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Relationship of Central Post-Stroke Pain with Location and Type of Lesions in Brain among Thalamic Stroke Patients

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Abstract

Background: Central post-stroke pain (CPSP) is a neuralgic pain syndrome following a stroke in thalamic region. **Objective:** The purpose of the present study was to see the relationship of Central Post-Stroke Pain with Location and Type of Lesions in Brain among Thalamic Stroke Patients. **Methodology:** This analytical cross-sectional study was carried out in the Department of Neurology at Dhaka Medical College and Hospital, Dhaka, Bangladesh during July 2013 to June 2015 for a period of two years. Patients with CPSP and without CPSP with isolated thalamic stroke within one year of event who were communicable with sufficient cognitive function were selected as study population. Demographic variables and clinical features were recorded by face to face interview, examination and by evaluating medical records. Pain perception was tested with the use of pinprick; temperature sense was tested with a cold tuning fork. Intensity of pain was graded on visual analogue scale (VAS). **Results:** This study was included 100 patients of which 50 cases were with CPSP and 50 cases were without CPSP. The mean age with SD of the study population were 57.2±11.4 years. 46% female, with isolated thalamic stroke. There was no significant difference between CPSP and non-CPSP groups in relation to age ($p>0.05$), gender (($p>0.05$), area of living ($p>0.05$) or frequency of risk factors ($p>0.05$). Frequency of participants with impairment of pain and thermal sensation as well as allodynia and dysesthesia were significantly higher in CPSP group in comparison to those in non-CPSP group ($p<0.05$ for all). Most of the participants with CPSP developed pain within one month of stroke event (60.0%), and had burning type of pain (74.0%). Majority of participants had moderate pain (56%), followed by severe and mild pain, 24% and 20% respectively. Participants with right sided lesion had higher risk of CPSP (OR 3.4; 95% CI 1.5-8.4; $p=0.003$) in comparison to those with lesions in the left. Similarly, participants with ischemic stroke had higher risk of CPSP (OR 3.5; 95% CI 1.4-9.0; $p=0.007$) in comparison to those with hemorrhagic stroke. **Conclusions:** Right sided lesions are more commonly found among subjects with CPSP and thalamic ischemia is more vulnerable than thalamic hemorrhage to develop CPSP after thalamic stroke. *[Journal of National Institute of Neurosciences Bangladesh, January 2022;8(1): 9-13]*

Keywords: Central Post-Stroke Pain; CPSP; thalamic stroke; location; type of lesions

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Introduction

Stroke is defined as rapidly developing clinical signs of focal (at times global) disturbance of cerebral function, with symptoms lasting for 24 hours or longer or leading to death, with no apparent cause other than that of non-traumatic vascular origin[1]. Significant physical,

emotional, and cognitive disabilities are caused by it, accounting for 3.6% of the total disability-adjusted life years (DALYs). Stroke is one of the 10 leading cause of disability irrespective of the development status of countries[2]. Prevalence of stroke in Bangladesh is approximately 3 per 1000 person-year overall and 10 per 1000 person-year in people aged 70 years or more[3]. Seven percent of all stroke patients have been reported to have isolated thalamic stroke[4].

Chronic pain is common in stroke patients[5]. Patient with stroke may suffer from a range of pain types such as central post-stroke pain (CPSP), hemiplegic shoulder pain, musculoskeletal pain or headache[6].The term CPSP, is a type of neuropathic pain, caused by damage to the central nervous system following cerebrovascular accident[5]. The reported prevalence of CPSP varies from 8% to 35% in literatures[7]. Lesions involving the spinothalamic and sparing of proprioceptive pathways at any level of the neuroaxis including the medulla, pons, midbrain, thalamus, sub-cortical white matter and the cortex may produce CPSP syndrome. However, the thalamus and brainstem are common sites for CPSP; 8.0% to 16.0% of thalamic stroke may lead to chronic pain. The frequency of pain after a geniculothalamic artery stroke is even higher (13%-59%) and right-sided lesions predominate among reported cases of the thalamic pain syndrome[8]. In studies reported consecutive patient with CPSP, thalamic lesions account for 33.0% to 47.0% of cases. Electrophysiologic evidence suggests that thalamic processing is a key element in the generation of central pain even when the injury is distant from the thalamus. Sensory loss of spinothalamic modalities is consider necessary for the development of CPSP[9]. The exact pathogenesis of CPSP is not yet known. However, it has been suggested that hyperexcitation in the damaged sensory pathways, damage to the central inhibitory pathways, or a combination of the two may be responsible for the onset of CPSP. Thalamic hemorrhage constitutes 6% to 25% of intracerebral hemorrhages[10]. Clinical presentation of thalamic hemorrhage in the form of a lacunar syndrome is very rare and pure sensory stroke is classically due to a small (lacunar) thalamic infarction[11].

