FREQUENCY OF SEIZURES AND EPILEPSY AFTER ISCHAEMIC STROKE

Adnan Khan, Sadaf Chiragh, Muhammad Irfan, Akhtar Sherin

Department of Neurology, Department of Psychiatry and Department of Medicine,
Postgraduate Medical Institute, Lady Reading Hospital, Peshawar and
KUST Institute of Medical Sciences, Kohat - Pakistan

ABSTRACT

Objective: *To evaluate the frequency and risk factors of seizures and epilepsy after ischemic stroke.*

Material and Methods: *This prospective observational study was conducted on patients with Ischemic Stroke in the Department of Neurology; Postgraduate Medical Institute, Lady Reading Hospital, Peshawar. These stroke patients were followed up for a total period of 2 years. Initially 210 patients were enlisted in the study. Out of these, 10 patients died or lost to follow up so they were excluded from the final analysis leaving a figure of 200. The main outcome measures were the occurrence of single or recurrent seizures as well as the occurrence of both early (within 2 weeks) and late (after 2 weeks) seizures were recorded. Patients who already had history of seizures, those with intra-cerebral bleed and sub-arachnoid hemorrhage were excluded from the study.*

Results: *Out of 200 patients (130 males and 70 female), 6 (3%) patients had early seizures while 10 (5%) patients presented for the first time with late onset seizures. So a total of 16 (8%) patients had post stroke seizures. Early seizures were mostly generalized tonic clonic seizures, while late seizures were mostly partial with or without secondary generalization. Epilepsy characterized by recurrent seizures occured in 3 patient's (1.5%).*

Conclusion: *Stroke patients have overall 8% risk of seizures and 1.5% risk of epilepsy in the first 2 years after an ischemic stroke. Majority of these seizures occurred after 2 weeks of onset of stroke.*

Key Words: *Seizures, Epilepsy, Ischemic Stroke.*

INTRODUCTION

One of the many sequellae of stroke is the development of epileptic seizures. Among the elderly people in whom seizures occur as a new onset disorder, stroke is most often the underlying cause.

Post stroke seizures and epilepsy have been described in numerous clinical studies for many years[1]. Post stroke seizures can occur soon after the onset of ischemia or can be delayed[2].

Seizures can be precipitated by strokes by a number of mechanisms. Early onset seizures are considered to be provoked seizures[2]. They are thought to result from cellular biochemical dysfunction, leading to electrically excitable tissue. Increased extracellular concentrations of glutamate, an excitatory neurotransmitter is presumed to cause secondary neuronal injury[2-4]. Secondly, blockage of a blood vessel deprives a portion of the brain of blood flow, and hence oxygen, producing anoxia. Either or both of these mechanisms may precipitate a seizure during or shortly after an ischemic stroke.

The most common seizures resulting from strokes are those that occur weeks or months after the initial event i.e. *late seizures*.

Late onset seizures occur after 2 weeks of ischemic insult. They are thought to be caused by gliosis and the development of meningo-cerebral cicatrix[1,2]. When a region of brain tissue dies during a stroke, it begins to degenerate into scar tissue after a few weeks. The dead area contracts into a fibrous nodule of scar tissue. The presence of this scar tissue acts as a provocative irritant to the normal neurons adjacent to it, precipitating a

TYPES OF SEIZURES IN EARLY AND LATE SEIZURES

	Type of Seizures		
	Partial Seizures	Generalized Tonic Clonic Seizures	Total
Early Seizures < 2 weeks	4 (66.7%)	2 (33.3%)	6 (100%)
Late Seizures >2 weeks	9 (90%)	1 (10%)	10 (100%)

Table 1

seizure months or even years later. Because scar tissue is permanent, late onset seizures have greater chance for recurrence.

MATERIAL AND METHODS

This prospective observational study was conducted at Neurology Department Lady Reading Hospital, starting from June 2004 to December 2007.

210 patients with ischemic stroke were initially enlisted in the study. They were followed up for a period of 2 years onwards, after being discharged from the hospital. Their age ranged from 10-70 years.

Ten patients died during the initial hospital stay or were lost to follow up period. They were excluded from the final analysis making the final figure of 200 (130 males and 70 female patients) patients that were followed up in the OPD.

Inclusion Criteria:

Patients with either first or recurrent CVA, in the age range of 10-70 years.

Exclusion Criteria:

Patients with intra-cerebral bleed, cerebellar bleed, sub-arachnoid hemorrhage, venous infarcts and those with a previous history of known epilepsy were excluded from the study.

