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Two-year prospective study on efficacy of various anti-epileptic drugs in drug-resistant epilepsy patients and parameters affecting seizure-freedom in Eastern Indian subcontinent

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ABSTRACT

Background: Epilepsy is a disease of suffering. Drug-resistant epilepsy (DRE) takes a heavy toll on patients, family and society in the form of prolonged treatment, expenditure, unemployment and disability. Successful treatment depends on appropriate antiepileptic drug (AED) use in appropriate dosage, which varies in different parts of the world. **Aims and Objectives:** To find out AED efficacy in Indian subcontinent and factors affecting seizure freedom. **Materials and Methods:** We explored many characteristics of DRE patients, compared in between seizure-free and seizure-persisting patients to find out the variables more affecting seizure-freedom. We measured minimum effective dose and maximum tolerable dose of different AED in child and adult subgroups in patients of the Indian subcontinent. **Results:** Lamotrigine was most efficacious in various seizure-types and phenytoin was the least one as first add-on AED. Clobazam was efficacious and good-compliance second add-on AED. AED compliance was significantly reduced as the number of AED was increased above two. AED monotherapy was most effective and the effectiveness decreased as subsequent AED was added as per need. **Conclusion:** Our study enlightened about various aspects of drug-resistant epilepsy patients in Indian sub-continent and their treatment.

Key words: Drug-resistant epilepsy; Anti-epileptic drug; India, Seizure-freedom; Compliance

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INTRODUCTION

Sir Charles Locock used potassium bromide in young women with hysterical epilepsy connected with menstrual period in 1857. Potassium bromide was the first anti-epileptic drug (AED).[1] Alfred Hauptmann discovered the anticonvulsant properties of phenobarbitone and the pharmacological age of AED therapy begun in the early part of twentieth century.[2] Many anti-epileptic drugs were discovered in last 100 years and many more to come to fight against epilepsy, a great suffering. Even if we administer a highly efficacious AED, the patient might not get the desirous result due to many factors including demographic factors, disease factors, compliance factors etc. We need to identify the factors hindering the patients from seizure-freedom. India was the home of 10 million people with epilepsy whereas 50 million patients were suffering worldwide.[3] Though Indian subcontinent had huge burden of epilepsy, large studies were lacking on the experience of AEDs on patients of this region. An highly efficacious AED of Western world might not be that efficacious in this part of the world and might have a different pattern of side-effect profile due to ethnic variation. People could have different minimum efficacious dose and maximum

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tolerable dose than western countries where most of the dosage guidelines were structured. Our tertiary care hospital was situated in Eastern India and caters most part of the Eastern Indian subcontinent including the countries of Bangladesh, Nepal and Bhutan.

MATERIALS AND METHODS

We studied drug-resistant epilepsy (DRE) patients in intractable epilepsy clinic from the month of December, 2015 to the month of November, 2017 in Nil Ratan Sircar Medical College & Hospital, Kolkata, Eastern India. Drug-resistant epilepsy was defined by International League Against Epilepsy (ILAE)[4] as failure of adequate trials of two tolerated and appropriately chosen and used anti-epileptic drug schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom. Seizure freedom is defined as freedom from seizures for a minimum of three times the longest pre-intervention inter-seizure interval (determined from seizures occurring within the past 12 months) or 12 months, whichever is longer. We labeled the patients as 'seizure-free' who achieved seizure freedom during the study period of two years; failing which patients were categorized as 'seizure-persisting'. We collected detailed history and examined the patients and investigated with EEG and MRI brain. We categorized the patients according to various etiology. The term 'idiopathic' was used for those patients who did not have structural lesion in MRI brain, though it was known that some patients with normal MRI brain might have secondary cause for their epilepsy. We used sodium valproate or appropriate alternative AED according to seizure type as first drug and titrated the dose. If the patient did not tolerate or seizure was not controlled then we tried alternative appropriate AED. Then we used subsequent appropriate AED if needed in addition and titrated the dose as needed by the patients. We tried to keep the patients on minimum number of AED in minimum dose as their seizure-control was concerned. Some patients achieved seizure-freedom during the study period with changing AED schedule. We marked the 'minimum effective dose' for an AED defined as the minimum dose which rendered the patient seizure-free and 'maximum tolerated dose' for an AED defined as the maximum dose of the drug that was safely used in the population without adverse effect. Then we calculated the median dose and range also. 'Number Needed to Treat' for all anti-epileptic drugs in our series was measured. Pediatric age group was considered up to age 12 years and adult age group was considered beyond that. We compared various parameters in seizure-free and seizure-persisting patients to find out risk factors for seizure persistence. All types of psychiatric symptoms were grouped together. Some symptoms came early, some symptoms late during treatment and some symptoms were present before the start of the data collection. Cognitive decline was defined as patients who initially had normal cognitive function but cognitive function was declined later on during disease and/or therapy. Developmental delay was denoted to those patients who had delay in achieving their motor and/or language milestones within proper time. Some patients had both delayed developmental milestones and cognitive decline. The data was put on WPS office 2016 spreadsheet (Kingsoft Corporation, CA, USA) and analyzed with Instat GraphPad (GraphPad Software Inc., CA, USA) using unpaired t-test and Fisher's exact test assuming $p < 0.05$ as statistically significant.

