Early post-acute stroke seizures: Clinical profile and outcome in a Nigerian stroke unit

Imarhiagbe Frank Aiwansoba, Ordia Wallace Chukwuyem
Department of Medicine, University of Benin Teaching Hospital, Benin City, Nigeria

Correspondence to: Dr. Imarhiagbe Frank Aiwansoba, P.O. Box 7184, GPO, Benin City, Nigeria. E-mail: dnimei@yahoo.com

Abstract

Aim: To describe the basic clinico-demographic profile and outcome of Early Post-Acute Stroke Seizures (EPASS).

Materials and Methods: Two-hundred and fifty one patients admitted within 24 h of onset of stroke symptoms into the stroke unit of a tertiary care hospital were followed up for convulsive seizure(s) within 7 days of admission and for disease outcome in 42 days. Stroke subtype was defined by cranial computed tomography and ictal phenomenon was as described by the stroke unit doctors. Stroke severity was by the Canadian Neurological Scale (CNS) and Glasgow Coma Scale (GCS). Seizures were characterized as partial, generalized, or status. Stroke outcome was defined as discharge from inpatient care to follow-up or still in care and all cause in-hospital death. Data was compared between the group with and without seizures. The effect of age, sex, blood sugar, GCS, CNS, and seizure type on stroke outcome and time to in-hospital death in EPASS was tested on logistic regression and Cox proportional hazard regression.

Result: EPASS occurred in 9.96% of subjects and intracerebral infarct was more associated with EPASS, a finding different from what is dominant in western literature.

Conclusion: Profile of EPASS may appear different in terms of stroke subtype in Sub-Saharan African populations. Larger prospective studies may clarify the position better.

Keywords: Africans, outcome, profile, seizures, stroke

Résumé

Objectif : Pour décrire le profil clinico-démographiques de base et les résultats des saisies précoce de l’AVC Post-Acute (EPASS).

Matériaux et Méthode: Deux - cent cinquante un patients admis dans les 24 heures précédant l’apparition des symptômes de l’AVC dans l’unité de temps, d’un hôpital de soins tertiaires ont été suivis pour seizure(s) convulsif dans les 7 jours d’admission et pour le résultat de la maladie en 42 jours. Sous-type de course a été défini par crânienne une tomodensitométrie et phénomène ictal était tel que décrit par les médecins d’unité de temps. Gravité de l’accident vasculaire cérébral a été par l’échelle neurologique canadienne (SNC) et échelle de Coma de Glasgow (GCS). Saisies ont été caractérisées comme partielle, généralisée, ou statut. Résultat de la course a été défini comme décharge de soins aux patients hospitalisés au suivi ou encore dans les soins et toutes causes de décès à l’hôpital. Données a été comparées entre le groupe avec ou sans convulsions. L’effet de l’âge, le sexe, sucre dans le sang, GCS, SNC et type de saisie sur le résultat de la course et le temps à mortalité à EPASS a été testé sur la régression logistique et la régression de Cox risque proportionnel.

Résultat : EPASS éclata en 9,96 % des sujets et des infarctus intracérébral fut plus associé à EPASS, une conclusion différente de ce qui est dominant dans la littérature occidentale.

Conclusion : Profil de EPASS peut sembler différente en termes de sous-type d’AVC chez les populations d’Afrique subsaharienne. Grandes études prospectives peuvent clarifier la position mieux.

Mots-clés : Africains, résultat, profil, convulsions, accidents vasculaires cérébraux
Introduction

Stroke results in several-fold increase in seizure incidence. Early Post-Acute Stroke Seizures (EPASS) is a seizure occurring in the early period following a stroke and it occurs in 2-18% of acute strokes. There are no strict guidelines currently in the definition of EPASS in reference to the number of days after a stroke; however, between 7 and 14 days have been used operationally. EPASS usually begins within the first 24 h of a stroke, it could be solitary or multiple, focal or generalized, it may occasionally present as status epilepticus, and it is found more frequently in males than in females. The pathophysiological changes that occur in the brain's cortical function shortly after a stroke is believed to be the neutral substrate for EPASS and more often than not, as the acute alterations resolve, EPASS also resolves and usually does not progress to epilepsy (a tendency to recurrent seizures). The risk of late post-stroke seizures (seizures occurring after 14 days of acute stroke), epilepsy, and cognitive decline is however known to increase with EPASS and it has also been associated more with increasing severity of stroke and cortical location of the stroke rather than the pathologic subtype of stroke, as both cerebral infarct and hemorrhage are associated with it. EPASS is advisedly aborted with anticonvulsants as a result of the potential effect on morbidity and disease outcome, which are withdrawn as soon as the seizures stop as they rarely recur.

