

The Frequency of Neuropathic Pain In Stroke Patients and Medical Treatment Approaches

İnmeli Hastalarda Nöropatik Ağrı Sıklığı ve Medikal Tedavi Yaklaşımları

Nurten NAS KIRDAR¹, Hande ŞENOL¹

¹Denizli State Hospital, Department of Physical Medicine and Rehabilitation, Denizli

Yazışma Adresi / Correspondence:

Nurten NAS KIRDAR

Denizli State Hospital, Department of Physical Medicine and Rehabilitation, Denizli

E-mail : nrttns@gmail.com

Geliş Tarihi / Received : 08.07.2022 Kabul Tarihi / Accepted: 25.08.2022

Orcid :

 Nurten NAS KIRDAR <https://orcid.org/0000-0002-6507-7880>

 Hande ŞENOL <https://orcid.org/0000-0001-6395-7924>

Hippocrates Medical Journal / Hippocrates Med J 2022, 2(2): 24-28 DOI: <https://doi.org/10.29228/HMJ.16>



Abstract

Objective Neuropathic pain is a condition that can be seen in the post-stroke period and affects the patient's quality of life, mood, and participation in the rehabilitation program. Our aim in this study is to investigate the frequency of neuropathic pain in stroke patients and to examine whether they receive appropriate treatment.

Materials and Methods This study was designed as a retrospective, single-center clinical trial. Patients with stroke who applied to our physical medicine and rehabilitation outpatient clinic between June 2021 and June 2022 were included in the study. Patients with history of aphasia, cognitive dysfunction, subarachnoid hemorrhage, arteriovenous malformation, tumor, traumatic brain injury, complex regional pain syndrome were excluded from the study. The plegic side, the severity of pain with the numerical pain scale (NPS) and neuropathic pain with the S-LANSS (Self - Leeds Assessment of Neuropathic Symptoms and Signs) questionnaire were questioned by making phone calls with the patients. The drug treatments they used were questioned.

Results A total of 41 patients (22 male, 19 female) were included in this study. The mean age of the patients was 63.54 ± 10.97 years. There were 22 right hemiplegic and 19 left hemiplegic patients. Neuropathic pain frequency was 41.5% (17 patients). NPS, S-LANSS (p = 0.0001) and gabapentinoid use (p = 0.014) were found to be significantly higher in people with neuropathic pain.

Conclusion The frequency of neuropathic pain was found to be significantly higher in stroke patients. Detecting neuropathic pain and treating it appropriately will improve the quality of life of stroke patients.

Keywords Stroke, gabapentinoid, neuropathic pain

Özet

Amaç Nöropatik ağrı, inme sonrası dönemde görülebilen ve hastanın yaşam kalitesini, ruh halini ve rehabilitasyon programına katılımını etkileyen bir durumdur. Bu çalışmadaki amacımız inmeli hastalarda nöropatik ağrı sıklığını araştırmak ve uygun tedavi alıp almadıklarını incelemektir.

Gereç ve Yöntemle Çalışma retrospektif, tek merkezli bir klinik araştırma olarak tasarlandı. Haziran 2021-Haziran 2022 tarihleri arasında hastanemizin Fizik Tedavi ve Rehabilitasyon polikliniğine inme tanısıyla başvuran hastalar çalışmaya dahil edildi. Afazi, kognitif disfonksiyon, subaraknoid kanama, arteriyovenöz malformasyon, tümör, travmatik beyin hasarı, kompleks bölgesel ağrı sendromu öyküsü olan hastalar çalışma dışı bırakıldı. Hastalarla telefon görüşmesi yapılarak, plegik tarafı ve ağrısının şiddeti (numerik ağrı skalası ile) soruldu. Nöropatik ağrı açısından S-LANSS (Self - Leeds Assessment of Neuropathic Symptoms and Signs) anketi yapıldı. Hastanın bu ağrı için kullandığı ilaçlar sorgulandı.

