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Profile of Post-traumatic Epilepsy in Benin City, Nigeria

Profil de l'épilepsie post-traumatique dans la ville de Bénin, Nigéria

O. A. Ogunrin*, A. A. Adeyekun†

ABSTRACT

BACKGROUND: **Post traumatic epilepsy is recurrent chronic seizures occurring after four weeks following brain injury. It commonly occurs after road traffic accidents thus making it a preventable cause of chronic seizures. The prevalence and pattern of this disorder is not known among Nigerian patients with epilepsy.**

OBJECTIVE: **This study aimed at determining the prevalence of and predisposing type of head injury to developing post traumatic epilepsy.**

METHODS: **We studied 244 consecutive patients with epilepsy attending the neurology clinic of a tertiary health facility in an urban Nigerian city by analyzing the details of their demographic and clinical data obtained with the aid of a structured questionnaire and from the Epilepsy Registry of a Neurology Unit between January and December 2006.**

RESULTS: **Thirty-eight patients with a mean age of 38.6 ± 7.3 years (age range 15 – 75 years) had posttraumatic epilepsy comprising 15.57% of all cases of epilepsy. Thirty-three (86.8%) had closed head injury. Thirty-two (84.2%) of the patients had positive history of loss of consciousness. Twenty-two patients (57.9%) sustained head injury from motor vehicle accidents. Majority of the patients had secondarily generalized seizures (73.7% of the cases). Twenty-seven (71.4%) of the 38 patients had seizure onset in the first year after brain injury. Depressed skull fracture (19/38; 50%) was the most common abnormal CT finding.**

CONCLUSION: **Post traumatic epilepsy contributes significantly to the number of patients with epilepsy presenting to our neurology services. There is need to educate people on the usefulness of seat-belts and helmets while driving. WAJM 2010; 29(3): 153–157.**

Keywords: **Epilepsy, Nigeria, post-traumatic, prevalence, risk factors, road trafic accident**

RÉSUMÉ

CONTEXTE: *épilepsie post-traumatique est chronique récidivante crises survenant après quatre semaines après une lésion cérébrale. Il se produit généralement après les accidents de la circulation routière est ainsi devenue un cause évitable de crises chroniques. La prévalence et modèle de ce trouble n'est pas connue chez les patients nigérians souffrant d'épilepsie.*

OBJECTIF: *Cette étude visait à déterminer la prévalence de prédisposition et de type de blessure à la tête de développer post l'épilepsie traumatique.*

METHODES: *Nous avons étudié 244 patients consécutifs atteints d'épilepsie assistant à la clinique de neurologie d'un établissement de santé tertiaire une grande ville du Nigeria, en analysant les détails de leur données démographiques et cliniques obtenus avec l'aide d'un questionnaire structuré et de la greffe d'une épilepsie Neurologie Unité entre Janvier et Décembre 2006.*

RÉSULTATS: *Trente-huit patients avec un âge moyen de 38,6 ± 7,3 ans (extrêmes de 15 ans - 75 ans) avaient une épilepsie post-traumatique comprenant 15,57% de tous les cas d'épilepsie. Trente-trois (86,8%) avaient un traumatisme crânien. Trente-deux (84,2%) de la patients avaient des antécédents de perte de conscience. Twenty-two patients (57,9%) ont subi un traumatisme crânien de véhicules automobiles accidents. La majorité des patients ont secondairement généralisées saisies (73,7% des cas). Vingt-sept (71,4%) de la 38 patients avaient début des crises dans la première année suivant le cerveau blessures. Déprimé fracture du crâne (19/38; 50%) était la plus commune de trouver CT anormal.*

CONCLUSION: *épilepsie post-traumatique contribue de manière significative le nombre de patients présentant une épilepsie à nos services de neurologie. Il est nécessaire d'éduquer les gens sur l'utilité des ceintures de sécurité et des casques en conduisant.* ***WAJM 2010; 29 (3): 153–157.***

Mots-clés: *épilepsie, le Nigeria, post-traumatique, la prévalence, le risque facteurs, accident de la route*

***Neurology Unit, Department of Medicine, †Department of Radiology, University of Benin Teaching Hospital, Benin City, Nigeria**

