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Post Stroke Seizures: Descriptive Study From A Tertiary Care Centre In Pakistan

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Abstract

Objective: To determine the frequency, mode of onset and outcome of post stroke seizures in a local setting.

Methods: The retrospective (Aug1999 to July 2001) and prospective (August 2001 to July 2002) data of patients aged 14 years and above, with post stroke seizures was collected from a tertiary care centre in a metropolitan city. The demographic, clinical, radiological, laboratory, neurophysiologic and outcome data was recorded and analyzed.

Results: During the three year period 1548 patients with stroke were admitted to the hospital. Four hundred thirty one (28%) had intracerebral haemorrhage (ICH) and 1117 (72%) had ischaemic stroke. One hundred seventeen (8%) of the 1548 had seizures. Their mean age was 63 ± 12 (range; 15-70) years. Fifty-nine (50%) were men and 58 (50%) were women. Twenty of 431(5%) patients with ICH and 97/1117 (9%) with ischaemic stroke, developed seizures. Nine of 117 (8%) developed a seizure within 14 days of stroke and 108/117 (92%) developed seizures after 14 days of stroke. Twenty-six (22%) had partial and 91 (78%) had generalized seizures. Two patients expired early in the course. Twenty four (21%) of these continued to have seizures at one year follow up. Fifteen of 37 (40%) patients who had systemic infections early in the course continued to have seizures at one year as compared to 9/80 (11%) who did not ($p = 0.001$).

Conclusions: Frequency of post stroke seizures is the same as reported in western literature. Post stroke seizures are more common in patients with ischaemic stroke. Generalized seizures are more common than partial seizures. Systemic infections early in the course are associated with recurrence of seizures at one year (JPMA 58:365;2008).

Introduction

Epilepsy is a common neurologic disorder. Age specific prevalence of epilepsy in Southern Pakistan is reported to be approximately 1%.¹ It manifests by seizures and prevalence of single seizure or multiple symptomatic seizures is higher than epilepsy. Stroke is most common cause of seizures in the elderly.^{2,3} Stroke increase the risk of seizures by several folds and the reported relative risk of developing seizures after stroke as compared to general population is as high as 35 times.⁴ Cortical location of stroke and stroke severity are reported, consistently, to be independent predictors of post stroke seizures.⁴⁻⁶ Post stroke seizures may have a negative impact on outcome of stroke. Some investigators observed that seizures in post stroke period are independent predictors of mortality in acute stroke.^{7,8} Others noted no significant effect.^{9,10} Recently Cordonnier et al reported that post stroke seizures may increase risk of development of dementia.¹¹ There are several published reports, throughout the world, reporting prevalence, clinical characteristics, risk factors and outcome, but to our knowledge there is no published literature on this subject from our country. We report the frequency, characteristics and outcome of post stroke seizures.

Methods

Patients (age 14 years and above), admitted consecutively to Aga Khan University Hospital with diagnosis of stroke, either ischaemic or haemorrhagic, over a period of three years (August 1, 1999 to July 31, 2002) were noted, using ICD-9 coding system of the hospital medical records. The patients who developed seizures were then identified from this cohort and their charts were reviewed to extract their demographic, clinical, radiological, laboratory, neurophysiologic and outcome data. Data from August 2001 to July 31, 2001 was reviewed retrospectively while data from August 1, 2001 to July 31, 2002 was collected prospectively.

All patients underwent brain imaging (CT scan, MRI or both) and were reviewed by trained neuroradiologists. Stroke subtype i.e. haemorrhagic or ischaemic was determined on the basis of well established radiologic criteria.¹² Patients with clinical picture of stroke and normal scans were classified as ischaemic stroke.