All the patients were given the protocol treatment for stroke according to guidelines [5]. They were observed for the occurrence of epileptic seizures occurring at before or after 2 week of the onset of ischemic stroke according to the guidelines developed by the International League Against Epilepsy (ILAE) [6].

For clinical assessment of neurologic impairment the Scandinavian stroke scale (SSS) was used, at hospital admission and after 1, 2, 6, 12, 18 and 24 months. Upon discharge from the hospital, they were given a fit record chart and asked to report if they developed a seizures any time.

Patients were interviewed in the OPD at the aforementioned times. At each follow up the patients and caregivers were specifically asked about whether any possible seizure had occurred. Patients with suspected seizures were reassessed.

Generalized seizures were diagnosed with reference to statements of witnesses while focal seizures were distinguished clinically from clonus, spasms and recurrent strokes. EEG was done, where considered appropriate.

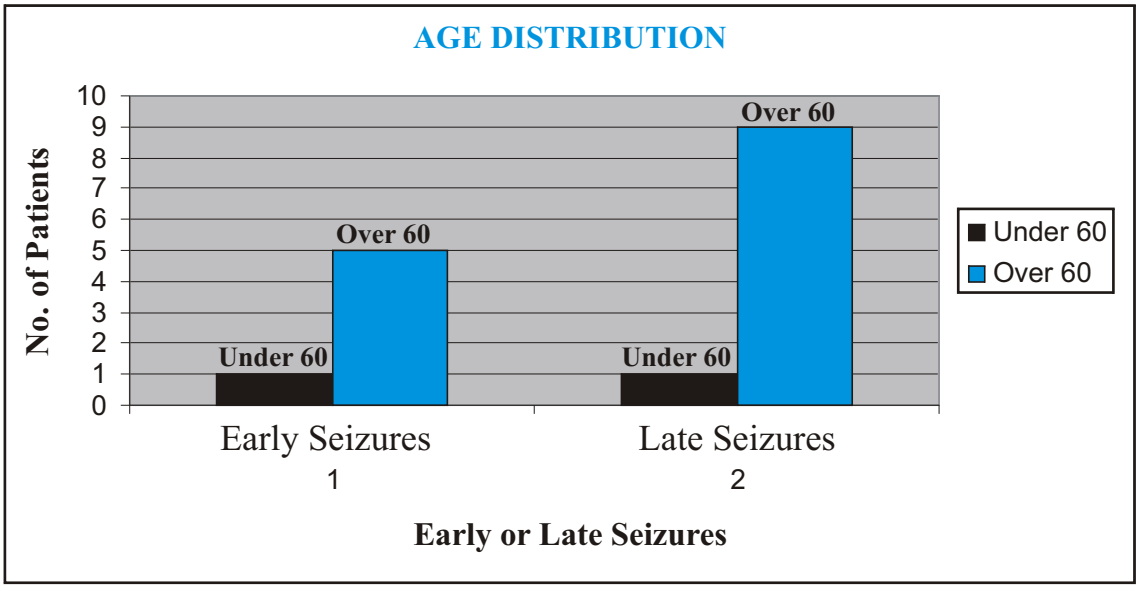

Figure 1

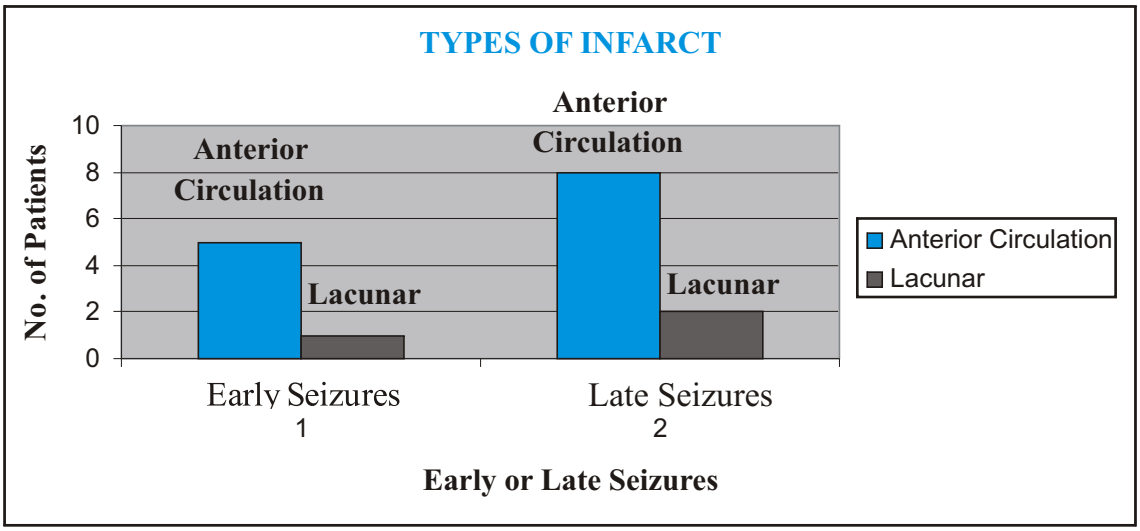

Figure 2

RESULTS

Out of 200 patients with ischemic stroke 130 (65%) were male and 70 (35%) were female patients. Mean age of these patients was 59.17 ±10.52 years.