RESULT

We studied 154 Intractable epilepsy patients for two years. At the end of second year, 121 (78.6%) patients continued follow up. Rest of the patients lost it. So we analyzed the data of 121 patients for our study. We found males (n=81, 67%) outnumbered females (n=40, 33%). People from rural areas (n=63, 52%) outnumbered people from urban areas (n=58, 48%). Majority of the patients were from lower socioeconomic class (n=89, 73.6%), rest were from middle class (n=32, 26.4%).

We found forty-eight (39.7%) patients were seizure-free according to ILAE criteria[4] in our study period. Patients at younger age, with normal activity of daily living, with positive neurological sign & symptoms, treated with one or two AED had statistically significant higher percentage of seizure freedom than their counterparts (Table 1). Although male gender, lower body weight, rural residence, higher socioeconomic status, focal onset seizure type, cognitive decline, lower seizure frequency, lower seizure duration, positive family history, normal EEG, focal discharge in EEG, MRI brain lesion had higher percentage of seizure-free patients but the difference with seizure persisting patients being statistically insignificant (Table 1). History of psychiatric symptoms was present near equally in seizure-free and seizure persisting patients (37.5% vs 38.4%, p =1.00) and so history of febrile seizure (14.6% vs 16.4%, p = 1.00) (Table 1).

Poor AED compliance was significantly higher in seizure persisting patients (Table 1). Patients had good compliance till one or two AED was used. As the number of AED was increased to control seizure, drug compliance decreased, which was statistically significant (Table 2). We also found statistically significant lower seizure control when AED number was increased from two (Table 1).

Lamotrigine was found to be the most effective to be followed by oxcarbazepine and phenytoin was least

Table 1: Comparison between seizure-free patients and patients having persistent seizure after the end of two-year follow-up

Parameter	Seizure-free patients (n=48)	Seizure-persisting patients (n=73)	P value
Age (mean)	16.6 year	21.2 year	0.0137
Gender			
Male	28 (58.3%)	53 (72.6%)	0.12
Female	20 (41.7%)	20 (27.4%)	
Body weight	42.2 Kg	46.3 Kg	0.20
Rural	26 (54.2%)	37 (50.7%)	0.71
Urban	22 (45.8%)	36 (49.3%)	
Lower socioeconomic class	33 (68.8%)	56 (76.7%)	0.40
Middle socioeconomic class	15 (31.2%)	17 (23.3%)	
Focal onset Seizure only	25 (52.1%)	34 (46.5%)	0.55
Generalized onset Seizure only	17 (35.4%)	31 (42.5%)	
Multiple Seizure type	6 (12.5%)	8 (11%)	0.78
Impaired activity of daily living (ADL)	16 (33.3%)	41 (56.2%)	0.016
Cognitive decline	25 (52.1%)	31 (42.5%)	0.35
Psychiatric symptoms	18 (37.5%)	28 (38.4%)	1.00
Headache, vertigo & other neurological complaint in any point of time	44 (91.7%)	52 (71.2%)	0.006
Median Seizure frequency per month	0.5	3	0.45
Median Seizure duration in minutes	2	3	0.16
Family history of Seizure	7 (14.6%)	7 (9.6%)	0.40
History of febrile seizure	7 (14.6%)	12 (16.4%)	1.00
Delayed Milestones	15 (31.3%)	28 (38.4%)	0.45
EEG normal	19 (39.5%)	27 (37%)	0.85
EEG focal epileptiform discharge	14 (29.2%)	20 (27.4%)	0.81
EEG generalized epileptiform discharge	15 (31.3%)	26 (35.6%)	
MRI brain lesion	24 (50%)	33 (45.2%)	0.71
MRI brain normal	24 (50%)	40 (54.8%)	
Number of AED used			
One	9 (18.8%)	3 (4.1%)	One vs multiple AED p=0.012
Two	25 (52.1%)	32 (43.8%)	One/Two vs > two AED p=0.015
Three	11 (22.9%)	33 (45.2%)	< four vs four AED p>1.00
Four	3 (6.2%)	5 (6.9%)	
Poor AED compliance	3 (6.2%)	22 (30.1%)	0.0012