Bulgular Bu çalışmaya toplam 41 hasta (22 erkek, 19 kadın) dahil edildi. Hastaların ortalama yaşı 63,54 ± 10,97 yıl idi. 22 sağ hemiplejik ve 19 sol hemiplejik hasta vardı. Nöropatik ağrı sıklığı %41,5 (17 hasta) idi. Nöropatik ağrısı olan kişilerde Numerik ağrı skalası, S-LANSS skoru (p=0,0001) ve gabapentinoid kullanımı (p=0,014) anlamlı olarak daha yüksek bulundu.

Sonuç İnmeli hastalarda nöropatik ağrı sıklığı belirgin şekilde yüksek bulunmuştur. Nöropatik ağrının saptanması ve uygun şekilde tedavi edilmesinin inme hastalarının yaşam kalitesi üzerine olumlu etkileri olacaktır

Anahtar Kelimeler İnme, gabapentinoidler, nöropatik ağrı

INTRODUCTION

Stroke is a disease caused by brain nerve injury. It is one of the diseases common among elderly and the second leading cause of death (1). Signs and symptoms of a stroke may include an inability to move or feel on one side of the body, understanding or speaking problems, dizziness, or loss of vision to one side (2).

Sensory impairment can be seen after stroke. Thalamus lesions can cause severe contralateral sensory loss and central pain. Especially in strokes affecting the spino-thalamo-cortical pathway, central pain may occur a few weeks after the onset of the stroke. Anticonvulsants such as gabapentin and pregabalin can be used in the treatment of these neuropathic pains that we encounter in stroke patients (3). In a review that evaluated many studies investigating the prevalence of central pain in stroke patients and comparing treatment options; it was stated that care should be taken in this regard, especially in the first 12 months after stroke, and pharmacological and non-pharmacological options can be used in treatment (4). In another study investigating the effect of post-stroke central pain on quality of life and depression, it was concluded that quality of life was affected, but mood was not (5).

Our aim in this study is to investigate the frequency of neuropathic pain in stroke patients who applied to the Physical Medicine and Rehabilitation outpatient clinic of our hospital, and to question whether they received an effective medical treatment for this pain. We think that the results of our study will draw attention to the presence of neuropathic pain in stroke patients, and it will be beneficial in treatment management.

METHODS

Our study was designed as a retrospective, single-center clinical trial.

Participants: patients with a diagnosis of cerebrovascular disease and hemiplegia (ICD-10 codes are: I67.8, I67.9, G81.0, G81.1, G81.9) who applied to the Physical Medicine and Rehabilitation outpatient clinic between June 2021- June 2022 were retrospectively screened. Local ethi-

cs committee approval was obtained (Pamukkale University non-interventional clinical research ethics committee, date: 28/06/2022, number: E-60116787-020-228512). Inclusion criteria; to be aged 18-80, ischemic cerebrovascular disease, hemorrhagic cerebrovascular disease. Exclusion criteria; aphasia, cognitive dysfunction, subarachnoid hemorrhage, arteriovenous malformation, tumor, traumatic brain injury, history of complex regional pain syndrome. Forty one patients who met these criteria were included in this study.

Methods: The musculoskeletal system pain that started after stroke was questioned by calling the patients by phone. Numerical Pain Scale was used for the severity of the pain, S-LANSS (Self – Leeds Assessment of Neuropathic Symptoms and Signs) scale was used for the character of the pain (6). Drugs which used by patients with neuropathic pain were noted as gabapentinoid or non-gabapentinoid.

Statistical analysis: All statistical analyses were performed using SPSS 25.0 (IBM SPSS Statistics 25 software (Armonk, NY: IBM Corp.)) software. Continuous variables were defined by the mean \pm standard deviation, median, interquartile range (25. - 75. percentiles), minimum - maximum values and categorical variables were defined by number and percent. Shapiro Wilk test was used for determination of normal distribution. For independent groups comparisons, independent samples t test (parametric test assumptions were met) and Mann Whitney U test (parametric test assumptions were not met) were used for continuous variables. Chi Square test was used for categorical variables. Statistical significance was determined as $p \leq 0.05$.