Acute stroke outcome in EPASS has varied widely across different studies; although some report no difference, others report poorer outcomes with EPASS compared with stroke without EPASS, although the risk of death always exists after a generalized seizure particularly with status epilepticus.

This study prospectively profiled convulsive EPASS and its relationship with acute stroke outcome in a stroke unit in Sub-Saharan Africa.

Materials and Methods

A total of 251 patients consecutively admitted into the stroke unit within 24 h of onset of stroke symptoms at the stroke unit of a tertiary care hospital in Sub-Saharan Africa between March 2011 and April 2012 were prospectively followed up for clinical convulsive seizure(s) occurring within 7 days of admission after basic data of age, sex, blood sugar, stroke subtype, seizure type, and admission Glasgow Coma Scale (GCS) were captured and all patients were followed up for disease outcome in 42 days. Stroke subtype was defined by cranial computed tomography (CT) scan as either intracerebral hemorrhage or infarct and ictal phenomenon was as described by the stroke unit resident doctors or consultants and stroke severity was assessed by the Canadian Neurological Scale (CNS). Operationally, seizures were characterized as either partial or generalized and status seizure was defined as seizure persisting for longer than 5 min after the administration of intravenous diazepam to abort the seizure. Stroke outcome was defined as discharge from inpatient care to follow-up or still in care and all cause in-hospital death.

Exclusion-CT evidence of mass lesion or subarachnoid hemorrhage or inconclusive diagnosis; diagnosis other than stroke; history of epilepsy or head trauma; patients admitted after 24 h of onset of stroke symptoms; seizures occurring after day 7 on admission or patient discharged against medical advice.

Statistics-Basic data is described and expressed as mean and standard deviation or percentages and compared between the group with and without seizures with t-test for continuous variables and Chi square for discrete and categorical variables and the effect of the covariates of age, sex, GCS, CNS, stroke subtype, and seizure type on acute stroke outcome was tested with logistic regression and the effect on time to outcome (in-hospital death) was tested with Cox proportional hazard regression. Analysis was carried out with SPSS® version 17 and P ≤ 0.05 was taken as significant for all tests.

Results

A total of 251 patients were studied and divided into two groups comprising those with and without EPASS. The overall mean age of all study subjects was 59.97 ± 13.32 years (range 21-91 years, median 60) and sex distribution was 119 (47.4%) females and 132 (52.6%) males [Table 1].

Of the 251 cases, the period incidence of EPASS was 25 (9.96%) and 226 (90.04%) were without seizures. Seizures were partial in 14 (56%) and generalized in 9 (36%) and status seizures occurred in 2 (8%) [Table 1].

Mean age of the group with EPASS was not significantly different from that of the group without seizures (62.68 ± 15.70 vs. 59.67 ± 13.04 years), t = 1.071, P = 0.285; however, the sex distribution was significantly different with a male sex preponderance in the EPASS group, Chi square = 6.103, P = 0.013 [Table1].

