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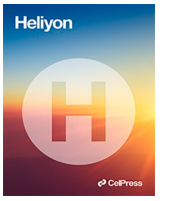

Research article

Persistent facial pain in post-stroke patients, a hospital-based cohort study; experience from North India

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ABSTRACT

Background: Post-stroke pain is common after a stroke and might be underreported. We describe Persistent Facial Pain (PFP) developed in post-stroke patients.
Method: ology: This was a prospective hospital-based cohort study of stroke patients, and patients were followed up. Out of 415 stroke patients, 26 developed PFP.
Result: Out of all PFP patients, six patients had an ischemic stroke, and 20 had a hemorrhagic stroke. 57.7% of patients had hypertension, while 34.6 patients had diabetes. The stroke location was left-sided in 12 patients and right-sided in 14 patients. 46.15% of patients responded to venlafaxine, 30.77% responded to amitriptyline, and 23.08% responded to pregabalin.
Conclusion: Persistent facial pain is a pain syndrome that might be missed in patients post-stroke. It might be more common in hemorrhagic stroke patients than in ischemic stroke patients. It responds adequately to antidepressants. A high index of suspicion is required to diagnose and appropriately manage these patients.

1. Introduction

Post-stroke pain (PSP) is common after stroke and varies from 10 to 55% across different studies [1,2]. There is a consensus that PSP might be underreported [2]. PSP includes several phenotypes. Common PSP subtypes are central, spasticity-related pain, complex regional pain syndrome, and post-stroke headache [3]. The pathophysiology of these post-stroke pain subtypes varies, and several theories have been postulated for various post-stroke pain subtypes. Post-stroke headaches seem to have a prevalence of 10 percent in multiple studies [4]. Atypical facial pain (AFP), also known as persistent idiopathic facial pain (PFP), is a chronic pain distributed along with the trigeminal nerve territory. A few case reports with atypical facial pain occurring post-stroke have been described previously [5,6]. Here, we report a prospective study of post-stroke persistent facial pain at three months of follow-up.

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2. Methodology

The study was part of an ongoing prospective hospital-based stroke registry. Patients from the stroke ward follow up in the stroke clinic after discharge. The registry has the hard copy and the electronic records of all the patients admitted to the stroke ward of the Department of Neurology. The patients were prospectively followed up in the stroke clinic after discharge, and those who could not come for the in-person visit were contacted on the phone for the modified Rankin Scale (mRS). All the patients' relevant clinical, biochemical, and radiological parameters were recorded. Odontogenic, inflammatory, and infective dental causes were excluded following clinical assessment and radiographic tests, and then the headache was assessed by the headache neurologist. Data were collected in an electronic password-protected spreadsheet. PFP was described as continuous facial and oral pain, with varying representations but recurring daily for most of the day without obvious dental or any local cause for the pain. All patients who developed PFP were adequately investigated for odontogenic, inflammatory, and infective dental causes and ruled out after dental examination and adequate radiological investigations.

3. Result

Out of a total of 415 patients, 26 patients developed PFP. The baseline characteristics of all stroke patients have been described (Supplementary Table S1). The baseline features of PFP have been described in Table 1. The mean age of patients in a PFP was 61.46 $\pm$ 12.5 years. There were eight females in comparison to 18 males. Out of all PFP patients, six patients had an ischemic stroke, and 20 had a hemorrhagic stroke. 57.7% of patients had hypertension, while 34.6% had diabetes. The stroke location was left-sided in 12 patients and right-sided in 14 patients. The mean days of onset of PFP were 10.38 $\pm$ 4.1 days. The reported severity ranged between 6 and 10 out of 10 on the verbal rating scale (VRS) in patients with PFP. All the patients of PFP described the character as a burning sensation on the face which was lateralized to the sites opposite to that of stroke. The duration of pain was continuous throughout the day before the initiation of the treatment. Two patients of PFP did have a throbbing quality associated with the pain.

There were no associated photophobia, phonophobia, or visual blurring associated with the pain. Four patients complained that the pain got aggravated by touch. There were no cranial autonomic features related to the pain. One patient had a history of migraine, while the rest 25 patients did not account for primary headaches. The patients were thoroughly investigated to rule out temporomandibular joint (TMJ) abnormalities. Of all patients with PFP and hemorrhagic strokes, 5 had thalamic hemorrhage; 10 had lobar bleeds, and 5 had a putaminal bleed. Out of the six patients of PFP with ischemic stroke, 3 had middle cerebral artery (MCA) infarct, 1 had anterior cerebral artery (ACA) infarct, and two had thalamic infarct, respectively.

4. Follow up

At three months follow-up, the pain intensity on VRS had decreased from the baseline. 46.15% of patients responded to venlafaxine, 30.77% responded to amitriptyline, and 23.08% responded to pregabalin. All the patients were on pharmacological management for the pain at the analysis time. Three patients with thalamic strokes, in follow-up, developed Hemi-sensory distribution.

5. Discussion

PFP is a pain syndrome that might be missed in patients post-stroke. It might be more common in hemorrhagic stroke patients than in ischemic stroke patients. It responds adequately to antidepressants. However, further extensive studies are required to identify and

Table 1
Clinical characteristics of patients with PFP.

