



STUDY OF IDIOPATHIC EPILEPSY AND EFFICACY AND ADVERSE EFFECTS OF ANTI EPILEPTIC DRUGS

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ABSTRACT **Aims And Objectives** (1)Study clinical profile of children with idiopathic epilepsy(2) Study efficacy and adverse effects of antiepileptic drugs in children with idiopathic epilepsy on long term drugs **Study Design** This is the prospective observational study in a random cohort of children (1-12 years old) with epilepsy on regular **Aed** **Inclusion Criteria**-Epilepsy patients between 1 to 12 years , on antiepileptic drug therapy for past 1 year **Exclusion Criteria**- Patient with Febrile seizure Neonates Patient with epileptic syndromes such as west syndrome and Loss to follow up **Study population** Random 61 idiopathic epilepsy patients on regular AEDs for at least last 1 year were identified during their regular visit to pediatric Department at DR.M.K SHAH MEDICAL COLLEGE AND Research Centre **Result** In present study 61 children among them 75.4.% children had epilepsy < 6 years and 24.59% had > 6 years. GTCS semiology 95% was commonest among children in both group followed by Focal, Among the 61 patients 48 received monotherapy and 13 polytherapy In present study reduction in GTCS seizure by >50% in patient treated with valproate was by 87.23% In all (100%) patients of focal seizure receiving carbamazepine levetiracetam and combination >50% reduction in seizure frequency

KEYWORDS :

INTRODUCTION

Epilepsy is a Greek word meaning "to be seized, to be possessed, or to be afflicted". It is a group of chronic neurological condition presenting with recurrent unprovoked "epileptic seizures".

About 50 million people worldwide are affected by epilepsy and the prevalence is much higher in developing countries. The prevalence rate is 5.59 per 1000 population in India with no gender or geographical differences.

Epilepsy has a bimodal peak with first peak in first two decades of life with second peak in sixth and seventh decade. It is one of the common neurological disorders occurring in childhood.

The International League Against Epilepsy (ILAE) formulated conceptual definitions of "seizure" and "epilepsy" in 2005 as: - An epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain.

Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures, and by the neurobiological, cognitive, psychological, and social consequences of this condition. The definition of epilepsy requires the occurrence of at least one epileptic seizure.

Epileptic seizures are paroxysmal events arising from neuronal hyper excitability and hyper synchrony of cerebral cortex, either locally or simultaneously in both hemispheres.

The vast majority of epilepsies encountered under the age of 12 years are idiopathic, developing without any identifiable or suspected cause, other than a genetic pre disposition in many cases. A large number of children with epilepsy-only are attended and followed-up even by general pediatricians in everyday clinical practice. Therefore, study of the clinical course and seizure out-come of idiopathic epileptic syndromes and epilepsies is of the utmost importance in the treatment of children with epilepsy.

The introduction of newer AEDs over the last three decades has expanded treatment options and increased the expectations about efficacy and tolerability. However, little is known about the effectiveness of AEDs in routine clinical practice. It is also unclear whether the treatment outcomes in epilepsy have improved in recent decades as a consequence of the availability of an increasing number of

AEDs. The present work attempts to provide a comprehensive evaluation of efficacy, and adverse effects of AED treatments in everyday clinical setting.

Patients with epilepsy often have cognitive or behavioral difficulties, which may include mild attention and concentration problems, difficulty in learning and recent memory, executive .Dysfunction as well as non-cognitive features of hyperactivity, irritability, and mood disturbance. Many factors potentially contribute to neuropsychological and cognitive performance in epilepsy patients including etiology and underlying brain substrate giving rise to a patient's epilepsy, seizure type and seizure syndrome, the age of seizure onset, and age at the time of the precipitating injury, as well as seizure- specific influences including seizure frequency, intensity, and duration (Lennox 1942; Meador 2005). Since AEDs act at the neuronal level causing inhibitory effect on neurons, they are associated with untoward side effects.[12] There are different types of adverse effects, idiosyncratic- rash, blood dyscrasia, dose related neurocognitive effects, and complications of long-term use.

Data obtained from cross-sectional studies and randomized controlled trials indicate that up to 80% of people with epilepsy taking AEDs experience an Adverse effect. Evidence indicates that AEDs also contribute to cognitive and neurological impairment and negatively impact quality of life (QOL). These could range from irritability, hyperactivity, to mood disturbances, behavior disturbances.

