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Clinical Characteristics and Current Medical Practice in a Group of Sudanese Patients with Epilepsy: A Cross Sectional Hospital Based-Study

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Abstract

Introduction: The epilepsy classification in under developed countries faces many difficulties in reporting, work-up and management strategies. Exploring local practice in general hospitals will positively add to the welfare of patients with epilepsy. The objectives of this study were to assess the current medical practice in epilepsy work up and to study the selection of AEDs as per ILAE guidelines. **Methods:** This was a cross sectional-retrospective hospital based study, conducted between April and September 2016 in Omdurman Teaching Hospital, Khartoum, Sudan. Patients aged 18 years old and above were enrolled. Epilepsy was defined as having at least two non-provoked seizures in the least 6 months in a patient who was assessed by clinical review and electroencephalogram (EEG). Epilepsy was classified as generalized, focal or unclassified. Medications refer to all internationally licensed antiepileptic medications (AEDs) in 2016. **Results:** One hundred adult Sudanese patients were enrolled for this study. The most common event described during the ictal phase was tongue biting in 50% of participants followed by body stiffness in 46%. Epilepsy was classified as generalized in 84%, focal in 11% and unclassified in 5% patients. In generalized epilepsy, the MRI detected 23.3% abnormal findings higher than the CT which detected 14.8% (4/27), p value = 0.032. In focal epilepsy, the CT detected 75% abnormal findings higher than the MRI which detected 33.3%, p value = 0.02. The AEDs used were as follows: Carbamazepine (CBZ) 48%, Na valproate (VP) 33%, Lamotrigine (LMT) 2%, Levetricetan (LVT) 1%, CBZ + VP 14% and CBZ + Oxcarbaze-

pine (OXC) 2%. **Conclusion:** The current medical practice in Omdurman teaching hospital should be modified to match the international league against epilepsy (ILAE) guidelines in workup, management, AEDs selection and classification of epilepsy.

Keywords

Anti-Epileptic Drugs, EEG, Epilepsy, Sudan

1. Introduction

Epilepsy is considered one of the most prevalent neurological disorders worldwide affecting over 45 million people [1]. The disease has a huge burden in the developing countries as over 80% of cases occurring in low- and middle-income countries [2] [3]. In Sub-Saharan Africa including Sudan, the prevalence of epilepsy was estimated to be 9 per 1000 persons [4].

The workup of epilepsy for the benefit of safe diagnosis and management options may differ due to the healthcare system criteria and many local, social, financial or environmental factors. The mixture of all those factors determines the strategy behind epilepsy management which may not be met by the international recommendations particularly in fragile healthcare systems.

Variations in prevalence of different types of epilepsy have been reported to vary across regions [5] [6] [7] [8]. In Sudan, the prevalence of generalized epilepsy was estimated to be 56% followed by focal epilepsy 36% and 8% for unclassified epilepsy [9]. The electroencephalography (EEG) is the main tool for potentiating the diagnosis, classification and prognostic criteria for epilepsy. It has a moderate sensitivity and a high specificity [10]. Further recording may increase the likelihood but around 10% - 40% may not show abnormalities on a routine EEG [11]. The recording in the first 24 hours after the seizure has a higher yield. Combining modern computer techniques, Magnetoencephalography (M/EEG), and in depth EEG may increase the yield of the EEG in classification of epilepsy [12]. The superiority of the magnetic resonance imaging (MRI) scans had bridged a large gap in the localization related epilepsies. A large study across 14 countries concluded that the MRI was the preferred imaging tool to detect cortical and subcortical changes in epilepsy [13].

The therapeutic paradigm of epilepsy should consider the rational selection of anti-epileptic drug (AED) in relation to the cause and classification of epilepsy. In addition, other factors are playing a major role in determining the selection process such as professional competency, location, and socio-economic status [14]. Generally, around 70% of epilepsy patients can be fairly controlled with medications and life style changes [15]. The persistent effort of the treating doctor to control intractable patients may be achieved in some through thoughtful AED changes [16].