Vraiables	Post stroke PFP (N = 26)
Age	61.46 $\pm$ 12.5
Female	8
Ischemic	6
Hemorrhagic	20
Location	
Left	12
Right	14
Onset (days)	10.3846 $\pm$ 4.1
Hypertension	15
Diabetes	9
Site of stroke-hemorrhagic Infarct	Thalamic-5 Putaminal-5 Lobar-10 MCA-3 ACA-1 Thalamic-2
Duration of pain	Continuous, lasting throughout the day

[a]PFP-persistent idiopathic facial pain; MCA-middle cerebral artery; ACA-anterior cerebral artery.

diagnose such patients. Early diagnosis would avoid unnecessary investigations and proper management of the patient.

Our cohort is the first cohort describing the PSP in stroke patients. The diagnosis of PSP was based on ICD beta criteria, (Headache Classification Committee of the International Headache Society, 2013) [7] and the symptoms are vague and still is the diagnosis of exclusion. The pathophysiology of PFP is less well understood, and it has been postulated that it might be due to abnormal trigeminovascular activation or psychological [8,9]. On the contrary, other researchers have suggested that the pain may have a central origin responsible for the pain. PFP has overlapping features with Central PSP [10]. The pain is ill-defined in both clinical diagnoses; In contrast, the pain in Central PSP occurs typically in the area of neurological insult, and PFP occurs only in the facial region [11]. In our cohort, the AFP was seen within the second week of the onset of the disease, was more common with hemorrhagic stroke, and thalamic pathology was the single most common site leading to atypical facial pain followed by cortical then subcortical pathology.

The patient responded adequately to antidepressants. The diagnosis of PFP was based on the international headache society. Clinical features and other characteristics ruled out other differentials for these pain, such as migraine, lower cluster headaches, orofacial migraine, regional myofascial pain, and trigeminal neuralgia. Out of the 26 patients, one patient developed typical hemisensory pain over one month of the development of PFP. The proposed pathophysiology of PFP is neuronal hyperexcitability at the brainstem level, along with the disturbed inhibitory function of the prefrontal cortex. The initial hypothesis suggested that PFP might be a heterogeneous entity that may be a syndrome of pure neuropathic pain on one extreme to the idiopathic pain of unclear etiology [8–10]. It shares exact pathophysiology or is different; PFP developing post-stroke needs further study in a larger population.

Post-stroke, various pain syndromes have been described, but PFP developing post-stroke has been described for the first time. Our cohort had one patient who subsequently developed typical thalamic pain in the follow-up, but the rest experienced continuous facial pain throughout the study. The persistent facial pain, quality of pain, and not following the vascular territory differentiated various other mimickers. The pain responded adequately to the medical treatment.

Our study had a few limitations; firstly, the patient with PFP was very small in number and was primarily complained by patients who were in a conscious state and could communicate. In long-term follow-up, there is a possibility that these patients might develop a phenotype that has been described earlier in the literature, namely, Complex regional pain syndrome (CRPS), and thalamic pain syndrome. However, three months follow-up is a significant period of follow-up in which one patient had developed pain in typical thalamic distribution. Out of the 26 patients with PFP, 20 had a hemorrhagic stroke, and only six had an ischemic stroke. The possible explanation for this could be the increased inflammation and severity of injury being more in hemorrhagic patients than in ischemic stroke patients.

Most importantly, we could not do the brain mapping and Blood oxygenation level-dependent MRI sequences due to non-availability, which could have added humoungously to our information. Secondly, because of the small sample size, the drug response could not be generalized, and further large studies are required to study the effect of the drugs on this particular entity. Thirdly the findings of this study find its drawback in that it lacks any radiological correlate. The addition of a functional MRI of the subjects would have helped us to understand the pathophysiology of the syndrome.

PFP may be a new pain syndrome that may develop post-stroke. A high index of suspicion is required to identify and adequately treat these patients. This may avoid unnecessary investigation and delay in the treatment. However, further long-term studies are needed to understand the pathophysiology of patients with post-stroke PFP.

Statement of ethics

Institutional Ethics Committee provided the ethical approval for the present study. The reference number is: ECR/526/lnst/UP/2014/RR-20.

Study approval statement

This study protocol was reviewed and approved by Institutional Ethics Committee, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India, and Reference number [Dean/2020/EC/2155].

Consent to participate statement

WRITTEN informed consent was obtained from participants or legal guardian to participate in the study.

Data availability statement

All data generated or analysed during this study are included in this article and its supplementary material file.

Authors agreement

All authors have viewed and agreed to the submission.

CRediT authorship contribution statement

Priya Dev: Writing – review & editing, Writing – original draft, Data curation. **Akhilesh Kumar Singh:** Data curation. **Devesh**

Kumar: Data curation. **Mareena Cyriac:** Data curation. **Varun Kumar Singh:** Data curation. **Anand Kumar:** Data curation. **Rameshwar Nath Chaurasia:** Resources. **Vijaya Nath Mishra:** Resources. **Deepika Joshi:** Resources. **Abhishek Pathak:** Writing – review & editing, Supervision, Project administration, Methodology, Conceptualization.

Declaration of competing interest

Abhishek Pathak reports financial support was provided by Banaras Hindu University Institute of Medical Sciences. Abhishek Pathak reports a relationship with Banaras Hindu University Institute of Medical Sciences that includes: employment. Abhishek Pathak has patent pending to N/A. N/A If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e28557.

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