There have been many new medications released since the 1990s, and although they tend to have more favorable side effect profiles compared to their older counterparts, there continues to be a risk of decreased cognitive function with the majority of these agents. [32]

AIMS AND OBJECTIVES

- 1) To study clinical profile of children with idiopathic epilepsy .
- 2) To study efficacy and adverse effects of antiepileptic drugs in children with idiopathic epilepsy on long term antiepileptic drugs

MATERIAL AND METHOD

Study Design:

This is the prospective observational study in a random cohort of children (1-12 years old) with idiopathic epilepsy on regular AED.

Inclusion Criteria-

Epilepsy patients between 1 to 12 years of age; who were on antiepileptic drug therapy for past 1 year.

Exclusion Criteria-

Patient with Febrile seizure Neonates Patient with epileptic syndromes such as west syndrome and lennox gastaut syndrome

Loss to follow up
Drop out

Study Population

Random 61 idiopathic epilepsy patients on regular AEDs for at least last 1 year were identified during their regular follow up visit to pediatric department IPD AND OPD at DR. M.K. SHAH MEDICAL COLLEGE AND RESEARCH CENTRE.

Demographic details, age of onset of epilepsy, semiology of seizures and its frequency, family history, co-morbidities if any, clinical examination and neurological examination were noted. Investigations like EEG, CT brain and MRI brain are also noted. AEDs dosage and duration, seizure frequency prior and after treatment were recorded. EEG done in all cases. Blood samples were collected for complete blood count, liver function test and renal function test from all participants. All participants were following up regularly for clinical examination at 4 weekly intervals and blood parameters at 3 monthly intervals. ILAE CLASSIFICATION was followed for defining seizure semiology. Antiepileptic drugs were given to all epileptic children by the supervision of pediatrician. Polytherapy was given when monotherapy failed. They were asked to follow up in between if any new neurological symptoms, seizures and other new symptoms develop in participants were observed. Any patient or parent complaining directly of any adverse effects was noted. Weight gain was considered when patient gained more than 10% of their pretreatment weight. Response to treatment based on assessment over study time period was classified as follows

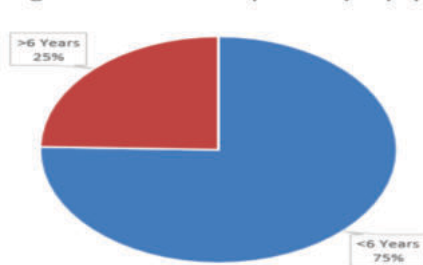
Excellent control or seizure free : complete freedom from seizures
Good control: greater than 50% reduction in seizure frequency
Poor control: no response or less than 50% reduction in seizure frequency

OBSERVATION AND DISCUSSION**Table 1**

Table showing age of onset in children with idiopathic epilepsy

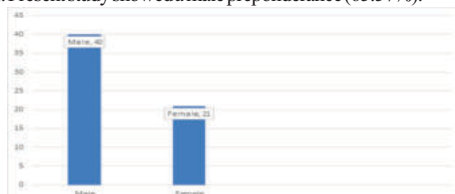
Age of onset	Percentage present study
<6 YEARS	(75.4%) 46
>6 YEARS	(24.59%) 15

In present study 61 idiopathic epileptic children were enrolled among them 75.4% children had epilepsy onset before 6 years and 24.59% had onset after 6 years.

Age of Onset for idiopathic epilepsy**Table 2** Table showing sex distribution of children with idiopathic epilepsy

Sex	Percentage present study
Male	(65.57%) 40
Female	(34.42%) 21

Out of 61 enrolled idiopathic epileptic children 40(65.57%) were male and remaining were female (34.42%) This findings were observed in a study that showed males were affected almost twice more commonly as compared to females. Present study showed a male preponderance (65.57%).

**Table 3** Table showing family history of epilepsy in children with idiopathic epilepsy

	1st degree	2nd degree	3rd degree	Children with no family history	Total
Family history of epilepsy	4	0	0	57	61

In present history family history of epilepsy 6.5 % among first degree relative and 0% among second degree and third degree relative among idiopathic epileptic children.

Table 4 showing distribution of seizure semiology among children with idiopathic epilepsy

Seizure semiology	Total
GTCS	58(95%)
Focal seizures	3(5%)
Focal with secondary generalization	0
Atonic seizures	0
Absence seizures	0
Myoclonic seizures	0

Seizure semiology	Age of onset <6years	Age of onset >6years	Total
GTCS	38	19	57
Focal seizures	4	0	4
Focal with secondary generalization	0	0	0
Atonic seizures	0	0	0
Absence seizures	0	0	0
Myoclonic seizures	0	0	0
Total	42	19	61

GTCS semiology 95% was commonest among enrolled idiopathic epileptic children in both group 66.6% & 33.33 % respectively followed by Focal 9.5%

In present study GTCS semiology 95% was commonest among enrolled idiopathic epileptic children in both group 66.66% & 33.33% less than 6 year and more than 6 years respectively followed by Focal 9.5%, No cases among absence, myoclonic, atonic, Focal with secondary generalization.