Table 2: AED compliance varying with number of AED used

Number of AED	AED compliance good	AED compliance poor	P value
One	12	0	One AED vs multiple AED p=0.07
Two	48	9	
Three	30	14	Upto two AED vs > two AED p=0.0231
Four	6	2	

Table 3: Comparison between first add-on AEDs

First add-on AED	Seizure controlled (n=48) (%)	Seizure persisting (n=71)	Number needed to treat (NNT)
Lamotrizine	5 (62.5%)	3	1.6
Oxcarbazepine	5 (55.6%)	4	1.8
Clonazepam	3 (42.9%)	4	2.3
Clobazam	11 (42.3%)	15	2.4
Levetiracetam	10 (41.7%)	14	2.4
Carbamazepine	5 (33.3%)	10	3
Phenobarbitone	2 (18.2%)	9	5.5
Phenytoin	1 (7.7%)	12	13

effective to be followed by phenobarbitone as first add-on AED (Table 3 and Figure 1). We compared clobazam and lacosamide as second add-on AED and found clobazam to be superior (Table 4). Compliance factor was present in the difference between clobazam and lacosamide effectiveness. 5 out of 17 patients (29.4%) from clobazam group were non-compliant but 8 out of 20 patients (40%) from lacosamide group were non-compliant, but the difference was not statistically significant (p=0.73). We calculated minimum effective dose and maximum tolerated dose of the AEDs in pediatric and adult population in our series (Tables 5-8).

In our series, Idiopathic epilepsy patients were highest in number to be followed by hypoxic-ischemic encephalopathy and brain atrophy and others (Figure 2). Seizure-control was also varied in different etiologies (Figure 3). Ignoring two small observation, it was evident that seizure-freedom was highest in neurocysticercosis patients and lowest in sclerosis patients.

Thirty-three patients lost follow up. Four patients had freedom from seizure but seizure was persisting in the

