication Steroid only Steroid+local anesthetic
	Approach of ESI Interlaminar Transforaminal
-	location of cutaneous rash

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Table 3 (Continued).

Variable	Number of patients (%)	Odds ratio (95% CI)	P-value			
Demographic variables						
Yes	1/2 (50)	1.22 (0.07–20.84)	0.89			
Gabapentin						
No	8/18 (44)	Reference				
Yes	11/24 (46)	1.05 (0.31–3.59)	0.93			
Local anesthetic						
No	18/37 (49)	Reference				
Yes	1/5 (20)	0.35 (0.04–2.94)	0.33			
Opioid						
No	14/29 (48)	Reference				
Yes	5/13 (38)	0.69 (0.18–2.62)	0.58			
SSRI or SNRI						
No	19/40 (48)	Reference				
Yes	0/2 (0)	0.22 (0.01–9.57)	0.43			
Steroid						
No	19/41 (46)	Reference				
Yes	0/1 (0) 0.38 (0-37.09)					
Tricyclic antidepressant						
No	15/36 (42)	Reference				
Yes	4/6 (67)	2.5 (0.41–15.05)	0.31			
Symptoms and interventions						
Level of ESI						
Thoracal	15/29 (52)	Reference				
Cervical	3/7 (43)	0.94 (0.05–16.43)	0.95			
Lumbar	1/2 (50)	0.73 (0.14–3.83)	0.78			
ESI medication						
Steroid only	8/15 (53)	Reference				
Steroid+local anesthetic	11/22 (50)	0.88 (0.24–3.28)	0.85			
Approach of ESI						
Interlaminar	18/37 (49)	Reference				
Transforaminal	1/1 (100)	3.22 (0.03–318.54)	0.61			
Location of cutaneous rash						
Thoracic	15/34 (44)	Reference				
Cervical	1/1 (100)	3.79 (0.04–370.99)	0.58			
Extremity	1/2 (50)	1.26 (0.07–21.82)	0.91			
Lumbar	2/5 (40)	0.9 (0.13–6.02)	0.62			
Likelihood of treatment response based on duration of PHN						
≤II months	16/29 (55)	Reference				
		0.27 (0.06–1.17)				

Note: <sup>a</sup>No patients concurrently used nonsteroidal anti-inflammatory drugs.

Abbreviations: ESI, epidural steroid injection; PHN, postherpetic neuralgia; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

who reported moderate-to-good treatment efficacy 2 weeks after ESI had continued efficacy at 12 weeks. However, none of the patient characteristics, concurrent medications, or type of intervention administered were associated with efficacy of ESI in PHN. Future studies warranted to verify this observation. The are

Table 4 Sensitivity, specificity	, PPV, NPV, and accurac	cy of likelihood of treatment respo	nse based on the duration of PHN

PHN dura- tion <sup>a</sup>	Moderate-to good pain relief, n	Poor pain relief, n	Sensitivity	Specificity	PPV	NPV	Accuracy
≤II months >II months	16 3	3  0	84.2%	43.5%	55.2%	76.9%	61.9%

**Note:** <sup>a</sup>We sought to establish the optimum cutoff point for PHN duration that would be predictive of moderate-to-good pain relief at 12 weeks. **Abbreviations:** NPV, negative predictive value; PHN, postherpetic neuralgia; PPV, positive predictive value.

effectiveness of ESI in PHN is not dependent on patient characteristics, concurrent medications, block numbers, or type of ESI.

### **Abbreviation list**

ESI, epidural steroid injection; HZ, herpes zoster; PHN, postherpetic neuralgia.

## Disclosure

All authors report no conflicts of interest in this work.

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