CPSP is associated with significant morbidity. Assessment of the risk of CPSP is an important part in the management of stroke as pain is commonly a great burden to the patient, even when the intensity is low. It can reduce quality of life in patients who have had stroke, compromise rehabilitation, interfere with sleep, and lead to self-mutilation and even push patients to suicide[12]. Pain can develop immediately after stroke but in many cases, the pain develops with a delay of weeks to months after the stroke[4]. This pain free interval after the stroke event theoretically opens the door for prophylactic pharmacological strategies and predictors would allow the early identification of patients at risk of developing CPSP of thalamic origin.

Post-stroke disability is a great burden in the society of Bangladesh. Many of them suffer from CPSP, which is overlooked most of the time, particularly in the elderly and aphasic patients. It is easy to diagnose CPSP by clinical examination in follow up visit which needs no cost. However, by proper diagnosis and treatment quality of life can be improved. So this study was intended to observe whether the CPSP of thalamic origin differed by location and type of stroke.

Methodology

Study Population & Settings: This observational study was carried out in Department of Neurology of Dhaka Medical College and Hospital during July, 2013 to June, 2015. It included 100 patients (50 with CPSP and 50 without CPSP) with isolated thalamic stroke confirmed by CT scan of head and/or MRI of brain admitted in or attending to the stroke clinic and out-patient departments of Neurology and Internal Medicine, Dhaka Medical College and Hospital by purposive sampling. Patients who were communicable with sufficient cognitive function were included within one year of stroke event. Recurrent stroke patients were excluded from the study. Prior to the commencement of this study, the research protocol was approved by the Local Ethical Committee.

Study Procedure: Important demographic variables and risk factors were recorded by face to face interview and evaluating medical records. The onset of pain from the day of stroke was noted. Pain perception was tested with the use of pinprick, temperature sense was tested with a cold tuning fork. Sensation of each modality (pinprick and temperature) was graded as either normal or impaired using non-affected side as reference. Intensity of pain was graded on visual analogue scale (VAS). Patients were asked to indicate their worst self-perceived pain during the previous 48 hours period on a 0 to 100 mm VAS, marked at one end 'no pain' and at the other end 'worst imaginable pain'. VAS score was registered in 10-mm intervals, where 0 was defined as no pain, 10-30 as mild pain, 31-70 as moderate pain and 71-100 as severe pain (7). CPSP was considered present if the patient complained of unilateral pain occurring after the stroke episode and when peripheral, neurogenic or psychogenic origin for the pain was

highly unlikely (5).

Statistical analysis: The data analysis was performed using standard statistical procedures (SPSS version 16). Quantitative data were expressed as mean and standard deviation while qualitative data were expressed as frequency and percentage. For continuous variables, comparison between groups was made by the Students T-test. Categorical variables were analyzed by the Chi-square test. Odds ratio with 95% confidence interval were calculated to see the risk of CPSP according to side and type of stroke. Statistical significance was accepted at p value 0.05.

Results

Total 100 patients were included in this study of which 50 cases were with CPSP and 50 cases were without CPSP. The mean age with SD of the participants was 57.2±11.4 years. Most were male (54.0%) and lived in rural area (65.0%). Hypertension was present in 78.0% participants followed by dyslipidemia (56%), smoking (53%), heart disease (18%) and diabetes mellitus (14%). There was no significant difference between CPSP and non-CPSP groups in relation to age, gender, area of living or frequency of risk factors ($p>0.05$) (Table 1).

Frequency of participants with impairment of pain and thermal sensation as well as allodynia and dysesthesia were significantly higher in CPSP group in comparison to that in non-CPSP group ($p<0.05$ for all). Features like motor weakness, hemiataxia, choreoathetosis and visual field defect had no significant difference in frequencies between two groups (p=not significant for all) (Table 2).