All patients were evaluated by at least one trained neurologist. Post stroke seizures were classified in to 'early onset seizures' if seizures manifested within 14 days of stroke onset and 'late onset seizures', if seizures manifested after 14 days of stroke onset.¹¹ Seizures were classified according to

criteria laid by International League against Epilepsy.¹³ Patients with prior history of seizures, transient ischaemic attacks (TIAs) preceding the index seizure, hypoglycaemia, hyponatraemia, hypocalcaemia, hypomagnesaemia, hepatic encephalopathy and uraemia were excluded. The outcome measures were death during hospital stay or seizure recurrence at one year.

Statistical analysis employed descriptive, univariate (chi square, t-test) and multivariate (logistic regression) methods. Data was analyzed on SPSS version 10.0.

Results

During the three year period 1548 patients with stroke were admitted to the hospital. Four hundred thirty one (28%) had intracerebral haemorrhage (ICH) and 1117 (72%) had ischaemic stroke.

One hundred seventeen (8%) of the 1548 had seizures. Demographic and clinical characteristics are summarized in Table.

Twenty of 431 (5%) patients with ICH had seizures. Most common site in affected persons was the cerebral cortex (13/20; 65%), followed by basal ganglia (5/20; 25%). Most commonly affected cortical regions were parietal and temporal accounting for approximately 40% each from cortical haemorrhages.

Ninety seven of 1117 (9%) ischaemic stroke patients

Table. Demographic and clinical characteristics.

Mean age (years)	63 ± 12
Gender	
Male : Female	1:1
Seizure Frequency in Stroke subtypes (%)	
Ischaemic	9
Haemorrhagic	5
Seizure onset	
Early onset (%)	8
Late onset (%)	92
Seizure type	
Partial (%)*	22
Generalized (%)	78
Co-morbidity	
Fever at presentation (%)	13
Hypertension (%)	85
BP >140/90 mmHg at admission (%)	50.5
Diabetes mellitus (%)	30
RBS >180mg% at admission (%)	28
Coronary artery disease (%)	35
Dyslipidaemia (%)	16

*One had complex partial, 4 had simple partial and 21 had complex partial seizures with secondary generalization.

developed seizures. Most common involved arterial territory was pure middle cerebral artery (MCA) (70/97;72%), followed by mixed middle and posterior cerebral arteries (9/97; 9%), and pure posterior cerebral artery (PCA) (6/97; 6%). Cortical involvement was noted in 75% of MCA strokes and 60% of PCA strokes. Six (5%) patients had status epilepticus, all in late onset group.

One hundred of the 117 (85.5%) patients achieved seizure control with one antiepileptic drug (AED), 16/117 (13.7%) required two AEDs and one (0.8%) patient required three AEDs. Phenytoin and valproic acid were most commonly prescribed AEDs followed by carbamazepine.

EEG was performed in 89/117 (76%) and 78 (87%) had abnormal findings. Diffuse slowing of background activity was most common finding (38/89; 42%), followed by focal slowing (23/89; 26%). Epileptiform activity was noted in 14/89 (16%). Of these 14, 11 had focal activity and 3 had generalized activity.

Thirty seven (32%) patients had systemic infection during hospital stay. Respiratory tract infection was the most common infection (22/32; 69%) followed by urinary tract infection (12/32; 37.5%).

Two patients expired early in the course. Twenty four (21%) patients continued to have seizures at one year. No statistically significant effect of age, gender, stroke subtype, stroke location, seizure type, or EEG findings was observed on seizure recurrence at one year. However, 15/37 (40%) patients who had systemic infections early in the course, continued to have seizures at one year as compared to 9/80 (11%) who did not (p = 0.001).

Discussion

The frequency of post stroke seizures has been reported from 5-10% in the West.^{4,13,15,16} A slightly higher frequency i.e. 13% is reported from India.¹⁷ A lower frequency is reported from China i.e. 3.4%.⁶ We noted that 8% of our stroke patients had post stroke seizures which is close to earlier reports.

