Post Stroke Seizure in Group of Hospitalized Patient in Baghdad Teaching Hospital

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Abstract: Background: Stroke is the most common causes of seizures in adulthood. The incidence of seizures after stroke varies widely between 3.7% to 42.8%. Objectives: To assess the incidence of post – stroke seizures, the time of onset of seizures and, the type of seizures, also to evaluate the relationship between the development of seizures with subtypes of stroke, stroke size, and stroke site. Patients and methods: Data of 380 stroke patients were collected consecutively in Baghdad Teaching Hospital from Oct. 2013 to Nov. 2014; age, sex, date of stroke, symptoms and signs of stroke, time of seizures onset, patterns of seizures, neuroimaging findings, and the findings of both carotid Doppler and echocardiography were studied in both ischemic and hemorrhagic stroke. . Statistical analyses were performed using the SPSS software package for Windows 6.0. Results: Post – stroke seizures were developed in (9.73%) of our patients, furthermore, (8.5%) of patients with ischemic stroke and (18%) of patients with hemorrhagic stroke developed seizures. early onset seizures occurred in (56.76%) of patients with post – stroke seizures, while (71.43%) developed seizures within the first 24 hours. status epilepticus was seen in (10.8%). partial seizures developed in (61.9%) of patients with early onset seizures, while, (75%) of patients with late onset seizures had Secondarily generalized seizures. post – stroke seizures were occurred in (81.1%) of patients with cortical lesions, (P< 0.00005). Also (20%) of patients with large size lesion developed seizures, while (5.3%) of patients with small lesion developed seizures, (P < 0.0002). Post – stroke seizures developed in; (17.53%), (6.06%), (1.47%), of patients with embolic, thrombotic, and lacunar subtype of stroke, (P = 0.0004). Conclusions: The post – hemorrhagic stroke seizures more frequently within the first 24hr after the onset of stroke, while the post – ischemic stroke seizures occur equally at early onset and at late onset seizures, early onset seizures are more likely to be simple partial seizures, while late onset seizures are more likely to be secondarily generalized, further more status epilepticus occur more frequently within the first week after the onset of stroke. The hemorrhagic stroke, the embolic stroke, the cortical lesion and the large size lesion are associated with a higher risk for the development of the post – stroke seizures.

Keywords: Post – Stroke Seizures, Post – Hemorrhagic Stroke Seizures, Post – Ischemic Stroke Seizures

1. Introduction

Stroke is one of the most frequent causes of seizures in adulthood, particularly in elderly [1]. The relationship between seizures and stroke was recognized since 1864 by Jahan Hughling Jackson [2], and the reported incidence of seizures after stroke varies from (3.75 % to 42.8%) [2, 3, 4]. Acute ischemia leads to increase extracellular concentrations of glutamate, an excitatory neurotransmitter that has been associated with epileptiform neuronal discharge [5, 6, 7] Further, transient peri- infarct depolarization have been observed in the penumbra after experimental occlusion of the middle cerebral artery [6, 8]. In hemorrhagic stroke the blood products result in exposure of neurons to iron containing compounds which may lead to peroxidation of lipid membrane and promote excitatory ionic currents, the neuronal membrane more excitible producing epileptic focus [9,10]. seizures that occur after acute phase of infarction are considered to be unprovoked [11], arising from area of partially injured brain where neuronal networks have undergone anatomic and physiologic alteration, gliosis and development of meningeocerebral cicatrix, changes in membrane properties, deaffentation, selective neuronal loss, and collateral sprouting, may result in hyperexcitability
and neuronal synchrony sufficient to cause seizures[12,13,14]. The aims of the study were to determine the proportion of post stroke seizures in a group of Iraqi patients with stroke admitted at Baghdad teaching hospital and to evaluate the relationship between subtypes, site and size of stroke with the development of seizures, and to determine the time of onset of seizures in relation to the onset of stroke, and lastly to describe the type of post stroke seizures.