Table 5 showing precipitating factors responsible for breakthrough seizure

Precipitating factors	No of patients
Febrile illness	2
Drug defaulter	7
Flashes of light	0
Sleep deprivation	0
Stress	0
No precipitating factor	52
Total	61

In present study drug defaulter (11.4%) as most common precipitating factor for breakthrough seizures followed by febrile illness (3.2%). This study observed Drugs defaulter was most common precipitating factor followed by Febrile illness, psychological stress, flickering of lights, physical and mental stress.

Table 6: showing comparison of patient developing status epileptic episodes on various AEDs during study period

Status Epileptic episode	Present study
Yes	9 (14.7%)
No	52(85.2%)

In present study 14.7 % of status epilepticus episodes in idiopathic epileptic children on antiepileptic drugs. Poor drug compliance was the reason for high status epileptic episodes

Table 7 : Table showing number of patient developing status epileptic episodes on various AEDs during study period

Drug	No of patient receiving drug	No of patient who had status epilepticus	Percentage
Phenobarbitone	0	0	0
Phenytoin	0	0	0

Valproate	48	4	8.3
Carbamazepine	1	0	0
Oxcarbazepine	0	0	0
Lamotrigine	0	0	0
Leviteracetam	3	0	0
Valparin +levipil	3	1	33
Valparin +carbamazepine	2	0	0
Valparin +levipil+oxcarbazepine	2	1	50
Valparin +lamotrigine +oxcarbazepine +Clobazam	1	0	0
Phenobarbitone +valparin +lamotrigine +leviteracetam	1	0	0
Total	61	6	

In present study 6 patient had status epilepticus episodes out of this 8.3 % on valproate and 50 % on combination drugs.

Table 8 : showing Co-morbidities in children with idiopathic epilepsy

Comorbidities	No of patients
Vision	0
Hearing	0
Microcephaly	6
Intellectual disability	2
Congenital heart diseases	0
Mental Retardation	2
ADHDS	0

In present study Microcephaly in 6 (9.8%) patient , Intellectual disability and mental retardation in 2 (3.2%) patient.

Table 9: Table showing electroencephalographic findings in idiopathic epilepsy children

EEG FINDING	Number	Percentage
Abnormal	42	68.85
Normal	19	31.14
Total	61	

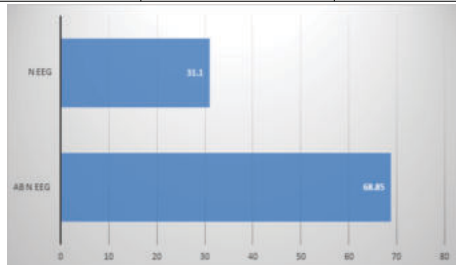


Table 9 A: Table showing distribution of abnormal electroencephalographic patterns

Patterns	Percentage
Normal	19(31.1%)
Abnormal	42(68.8%)
Focal spike wave	4(9.5%)
Generalized spike	36(85.7%)
Diffuse slowing	1(2.38%)
Mixed	1(2.38%)
Total	

In present study 19 (31.1%) had normal EEG and 42 (68.8%) had EEG changes among them generalized spike 36 (85.7%) commonest followed by focal spike 4(9.5%) .Diffuse slowing and Mixed EEG changes was found in 2.38% of patient.

EEG is important investigation for epilepsy but it is not always diagnostic.

In present study EEG findings were normal in 19 (31.1%) of patients, generalised in (85.7%), followed by focal in 9.5% .

Table 10: Table showing antiepileptic drugs used in idiopathic

epilepsy children

Drug	Present study
Phenobarbitone	0
Phenytoin	0
Valproate	46(75.4%)
Carbamazepine	2(3.2%)
Oxcarbazepine	0
Lamotrigine	0
Leviteracetam	2(3.2%)
Valparin +levipil	5(8.19%)
Valparin +carbamazepine	3(4.9%)
Valparin +levipil+oxcarbazepine	1(1.63%)
Valparin +lamotrigine +oxcarbazepine +Clobazam	1(1.63%)
Phenobarbitone +valparin +lamotrigine +leviteracetam	1(1.63%)

Among the 61 patients 48 (78.86 %) received monotherapy and 13 (21.3%) received polytherapy In present study AEDS use of valproate (75.4%) were commonest followed by carbamazepine and leviteracetam (2.3%) and respectively .In polytherapy valproate + levitaracetam (8.19%) were used commonly.