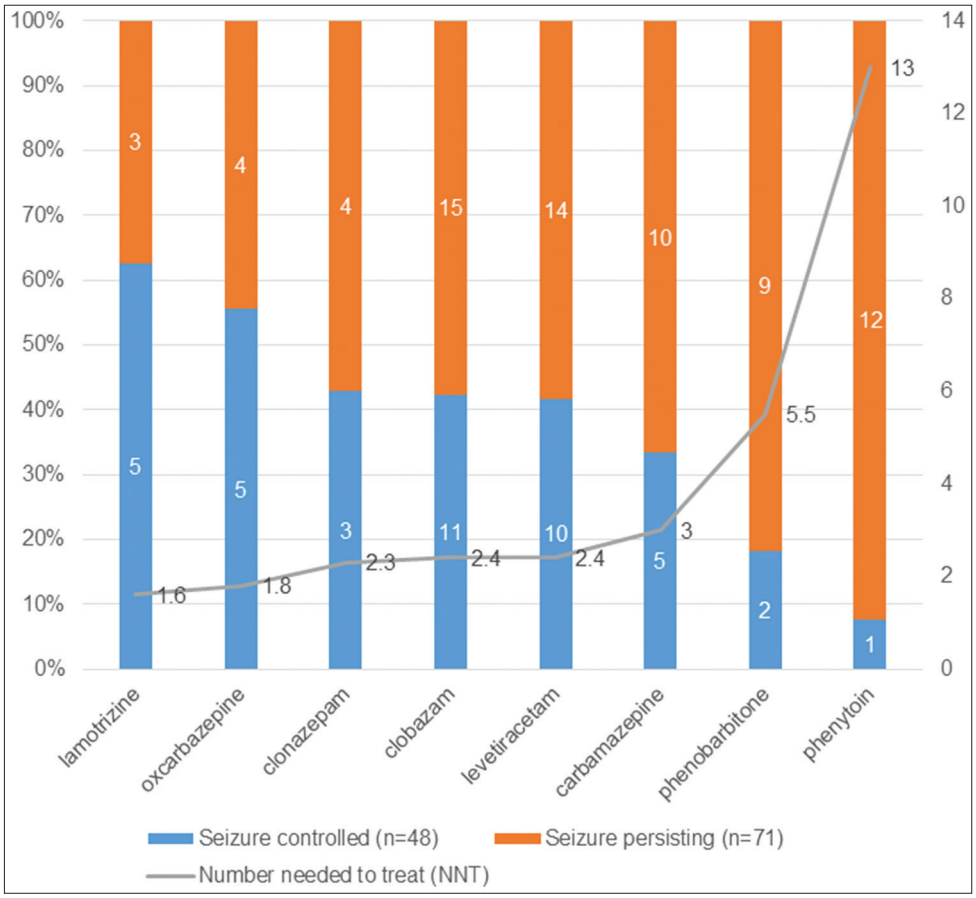

Figure 1: Effectiveness of first add-on AED

Table 4: Comparison between clobazam and lacosamide as second add-on AED

Second add-on AED	Seizure-free (one year)	Seizure persisting (one year)	P value	Number needed to treat (NNT)
Clobazam	9	8	0.002	1.9
Lacosamide	1	19		20

Table 5: Minimum dose of AED required in Seizure-controlled adults (mg/kg b.w.)

Parameter	Carbamazepine	Levetiracetam	Oxcarbazepine	Clobazam	Valproate	Clonazepam	Phenobarbitone
Mean	17.37	21.96	16.20	0.197	18.57	0.012	2.34
Standard deviation	6.89	5.46	7.79	0.113	4.48	0.00626	0
Sample size	6	10	7	15	21	3	1
Std error of mean (SEM)	2.81	1.72	2.94	0.029	0.97	0.0036	0
Lower 95% conf. limit	10.14	18.06	9.0	0.134	16.53	-0.00356	2.34
Upper 95% conf. limit	24.60	25.87	23.40	0.259	20.61	0.0275	2.34
Minimum	11.76	11.76	4.62	0.077	12	0.0078	2.34
Median	15.19	22.22	18.0	0.19	18.75	0.0090	2.34
Maximum	31.11	30.77	26.67	0.53	30.77	0.0192	2.34

Parameter	Lacosamide	Lamotrigine	Phenytoin	Zolpidem	Zonisamide	Topiramate	Divalproex
Mean	1.11	3.02	3.51	0.1	0.96	3.09	16.67
Standard deviation	0	1.001	1.126	0	0	0.83	0
Sample size	1	3	4	1	1	2	1
Std error of mean (SEM)	0	0.57	0.56	0	0	0.59	0
Lower 95% conf. limit	1.11	0.53	1.72	0.1	0.96	-4.40	16.67
Upper 95% conf. limit	1.11	5.51	5.30	0.1	0.96	10.58	16.67
Minimum	1.11	2	2.38	0.1	0.96	2.5	16.67
Median	1.11	3.08	3.34	0.1	0.96	3.09	16.67
Maximum	1.11	4	5	0.1	0.96	3.68	16.67