The epidemiological features, workup and diagnostic accuracy might differ across countries and regions. The aim of this study was to examine the current workup for epilepsy in medical practice and selection of AEDsa tertiary hospital in Sudan. Specifically, the study determined the diagnostic approach for epilepsy, verified the selection of AEDs in relation to seizure semiology and EEG findings, and evaluated the current practice of clinicians in the selection of AEDs.

2. Methods

This was a cross sectional-retrospective hospital based study conducted between April to September 2016 in Omdurman Teaching Hospital Khartoum Sudan. It is the second central hospital in the country. Adult Sudanese patients above the age of 18 years old and above were included after their consent. Patients presenting either to the emergency room or outpatient department were included. Their diagnosis was confirmed by history, examination, imaging and EEG. All patients were on anti-epileptic drugs (AEDs) for at least 6 months. Patients with an uncertain diagnosis or symptomatic seizures were excluded. The study sample was collected through total coverage sampling technique. The sample size was 100 patients representing complete coverage. Epilepsy was defined as having at least two non-provoked seizures for in the least 6 months in a patient who was assessed by clinical review and EEG. Antiepileptic medications refer to all internationally licensed AEDs in 2016. The EEG represented the standard 16 channel EEG recording for at least 20 minutes or more with photic stimulation and hyperventilation techniques. Seizures were defined as generalized, partial, complex partial and secondary generalized and epilepsy was classified as generalized or focal. Information was collected using a questionnaire containing personal data, important history points in regard to the symptomatology, diagnosis, EEG report and the details of AEDs that were used. The questionnaire was validated with Cronbach's alpha of 86.

2.1. Ethical Approval

Institutional ethical committee approval was obtained prior the start of study and informed consent was taken from all the study participants.

2.2. Statistical Analysis

Mean (standard deviations, SD) were reported for numerical variables. Frequencies with percentages were reported for categorical variables. Pearson Chi squares test was used to examine the association between categorical variables. Statistical significance was set at $p < 0.05$.

Analysis was performed using Statistical Package for Social Science (SPSS), version 23 (IBM, Armonk, NY, USA).

3. Results

Males were found to be 52% with a mean age of the entire participants was 31.5

years (standard deviation ±15.3 years).

Table 1 shows types and clinical characteristics of epilepsy. In this study the symptomatic description of the seizure was 84% generalized, 11% focal and 5% unclassified. Visual aura was reported in 20%, somatosensory aura in 10%, abdominal aura 8%, psychic aura 7%, autonomic aura 5% and olfactory aura 3%. The most common events described during the ictal phase was tongue biting in 50% of participants followed by body stiffness in 46%. In 37% there was collapse and loss of body posture while 30% had myoclonic jerks. Incontinence of sphincters was in 20%, 10% were hypotonic, 10% had lip smacking, chewing movements were in 6% and 4% had undressing. The duration of the seizure was described to be < 2 minutes in 48%, more than that in 47% and 5% had last for

Table 1. Types and clinical characteristics of epilepsy.

Variables	Percentages %	Number of patients
Type of auras		
Visual	20	20
Somatosensory	10	10
Abdominal	8	8
Psychic	7	7
Autonomic	5	5
Olfactory	3	3
Types of epilepsy		
Generalized	84	84
Focal	11	11
Unclassified	5	5
Duration of seizure, minutes		
<1	5	5
1 - 2	48	48
>2	47	47
Events during the ictal phase		
Tongue biting	50	50
Body stiffness	46	46
Collapsed	37	37
Myoclonic jerks	30	30
Incontinence	20	20
Hypotonia	10	10
Lip smacking	10	10
Chewing	6	6
Undressing	4	4
Neurological examination		
Normal	78	78
Focal signs	22	22

few seconds. The majority of patients had normal neurological examination (78%), while 22% had focal neurological signs either old or new (Table 1).

Distribution of the patients according to neuroimaging (CT/MRI) is shown in Table 2. From the total enrolled patients, a brain MRI was performed in 46% CT brain was done in 31%, both MRI and CT were done in 6% and 23% of patients could not afford a brain image. In generalized epilepsy, the MRI detected 23.3% (10/43) abnormal findings higher than the CT which detected 14.8% (4/27), p value = 0.032. In focal epilepsy, the CT detected 75% (3/7) abnormal findings higher than the MRI which detected 33.3% (1/8), p value = 0.021 (Table 2).