In present study 48 patients were on monotherapy and 13 were using more than one antiepileptic drugs.

Sodium valproate being a broad spectrum ,time tested and reasonable Antiepileptic drug still remains the drug of choice .In developing countries ,economic constraints and lack of evidence as a monotherapy for many of the newer generation drugs hinder their use in routine practice.

Table 11: showing Relative efficacy of AEDs among children with idiopathic epilepsy

Semio logy	AED	Present study				Total
		No reduction	<50% reduction	>50% reduction	Complete remission	
GTCS	Valproate	2(4.2%)	4 (8.5%)	30 (63.8%)	11 (23.4%)	47
	Leviteracetam			2		2
	Valproate +leviteracetam			3	1	4
	Valproate + carbamazepine			2		2
	Valparin +lamotrigine +oxcarbazepine +Clobazam		1			1
Focal	Phenobarbitone +valparin +lamotrigine +leviteracetam		1			1
	Valparin +leviteracetam +oxcarbazepine			1	1	2
	Leviteracetam			1		1
	Carbamazepine				1	1

At the end of follow up period patient were considered to be in " remission" if they not had seizures of any type for minimum of one year while receiving appropriate antiepileptic drug treatment

In present study reduction in GTCS seizure by >50% in patient treated with valproate was by 87.23%

In all (100%) patients of focal seizure receiving carbamazepine levitaracetam and combination >50% reduction in seizure frequency

Table 12: Table showing adverse effects in idiopathic epileptic children on long term AEDs

Drug	Drowsiness	GI distress	liver dysfunction	weight gain	Academic underachievement	No of patient receiving drug	Percentage
Phenobarbitone						0	0
Phenytoin						0	0

Valproate	3	2		4	5	47	77.04
Carbamazepine						1	1.63
Oxcarbazepine						0	0
Lamotrigine						0	0
Levetiracetam						3	4.91
Valparin + levipil			1			4	6.55
Valparin + carbamazepine		1				2	3.27
Valparin + levipil + oxcarbazepine		1				2	3.27
Valparin + lamotrigine + oxcarbazepine + Clobazam				1	1	1	1.63
Phenobarbitone + valparin + lamotrigine + levetiracetam						1	1.63
Total						61	

Valproate

Adverse effects	Present Study
weight gain	8.5%
Drowsiness	6.3%
GI DISTRESS	4.2%
Academic underachievement	10.6%
Liver dysfunction	

In present study we observed patient on long term AEDs had weight gain, GI distress, drowsiness and academic underachievement with valproate which was the most commonly used drug.

Summary

- 1) The present study was prospective observational study titled Study of clinical profile, efficacy of drugs and its adverse effects in children with epilepsy on long term antiepileptic drugs.
- 2) Of 61 consecutive Idiopathic epilepsy patients age of onset of epilepsy was more in <6 years of age 44(72.13%).
- 3) Male predominance was seen in our study.
- 4) 96.7% patients enrolled had no family history of epilepsy whereas 3.2% had history of epilepsy in family among first degree relatives.
- 5) Among the various seizure semiology generalized tonic clonic type of seizure semiology was commonest below six years of age.
- 6) The occurrence of breakthrough seizure was multifactorial in our study with drug non compliance was most common cause.
- 7) Status epileptic episodes seen among 8 patients during study more common observed in patients. Poor drug compliance was most common reason for status epileptic episodes
- 8) Amongst the co-morbidities microcephaly was the most common.
- 9) 70.49% patient had EEG abnormalities. Generalized spike /sharp waves was most common EEG abnormality.
- 10) The reduction in GTCS seizure by >50% in patient treated with valproate was 87.2%.
- 12) 24.5% of patient had adverse effects of drugs.

CONCLUSION

Phenobarbitone
Phenytoin
Valproate
Carbamazepine
Oxcarbazepine
Lamotrigine
Levetiracetam
Valparin +levipil
Valparin +carbamazepine
Valparin +levipil+oxcarbazepine
Valparin +lamotrigine +oxcarbazepine +Clobazam
Phenobarbitone +valparin +lamotrigine +levetiracetam

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