Correspondence: **Dr. A. O. Ogunrin,** Department of Medicine, PMB 1154, University of Benin, Benin City, Nigeria, E-mail: bunmifunmi@hotmail.com Telephone: 2348038818707 (Mobile), Fax: 23452251859

Abbreviations: CT, Computerised tomographic; **PTE,** Post traumatic epilepsy; **PTS,** Post traumatic seizures

INTRODUCTION

Post traumatic epilepsy (PTE) is a preventable cause of chronic seizures. This condition often occurs following head injury resulting from motor vehicle accidents. The mechanisms underlying the development of post traumatic seizures remain unclear but several theories including free radical damage caused by blood in the brain parenchyma, increases in excitatory activity and changes in inhibitory functions in the brain have been put forward to explain its pathogenesis.[1,2]

In PTE, the head injury is believed to be the initiating event resulting in a cascade of processes that culminates in epileptogenesis. Following either closed or open head trauma, two categories of post traumatic seizures (PTS) may occur – early or late. Early seizures occur as a result of the physical effects of the trauma and usually within one to two weeks after injury.[3] Late seizures occur after the patient has recovered from the effects of the injury, often weeks, months or even years after the original injury. The seizures may be single or recurrent. It has been reported that about 20% of those with one late PTS do not progress to having recurrent seizures.[3] Post traumatic epilepsy is diagnosed in the presence of recurrent late seizures.[4, 5] Seizures that occur within the first 24 hours following head injury (either trauma or due to brain surgery) have been distinguished from early seizures and termed immediate post traumatic seizures. The pathogenesis of immediate PTS remains unclear though it has been attributed to non-specific response to the physical insult.[5]

The risk of developing PTE is determined by the type of injury and the severity of injury, but why certain people develop seizures after only a mild insult yet others sustaining more severe traumatic brain injury do not, remains a mystery. It has been reported that individuals sustaining head injury have a threefold higher risk of developing epilepsy than the general population.[3] Furthermore, the Olmsted County study showed that increased risk of PTE is associated with these factors; brain contusion with subdural hematoma, skull fracture, presence of loss of consciousness, amnesia of more than 24 hours duration and the presence of persistent neurological injury, retention of fragments in the brain and intracranial hematoma.[6] It has also been observed that the degree of loss of brain tissue from injury positively correlated with likelihood of developing seizures.[7] The period it takes for seizures to develop after head trauma varies and the determining factor remains unclear. The Vietnam Head injury study reported that 50% of patients developed recurrent seizures within the first year after injury and seizures did not occur in 15% of them until five or more years.[7]

Reports on prevalence and incidence of post traumatic seizures are lacking in the Nigerian population. In the United States, an incidence of 53% was reported by Annegers *et al* among war veterans with head injuries and incidence of between 1.8% and 5% in civilian populations.[6] This study describes the profile of post traumatic seizures among Nigerian patients with epilepsy attending the neurology clinic of a tertiary health facility, with emphasis on the prevalence, the time frame or period that elapsed between sustenance of head injury and occurrence of seizures, and the severity and type of head injury found in these patients.

SUBJECTS, MATERIALS, AND METHOD

A total of 244 consecutive patients diagnosed as having epilepsy based on history of recurrent afebrile seizures unrelated to alcohol or substance abuse, metabolic disorders or drug withdrawals with eye-witness corroboration were recruited from the neurology clinic of the Benin University teaching hospital, a tertiary health facility in metropolitan Nigeria between January and December 2006. Details of demographic information (including age, sex, domicile, occupation and marital status), history of seizure variables (duration of seizures, type of seizures, onset, periodicity and frequency of seizures) and possible aetiology were obtained from all patients using a questionnaire administered by one of the authors (OAO) and from the Epilepsy Register of the Neurology Unit. All patients had detailed neurological evaluation and electroencephalographic (EEG) examination done. The classification of epilepsy was based on the International League Against Epilepsy (ILAE) criteria.[8]

Thirty-eight patients of the 244 were diagnosed as having post traumatic epilepsy based on history of recurrent chronic seizures with onset after four weeks of head trauma. The exclusion criteria included patients less than 14 years of age, early post-traumatic seizures (i.e. seizures occurring within first four weeks after head trauma), seizures from other causes (infections, post-stroke, hypoxic encephalopathy, etc) and those with unidentifiable aetiology. The thirty-eight patients had cranial computerized tomographic (CT) scan done. Information on causes of head injury, type of head injury, presence or absence of loss of consciousness, findings on CT scan, onset time of seizures after head trauma, type of seizure and anti-epileptic medication were documented and analyzed. The severity of head trauma was assessed using the presence or absence of loss of consciousness and CT brain findings of skull fractures, subdural hematoma or intracranial hematoma. The study protocol was approved by the hospital ethics committee.