Table 3 shows the distribution of the patients according to the electroencephalogram (EEG) findings by their clinical diagnosis and epilepsy type. Generalized epileptiform discharge was found in 22%, focal epileptic form in 12%, abnormal findings in 4% and normal findings in 16% of the patients. The patients who were diagnosed clinically as generalized epilepsy and their EEG confirmed the diagnosis were 37.5%, while 20.8% of those patients their EEG showed focal epileptic form discharge, p value = 0.011. The patients who were diagnosed clinically as focal epilepsy and their EEG confirmed the diagnosis were 40%, equal to those patients their EEG showed generalized epileptic form discharge, p value = 0.930.

Table 4 shows the types of anti-epileptic drugs (AEDs) used in this study and their prescribed total daily doses. The AEDs used in this group of patients were

Table 2. Brain imaging stratified by types of epilepsy.

Brain Imaging	Findings	Generalized Epilepsy		P value
		N	%	
MRI	Normal	33	76.7	0.032
	Abnormal	10	23.3	
	Total	43	100.0	
	Not done	45	51.1	
CT	Normal	23	85.2	
	Abnormal	4	14.8	
	Total	27	100.0	
	Not done	61	69.3	
		Focal Epilepsy		
MRI	Normal	2	66.7	0.021
	Abnormal	1	33.3	
	Total	3	100	
	Not done	8	72.7	
CT	Normal	1	25	
	Abnormal	3	75	
	Total	4	100	
	Not done	7	63.6	

Table 3. Electroencephalogram (EEG) findings stratified by clinical diagnosis and types of epilepsy.

EEG finding	Generalized Epilepsy (semiology)				P value
	Yes		No		
	N	%	N	%	
Normal	15	31	1	13	0.011
Generalized epileptiform discharge	18	38	4	50	
Focal epileptiform discharge	10	21	2	25	
Abnormal EEG	5	10	1	13	
Total	48	100	8	100	
Not done	40	46	8	50	
	Focal Epilepsy (semiology)				
Normal	0	0.0	16	33	0.930
Generalized epileptiform discharge	2	40.0	20	41	
Focal epileptic discharge	2	40.0	10	20	
Abnormal EEG	1	20	3	6	
Total	5	100	49	100	
Not done	6	55	40	82	

Table 4. Antiepileptic drugs (AED) stratified by daily doses.

AED	Daily Dose/mg	N	%
Carbamazepine	200	3	2
	400	22	22
	600	17	15
	800	3	3
	1200	3	3
Na valproate	200	6	6
	400	12	11
	600	5	5
	800	6	6
	1000	2	2
	1500	2	2
Lamotrigine	100	2	2
Levetricetan	250	1	1
Carbamazepine + Na valproate	200/400	14	14
Oxcarbazepine + Carbamazepine	400/600	2	2
Total		100	100

as follows: Carbamazepine (CBZ) 48%, Na valproate (VP) 33%, Lamotrigine (LMT) 2%, Levetricetan (LVT) 1%, CBZ + VP 14% and CBZ + Oxcarbazepine (OXC) 2%.

The management of the patients based on clinical grounds shows that patients

diagnosed as generalized epilepsy received were mainly received CBZ 48.9% (43/88) and VP 33% (29/88) almost similar to patients diagnosed as focal epilepsy who received CBZ 41.7% (5/12) and VP 33.3% (4/12), (Table 5). Combinations of CBZ & VP were prescribed for 13.6% (12/88) with generalized epilepsy and for 16.7% (2/12) with focal epilepsy (Table 5).

4. Discussion

Our findings in semiology of generalized seizures (84%) was higher than a hospital based study in Iran (78%) [17] and also higher than the French and Spain studies (31% & 13.8%), in hospital and primary care setting respectively [18] [19]. The tonic clonic seizures here was 75% which was partially matching a previous study in the same hospital which was 72.3% [20]. The differences in design and methodologies had affected our hospital based results. The common semiology's which helped to diagnose epilepsy in this study were tongue biting in 50%, body stiffness in 48% and collapse in 37%. All patients had a usual duration of events that last between few seconds to maximum 2 minutes for a single event. This is well convenient with the natural history of seizures.