Early onset seizures:

Six (3%) patients had early seizures i.e., they developed seizures within 2 weeks of the onset of stroke, despite no previous history of seizures. Four (66.6%) of these patients developed the seizures within 24 hours of the onset of stroke. They were all generalized tonic clonic seizures (GTCS). Two (33.3%) patients had simple partial seizures (Table 1). The occurrence of an early onset seizure was, however not associated with a worse outcome although being associated with an increased risk of having further seizures.

Two of the patients with GTCS went to have one or more post stroke seizures, when followed up in the OPD. The other 2 with generalized tonic clonic seizure and the two with partial seizures did not have further fits during their 2 years follow up in the OPD.

All the 4 patients with GTCS were in the age range 40-70 years (Figure 1). They had concomitant illnesses and underlying risk factors, i.e., diabetes mellitus, hypertension, hyper-lipidaemia and diastolic dysfunction on echocardiogram. One patient with partial seizures was diabetic and hypertensive. While the other one with partial seizure was young patient with valvular heart disease having Atrial Fibrillation causing Cerebrovascular Accident.

Renal functions were impaired in one patient with GTCS and the same patient continued to have post stroke seizures as well. He was continued with the anti-epileptics with renal safety.

Out of 6 patients having early seizures, 5 had extensive anterior circulation infarct, while one patient had lacunar infarcts (Figure 2). None of them had posterior circulation infarct. Except for one patient, whose age was 30 with valvaular heart disease, the rest five patients were above 60.

Late onset seizures:

Out of 10 patients with late onset seizures, 9 patients had a single fit during their 2 years follow up, while 1 patient had recurrent seizures. Two patients with early onset seizures also progressed to have late onset seizures. One had a single late onset seizure while the other one had 2 late onset seizures. So overall three (1.5%) patients had recurrent seizures

Three patients i.e., 30% presented in the first year at 6, 10 and 12 month post stroke (Figure 3). Seven patients i.e., 70% presented in the second year, all between 18 and 24 months. One patient who had recurrence of seizures presented with late onset seizures at 12 months and then 16 months. He was controlled with increasing the dose of anti-epileptic drugs. Two patients with early onset GTCS progressed to late onset seizures as well.

Out of these 10 patients, 9 were in the age range of 60–65 years. One patient was young, age 30–32 years with cardiogenic embolism.

All these patients had anterior circulation infarcts. None of the patients recruited in the study went into status epilepticus. Eight patients out of 10, who presented with first late onset seizure had partial seizures while one patient had partial seizures with secondary generalization. One patient

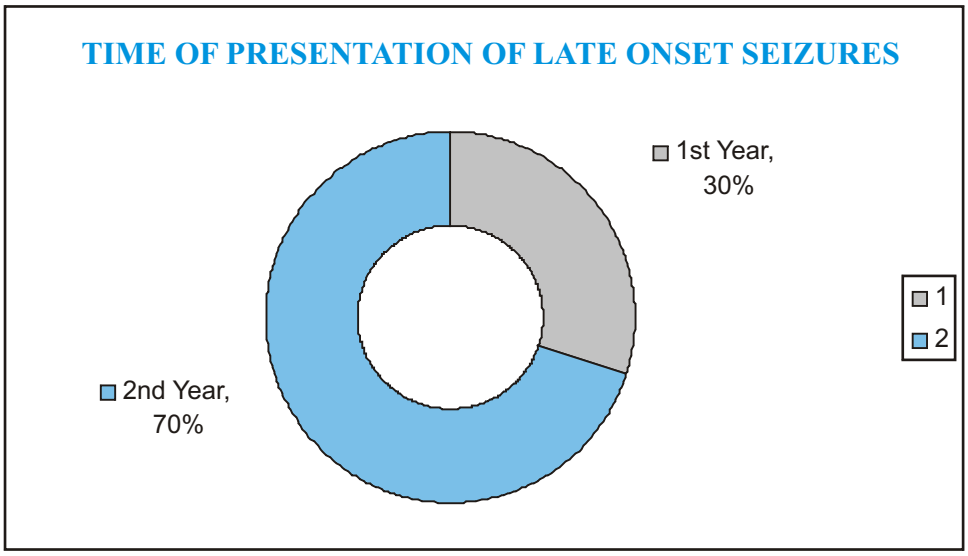

Figure 3

presented with GTCS.