Statistical Analysis of Data

Data was analyzed with the aid of Statistical Package for Social Sciences (SPSS) version 11. The proportions of patients in relation to seizure variables and time of onset of seizures were expressed as percentages and means (±

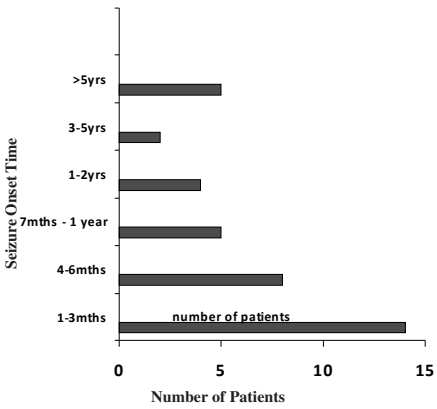

Figure 1: Time interval between head injury and onset of seizures

Table 1: Age and Sex Distribution of the Patients

Age group(years)	Number(%)		
	Male	Female	Total
15 – 25	2 (5.3)	4 (10.5)	6 (15.8)
26 – 35	8 (21.1)	3 (7.9)	11 (28.9)
36 – 45	9 (23.6)	2 (5.3)	11 (28.9)
46 – 55	3 (7.9)	2 (5.3)	5 (13.2)
56 – 65	2 (5.3)	1 (2.6)	3 (7.9)
66 – 75	1 (2.6)	1 (2.6)	2 (5.3)
Total	**25 (65.8)**	**13 (34.2)**	**38 (100.0)**

Table 2: Causes of Head Trauma among Patients with Post-traumatic Epilepsy

Cause of Head Injury	Number (%)	Average (Range) Period of Seizure Onset (Months)
Motor vehicle accident	22 (57.9)	17 (2 – 96)
Falls (domestic & work place)	6 (15.8)	12 (4 – 60)
Assault	3 (7.9)	12 (3 – 24)
School accident*	2 (5.3)	8 (6– 9)
Object fell on head†	1 (2.6)	3 (0 – 3)
Armed robbery victims	4 (10.5)	5 (4 – 12)
Total	**38 (100.0)**	