The type of epilepsy classified as generalized epilepsy (61%) in this study did not match a previous study in Omdurman teaching hospital (38%). However, in the later study all patients have EEG while in our patients only 55% had EEG access. The focal epilepsy partially matched the previous study as it was 26% versus 29% [20].

The management of patient's resources in under developed countries affects the management decisions including imaging selection. The Brain MRI in the

Table 5. Antiepileptic drugs (AEDs) stratified by types of epilepsy.

AED	Generalized epilepsy	
	N	%
Carbamazepine	43	49
Na valproate	29	33
Lamotrigine	2	2
Levetiracetam	1	1
Carbamazepine + Na valproate	12	14
Oxcarbazepine + Carbamazepine	1	1
Total	88	100
	Focal epilepsy	
Carbamazepine	5	42
Na valproate	4	33
Lamotrigine	0	0
Levetiracetam	0	0
Carbamazepine + Na valproate	2	17
Oxcarbazepine + Carbamazepine	1	8
Total	12	100

enrolled patients was significantly more cost effective (8%) in detecting lesional epilepsy than CT Brain (3.5%) even in patients thought to have Idiopathic epilepsy. This had added to epilepsy classification.

The statistical significance of imaging findings between the MRI & CT Brain in this study conforms to the literature recommendation about the superiority of MRI scans against CT in imaging of epilepsy patients [21] [22]. Moreover, the MRI was the preferred tool the ENIGMA-Epilepsy consortium [13].

The electroencephalography was normal in 16% of our patients in comparison to 29% in a larger multi center Iranian study [17]. As known about the increased sensitivity of 3 EEGs, it worth mentioning here that our patients had one EEG during the time of this study. Moreover, the poor significance of the clinical impression in classification of epilepsy was revealed here as 20% of the patients assumed to have idiopathic generalized epilepsy were relay having generalized epileptiform discharges on their EEGs. In 11% of the assumed cases of generalized epilepsy had focal discharges altering their epilepsy classification.

On the other hand, 18% of the clinically assumed focal epilepsy had focal discharges while 18% of the assumed focal epilepsy had generalized epileptiform discharges on EEG, again altering their epilepsy classification and management.

So the likelihood of having a wrong clinical judgment on epilepsy classification without performing an EEG is higher in focal epilepsy than generalized epilepsy.

The total percentage of patients finally classified as a generalized form of epilepsy was 38% versus 29% for focal epilepsy. This is slightly higher in the Market scan data study but the difference is related to sample size, EEG technique, age, demographic features and accuracy of epidemiological studies [23].

Our epilepsy classification figures are quite different from the hospital study that targeted elderly population including brain tumors and stroke. The generalized epilepsy was found in 65% and focal was only 13% [24]. This can be explained by the young age in our study.

In our sample, the IGE percentage was approaching the percentage of a retrospective tertiary hospital study which was 33% [25]. However, EEG was applied for all patients and some had multiple EEGs.

Our data were different from the Egyptian school children study. However, the difference is due to differences in design, target population and 49% in the Egyptian study were diagnosed with specific epileptic syndromes where we expect multiple seizure types in this group of patients [25].

This essential part of the study matched a research question of the authors that the selection for AEDs was not suitable in respect to the type of epilepsy and EEG diagnosis. It was clearly found that CBZ was used as major choice in almost half of patients regardless of having focal or generalized epilepsy. This is not suitable as CBZ is licensed for focal epilepsy and it is a second line drug for generalized seizures. However, CBZ was reported as the second used AED (18.7%) for generalized epilepsy in the Northern Iran study while VLP was the first

choice as 27.7% were using it [17]. One of the interesting observations was the unsuitable use of combinations of CBZ and OXC which is not recommended depending on the indications, target receptor and side effects. The use of CBZ in our study, partially matched a previous primary care study which reported it as the second choice [19]. In one study addressing only idiopathic generalized epilepsy, LMT was prescribed in 3% of the cases and this conforms to our findings [25].