The distribution of stroke subtypes showed that intracerebral hemorrhage and intracerebral infarct accounted for 5 (20%) and 20 (80%), respectively.
Table 1: Basic data of study participants compared between early post-acute stroke seizures and no early post-acute stroke seizures groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean (EPASS)</th>
<th>Mean (no EPASS)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean±SD) in years</td>
<td>62.6±15.70</td>
<td>59.6±13.04</td>
<td>0.285</td>
</tr>
<tr>
<td>Sex-F/M (%)</td>
<td>6/19 (24/76)</td>
<td>113/113 (50/50)</td>
<td>0.013</td>
</tr>
<tr>
<td>Blood sugar (mean±SD) mg/dl</td>
<td>156±25.36*</td>
<td>139.58±41.37</td>
<td>0.163</td>
</tr>
<tr>
<td>GCS (mean±SD)</td>
<td>8.56±3.98</td>
<td>8.65±3.13</td>
<td>0.899</td>
</tr>
<tr>
<td>CNS (mean±SD)</td>
<td>5.16±3.83</td>
<td>5.17±3.09</td>
<td>0.977</td>
</tr>
<tr>
<td>Stroke subtype-infarct/haemorrhage (%)</td>
<td>20/5 (80/20)</td>
<td>130/96 (57.5/42.5)</td>
<td>0.030</td>
</tr>
<tr>
<td>Seizure type-partial/generalized/status (%)</td>
<td>56/36/8</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>In-hospital death (%)</td>
<td>11 (44)</td>
<td>–66 (29.20)</td>
<td>0.128</td>
</tr>
<tr>
<td>n (% of total)</td>
<td>25 (9.96)</td>
<td>226 (90.04)</td>
<td></td>
</tr>
</tbody>
</table>

EPASS=Early post-acute stroke seizures, SD=Standard deviation, GCS=Glasgow coma scale, CNS=Canadian neurologic scale.

Table 2: Early post-acute stroke seizures outcome stratified between status and non-status seizures

<table>
<thead>
<tr>
<th>Seizure</th>
<th>Status</th>
<th>Non-status</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>outcome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discharge/still-in care</td>
<td>14</td>
<td>0</td>
<td>0.096</td>
</tr>
<tr>
<td>In-hospital death</td>
<td>9</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>n=25</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Predictors of acute stroke outcome in early post-acute stroke seizures

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>CI (95%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>age</td>
<td>0.956</td>
<td>0.901-1.015</td>
<td>0.142</td>
</tr>
<tr>
<td>Sex</td>
<td>0.727</td>
<td>0.115-4.585</td>
<td>0.735</td>
</tr>
<tr>
<td>RBS</td>
<td>1.003</td>
<td>0.996-1.010</td>
<td>0.426</td>
</tr>
<tr>
<td>GCS</td>
<td>0.545</td>
<td>0.357-0.832</td>
<td>0.005</td>
</tr>
<tr>
<td>CNS</td>
<td>0.538</td>
<td>0.351-0.825</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Seizure type 2.333 0.606-8.990 0.218, OR=Estimated odds ratio, RBS=Admission random blood sugar, GCS=Glasgow Coma Scale, CNS=Canadian neurologic scale, CI=Confidence interval.

Table 4: Predictors of time to in-hospital mortality in early post-acute stroke seizures

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR</th>
<th>CI (95%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.970</td>
<td>0.933-1.008</td>
<td>0.120</td>
</tr>
<tr>
<td>Sex</td>
<td>1.176</td>
<td>0.248-5.581</td>
<td>0.839</td>
</tr>
<tr>
<td>RBS</td>
<td>1.003</td>
<td>0.999-1.008</td>
<td>0.140</td>
</tr>
<tr>
<td>GCS</td>
<td>0.699</td>
<td>0.559-0.874</td>
<td>0.002</td>
</tr>
<tr>
<td>CNS</td>
<td>0.703</td>
<td>0.562-0.880</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Seizure type 1.687 0.559-5.089 0.354, HR=Hazard ratio, RBS=Admission random blood sugar, GCS=Glasgow Coma Scale, CNS=Canadian Neurologic Scale, CI=Confidence interval.

Discussion

The 10% period incidence of seizures in this study is close to figures found in earlier related studies.[3,4,7,13] The distribution of seizure types showed that partial seizures were more than generalized and status seizures, a finding which may be explained by the fact that the underlying stroke usually excites first a focal neurologic injury.