**Students beaten on the head in school.*
†*Case of a lumberjack who a tree fell on his head.* (χ^2 = 18.728; P=0.54)

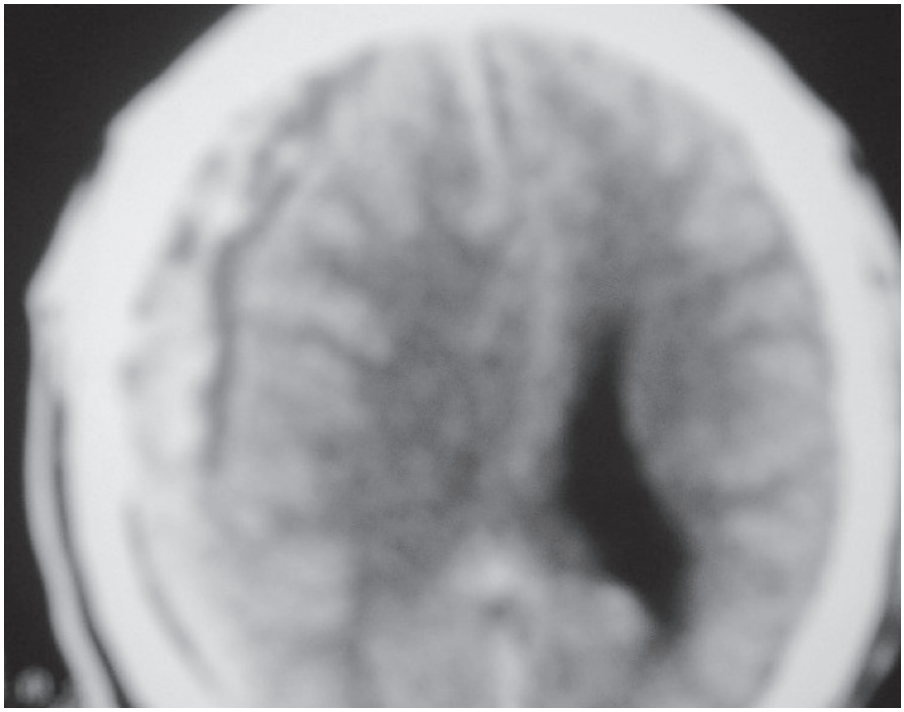

Figure 2: The computerized tomographic scan showing a right-sided acute-on-chronic subdural hematoma with ipsilateral ventricular effacement and midline shift to the left.

SD) as appropriate. The effect of the type of head injury on onset time of seizures was assessed using chi-square analysis (with level of significance taken as $p<0.05$).

RESULTS

Thirty-eight patients were diagnosed as having post traumatic epilepsy comprising 15.57% of all cases of epilepsy seen in the clinic during the one year period. The mean age of the patients was 38.6 ± 7.3 years (age range 15–75 years) with a male preponderance, M/F ratio of 1.9:1 (Table 1). The highest number of cases was recorded among patients in the age group 26 – 45 years. Thirty-three (86.8%) of the patients had closed head injury while the remaining five (13.2%) patients had open head trauma. Thirty-two (84.2%) of them had positive history of loss of consciousness. Of the remaining six patients without loss of consciousness, four had open head injuries.

Twenty-two (57.9%) patients sustained head injury from motor vehicle accidents. The other causes of head trauma included domestic assaults, blunt head injuries from armed robbery attacks, falls and objects falling on the head (Table 2). Thirty (78.9%) of the patients had clinical history of partial epilepsy with secondary generalization while two patients had akinetic epilepsy and four had primarily generalized tonic-clonic epilepsy. The remaining two patients had simple partial epilepsy (Jacksonian type). The EEG recordings showed that majority of the patients had secondarily generalized seizures, constituting 28(73.7%) of the cases. The remaining ten patients had primarily generalized (n=6) and localization-related seizures (n=4) on EEG.

The onset of recurrent seizures was observed in the first 3 months in fourteen patients (36.8%). Twenty-seven (71.4%) of the thirty-eight patients had seizure onset in the first year after brain injury. Details of seizure onset are illustrated on Figure 1. The type of head trauma did not significantly predict or affect the time of onset of seizures (p=0.54).

The computerized tomography of the brain revealed findings outlined on Table 3. Depressed skull fracture was the

Table 3: Frequency of CT Scan findngs in 38 Patients with Post-traumatic Epilepsy

CT Brain Scan Findings	Frequency N (%)
Normal	10(26.3)
Depressed skull fracture	19(50.0)
Subdural hematoma	4(10.5)
Intra parenchymal hematoma	3(7.9)
Subdural and intra-parenchymal hematoma	2(5.3)
Total	**38(100.0)**

most common abnormal CT finding, present in 50 percent of the patients. Ten (26.3%) of the patients had normal CT brain scan while four (10.5%) had subdural haematoma (Figure 2).

Twenty (52.6%) received phenytoin sodium (at an average dose of 200mg/day), 14 (36.8%) received controlled-release formulation of carbamazepine (at an average dose of 800mg/day in two divided doses) and the outstanding four patients were treated with sodium valproate (at an average dose of 600mg/day in three divided doses). Thirty-four (89.5%) were seizure-free within the first 3 months of anti-epileptic medication. All the patients were seizure free after six months of therapy.

DISCUSSION

The development of recurrent seizures following injury to the brain is a matter of concern in neurological and neurosurgical practice for several reasons. First it is difficult to measure the incidence of post traumatic seizures taking into account the incidence of epilepsy in the general population,[3] and second it is difficult to optimize effective treatment because of the poor understanding of the pathogenesis, presence of other risk factors of seizures, loss to follow up and confusion with single late seizures after the initial injury in this group of patients. Despite these pitfalls, it is apparent that post traumatic epilepsy accounts for a significant portion of all cases of epilepsy. The prevalence of approximately 16% recorded in this study may just be a 'tip of the iceberg' as the incidence of post traumatic epilepsy may be more especially in a developing country like Nigeria where the issues of stigmatization and banishment of patients with epilepsy are rampant,[9] hence we may not be seeing some who develop seizures following brain injury.