RESULTS

A total of 41 patients (22 male, 19 female) were included in this study. The mean age of the patients was 63.54 ± 10.97 years. There were 22 right hemiplegic and 19 left hemiplegic patients. Descriptive statistics are given in Table-1.

When we evaluated the S-LANSS questionnaire results of the patients, we found that 17 patients (41.5%) had neuropathic pain. The mean S-LANSS score of patients with neuropathic pain was 14 ± 1.87 (min 12- max 18).

	N	(%)
Gender		
Male	22	53.7
Female	19	46.3
Age		
Mean ± S.D	63.54 ± 10.97	
Med (IQR)	66 (55.5 - 72)	
Min - max	38 - 78	
Plegic side		
Left	19	46.3
Right	22	53.7
Neuropathic pain		
No (S-LANSS<12)	24	58.5
Yes (S-LANSS ≥ 12)	17	41.5
Treatment approach		
non-gabapentinoid	34	82.9
gabapentinoid	7	17.1
Numeric pain scale		
Mean ± S.D	3.49 ± 1.61	
Med (IQR)	4 (2 - 4)	
Min - max	0 - 7	
S-LANSS		
Mean ± S.D	6.71 ± 6.69	
Med (IQR)	5 (0 - 13)	
Min - max	0 - 18	

Table-1: Descriptive statistics
S.D: Standard Deviation; Med (IQR): Median (25. - 75. Percentiles)

When we examined the difference between the group with and without neuropathic pain, no significant difference was found in terms of gender, age and plegic side. NMS, S-LANSS (p = 0.0001) and gabapentinoid use (p = 0.014) were found to be significantly higher in people with neuropathic pain. The examination of the difference between the group with and without neuropathic pain is given in Table-2.

DISCUSSION

In our study, the frequency of neuropathic pain in stroke patients was found to be 41.5%. This is a rate that cannot be underestimated. Kiliç et al. (7) in a study in which they investigated the frequency of central pain after stroke, they found this rate to be 12%. The reason why the rates were so different was accepted as the design of the study. Because the study we mentioned was designed as cross-sectional

	Neuropathic pain- (S-LANSS <12)	Neuropathic pain+ (S-LANSS ≥ 12)	p
Gender			
Male	13 (%54.2)	9 (%52.9)	0.938
Female	11 (%45.8)	8 (%47.1)	
Age			
Mean ± S.D	64.71 ± 10.26	61.88 ± 12.02	0.427
Med (IQR)	66.5 (61.25 - 71.5)	62 (50 - 74.5)	
Min - max	38 - 78	41 - 77	
Plegic side			
Left	12 (%50)	7 (%41.2)	0.577
Right	12 (%50)	10 (%58.8)	
Neuropathic pain			
No (S-LANSS<12)	23 (%95.8)	11 (%64.7)	0.014*
Yes (S-LANSS ≥ 12)	1 (%4.2)	6 (%35.3)	
Numeric pain scale			
Mean ± S.D	2.67 ± 1.52	4.65 ± 0.86	0.0001*
Med (IQR)	2.5 (2 - 3.75)	4 (4 - 5.5)	
Min - max	0 - 7	4 - 6	
S-LANSS			
Mean ± S.D	1.54 ± 2.89	14 ± 1.87	0.0001*
Med (IQR)	0 (0 - 3.75)	13 (13 - 15)	
Min - max	0 - 10	12 - 18	

Table-2: The difference between the group with and without neuropathic pain
S.D: Standard Deviation; Med (IQR): Median (25. - 75. Percentiles)
, *p<0.05 statistically significant

and it was questioned whether the patients had neuropathic pain at the time of admission. Whereas our study was designed retrospectively and we questioned whether patients who applied to us for stroke within the last 1 year had neuropathic pain at any time after stroke. This explains why the frequency of neuropathic pain was higher in our study compared to other studies (7-10).