Hence, we observed a significant practice gap noticed by the less use of LMT in generalized epilepsy and more use of CBZ for generalized epilepsy. The same concept was observed in the use of LVT for generalized epilepsy despite the small number of patients suing LVT due to cost and availability issues.

The observed selection bias of AEDs reflects the suboptimal knowledge about epilepsy classification, selection mechanism, drug action and potential side effects. Despite the percentage was small here but it necessitates more target oriented educational effort to be taken by the clinical pharmacists and neurologists to modulate this practice. The current practice needs to be improved by the local application of international guidelines of diagnosis, EEG and selection of AEDs. The ILAE classification of seizures and epilepsy should be made more available and accessible to physicians talking care of epilepsy patients in the under developed world.

This paper comes as a closing workfor 2 previous papers in the same hospital addressing precipitating factors of seizures and adherence to medications in the same hospital. However, it also faced some limitations. The limitation of this study is being that it was hospital based and was performed in a single tertiary center. Moreover, the sample size is relatively small for quite a common neurological disease. The EEG service was not manageable for 45% of participants which impaired the goal of the 3rd minor objective. There was no follow up to determine emergence of other seizure semiology which may have affected the initial impression about the seizure type.

5. Conclusion

The clinical diagnoses of epilepsy type should be potentiated by the electro-encephalography to guide the best epilepsy classification. The EEG has good sensitivity for generalized epilepsy in patients who were suspected to have generalized epilepsy in this study group in contrast to mildly lower sensitivity for patients clinically suspected to have focal epilepsy. The EEG has high positive predictive value in partial epilepsy diagnosis for this group. The MRI scan had a higher predictive value in epilepsy patients. Selection of AEDs for the type of epilepsy in our hospital medical practice is not matching the ILAE recommendations which are reflected as unsatisfactory selection of AED. More structured awareness is needed to raise the knowledge and modify medical practice, verify semiology, EEG importance and selection of AEDs to help the wellbeing of epilepsy patients in this area. Collaboration of the related local and international bodies will help

to improve this situation.

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Authors Contributions

Thee corresponding author contributed to the abstract, introduction, discussion and refrences sections. Dr. Mohamed Issa collected the data and initial references. Dr. Ibrahim Mahmoud contributed to re-writing of methodology and results plus updating references. Dr. SarahIman had edited the manuscript and revised the introduction and discussion.

Conflicts of Interest

Authors declare no conflict of interest.

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Questionnaire

A-Personal data:

- NAME……..
- AGE……
- Gender: Male ☐ Female ☐
- Residence……
- Occupation……..……
- Contact phone number:……..

B-Type of seizure: Generalized ☐ Focal ☐

C-Seizure semiology:

Precipitating factor: Tiredness ☐ Hunger ☐
Insomnia ☐ non-adherence ☐
Current infection ☐

Mood change: Excited ☐ Anxious ☐ Depressed ☐

Sounds: Crying ☐ Mumbling ☐

Unusual sensation: Odd smell ☐ Odd taste ☐

Rising feeling in stomach ☐ visual features ☐

Body numbness ☐

Activity: Normal daily ☐ Hard ☐ Light ☐

Intra ictalsemiology: Blank ☐ Starring into space ☐
Loss consciousness ☐ Confused ☐

Color change: Pale ☐ Flushing

Breathing change: Noisy ☐ Difficult ☐

Abnormal movement: Jerky ☐ Twitch ☐

Posture: Collapsed ☐ Stiff ☐ Floppy ☐ Got wet ☐ Tongue bitten☐

Post ictal: Drowzy Tired ☐ Sleepy ☐

Duration of seizure: Seconds ☐ Minutes ☐ Hours ☐

C-EEG finding: Consistent ☐ Inconsistent ☐

D-AEDs taken: Carbamazepine ☐ Na.Valproate ☐ Lamotrigine☐
Oxcarbazepine ☐ Levetiracetam ☐
Phenytoin ☐ Phenobarbitone ☐ Others ☐