Several studies have reported the high percentage of patients who present with recurrent post traumatic seizures (PTS) within the first one or two years,[3, 10,11,12] thus corroborating our finding. Early PTS has been observed to be more common in children while late PTS more common in adults but the role of genetic susceptibility remains controversial.[3,5] Most of the early PTS are usually of the generalized tonic-clonic type whereas in late post traumatic seizures the seizure types are varied.[3] There was a decline in the percentage of patients with recurrent post traumatic seizures after the first year until after five years when there was an increase in the percentage, an observation similar to what was reported by Jennett.[10] What explains the time delay between the initial brain insult and the 'epilepsy' phenotype remains unclear. It may however be related to the gradual and selective neuronal loss initiated by the injury, alteration in the expression of neurotransmitters and their receptors, axonal and dendritic re-organization, and subsequent changes in glial architecture.[10]

The important risk factors for PTE which have been identified include severity of trauma, penetrating head injury, intracranial hematoma, depressed skull fracture, haemorrhagic contusion early post traumatic seizures and coma lasting for more than (24) hours.[5,6,13] Significant proportions of our patients had depressed skull fracture, loss of consciousness (though we could not determine the duration of coma because of late presentation to the tertiary hospital as most patients seek care at private health facilities or traditional medical homes initially) and intracranial hematomas. The increased risk after intracranial hematomas is particularly important because the presence of blood in the parenchyma of the brain is one of the elements incriminated in the pathogenesis of post traumatic epilepsy. The formation of damaging free radicals by blood in the parenchyma causes increase excitatory activity and changes in the inhibitory functions of the brain. The breakdown products of hemoglobin have been shown to affect synaptic transmission that may lead to epileptogenesis.[1] This is thought to be related to the formation of free radicals by iron causing direct injury to neuronal membrane and subsequently resulting in cell death. In addition iron has been demonstrated in animal models to increase the release of excitatory neurotransmitter glutamate and reduce the activity of glutamate transporter protein (a protein expressed by astrocytes responsible for glutamate re-uptake).[2,14]

Post traumatic epilepsy is more common among young adults as they are more likely to be involved in activities that predispose to head injuries. It is also more common in males than females for same reason. Our study revealed that most of the patients suffered brain injury from road traffic accidents. This observation is in agreement with the recent publication by Nzegwu et al who attributed a mortality of 22.7% to road traffic accidents among 308 deaths that occurred in Benin City between August 2002 and July 2003(15). It was observed that most of the deaths were due to intracranial hemorrhage.[15] The use of seat belts and helmets thus make PTE a preventable cause of epilepsy.

Magnetic resonance imaging is the investigation of choice in PTE. This facility is however not available in our centre. The option available to us is the cranial computerized tomography which is an acceptable alternative.[5] The electro-encephalography is of limited use in post traumatic epilepsy as it does not predict the onset of PTE. It may be useful in focus localization and prognosticating the severity of brain involvement. Neuro-psychological assessment is advised before the commencement of anti-epileptic drug[16, 17] and if surgery is contemplated.

The prophylactic use of phenytoin in patients with severe head injury has been questioned in recent times. The initial prevention of seizures after brain injury results in delayed recovery.[18] Early treatment with phenytoin has not been shown to reduce the incidence of late

seizures[19] suggesting that it does not seem to have an effect on the epileptogenesis of post traumatic seizures. The current practice is to provide early treatment for two to three weeks in those with moderate to severe head injury to prevent early post traumatic seizures that may complicate the management of the patient in the critical phase of the illness. The use of anti-epileptic drug in patients with single unprovoked seizure depends on the risk of developing further seizures. Since a singular late seizure has a 65% to 90% chance of progressing to recurrent seizures[3] it has been advocated that long term treatment should be instituted in patients with single late seizures.[20] Though phenytoin is the preferred drug in the management of early post traumatic seizures, carbamazepine and sodium valproate have been found beneficial in patients with post traumatic epilepsy.[21,22]

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