The similar age distribution of subjects with EPASS and no EPASS suggests that age may not be a contributing factor in the occurrence of EPASS.[14] However, the relationship between age and seizures occurring after stroke from related studies has shown that stroke is a relatively frequent cause of new-onset seizures in the elderly.[15] The significant difference in the sex distribution between EPASS and no EPASS indicated a predominance of the male sex in EPASS, which is consistent with results from related studies.[9,12]

Remarkably, the distribution of stroke subtype showed a significant preponderance of cerebral infarct in EPASS compared with no EPASS, a finding in consonance with some earlier studies that associated EPASS more with cerebral infarct compared with intracerebral hemorrhage.[16,17] The

in the group with EPASS and 96 (42.47%) and 130 (57.52%), respectively, in the group without seizures, with a significant difference (Chi square = 4.730, P = 0.03). Admission GCS and blood sugar were not significantly different between the two groups (P = 0.899 and 0.163, respectively) and mean CNS scores were also not different (P = 0.977).

Through there were more in-hospital deaths with EPASS compared with subjects without seizures –11/25 (44%) versus 66/226 (29.20%) – and remarkably the two patients with status seizures died, stroke outcome was not statistically different between the two groups, (P = 0.128) [Table 1]. Acute stroke outcome was stratified between status and non-status seizures, and showed a poorer trend with status seizures though the difference was not statistically significant (P = 0.996) [Table 2].

Lower GCS and CNS predicted poorer stroke outcome in subjects with EPASS (P = 0.005, P = 0.004) as shown in Table 3.

GCS and CNS also significantly influenced time to in-hospital mortality in EPASS, P = 0.002 and 0.002, respectively, as shown in Table 4.
dominant majority of western literature however associates EPASS more with hemorrhage than infarct.\[1,2,6\] This epidemiologic difference in the presentation of EPASS and the subtype of stroke may not be unrelated with the very high proportion of putaminothalamic (deep) bleeds of ruptured lenticulostriate arteries from chronic severe hypertension in Africans, which may provoke less seizures in contrast to cortical (superficial) bleeds as shown in the recent Kinshasa intracerebral hemorrhage score study in rural Congolese Africans.\[16\] Similar studies have divested EPASS to an extent from pathologic subtypes of stroke and have instead associated EPASS more with cerebral cortical location of a stroke than with the subtype of stroke.\[4,14,19,20\] Hemorrhagic transformation of an infarct and multi-lobar or hemispheric involvement of a stroke have also been linked with increased propensity for early seizures after stroke.\[14\]

We note also that the mean admission GCS of the two study groups was not significantly different. This suggests that GCS did not influence the incidence of EPASS. Stroke severity as assessed by the CNS was also not different between the groups, which suggests that stroke severity did not influence the occurrence of seizures. Severe strokes have, however, been found to be more associated with non-convulsive electrographic seizures in related studies.\[21\] It bears reiteration that in this study convulsive seizures were only clinically assessed, which may explain the absence of any association between stroke severity and EPASS.

Mean admission blood sugar was also not significantly different between the two study groups. Elevated blood sugar lowers seizure thresholds in acute stroke patients and increases the propensity for seizures and this picture is the same for hypoglycemia.\[12\]

Although stroke outcome was not significantly different between the groups, the higher proportion of in-hospital deaths in the EPASS group is noteworthy. The relationship between EPASS and acute stroke outcome varies widely across different studies and somewhat appears to be influenced more by other clinicodemographic factors of the stroke other than the seizures even though the risk of sudden death always exists in generalized seizures and particularly in status seizures.\[3,4,22\] Status seizures are associated with poorer outcome of EPASS, a trend that is also noted in this study.\[22\]

Acute outcome of EPASS was predicted by GCS and the CNS. GCS correlates with well-known stroke severity assessment tools such as CNS and National Institutes of Health Stroke Score, and stroke severity is generally an independent predictor of acute stroke outcome.\[23,24\]

The influence of GCS and CNS on time to in-hospital death is noted. Lower GCS and CNS predicted shorter time to in-hospital mortality. This is consistent with earlier related studies.\[25,26\]

We conclude that the incidence of EPASS in this study is similar to that in previous works carried out in other climes and importantly, intracerebral infarct was associated more with EPASS than with intracerebral hemorrhage – a finding different from the dominant one in western literature. Acute stroke outcome in terms of in-hospital mortality was not significantly different in EPASS compared with no EPASS and status seizures were associated more with poorer outcomes than with non-status seizures. Severe strokes and lower GCS predicted poorer acute outcome and a shorter time to in-hospital mortality in EPASS. A larger prospective study would probably better clarify the issues raised.

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