In our study, 5% (20/431) of post stroke patients had seizures after ICH which is comparable to 5% (64/1402 patients) reported in a series from Taiwan.¹⁸ However, a higher frequency is reported from the West.^{9,10,15,16} Western literature reports a similar or higher frequency of seizures in haemorrhagic strokes as compared to ischaemic strokes.^{9,15,16,19} Conversely, we noted a higher frequency of seizures in ischaemic strokes i.e. 9% versus, 5% in haemorrhagic strokes. Reasons for this difference are not clear.

Majority (92%) of our patients had late onset seizures and only 9% had early onset seizures. This is in

sharp contrast to earlier reports where early onset seizures comprised 35-77% of all post stroke seizures.^{6,11,17} There is no explanation for this difference. Further prospective studies are required to determine if there are different predictors for early and late onset seizures and to find out whether these are different from what has been reported in literature.

Twenty six (22%) of our patients had partial onset seizures while 91/117 (78%) had generalized seizures at onset. A French study reported that 89% of the post stroke seizures were partial seizures and about a third of these patients had secondarily generalized seizures.²⁰ A Chinese study reports that partial seizures were more frequent in early onset (56%) while generalized seizures were more common in late onset group (72%).⁶ We also noted almost a similar frequency of generalized seizures in late onset group i.e. 82/108 (76%). However, we also observed that all early onset seizures were generalized ($p=0.03$). This discrepancy might be a result of bias related to retrospective record review with possible improper documentation. However, this distinction is based on clinical characterization only which may not be a true reflection of underlying pathophysiology, as focal onset seizures may rapidly progress to secondarily generalization without apparent clinically appreciable focal onset.

Cortical involvement has been reported as the most important predictor of development of post stroke seizures, related to both types of stroke i.e. haemorrhagic and ischaemic.^{4,5,6,15,16} Though we did not compare patients of post stroke seizures with stroke patients who did not develop seizures but 70/117 (60%) of the ischaemic stroke had MCA territory cortical strokes and 65% of all the haemorrhages were located in cortical region. Clearly a high proportion of cortical stroke in this cohort suggests its being an important predictor of post stroke seizures in our setting too.

Status epilepticus developed in 5% (6/117) of our patients and one of them died. All were late onset seizures. Proportion of status epilepticus in post stroke seizures has variably been reported from 9-27%.^{9,21}

EEG was performed in 89 (76%) patients, was normal in 11 patients. The abnormalities included ictal activity in 16 (18%; focal:13, generalized:3), focal slowing in 31 (34%) and diffuse slowing in 48 (54%) patients. None of our patients had PLEDs (periodic lateralized epileptiform discharges) or FIRDA (Frontal intermittent rhythmic delta activity). Both of these EEG patterns are reported to be more in stroke patients with post stroke seizures.²² The same study reported a higher frequency of diffuse slowing and other abnormal EEG findings in patients with post stroke seizures.²² We also noted a very

high proportion of over all abnormal EEG and about half of these had diffuse slowing. Since, our study was not designed to determine differences between stroke patients who did or did not develop seizures, in the post stroke period we cannot comment on the significance of EEG findings in our cohort.

Effect of post-stroke seizures on mortality is controversial. Some investigators noted no effect while others have observed a significant impact on mortality.⁷⁻¹⁰ Two of our patients died during initial hospital stay.

The association of systemic infection on the course of post stroke seizures has not been evaluated previously. We observed that 40% (15/37) of the patients who had systemic infection early in the course continued to have seizures at one year as compared to 11% (9/80) who did not ($p = 0.001$).

Our study is limited by being partly retrospective and at a single center. Another important limitation was that our study was not designed to assess predictors of post stroke seizures. Multicenter prospective studies are required to assess this aspect.

The frequency of post stroke seizures in our country is similar to reported literature from West and usually manifest after two weeks of stroke onset. Post stroke seizures are more common in patients with ischaemic stroke, contrary to previously reported literature. Systemic infections early in the course are associated with persistence of seizures at one year.

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