Clinical features of post stroke seizure in Babol, northern Iran

Alijan A. Ahangar, *MD,* ***Seidreza Hosseini,*** *MD,*
Roshanak Saghebi, *MD.*

Seizures are one of the most common and dangerous complications of stroke, and approximately 10% of all stroke patients experience one or more seizures.[1] Stroke accounts for 30% of newly diagnosed seizures in patients >60 years old.[2] Early post stroke seizures are thought to result from cellular biochemical dysfunction whereas late-onset seizures are thought to be caused by gliosis and the development of a meningocerebral cicatrix. Post stroke seizures are more frequent in severe and disabling strokes and in hemorrhagic strokes.[3] Due to the lack of reported clinical and epidemiological data on the aspects of post stroke seizures in our region, this study was conducted to describe the immediate and long term risk of seizures after stroke and its relation to the subtype of the first stroke

Using the results from our previous study,[4] we carried out this historical cohort study on the recorded data of 250 consecutive stroke patients admitted to Yahanejad Hospital in Babol in Northern Iran from April 2001 to April 2003 to monitor the occurrence of seizure(s). Diagnosis of stroke and its subtypes was made by a neurologist based on the clinical signs and symptoms. The diagnosis of all cases was confirmed by neuroimaging investigation (brain CT scan or MRI). The classification of seizure types was according to international classification of epileptic seizures. Post stroke seizure was defined as a single seizure or as recurrent seizures occurring after the stroke and seizures that occurred without any identifiable acute precipitants other than stroke. Early post stroke seizures were defined as seizures occurring within one week after stroke,[5] including onset seizures, and seizures developing beyond one week after stroke were termed as late seizures. Patients with a history of epileptic seizures and acute symptomatic seizure due to other causes were excluded from the study. Anticonvulsants such as phenobarbital or phenytoin were prescribed for every patient who had early- and late-onset post stroke seizure. Study inclusion criteria were stroke patients with seizure after stroke with no prior history of unprovoked seizures and epilepsy. For each patient a file was recorded including age, gender, stroke subtypes: hemorrhagic stroke type [deep or lobar with a small (less than 2 cm) or large (more than 2 cm) hematoma] and ischemic stroke type (thrombotic and embolic), based on clinical diagnosis and neuroimaging findings, seizure type, first seizure occurrence time in early or late seizure and single or recurrent seizures, EEG findings, the severity of the neurological impairment on admission as: alert, confused, sub coma and comatose, and the functional outcome at discharge time, which was assessed using the modified Rankin scale. Statistical tests used in this study were Fisher's exact test and chi-square. Risk Ratio was calculated using the formula of [Risk (exposed)/Risk (unexposed)]. A p-value of ≤0.05 was considered to indicate a significant difference. Ethical approval was received from the local ethics committee prior to the start of the study

During the 2-year follow-up of these stroke patients, one or more seizure(s) due to causes other than stroke occurred in 7 cases. In the remaining 243 patients, 163 cases were diagnosed with ischemic stroke (67.1%), 87 cases were thrombotic and 76 cases were diagnosed with embolic subtype, and the remaining 80 patients (32.9%) with hemorrhagic type of stroke (RR=1.683, CI: 0.975-2.904). Among these stroke patients, in 42 (17.3%), one or more seizures developed within 2 years after acute stroke. In 16 of these post stroke seizures cases, the seizures were generalized, whereas in 18 of them simple partial seizure occurred and complex partial seizure in 8 of the patients was recorded. Twenty-eight cases of these post stroke seizures had a single seizure, and 14 had repetitive seizures. Recurrent seizures developed in 4 cases of early- and 10 of late-onset seizures (p=0.495, Risk Ratio (RR)=1.389, CI: 0.525-3.67). The timetable of the occurrence of other seizures after different stroke subtypes is shown in **Table 1**. Nineteen patients of those with post stroke seizures were hemorrhagic, 12 were thrombotic, and 11 were embolic subtypes (p=0.174). On admission to the hospital, 131 stroke cases (53.9%) had decreased level of consciousness and 112 cases (46.1%) were in an alert state, while the rate in post stroke seizure cases in respect to consciousness state were 28 (66.7%) decreased, and 14 (33.3%) alert. Comparison between the degree of disability on discharge time of all of the stroke patients with Modified Rankin scale disclosed that 42.9% of survivors of stroke had no disability, while this rate was 34.6% in post stroke seizures. Rate of mild to moderate disability was 41.1% in stroke survivors and 26.9% in post stroke seizure cases. Rate of moderate to severe disability was 15.9% in stroke survivors and 38.5% in post stroke seizure cases. Sixteen patients with seizures died during the 2-year follow-up period, 11 cases were hemorrhagic stroke type and 5 cases were ischemic stroke type. In general, of 19 post hemorrhagic stroke patients developing seizure, 11 cases died and 5 cases of 23 post ischemic stroke seizure patients died during the 2-year study period (p=0.16, RR=2.663, CI: 1.121-6.325). However, among all of these ischemic

Table 1 - Frequency of first seizures after stroke in stroke patients in Babol.

