Clinical Predictor For Drug Response Among Idiopathic Epilepsy Patients In Sudan

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Abstract: Epilepsy is one of the common chronic neurological diseases. It spreads widely in Sudan interrupting patients, life and annoying their care givers. Antiepileptic drugs are the corner stone in the management of epilepsy. It carries a good outcome which may be enrolled by some clinical factors. These factors help in determine treatment modality. Aim of the study To identify the clinical prognostic factors of idiopathic epilepsy in Sudanese patients. Methods there were 99 patients with idiopathic epilepsy recruited from Sheikh Mohamod Kheer health centre, Omdurman, Khartoum state, Sudan; between August 2016 and February 2019. There demographic data, seizure characteristics, drugs, and concomitant conditions were recorded in dc-hoc forms. The data was analysed using excel and SPSS program to compare between good and bad outcome of patients regarding different prognostic factors, and determine the likelyhood ratio and significance by chi square test. Results over all response to treatment were good in 89%. This response was associated insignificantly with age group above 65 years, focal seizure, duration less than 5 years, or monotherapy while frequency of seizure pretreatment and good response to first regiment has significant statistical response. Conclusion There was good response to treatment especially if the seizure frequency pretreatment was low, and the patient respond well to the first treatment regimen..

Keywords: Epilepsy, Predictor, Factor, Pharmacoresistance, Remission.

1.Introduction

Epilepsy is an overwhelming disease ; the patients and their caregivers are usually worried about its further sequel .In the past it was considered as untreatable disease. [1] Rodin concluded that only about one third of epileptic patients were likely to achieve a terminal remission of at least two years may because this study was conducted in a in tertiary centre. [2] That had been change recently, when community based researches were published reporting more preferable outcome. [1]The Rochester, Minnesota, U.S.A. group reported in 1979 that in a retrospective community-based study as many as 76% of patients achieved long term remission. [3]. In 1982, many researches were done to study the efficacy of the anticonvulsants carbamazepine and phenytoin for new and chronic patients reporting that they have similar response. [4],[5] Although in countries with treatment gap epilepsy had similar prognosis to the industrial one reflecting that there is spontaneous remission pattern . [1] The epilepsy outcome course is determined by many factors. The most obvious prognostic factor was concomitant neurological or psychosocial handicap, and the overall outcome was determined by the early prognosis determining, [4],[5] This findings were confirmed more by a multicenter study done in Italy which reported that the first year outcome together with aetiology and seizure frequency , has a significant role in predicting the prognosis. [6] Some studies also concluded that the presence of multiple seizure type and history of migraine may reflect poor outcome. Shinnar and his colleague emphasized the need to cover the psychosocial effect of childhood's epilepsies in the outcome. [7] while the role of Electroencephalogram (EEG) as prognostic predictor is controversially. [8] some clinical factors like epilepsy syndrome and the social, psychological and emotional profile of the patient may help in deciding wither to stope treatment or not after long term remeission. [9], [10]That means continuous of treatment is depending on the clinical predictors for that this study is going to highlight some clinical prognostic factors in Sudan .

2.Methods

This study was done at Sheikh Mohammed Kheir centre, Banat, Omdurman, Khartoum state. This centre is primary health care centre however epilepsy diagnosis was provided by neurology physician depending mainly on the description of eyewitness to the seizure attack, 99 patients with idiopathic epilepsy during the period (9/2016 to 2/2019) .The patients with idiopathic epilepsy who were attending the clinic for follow up regardless to the time of diagnosis, only those who refused to joint the study and pregnant women were excluded . Patients demographic, and clinical data including :onset of seizure, seizure classification, precipitating factor, modality of treatment, compliance, change of medication, drugs adverse effect , psychosocial aspects, concomitant illness, and family history were recorded. Analyses was done using Microsoft Office Excel 2010, and Statistical Package for Social Science Program (SPSS version 25). Logistic regression was used for multi-variants analysis, to highlight the relationship between outcome and some prognostic factor such as age, gender, ethnicity, class of seizure, onset of seizure, frequency of seizure, treatment, compliance and the drug regimen used. Good outcome was defined by less than 1 per month seizure attacks after initiation of treatment. Chi-square test was used to determine the significance of the study