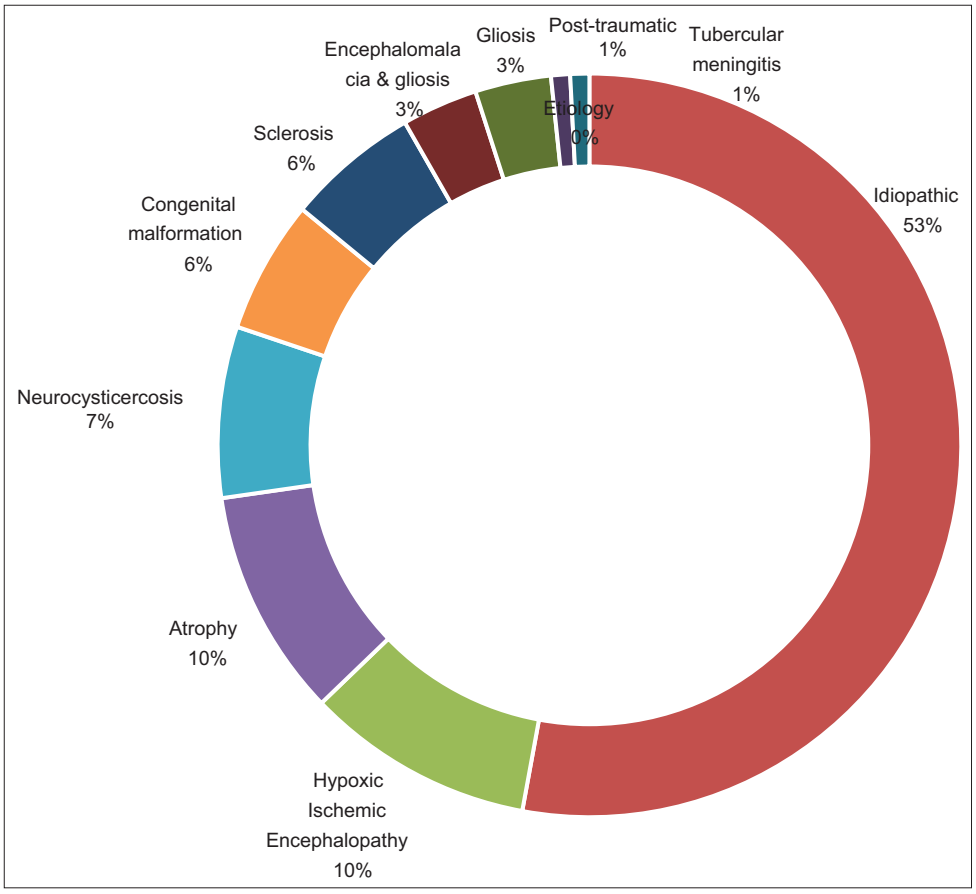

Figure 2: Etiology of Intractable epilepsy in our series

Table 6: Minimum dose of AED required in Seizure-controlled children (mg/kg b.w.)

Parameter	Carbamazepine	Levetiracetam	Oxcarbazepine	Clobazam	Valproate	Clonazepam	Phenobarbitone
Mean	19.47	33.33	28.64	0.238	28.82	0.027	2
Standard deviation	9.96	0	8.004	0.055	10.10	0.0308	0
Sample size	4	1	4	5	13	3	1
Std error of mean (SEM)	4.98	0	4.002	0.0247	2.803	0.0178	0
Lower 95% conf. limit	3.63	33.33	15.91	0.169	22.71	-0.0495	2
Upper 95% conf. limit	35.32	33.33	41.38	0.306	34.93	0.1037	2
Minimum	11.25	33.33	20.45	0.200	16	0.00625	2
Median	16.66	33.33	27.50	0.210	26.08	0.0125	2
Maximum	33.33	33.33	39.13	0.330	50	0.0625	2

rest of the patients. There were no significant difference in gender (female 33.1% vs 33.3%, p= 1.00) and age (mean 19.4 year vs 18.6 year, p = 0.70) between those who continued follow-up and who lost it. No significant difference were found in activity of daily living (p = 1.00), family history of seizure (p = 0.52), delayed milestones (p = 1.00), history of febrile seizure (p = 0.44) among the two cohorts.

DISCUSSION

The prevalence of epilepsy was higher in rural India (1.9%) than in the urban areas (0.6%).[5-7] Our findings were corroborating the reports. In addition, higher percentage of rural patients and patients of lower economic status were drug-resistant than their counterparts in our study. Inadequate health-care set-up, poor availability of medicines, lower educational standard of the families might be the reason behind intractability.

Tripathi M et al from North-India found 71% male in their DRE series[8] whereas Ramos et al[9] found 59 % and Wirrell et al[10] found 51%. All recent studies on epilepsy from many parts of India showed male predominance,[11-17] except the study done by Pandey et al.[18] in Chandigarh, North India; females were predominant in their DRE series. Not only

Table 7 Maximum dose of AED tolerated in adults (mg/Kg b.w.)