2. Patients and Method

We consecutively collected patients with stroke admitted at the department of neurology at Baghdad teaching hospital between oct.2013 to nov.2014.Patients with first stroke were 380, ischemic stroke seen in 330 (86.85%) while 50 patients (13.15%) had hemorrhagic stroke. Their age range between 32-88; male were 210 and female were 160. We excluded patients with transient ischemic attack, subarachnoid hemorrhage, imaging evidence of aneurysm or arteriovenous malformations or brain tumor, features of cerebral venous thrombosis, evidence of hypertensive encephalopathy, recent history of head trauma: history of: previous seizures, previous stroke and previous brain surgery. We included only patients with first attack of stroke, thus only 380 patients with first stroke admitted during this period were included in our study. Demographic factors including age, sex, date of stroke, patterns of seizures, neuroimaging findings, and the findings of both carotid Doppler and echocardiography, were studied. We classified stroke into ischemic and hemorrhagic stroke depending on the findings of neuroimaging.

Classification into cardio embolic, thrombotic and lacunar strokes depends on typical clinical syndromes as well as typical brain imaging and the presence or absence of myocardial infarction orcardiac valvular disease, we classified post stroke seizures into immediate seizures when occurred within the first 24 hours after the onset of stroke and early onset when occurred between second day and the seventh day after the onset of stroke and late onset when occurred more than 7 days after onset of stroke, [15, 16,17]. We classified the seizures by type into partial, generalized and status epilepticus depending on the recommendation of international league against epilepsy 2010 classification [18, 19, 20].The presence or absence of status epilepticus, the timing of occurrence after stroke, and seizure frequency was determined. CTscan was performed for all patients and MRI was done for patients if indicated clinically with a negative brain CT scan.

Statistical analyses were performed using the SPSS software package for Windows 6.0. Student’s t test and the chi squaretest were used. The level of significance was set at P< 0.05.

3. Results

Patients with first time stroke were 380, ischemic stroke seen in 330 (86.85%) while 50 patients (13.15%) had hemorrhagic stroke. Their age range between 32-88; male were 210 and female were 160.

Post stroke seizures were seen in 37 out of 380 patient(9.7%) who suffered first time stroke, their age range from (41 to 83) with age mean was (58.9) years, male forms 22 (59.46%) of them.

Post – ischemic stroke seizures developed in 28 (8.5%) patients out of 330 suffered ischemic stroke, whereas 9 (18%) of 50 patients with hemorrhagic stroke suffered seizures (28/330 versus 9/50, P=0.062) [see Table.1].

Early onset post – stroke seizures were seen in 21 (56.75%) patients and 16 (43.25%) patients had late onset post – stroke seizures, (21/37 versus 16/37, p > 0.05), this result showed a significant higher statistical early post stroke seizure [see table 2]. The majority of the early onset post stroke seizures occurred within the first 24 hours after the onset of stroke in 15 out of 21 (71.43%) patients with early onset post stroke seizures, the seizures occurred within the 24 hours, while the remaining 6 (28.57%) patients had an early onset post – stroke seizures occurred more than 24 hours to one week after the onset of stroke (15/21 versus6/21, P = 0.013) this results was statistically significant. [See Table. 2].

Among patients with post ischemic stroke seizures, 15(53.57%) were early onset post – stroke seizures, also 10(35.7%) of them had seizures within the first 24 hours after the onset of stroke. While of 9 patients with post – hemorrhagic stroke seizures 6 (66.67%) were early onset post – stroke seizures, also 5 (55.6%) of those patients had seizures within the first 24 hours after the onset of stroke. (15/28 versus6/9, P= 0.76), (10/28 versus5/9, P = 0.05).late onset post – stroke seizures developed in 13 out of 28 (46.43%) patients with post ischemic stroke seizures, while of 9 patients with post – hemorrhagic stroke seizures, 3 (33.33%) patients had late onset seizures (13/28 versus3/9, P=0.76). [see Table 3.]

Partial seizure was reported in 61.9% (13/21) and 25% (4/16) of early onset post stroke seizures and late onset post stroke seizures respectively and this results was statistically significant (P = 0.05). Secondarily generalized seizures were developed in 38.1% (8/21) of early onset post – stroke seizures, while 75% (12/16) of late onset post – stroke seizures were Secondary generalized (12/16 versus8/21, P = 0.04). Among the early onset post – stroke seizures group 61.9% (13/21) of the patients had partial seizures and 38.1% (8/21) of them had Secondary generalized seizures, (13/21 versus8/12, P = 0.21), whereas among the late onset post – stroke seizures group 75% (12/16) of the patients had Secondary generalized seizures and 25%(4/16) of them had partial seizures, (12/16 versus 4/16 P = 0.01). Also we found that of 21 patients with early onset post – stroke seizures, 11 (52.4%) had simple partial seizures and 2 (9.5%) had partial complex seizures, whereas 8 (38.1%) had secondary generalized seizures. On the other hand, we found that of 16 patients with late onset post – stroke seizures, 3(18.8%) had simple partial seizures and 1 (6.2%) had complex partial
seizures, whereas 12 (75%) had secondary generalized seizures, status epilepticus was more common in early onset 14.3% (3/21), than in late onset post – stroke seizures 6.2% (1/16), (3/21 versus 1/16, P< 0.05).Table 3.