In our study, no significant relationship was found between the plegic side and the presence of neuropathic pain. In other studies conducted in this area, it has been determined that neuropathic pain is more related to the localization in the brain (thalamic-extrathalamic) rather than the plegic side (11,12).

Musculoskeletal pain is common in hemiplegic patients. This pain can be neuropathic pain or complex regional pain syndrome on the plegic side, as well as pain due to overuse on the non-plegic side. Traumas during transfers

can also cause pain. Therefore, differential diagnosis of the cause of pain in hemiplegic patients should be done well and treated accordingly. Sezgin Özcan D et al. (13), in a case report, drew attention to a case of knee osteonecrosis that can be confused with complex regional pain syndrome in hemiplegic patients. Although there are many treatment options from different pathways to reduce pain, there is no effective agent in the treatment of neuropathic pain yet. Since the role of serotonergic and noradrenergic systems in the pathophysiology of chronic pain has emerged, antidepressants and anticonvulsants have been used in treatment (14). There are other studies showing that gabapentinoid drugs are effective in treatment (15). In our study, gabapentinoid drug use was found to be statistically significantly higher in the group with neuropathic pain ($p = 0.014$). In other words, we can say that an effective treatment has been started for patients diagnosed with neuropathic pain.

It has been shown in many studies that neuropathic pain negatively affects quality of life, sleep patterns and mood in stroke patients (5,16,17). Koca TT et al. (18), investigated the relationship between neuropathic pain and kinesiophobia in post-stroke patients, but did not find a significant relationship.

In conclusion, with this study, we demonstrated how common neuropathic pain is seen in the post-stroke period. Unlike other studies, since we questioned the presence of neuropathic pain at any time after stroke rather than cross-sectionally, we showed how common it actually is. We have shown that the majority of patients diagnosed with neuropathic pain receive appropriate medical treatment. We recommend a detailed evaluation in terms of neuropathic pain in every patient who presents with pain in the post-stroke period. Thus, we think that with a more effective treatment, we will also improve the patient's quality of life.

Financial Disclosure: The authors declared that this study has received no financial support.

Conflict of Interest: The authors declare that there is no conflict of interest.

Ethics Committee: This study was approved by Pamukkale University Non-Interventional Clinical Research Ethics Committee (60116787-020/228512).