Anterior Circulation infarct was the best characterized risk factor for seizures after ischemic stroke.

DISCUSSION

Stroke is an important cause of symptomatic epilepsy[7]. Seizure and status epilepticus may be an early (<7 – 14days) or late (>14 days) complication of acute stroke[1,8]. Epilepsy defined by at least two unprovoked epileptic seizures, may also be a late complication[9].

This study was conducted to determine the incidence and risk factors for seizures after ischemic stroke. Overall seizures occurred in 8% of patients, and epilepsy occured in 3 patient's i.e 1.5%.

The main risk factors identifiable for seizures after stroke in the study were.

1. Anterior circulation syndrome, with cortical involvement, especially the parieto-temporal region involvement.
2. Old age patients
3. Early acute seizures

Cortical signs and large hemisphere strokes are also the identified risk factors[10].

In our study 6 patients had early seizures against the total 16 patients. The rate of early seizures was thus 3% in our study. It is comparable to the studies conducted by Camilo O et al, where the estimates of early post ischemic stroke seizures were as minimum as 2%[2].

A more representative study of 1000 consecutive patients admitted to an Australian hospital with acute stroke identified 4.4% patients with early onset seizures[11]. Within a population based study in Rochester 4.8% of patients had early onset seizures within 24 hrs of cerebral infarction. The Rochester series may have included patients with haemorrhagic stroke as the subjects sustained their first stroke before the use of Ct[11].

The rate of late onset seizures was 5% in our study. In the study conducted by Camilo O et al, the rate of late seizures was as minimum as 3%[2]. Aside from cortical location and stroke severity to some extent, no other risk factors for post ischemic stroke seizures have been clearly demonstrated.

Late onset seizures occurred between 6 months and 2 years after stroke. Patients with early acute seizures, those with anterior circulation syndrome, large cortical infarct with regular borders located in parieto-temporal regions, were mainly at risk. The increased incidence after total anterior circulation infarction may reflect the extensive damage frequently sustained to the frontal and temporal cortex, the most epileptogenic areas of the brain[12,13]. Early post ischemic seizures are associated with increased in hospital mortality [14]. This may be because of comorbid conditions. Post stroke seizures are again common causes of hospital admission either as a presenting feature or a complication after stroke[14].

The association of stroke and status epilepticus has been evaluated in several studies[15-18].

It is associated with higher functional

disability. An early Status Epilepticus is associated with higher risk of Status epilepticus recurrence and a higher mortality rate than late onset Status Epilepticus[19] but we did not observe Status Epilepticus in any of the patients recruited in the study.

Treatment options included phenytoin, carbamazepine, valproic acid and the new antiepileptic drugs. New anti epileptic drugs can be used to decrease the likelihood of drug interactions and adverse effects anti epileptic drugs and in treatment failures with the classic anti epileptic drugs[13].

The optimal timing and type of antiepileptic treatment for patients with post stroke seizures was not specifically assessed. The decision to initiate antiepileptic drugs therapy after first or a 2nd post stroke seizures was individualized. Generally the early onset seizures were not started on anti epileptic drugs, but observed for recurrence but in late onset seizures, even with the first fit, the patients were started on anti epileptic treatment. The new generations anti epileptic drugs were tried in those Patients who were on anticoagulants or receiving other medicines for concomitant illnesses. Among the new generation, lamotrigine alone or in combination with Gabapentin was used. They proved effective choice for elderly patients or in younger patients requiring anticoagulation. The first generation Anti epileptic drugs were a reasonable option for those not requiring anticoagulation. The lamotrigine treatment in post stroke seizures versus carbamazepine treatment was relatively better tolerated and can be accepted initial treatment[20].

CONCLUSION

Stroke patients have overall 8% risk of seizures in the first 2 years after an ischemic stroke. Majority of these seizures occurred after 2 weeks of onset of stroke. Only 3 (1.5%) patients had recurrence of seizures so, it is unusual for epilepsy to be a major problem among ischemic stroke survivors. However large scale study with more prolonged follow up is required to assess the frequency of seizures and epilepsy in ischemic stroke patients.

RECOMMENDATION

Considering anti epileptic therapy for those patients with two or more risk factors is important.

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Address for Correspondence:
D. Sadaf Chiragh
Department of Neurology,
Postgraduate Medical Institute,
Lady Reading Hospital,
Peshawar.