Most of the participants with CPSP developed pain within one month of stroke event (60%), while 36% cases developed pain within 1 week of stroke event followed by 20% cases in 1 to 6 months and additional 20.0% patients after 6 months. Most of the patients had

Table 1: Demographic and clinical characteristics of the participants (n=100)

Parameters		Groups		Total	P value
		CPSP (n=50)	Non-CPSP (n=50)		
Mean Age (Mean±SD), Years		56.9 ±11.8	57.5±11.0	57.2±11.4	0.31
Sex	Male	28(56.0%)	26(52.0%)	54(54.0%)	0.68
	Female	22(44.0%)	24(48.0%)	46(46.0%)	0.29
Residence	Rural	30(60.0%)	35(70.0%)	65(65.0%)	0.60
	Urban	20(40.0%)	15(30.0%)	35(35.0%)	0.56
Hypertension		40(80.0%)	38(76.0%)	78(78.0%)	0.52
Diabetes mellitus		8(16.0%)	6(12.0%)	14(14.0%)	0.54
Dyslipidemia		32(64.0%)	24(48.0%)	56(56.0%)	0.60
Smoking		28(56.0%)	25(50.0%)	53(53.0%)	0.69
Heart disease		10(20.0%)	8(16.0%)	18(18%)	
CKD		4(8.0%)	3(6.0%)	7(7.0%)	

p-value stands for comparison between CPSP and non-CPSP group; CPSP: Central post-stroke pain; CKD: Chronic kidney disease.

Table 2: Comparison of Clinical Abnormalities between Participants with or without CPSP

Characteristics	CPSP Group (n=50)	Non CPSP Group (n=50)	P value
Impairment of pain (pin prick) sensation	43(86.0%)	32(64.0%)	0.01
Impairment of thermal sensation	42(84.0%)	31(62.0%)	0.01
Allodynia	43(86.0%)	10(20.0%)	<0.001
Dysesthesia	44(88.0%)	11(22.0%)	<0.001
Motor weakness	30(60.0%)	29(58.0%)	0.83
Hemiataxia	17(34.0%)	16(32.0%)	0.83
Choreoathetosis	5(10.0%)	3(6.0%)	0.46
Visual field defect	5(10.0%)	6(12.0%)	0.74

Within parentheses are percentages over column total; CPSP: Central post-stroke pain

burning type of pain (74%), followed by 16.0% cases non-specific pain and 10% cases in numbness. Most of patients had moderate pain 56.0% cases followed by severe pain in 24.0% cases and mild pain in 20% cases (Table 3).

Table 3: Characteristics of Pain in Participants with CPSP

Characteristics	Frequency	Percent
Onset of pain after stroke event		
• <1 week	18	36.0
• 1-4 weeks	12	24.0
• 1-6 months	10	20.0
• >6 months	10	20.0
Type of pain		
• Burning	37	74.0
• Numbness	5	10.0
• Others	8	16.0
Severity of pain		
• Mild (VAS score 10-30)	10	20.0
• Moderate (VAS score 31-70)	28	56.0
• Severe (VAS score 71-100)	12	24.0

Within parentheses are percentages over column total; CPSP: Central post-stroke pain; VAS: Visual analogue scale

Participants with right sided lesion had higher risk of CPSP (OR 3.4; 95% CI 1.5-8.4; p=0.003) in comparison to those with lesions in the left. Similarly, participants with ischemic stroke had higher risk of CPSP (OR 3.5; 95% CI 1.4-9.0; p=0.007) in comparison to those with hemorrhagic stroke (Table 4).

Table 4: Side and type of lesion in the participants (n=100)

Characteristics	CPSP Group (n=50)	Non CPSP Group (n=50)	OR (95% CI)	P value
Side of lesion				
• Left	12(24.0%)	26(52.0%)	3.4(1.5-8.4)	0.003
• Right	38(76%)	24(48.0%)		
Type of lesion				
• Hemorrhagic	8(16.0%)	20(40.0%)	3.5(1.4-9.0)	0.007
• Ischemic	42(84.0%)	30(60.0%)		

Within parentheses are percentages over column total; CPSP: Central post-stroke pain; CI=Confidence Interval; OR=Odds ratio.