Parameter	Carbamazepine	Levetiracetam	Oxcarbazepine	Clobazam	Valproate	Clonazepam	Phenobarbitone
Mean	20.44	24.05	20.23	0.202	23.22	0.01508	2.25
Standard deviation	9.94	8.28	9.65	0.144	9.62	0.00782	0.706
Sample size	17	27	16	35	69	14	5
Std error of mean (SEM)	2.41	1.59	2.41	0.024	1.15	0.00209	0.315
Lower 95% conf. limit	15.33	20.77	15.09	0.153	20.91	0.01057	1.375
Upper 95% conf. limit	25.55	27.33	25.37	0.252	25.54	0.01960	3.129
Minimum	8.16	8.33	4.62	0.050	8.96	0.00560	1.64
Median	18.18	24.19	19.37	0.182	20	0.01175	2
Maximum	48	45.45	48	0.800	60	0.0300	3.43
	Lacosamide	**Lamotrigine**	**Phenytoin**	**Zolpidem**	**Zonisamide**	**Topiramate**	**Divalproe**
Mean	3	3.26	4.48	0.1	1.39	3.09	17.71
Standard deviation	1.43	0.77	1.15	0	0.608	0.834	1.471
Sample size	12	6	20	1	2	2	2
Std error of mean (SEM)	0.414	0.317	0.25	0	0.43	0.590	1.04
Lower 95% conf. limit	2.08	2.44	3.94	0.1	-4.07	-4.40	30.92
Upper 95% conf. limit	3.912	4.07	5.02	0.1	6.85	10.58	16.67
Minimum	0.91	2	2.38	0.1	0.96	2.5	16.67
Median	3.09	3.36	4.72	0.1	1.39	3.09	17.71
Maximum	4.87	4.0	6.67	0.1	1.82	3.68	18.75

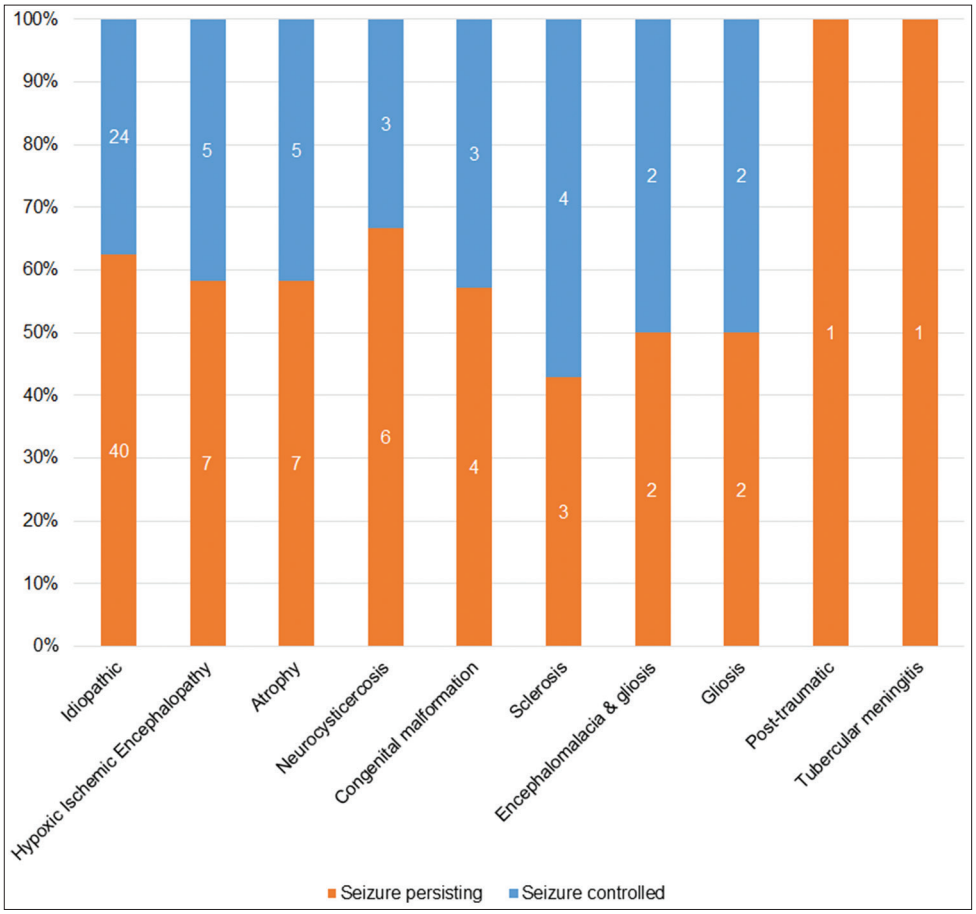

Figure 3: Seizure control in various etiologies

we found more male epilepsy cases in our cohort, but our findings also pointed out higher male preponderance in 'seizure-persisting' patients. After corroborating all those studies, it could be postulated that gender might have some propensity to get drug-resistant.