There was significant correlation between the cortical location of the lesion and the development of post – stroke seizures, of 37 patients with post – stroke seizures, 30 (81.1%) had cortical lesion, whereas of 265 patients with small lesion 14 (5.3%) had seizures. (23/115 vs 14/265, P < 0.0002).[see table 5]

The correlation between the size of the lesion and the development of post – stroke seizures was highly significant, of 37 patients with post – stroke seizures, 30 (81.1%) had seizures. (23/115 vs 14/265, P < 0.0002).[see table 5]

Table 3. Showing the relation of stroke site and size with post stroke seizure.

<table>
<thead>
<tr>
<th>Type of Stroke</th>
<th>Total patients</th>
<th>Percentage</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small size</td>
<td>14/265</td>
<td>20%</td>
<td></td>
</tr>
<tr>
<td>Large size</td>
<td>23/115</td>
<td>5.3%</td>
<td>0.0002</td>
</tr>
<tr>
<td>Cortical site</td>
<td>30/37</td>
<td>81.1%</td>
<td>0.00005</td>
</tr>
<tr>
<td>Subcortical sites</td>
<td>7/37</td>
<td>18.9%</td>
<td></td>
</tr>
</tbody>
</table>

The correlation between the subtype of ischemic stroke and the development of post – stroke seizures was statistically highly significant, of 97 patients with embolic stroke 17 (17.53%) had post – stroke seizures, while of 165 patients with thombotic stroke 10 (6.07%) had seizures and 1 (1.47%) of 68 patients with lacunar stroke had post – stroke seizures (1/68 vs 10/165 vs 17/97 P= 0.0004) Table.1.

4. Discussion

The proportion of post – stroke seizures in our study was (9.73%).The incidences of post – stroke seizures in other studies were varying between (3.7 – 42.8 %). The highest incidence (42.8%) was reported by “Meyer et al”[4], in embolic stroke.. Dhanuka et al”[21], “Lancman et al”[20], “Black et al”[22], “Bladin et al”[1] and “Tsoi et al”[3], studies the reported incidences of post – stroke seizures were (13%, 10.04%, 10%, 8.9%, 3.7%)respectively. This wide range and variability between studies was related to the difference between study inclusion criteria and difference of study design.

The hemorrhagic stroke was more frequently associated with the development of post – stroke seizures, (18%), than the ischemic stroke, (8.5%). These findings agree with those of “Lancman et al” study [20] and “Bladin et al” study [1]. This high rate of post stroke seizures in intracerebral hemorrhage is related to raised intracerebral pressure and more neuronal irritability. We found that there was no significant difference between the percentages of patients with early onset (56.7%), and those with late onset post – stroke (43.2%), These results agree with those of “Black et al”[22] “Lancman et al”[20] and "Rhadwan" [23] studies, which were reported (57% versus 43% 54.5% versus45.5% and 54% versus 46%)Respectively. The majority of the early onset seizures developed within the first 24 hours after the onset of stroke, (71.4%, P = 0.01)this result agree with “Copenhagen” stud [15] (66%), and “So El et al” study[24](78%).

The post – hemorrhagic stroke seizures were more frequently occurred within the first 24 hours after the onset of stroke, (55.6%), than the post – ischemic stroke seizures, (35.7%).These results agree with those in “Bladin et al” study [1] who report (57%) of patients with post – hemorrhagic stroke seizures, and (40%) of patients with post – ischemic stroke seizures, had seizures within the first 24 hr. after the onset of stroke. On the other hand, we found that the post –hemorrhagic stroke seizures more frequently occurred at early onset (66.7%) than to occurred at late onset (33.3%), but we did not find such differences among patients with post – ischemic stroke seizures. The apparent differences
observed may be due to: a higher initial stroke severity which has been shown to exist in hemorrhagic stroke [13, 25].