References

1. Belagaje SR. Stroke Rehabilitation. *Contin Lifelong Learn Neurol* [Internet]. 2017 Feb;23(1):238–53. Available from: <http://journals.lww.com/00132979-201702000-00017>
2. Donnan GA, Fisher M, Macleod M, Davis SM. Stroke. *Lancet* [Internet]. 2008 May;371(9624):1612–23. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0140673608606947>
3. Goodman CW, Brett AS. A Clinical Overview of Off-label Use of Gabapentinoid Drugs. *JAMA Intern Med* [Internet]. 2019 May 1;179(5):695. Available from: <http://archinte.jamanetwork.com/article.aspx?doi=10.1001/jamainternmed.2019.0086>
4. Liampas A, Velidakis N, Georgiou T, Vadalouca A, Varrassi G, Hadjigeorgiou GM, et al. Prevalence and Management Challenges in Central Post-Stroke Neuropathic Pain: A Systematic Review and Meta-analysis. *Adv Ther* [Internet]. 2020 Jul 23;37(7):3278–91. Available from: <https://link.springer.com/10.1007/s12325-020-01388-w>
5. Şahin-Onat Ş, Ünsal-Delialioğlu S, Kulaklı F, Özel S. The effects of central post-stroke pain on quality of life and depression in patients with stroke. *J Phys Ther Sci* [Internet]. 2016;28(1):96–101. Available from: https://www.jstage.jst.go.jp/article/jpts/28/1/28_jpts-2015-790/_article
6. Koc, R., & Erdemoglu, A. K. (2010). Validity and reliability of the Turkish Self-administered Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) questionnaire. *Pain Medicine*, 11(7) 1107-1114. [s-lanss-agri-skala-si-toad.](https://doi.org/10.1007/s12325-020-01388-w)
7. Kilic Z, Erhan B, Gunduz B, Iska Elvan G. Central Post-Stroke Pain in Stroke Patients: Incidence and the Effect on Quality of Life. *Türkiye Fiz Tip ve Rehabil Derg* [Internet]. 2015 Aug 4;61(2):142–7. Available from: <http://www.ftrdergisi.com/eng/makale/3836/293/Full-Text>
8. Bekircan-Kurt CE, Inan B, Bulut O, Sengun I, Karli N, Gunes HN, et al. Neuropathic Pain Frequency in Neurology Outpatients: A Multicenter Study. *Arch Neuropsychiatry* [Internet]. 2021; Available from: <http://submission.noropsikiyatriarsivi.com/default.aspx?s=public~kabule&mId=27549>
9. Klit H, Finnerup NB, Andersen G, Jensen TS. Central poststroke pain: A population-based study. *Pain* [Internet]. 2011 Apr;152(4):818–24. Available from: <https://journals.lww.com/00006396-201104000-00019>
10. Hansen AP, Marcussen NS, Klit H, Andersen G, Finnerup NB, Jensen TS. Pain following stroke: A prospective study. *Eur J Pain* [Internet]. 2012 Sep;16(8):1128–36. Available from: <https://onlinelibrary.wiley.com/doi/10.1002/j.1532-2149.2012.00123.x>
11. Misra UK, Kalita J, Kumar B. A Study of Clinical, Magnetic Resonance Imaging, and Somatosensory-Evoked Potential in Central Post-Stroke Pain. *J Pain* [Internet]. 2008 Dec;9(12):1116–22. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S152659008006457>
12. Bowsher D. The management of central post-stroke pain. *Postgrad Med J* [Internet]. 1995 Oct 1;71(840):598–604. Available from: <https://pmj.bmj.com/lookup/doi/10.1136/pgmj.71.840.598>
13. Sezgin Özcan D, Köseoğlu BF, Taşkın MK, Tekin B, Hatipoğlu ŞC. A Condition Confused with Complex Regional Pain Syndrome in Hemiplegia: Simultaneous Occurrence of Knee Osteonecrosis and Monoarthritis. *Fiz Tip ve Rehabil Bilim Derg* [Internet]. 2018;21(2):95–8. Available from: <http://www.jpmsr.org/current-issue/hemiplejide-kompleks-bolgesel-agri-sendromu-ile-karisabilen-bir-durum-es-zamanli-gorulen-diz-osteonekrozu-ve-monoartrit-654>
14. Gökçe Ş, Çigdem B. Efficacy of mirtazapine in neuropathic pain model. *Anatol J Psychiatry* [Internet]. 2020;21:1. Available from: <http://alpha-psychiatry.com/ent/efficacy-of-mirtazapine-in-neuropathic-pain-model-13987>
15. 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. *Eur J Neurol* [Internet]. 2010 Sep 7;17(9):1113. Available from: <https://onlinelibrary.wiley.com/doi/10.1111/j.1468-1331.2010.02999.x>
16. Tarsuslu T, Yümin ET, Oztürk A, Yümin M. [The relation between health-related quality of life and pain, depression, anxiety, and functional independence in persons with chronic physical disability]. *Agri* [Internet]. 2010 Jan;22(1):30–6. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/20209412>
17. Appelros P. Prevalence and predictors of pain and fatigue after stroke: a population-based study. *Int J Rehabil Res* [Internet]. 2006 Dec;29(4):329–33. Available from: <https://journals.lww.com/00004356-200612000-00010>
18. Koca TT, Gülkesen A, Nacitarhan V, Koca Ö. Does Kinesiophobia Associated with Poststroke Neuropathic Pain and Stroke Severity? *Fiz Tip ve Rehabil Bilim Derg* [Internet]. 2019;22(2):60–5. Available from: <http://www.jpmsr.org/current-issue/kinezyofobi-nme-sonrasi-noropa2k-agri-ve-nme-sidde2-ile-lis-kili-midir--686>