The median age of 'seizure-persisting' patients was 4.6 year higher than the 'seizure-free' patients (21.2 year vs. 16.6 year, p=0.0137). Sajobi et al[19] showed in their study that age was one of the most significant correlates of seizure-related disability in persons with epilepsy. Wu JY et al[20] found

Table 8: Maximum dose of AED tolerated in children (mg/kg b.w.)

Parameter	Carbamazepine	Levetiracetam	Oxcarbazepine	Clobazam	Valproate	Clonazepam	Phenobarbitone	Lacosamide
Mean	22.19	38.34	31.59	0.414	32.54	0.0390	4.04	2.91
Standard deviation	8.79	13.04	9.04	0.318	12.54	0.0242	1.56	1.39
Sample size	6	5	6	13	21	6	5	6
Std error of mean (SEM)	3.59	5.83	3.69	0.088	2.73	0.0099	0.70	0.56
Lower 95% conf. limit	12.96	22.14	22.10	0.221	26.83	0.0135	2.10	1.45
Upper 95% conf. limit	31.42	54.54	41.09	0.606	38.25	0.0645	5.99	4.38
Minimum	11.25	20	20.45	0.200	13.63	0.00625	2.00	1.85
Median	23.63	40	30	0.300	27.27	0.048	4.44	2.38
Maximum	33.33	55.56	45	1.330	53.33	0.0625	6.00	5.56

that surgery at younger age and shorter seizure duration was associated with higher rate of seizure freedom after surgery in patients of tuberous sclerosis in USA. Weiner HL et al[21] found similar results. Secondary epileptogenesis theory by Morrell[22, 23] or the theory of an epileptic network as a result of inter-connectivity and entrainment between different epileptogenic foci by Spencer[24] could explain the age-correlated increased epileptic attacks, because as age increases, newer epileptogenic foci may develop in brain.

Mohanraj et al,[25] in their review article, analyzed many studies and showed that the effect of seizure types was less important than other factors including early response to treatment in determining eventual outcome. We also found that there was neither significant difference between seizure-free and seizure-persisting patients in focal onset vs. generalized onset seizure nor patients with single vs. multiple seizure types.

Earlier studies[26-31] depicted that Epilepsies relating to structural brain abnormalities are less likely to enter remission compared that occurring in patients with structurally normal brains. But in our series we found higher percentage of seizure-free patients having structural abnormality in brain, though the difference was not statistically significant (Table 1).

Many studies[32-35] demonstrated that the presence of neurological deficit, especially if associated with intellectual impairment, was a poor prognostic factor. However those study population were children. But other studies,[36,37] which comprised all age group or adult population, failed to show the association. Impaired activity of daily living significantly affected seizure-freedom in our study. It might be due to degeneration of brain due to repeated seizure attacks or due to caregiver stress factor. We also reported that cognitive decline as well as other neurological complaints like headache, vertigo, tremor etc were higher in seizure-free patients. Neurological complaints had started during the two year study period or previously, but many of them were amenable to supportive therapy provided. Whether these deterioration of neurological status in seizure-free patients was due to the disease process itself or due to the effect of anti-epileptic drug was a matter of debate. The anti-epileptic regimen usually remained same for months or years in seizure-free patients, whereas various anti-epileptics were tried in changing pattern in seizure-persisting patients to find the relief from seizure. So it could be postulated that higher incidence of various neurological complaints in seizure-free patients might be due to prolonged exposure of same AED on brain.

Psychiatric symptoms were prevailing in epilepsy patients. Depression, anxiety and psychosis were present in more than a third of the patients in our series. In our study, it was present in near similarly (Table 1) in seizure-free and seizure-persisting patients. Earlier studies had evidence to support an association of depression with the pathogenesis of epilepsy 38. Multiple studies supported the view that psychiatric co-morbidity was closely associated with failure to achieve remission in epilepsy.[39-43]

Few studies[31, 39, 40] indicated an association of poorer prognosis with the family history of epilepsy. In our series, higher percentage of seizure-free patients had positive family history of epilepsy, though statistically insignificant. Racial and genetic variation in different parts of the world might explain this discrepancy.