In this study, the simple partial and the partial complex were predominant type of seizures among early onset seizures group (61.9%), the simple partial alone was seen in (52.4%) of the early onset seizures group. The Secondary generalized seizures were the predominant type of seizures (75%) in the late onset seizures group. These results agree with those of “Tsai et al” study [3], (56%) of early onset seizures were simple partial or partial complex, while (72%) of late onset seizures were Secondary generalized. Also agree partly with those of the “Gupta et al” study [26], who found that (57%) of the early onset seizures were simple partial or partial complex, while (65%) of the late onset seizures were Secondary generalized.

The cortical lesion was significantly more commonly associated with the development of post – stroke seizures (81.1%) than the subcortical lesion (18.9%), (P < 0.00005). These results agree with those of “Dhanuka et al” study [21], who reported that (85.7%) of patients with post – stroke seizures had cortical lesion. The post – stroke seizures that occur in the setting of subcortical stroke explained as a possible consequence of a substantial release of glutamate from axonal terminalis arising from injured thalamo – cortical neurons [27].

There was a significant association between the size of the lesion and the development of post – stroke seizures, (20%) of patients with a large lesion developed seizures, while (5.3%) of patients with a small lesion developed seizures (P < 0.0002). These results agree with those of “Lancman et al” study [20], who reported that the post – stroke seizures occurred in (21.2%) of patients with a small lesion, and in (5.3%) of patients with a large lesion. These results may be partly due to; neurons in the penumbra are still alive and able to discharge [28]. Epileptogenic processes such as enhanced release of exitotoxic glutamate, ionic imbalance, break down of membrane phospholipids and release of free fatty acid all are characterize the penumbra [12], so a larger infarct is associated with a larger ischemic penumbra which will in turn enhance the risk of seizures in metabolically disturbed tissue because the neurons are still able to discharge. Also a larger area of infarct results in a larger scar formation which will increase the risk of seizures development. On the other hand, in case of intracerebral hematoma, a larger hematoma will cause more severe tissue destruction and as a result lead to a larger scar formation which will enhance the risk of seizures, on the other hand, experimental models observed that the direct application of iron increases cortical irritability [29]. So the larger intracerebral hematoma will result in exposure of cortical neurons to a larger amount of iron which will cause more severe cortical irritability than in case of small size intracerebral hematoma.

In this study there was a significant difference between the different subtypes of ischemic stroke and the development of post – stroke seizures. The most common subtype of ischemic stroke that associated with the development of the post – stroke seizures was embolic stroke,(17.53%), followed by of patients with thrombotic stroke (6.07%), while (1.47%) of patients with lacunar stroke developed seizures. (P =0.0004). These results agree with the results of “Giroud et al” study [30] in which (16.6%) of patients with embolic stroke developed seizures, and (4.4%) of patients with thrombotic stroke developed seizures, whereas (1%) of patients with lacunar stroke developed seizures. The embolic stroke is most likely to involve the cortex directly, it is usually affected the cortex at the gray – white mater junction where blood flow is highest and end arteries predominate [1], also the embolic stroke is more likely to produce a large size lesion, on the other hand, the embolic stroke often include at least a small hemorrhagic component [11]. The occurrence of post – stroke seizures with lacunar stroke may be explained by the concurrent cortical involvement, patients with lacunar stroke showed evidence of cortical dysfunction on single photon emission CT scan and had lateralized EEG abnormalities even when the routine CT scan was normal [1, 31], also in a small study using quantitative EEG analysis reported lateralized abnormalities in (83%) of patients with lacunar infarctions [32].

5. Conclusions

The development of seizures as a sequellae of stroke is not common. The post – hemorrhagic stroke seizures commonly occur at early onset seizures and more frequently within the first 24hr. after the onset of stroke, while the post – ischemic stroke seizures occur approximately equally at early onset or late onset seizures, on the other hand the early onset seizures are more likely to be simple partial seizures, while the late onset seizures are more likely to be secondarily generalized, further more the status epilepticus occur more frequently within the first week after the onset of stroke. Also lacunar stroke may be associated with the development of seizures. The hemorrhagic stroke, the embolic stroke, the cortical lesion and the large size lesion are associated with a higher risk for the development of the post – stroke seizures.

References