Frequency	Type of stroke n (%)								Total
	Ischemic stroke 23 (54.8%)				Hemorrhagic stroke 19 (45.2%)				
	Embolic 11 (26.2%)		Thrombotic 12 (28.6%)		ICH 15 (35.7%)		SAH 4 (9.5%)		
	Male	Female	Male	Female	Male	Female	Male	Female	
<24 hours	1	1	1	0	1	1	0	1	**6**
1 week	2	1	1	1	2	1	1	0	**9**
1 month	1	1	2	1	3	2	0	1	**11**
1 year	1	2	1	2	3	1	0	0	**10**
2 years	1	0	2	1	1	0	1	0	**6**
Total	**6**	**5**	**7**	**5**	**10**	**5**	**2**	**2**	**42**

ICH - intracerebral hemorrhage, SAH - subarachnoid hemorrhage

cases, 24 (9.9%) patients, and among all hemorrhagic cases, 56 (23.4%) patients died during the study period (p=0.000, RR= 4.754, CI: 3.199-7.066). The number of deaths from these post stroke seizure patients was 16, with a mortality rate of 38.1%, while the total number of deaths during the follow-up period was 80 with a mortality rate of 32.9% (p=0.512, RR=1.157, CI: 0.756-1.77).

In the study subjects, the risk of occurrence of single or recurrent seizure(s) during a period of 2 years after a stroke was 17.3%. This is higher than the risk of occurrence of the seizures in other reports.[2] Obviously, the definition of post stroke seizure influences its frequency. Authors who included all seizures after a stroke without distinguishing them as acute, early, or late seizures reported a higher frequency. We included all the seizures occurring after the onset of stroke in our study findings as in our opinion, although these acute and early seizures may be related to non-cerebral disarrangements such as acid base disturbances, electrolyte imbalance, and so forth, however, these seizures were either directly or indirectly related to stroke. In our study, the mean age of the patients was 68 years ranging from 30-90 years, which is in agreement with other reports and no data suggest that the extent of a lesion caused by a cerebrovascular accident differs within these age groups. The number of female patients with stroke in this study was more than that of the males, however, the frequency of male cases (59.5%) of post stroke seizure was higher than females (40.5%). This might be due to the high rate of intracerebral hemorrhage (ICH) in our male subjects,[4] who developed more episodes of seizures. The high rate of simple partial seizure in our cases is in agreement with other studies. We found that most post stroke seizures were of the late onset type (64.3%), while in other studies the early-onset types are more common. In this study 14 (33.3%) cases showed repetitive seizures, which is lower than the findings of some other studies.[1] This may be due to our early treatment of every post stroke seizure, which might have prevented the recurrence of seizures; contrary to the results of some of the previous studies that indicate early treatment after the first early post stroke seizure has not been associated with a reduction of recurrent seizures after discontinuing the medication. The risk of seizures was higher in hemorrhagic subtype (45.2%) in comparison with thrombotic (28.6%), and embolic (26.2%) (RR=1.683, CI: 0.975-2.904), which is compatible with other reports.[2] Patients with lobar hemorrhage had seizures more often than deep ICH patients did. It should be noted that the volume of ICH had some predictive value because seizures were more frequent in patients with larger hematomas than those with small ones (p=0.725, RR= 0.764, CI: 0.284-2.058), and this was in accordance with other studies. Although results of clinical and autopsy studies[2] have suggested that seizures are more common with cardioembolic infarction than other types of ischemic stroke, Gilad et al[6] in their seizures after stroke study (SASS), found that patients who had a probable cardioembolic stroke were not at an elevated risk of development of a first seizure. However, according to the results of this study, seizures are more common with thrombotic ischemic stroke than with embolic subtype. This may be due to the high prevalence rate of thrombotic cases in comparison with embolic subtypes in these stroke patients.[4] Post-stroke seizures were more common in patients who, on their admission, had a more seriously decreased level of consciousness. Other researchers, such as Burn et al[7] reported the same. Another finding in this study is that

seizures after stroke worsen the disability of survivors of stroke. Some authors suggested that the occurrence of seizures after stroke might worsen the clinical outcome,[2] but others suggest the possibility that stroke with higher risk of long term disability might be more likely to generate seizure. The number of deaths from these post-stroke seizure patients was 6 with a mortality rate of 38.1%, while the total number of deaths in all of these stroke cases during the 2-year follow-up period was 80 and the mortality rate was 32.9% (p=0.512, RR=1.157, CI: 0.756-1.77). The mortality rate of post hemorrhagic stroke patients with seizure (26.2%) was more than that of post ischemic stroke seizure (11.9%). Therefore, post hemorrhagic stroke seizures worsen the prognosis of the stroke. This is in agreement with other studies.[2] Our main study limitation was the lack of a control group, and we recommend performing further case control-studies on this subject.

In conclusion, according to our results the rate of post stroke seizure was higher than other reports, which could be due to the high incidence of hemorrhagic stroke cases. The rate of late onset seizure was shown to be higher than early seizures, which cannot be explained. Moreover, these seizures increased the morbidity of stroke and the mortality rate among these patients as well. It can be concluded that treatment of every post-stroke seizure has some preventive efficacy in the recurrence of the seizures.

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From the Department of Neurology (Ahangar), Yahyanejad Hospital, Department of Social Medicine (Hosseini) and the Education Development Center (Saghebi), Babol Medical Sciences University, Babol, Iran. Address correspondence and reprint requests to: Dr. Alijan Ahmadi Ahangar, Neurology Department, Yahyanejad Hospital, Babol Medical Sciences University, 4714766855 Babol, Iran. Tel. +98 (111) 2290141. Fax. +98 (111) 22225035. E-mail: alijanahmadiahangar@yahoo.com

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