Though febrile seizure is a benign process, Lux AL[44] showed 3% of affected infants would develop epilepsy in later life. He also reported association of febrile seizures in infancy and the development of hippocampal sclerosis in later life. Hitiris et al[40] and Geerts et al[45] found febrile convulsion in infancy was closely related to poorer seizure outcome in later life. In our study, the history of febrile seizure in childhood was present in similar way in seizure-free and seizure-persisting patients.

We classified our EEG into normal, focal epileptiform discharge and generalized epileptiform discharge. We failed

to show any significant difference between the seizure-free and seizure-persisting patients in terms of EEG patterns. Though some studies in children[34, 46] found a correlation of background slowing and focal spike and wave activity with poor outcome, other studies in adults[40, 47] failed to show EEG predicting the outcome. So we cannot rely on EEG patterns to predict prognosis.

When we look into the number of AED a patient was taking and correlated with the prognosis, we got some interesting results (Table 1). Seizure freedom was significantly higher in patients taking one AED in comparison to patients taking multiple AED (18.8% vs. 4.1%, p=0.012) as well as in patients taking one/two AED in comparison to patients taking three/four AED (71.9% vs. 47.9%, p=0.015). Seizure-freedom was mostly decreased as the number of AED needed was increased from two. Several studies on children and adults[48-53] found that the response to first appropriate AED was a strong predictor of subsequent seizure-freedom.

In ILAE treatment guideline Glauser T et al[54] mentioned three seizure types had AEDs with level A or level B efficacy and effectiveness evidence as initial monotherapy: adults with partial-onset seizures (level A, carbamazepine and phenytoin; level B, valproic acid), children with partial-onset seizures (level A, oxcarbazepine; level B, None), and elderly adults with partial-onset seizures (level A, gabapentin and lamotrigine; level B, None). In the 2013 ILAE update, Glauser T et al[55] mentioned that new efficacy/effectiveness findings include the following: levetiracetam and zonisamide had level A evidence in adults with partial onset seizures and both ethosuximide and valproic acid had level A evidence in children with childhood absence epilepsy. There were no major changes in the level of evidence for any other subgroup.

Our patients suffering from focal onset seizure, generalized onset seizure and multiple seizure types. We analyzed the effectiveness of the first add-on AED in our series, with the percentage of patients becoming seizure-free after addition of the AED and with the value of 'number needed to treat'. We found lamotrigine was most efficacious and oxcarbazepine was a close contender in various appropriate types of seizure. Similarly phenytoins followed by phenobarbitone were the least efficacious in our series as first add-on AED. Lamotrigine was highly efficacious in GTCS, myoclonus and focal seizures in the study done by EbrahimiHA et al[56] from Iran. Messenheimer J et al[57] reported overall median seizure frequency decreased by 25% with LTG as compared with placebo ($p < 0.001$). In a study by Bang L et al[58], 43-71% of patients with partial-onset, generalized or undetermined epilepsy were seizure free after oxcarbazepine monotherapy (mean dosage 27.7-50 mg/kg/day; duration 1-5 years).

In an Indian study from North India Joshi R et al[59] reported that 35.5 % patients were seizure free, 37.1% patients were at 50% remission, 20.4% patients were at <50% reduction, no change in 7% patients with clobazam as second add-on AED. Another study from USA[60] showed good efficacy and retention rate of clobazam. On the other hand, as first add-on Lacosamide was found to be efficacious and well tolerated.[61, 62] But no data on lacosamide was found as second add-on. We compared clobazam and lacosamide as second add-on AED and found clobazam to be superior than lacosamide in terms of seizure control and compliance. Lower price and better availability could be the reason behind.

In earlier studies, monotherapy was the best therapeutic option when starting AED treatment.[63] Add-on therapy appears to be more effective when started immediately after first-drug failure rather than after a second drug has also failed.[64] It was our observation that, as the number of AED was increased, the drug-compliance was decreased (Table 2). We also noted that AED non-compliance was a significant risk factor for seizure persistence (Table 1).

In our series, we observed 'minimum effective dose' and 'maximum tolerated dose' of different AED in child and adult populations. The finding could become a guide for treating epilepsy patients of Indian subcontinent, however a larger study on the matter would be more appropriate.

DISCLOSURE

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