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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[1]
Christopher S Wie[2]
Rhonda S Low[3]
Richard J Butterfield[4]
Nan Zhang[4]
Gurman Singh Dhaliwal[5]
Jordan M Montoya[6]
David L Swanson[1]

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

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.[1–4] 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.[5] 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.[6,7] These changes contribute to increased *N*-methyl-D-aspartate glutamate receptor–dependent excitability of spinal dorsal horn neurons,[8–10] which contribute to the neuropathic pain of PHN.

Noninvasive management practices, which are widely used for PHN, have not been consistently effective.[11,12] Invasive treatment options have been developed, including

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

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local infiltration, sympathetic nerve blocks, and intrathecal injections. However, the reported efficacy of the invasive methods also is inconsistent.[13–17]

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.[18] 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.[19–22] 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 patient-specific identifiers were removed from the data set before analysis.

Univariate logistic regression using the Firth penalized likelihood approach[23] 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).

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.[24] Current American Academy of Neurology guidelines[13] 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.[25] 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.[13,14] Intrathecal injections have shown promise, but concerns regarding their safety remain.[11,13,14,26–30] The risk of arachnoiditis reported with intrathecal injections likely will prevent this treatment from becoming widely used.[27,28,30]

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 long-term PHN.[15]Two studies by Forrest[16,17] compared the effects

Table 1 Demographics and clinical characteristics (N=42)

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

Note: [a]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[5] 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[18] 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 published describing the application of interlaminar ESI in HZ and PHN.[15,31,32]

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.[33,34] 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.[35]

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

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[a]			
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*)

Table 2 (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	11/15 (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: [a]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	
Female	9/19 (47)	1.16 (0.34–3.94)	0.80
Diabetes mellitus			
No	16/37 (43)	Reference	
Yes	3/5 (60)	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[a]			
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*)

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)	0.68
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			
≤11 months	16/29 (55)	Reference	
>11 months	3/13 (23)	0.27 (0.06–1.17)	0.08

Note: [a]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 are warranted to verify this observation. The

Table 4 Sensitivity, specificity, PPV, NPV, and accuracy of likelihood of treatment response based on the duration of PHN

PHN duration [a]	Moderate-to good pain relief, n	Poor pain relief, n	Sensitivity	Specificity	PPV	NPV	Accuracy
≤11 months	16	13	84.2%	43.5%	55.2%	76.9%	61.9%
>11 months	3	10					

Note: [a]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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