3.Result

The study was conducted to estimate epilepsy outcome and identify clinical prognostic factor in 99 patients with Idiopathic Generalized Epilepsy. More than 50% were between 18-40 years, and females. Most of them (67%) situated in Khartoum state. Duration of the disease was less

than 5 years in 50% of the patients, in 22% the duration was more than 10 years, the rest of them it was between 5 and 10 years. Generalize epilepsy presented in 68%, focal to bilateral in 26% , and focal in 6 patients two of them developed impairment. High seizure frequency was reported in around 50%. Treatment is mainly monotherapy in 79% (Valproate in 59% and Carbamazepine in 41%), and the frequency of seizures reduced making good outcome in 89% The following tables display the association between different prognostic factors and outcome determined by seizure frequency after treatment considering frequency more than one attack per month as poor prognosis.

Table 1 *Age group and post treatment seizure attacks frequency*

Age Group	post_ttt attacks No						P-value
	1-11 yr		1-3/mth		1-6/wk		
	Frequency	Percentage %	Frequency	Percentage %	Frequency	Percentage %	
<65	2	100.0 %	0	0.0%	0	0.0%	.390
>18	27	84.4%	2	6.3%	3	9.4%	
18-40	44	80.0%	6	10.9%	5	9.1%	
41-65	6	54.5%	2	18.2%	3	27.3%	

Table 2 *Gender and post treatment seizure attacks frequency*

Gender	post_ttt attacks No						P-value
	1-11 yr		1-3/mth		1-6/wk		
	Frequency	Percentage %	Frequency	Percentage %	Frequency	Percentage %	
Female	41	77.4 %	7	13.2%	5	9.4%	.518
Male	38	80.9 %	3	6.4%	6	12.8%	

Table 3 *onset of seizure and post treatment seizure attacks frequency*

onset of seizure	post_ttt attacks No						P-value
	1-11 yr		1-3/mth		1-6/wk		
	Frequency	Percentage %	Frequency	Percentage %	Frequency	Percentage %	
<5 yr	43	86.0%	3	6.0%	4	8.0%	.390
5-10 yr	23	82.1%	2	7.1%	3	10.7%	
>10 yr	13	59.1%	5	22.7%	4	18.2%	

Table 4 *Class of seizure and post treatment seizure attacks frequency*

Class of seizure	post_ttt attacks No						P-value
	1-11 yr		1-3/mth		1-6/wk		
	Frequency	Percentage %	Frequency	Percentage %	Frequency	Percentage %	
Generalize	50	73.5%	9	13.2%	9	13.2%	.599
Focal	4	100.0 %	0	0.0%	0	0.0%	
Focal with impairment	2	100.0 %	0	0.0%	0	0.0%	
Focal to bilateral	23	88.5%	1	3.8%	2	7.7%	

Table 5 *Pre-treatment seizure attacks and outcome*

Pretreatment seizure attacks	post_ttt attacks No						P-value
	1-11 yr		1-3/mth		1-6/wk		
	Frequency	Percentage %	Frequency	Percentage %	Frequency	Percentage %	
1-11 yr	28	90.3 %	1	3.2%	2	6.5 %	.042
1-3/mth	10	71.4 %	4	28.6 %	0	0.0 %	
1-6/wk	41	75.9 %	5	9.3%	8	14.8 %	

Table 6 *Monotherapy vs polytherapy effect in outcome*

Number of used drug	post_ttt attacks No						P-value
	1-11 yr		1-3/mth		1-6/wk		
	Frequency	Percentage %	Frequency	Percentage %	Frequency	Percentage %	
Monotherapy	67	84.8 %	6	7.6%	6	7.6%	.067
Polytherapy	12	60.0 %	4	20.0 %	4	20.0 %	