Discussion

This observational study evaluate the relationship of location and type of stroke with CPSP by enrolling 100 thalamic stroke patients (50 with CPSP and 50 without CPSP) within one year of stroke event. There is significant higher risk of CPSP in thalamic stroke patients who had right sided lesion in comparison to those with left sided lesion This finding is consistent with recent experimental studies demonstrating right-hemisphere specialization for mediation of pain. In normal subjects, pain threshold and pain tolerance are lower on the left side of the body than the right for electrical, thermal, and focal pressure stimulation. Among patients with unilateral cerebral injury, individuals with right-hemisphere lesions tolerate pain longer than those with left-hemisphere lesions[9].

Similarly, significantly higher risk of CPSP was also observed in patients with ischemic stroke in thalamic region in comparison to those with hemorrhagic stroke in the same region. This can be explained by poor regeneration potential with more cellular damage by ischaemia and better regeneration potential with minimum cellular damage by haemorrhage. Another explanation is that the thalamus is the common site for lacunar stroke and clinical presentation of thalamic haemorrhage in the form of a lacunar syndrome is very rare but pure sensory stroke is classically associated with a lacunar thalamic infarction[9, 11, 14].

The important demographic and clinical characteristics are similar between participants of both the groups. There is no significant difference between participants with or without CPSP in relation to age, gender, area of residence or in relation to risk factors like hypertension, dyslipidemia, diabetes, smoking, heart disease and chronic kidney disease. Previous studies also could not recognize any difference in these parameters with regard to development of CPSP9,[13-16]. However, younger age and female sex were reported as higher risk for CPSP in a study[7]. In the present study, hypertension is found most common and dyslipidemia is found second most common risk factor: 80.0% and 64.0% respectively in CPSP and 76.0% and 48.0% respectively in non CPSP groups. Smoking is found in 56% CPSP and 50% non-CPSP patients, which is lower than the findings in most of the previous studies like[15]. This can be explained by the low smoking rate in females of Bangladesh due to religious background in comparison to the western world, where those studies were conducted. In 18.0% patients of CPSP and 16.0% patients of non CPSP group no risk factor is identified specially in younger patients.

Almost all CPSP patients in this study have abnormal pain and temperature sensibility, supporting the notion that a lesion of the spinothalamic tract is necessary for the development of CPSP. Positive somatosensory signs such as allodynia and dysesthesia are seen more often in

CPSP patients. These signs are assumed to reflect a neuronal hyperexcitability. Similar findings were observed by previous studies[15]. Motor weakness ipsilateral to pain, hemiataxia, abnormal movement like choreoathetosis and visual field defect do not differ between the two groups.

Onset of pain varies after stroke event which can develop immediately after stroke in some patients and up to several years later in others. Pain onset within the first few months is most common[5]. It has been observed that, onset of CPSP from the event of stroke was within one month in 60.0% participants, of which 36.0% developed pain within one week of stroke event. Additional 20.0% patients developed pain from one month to six months and another 20% patients developed pain after six months from the event of stroke. Similar pattern of pain onset from the event of stroke was found by other researchers[15]. This study reveals that majority of patients complained of burning type of pain, followed by numbness and non-specific type of pain, which have similarities with most of the previous studies[14,16]. Majority of patients in this study have moderate pain. The cause may be due to use of antineuralgic medication by most of the patients. This finding is consistent with Harno et al[17].

The study has several limitations. It is carried out in a single center in the capital of Bangladesh. So result of the study may not reflect the population as a whole, rather only the patients attending the study center is represented by it. The findings of this observational study need to be confirmed and amplified by prospective studies of consecutive patients of larger sample with new onset thalamic stroke and pain. Extrathalamic studies will also allow confirmation of whether the anatomic substrates for lateral asymmetries in pain processing principally involve thalamic nuclei, extrathalamic sites, or both.

Conclusion

It has been concluded that, right sided lesions predominate among study subjects with CPSP and thalamic ischemia is more vulnerable than thalamic hemorrhage to develop CPSP after thalamic stroke, but there is no statistically significant difference among demographic variables and risk factors between CPSP and non CPSP group.

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