Table 7 *Drug and post treatment seizure attacks frequency*

Drug	post_ttt attacks No						P-value
	1-11 yr		1-3/mth		1-6/wk		
	Frequency	Percentage %	Frequency	Percentage %	Frequency	Percentage %	
Valproate	44	75.9%	5	8.6%	9	15.5%	.119
Carbamazepine	41	80.4%	5	9.8%	5	9.8%	
Phenytoin	2	50.0%	2	50.0%	0	0.0%	
Lamotrigine	3	50.5%	1	16.7%	2	33.3%	

Table8 change in medication and post treatment seizure attacks frequency

change in medication	post_ttt attacks No						P-value
	1-11 yr		1-3/mth		1-6/wk		
	Frequency	Percentage %	Frequency	Percentage %	Frequency	Percentage %	
No	64	88.9 %	4	5.6%	4	5.6%	.001
Yes	15	55.6 %	6	22.2 %	6	22.2 %	

Table 9 *Patient adherence post treatment seizure attacks frequency*

Patient adherence	post_ttt attacks No						P-value
	1-11 yr		1-3/mth		1-6/wk		
	Frequency	Percentage %	Frequency	Percentage %	Frequency	Percentage %	
No	12	80.0%	1	6.7%	2	13.3%	.823
Yes	67	79.8%	9	10.7%	8	9.5%	

4. Discussion

Epilepsy is a serious neurological illness which is cost effective and time consuming for that there is a need to identify their response to medications and the factor that control these response to support the patients and prepare them to further modality of treatment like surgery, nerve stimulation, and ketogenic diet. Good outcome was detected in 89 % of our patients, that was similar to Dragoumi,s team; [11] another study reported good prognosis in 92% of the patients [8] while here in Sudan Dr Etadal and her colleague reported 70% good prognosis , [12] This variation may be attributed to the study population since good outcome was reported in population based studies rather than the hospital based ones. There were some clinical factors play major role in the prognosis of epilepsy such as age group, seizure class, type of treatment, and number of drugs used. Regarding age group old age was associated with good response while in many studies it carries risk of recurrency. [3] ,[6], [13]- [15] Female gender was associated with better outcome than Males, the same findings in Annegers,s study; however, that was controlled by age because some childhood studies found that boys have better outcome than girls, most of researches found no gender differences. [3] ,[16]-[18] Regarding the recent International League Against Epilepsy (ILAE) classification in 2017, we found that focal seizure had the best outcome, similar to results reported by Rochester, Minnesota in USA.1while others suggested that generalized epilepsy respond to treatment well [8], [15],[19]-[24] The strongest factor in reducing post treatment attacks was frequency of seizure before treatment which was reported also in a Nigerian study. Less frequent seizure pre-treatment has good prognosis because high frequency seizure will changes the brain electrical discharge and interferes with drug response [24] - [26] Number of the drugs used plays a major role in the outcome, as monotherapy had better prognosis than Polytherapy.[26], [27] However in Chinese study for prognosis in elderly the number of antiepileptic has no significant effect on the course of epilepsy. [28] Patients adherence has small change in remission, although another study reported it as significant factor. [24] The change of medication was an important factor as well. [24] , [29] , [30] From the previous data it was obvious that there were many modifiable factors. Controlling these factors will result in favourable epilepsy outcome. Due to the short duration of this study we were only able to detect these factors without monitoring them. We were not able to differentiate between long term& short term prognosis because of the variable seizure duration in our patients, also the lack of stratification of the patients according to the age group, seizure class, or drug regimen. For that we need more studies with longitudinal design adding containing more factors such as EEG, imaging studies, and genetics variables will help to emphasis the role of this factor in prognosis.

5. Conclusion

Idiopathic epilepsy carries good response to treatment however there is consideration for frequency of seizure before treatment and the response for first treatment. other clinical factors such as age, class of seizure, drug type, and patient adherence to treatment was not statistically significant. There is a need for more prognostic study including genetic and imaging study to identify more factors and predict patient with resistance epilepsy early to apply for them suitable interventions..

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