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Drug Utilization Pattern of Anti-epileptic Drugs in Idiopathic Childhood Epilepsy in a Tertiary Health Care Center

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ABSTRACT: Introduction - The study was conducted to know the prevalence of various types of Idiopathic Childhood Epilepsy and the utilization pattern of Antiepileptic drugs (AED) in the tertiary referral center.
Method - A total of 100 Idiopathic epileptic patients of both sexes below 15yrs of age who were prescribed an AED (Antiepileptic drug) were considered for analysis. Demographic profile, type of epilepsy, AED, number of epileptic events, biochemical, EEG and ADR (Adverse drug reaction) data were collected and analyzed.
Results - Among all subjects 58% (Male56%)are children <5yrs. Incidence of Generalized Tonic-Clonic Seizure (GTCS) was 80%, Complex Partial Seizure 60%, Partial Seizure with Secondary Generalization 32%, Simple Partial Seizure 8%, Myoclonic 8%, Absence 7% and Atonic 5%. Valproate was the most commonly prescribed drug in GTCS, Atonic, Myoclonic and Absence seizure. Carbamazepine was commonly prescribed drug in Partial seizure. A total of 110 AEDs (i.e.1.1 AED per patient) were prescribed. The majority of subjects (90%) required monotherapy. Overall, only 5% patients received newer AED and majority of patients (95%) were on older AED therapy. Only five patients reported ADRs. Phenytoin and Carbamazepine were the offenders but none received any treatment for adverse effects.
Conclusion-Idiopathic Childhood Epilepsy was more common in male children of 1 to 5yr age. GTCS was the commonest type of epilepsy. The majority of epileptic children received monotherapy and older AED. Valproate was the commonly prescribed drug in all type of epilepsy other than Partial seizure. It was the most cost effective and safest AED.

Keywords: Adverse drug reactions; Antiepileptic drugs; Sodium Valproate; Phenytoin; Drug utilization; Monotherapy and Polytherapy.

INTRODUCTION: Epilepsy is the most common neurological disorder in children, and it is characterized by a spontaneous propensity for recurrent and unprovoked seizures. Epilepsy, particularly childhood epilepsy, remains a challenge to treat. Despite the increase in the number of antiepileptic drugs (AEDs), more than 25% of children with childhood epilepsy continue to have seizures[1]. Around 4%–10% of children suffer at least one seizure in the first 16 years of life[2].The incidence is highest in children below 3 years of age, with a decreasing frequency in older children[3]. There are some special problems in the treatment of childhood epilepsy as they are more susceptible to the hepatotoxic effect of valproic acid[4] and phenobarbitone induced alteration of behavior and impairment of learning process[5]. In spite of continued emergence of newer drugs, the response to antiepileptic therapy is still unpredictable and unsatisfactory. The physicians and even the neurologists are in a dilemma and vary from one another in selecting the most appropriate drug in a particular type of epilepsy. Monotherapy is the usual dictum, but polytherapy is needed for patients with multiple seizure types or refractory disease[3]. It is felt, therefore, necessary to know the prevalence of various types of childhood epilepsy and the prescribing pattern of antiepileptic drugs. Epilepsy is a chronic disorder and requires a long continued treatment for at least 2 years. Naturally the cost of treatment produces a substantial financial burden to the family. It is therefore prudent to attach importance not only on efficacy and safety of the drugs, but also on cost-effective analysis of therapy.

Aims and objectives:

- To evaluate the utilization pattern of antiepileptic drugs in different types of idiopathic childhood epilepsy.
- To compare the efficacy and safety profile of commonly used AEDs

MATERIAL AND METHODS: The permission to conduct the study was obtained from the Institutional Clinical Ethics Committee June 2014. We conducted the study at R. G. Kar Medical College, Kolkata from

July 2014 to April 2015. During this time period, we analyzed the prescription data of 100 patients of seizures of both sexes below 15 yrs. from pediatric out-outpatient department (OPD). The diagnosis was confirmed by a pediatrician along with consultation with neurologist as and when required. Case categorization was done on the basis of clinical presentation of seizures, supported by electroencephalography (EEG) and radio imaging study on selected cases. Data collection proforma was pretested on a pilot group of patients and validated by the experts in pediatrics and pharmacology. A total of 109 patients were approached, of whom 100 agreed to participate in the study. We excluded all surgical causes of convulsion, febrile convulsion, cerebral palsy and patients with status epilepticus.

Study Variables:
1. Socioeconomic-demographic profile of the patient.
2. Type of epilepsy.
3. Drug utilization pattern.
4. Drug related information like: (a) Generic name of drugs. (b) Preparation of the drugs. (c) Monotherapy or polytherapy.

The information was compiled and the distribution pattern of various clinical types of epilepsy in relation to age and sex and the incidence of prescription of individual antiepileptic agent was calculated.

Adverse drug reaction (ADR) profile includes:
1. The incidence and type of adverse drug reaction.
2. The causality relationship of the ADR with suspected drug according to Naranjo ADR probability scale.
3. Whether the suspected drug was stopped after the ADR.
4. Whether any treatment was given for the ADR.
5. The drug(s) most commonly causing ADRs.

Statistical Analysis: Data generated from this study was analyzed by Graphpad Instat.As appropriate, paired t test and one–way Analysis of Variance [ANOVA] with post-hoc test Dunnet multiple comparison test was used to assess the statistical significance of differences in means. Values <0.05 were considered significant.

RESULTS AND DISCUSSION: The study was conducted on 100 epileptic patients and belonged to the age group of 1 to 5 years (58%). The result indicates the majority (56%) of the epileptic children were male. Distribution according to the type of epilepsy was shown in Table1.

The pattern of AEDs prescribed and the different therapeutic approaches of epilepsy treatment utilized are presented in Tables 2 & 3. Regarding the treatment, the majority of epileptic children received monotherapy (90%) and only a small percentage of patients (10%) required polytherapy for the control of seizures (Table 2). The majority of epileptic children received sodium valproate (74%), which was followed by carbamazepine (12%) and phenytoin (10%). Again valproate is the most common agent with other drug as combination. Only a small percentage of received either lamotrigine &topiramate (2% patients each) or oxcarbamazepine & phenobarbitone (1%) (Table 3).

Table 1: Distribution according to the type of epilepsy.

Type of Epilepsy(n=100)	**Sub-Type of Epilepsy**	**No. of Patients (%)**
Primary Generalized Seizure(n=75)	a) Tonic Clonic	60(80)
	b) Tonic	0(0)
	c) Atonic	4(5)
	d) Absence	5(7)
	e) Myoclonic	6(8)
Partial Seizure (n=25)	a) Simple Partial	2(8)
	b) Complex Partial	15(60)
	c) Partial Seizure with Secondary Generalization	8(32)

Table 2: Patterns of AEDs prescribed.

Type of therapy	**no. (%)**
Monotherapy	90 (90)
Polytherapy	10 (10)
Older AED	95(95)
Newer AED	5(5)
Older/Newer AED	19 (19)
Dosage form Tablet Syrup	 69(69) 31(31)
Generic name	4(4)
Brand name	96(96)

Table 3: Distribution of AED prescribed.

Type of therapy	no. (%)
Most frequent dual combination (n = 10)	
Valproate/ Topiramate	2(20)
Valproate/Phenytoin	2(20)
Valproate/ Lamotrigine	2(20)
Others	4(40)
Most frequent AED as monotherapy (n = 90)	
Valproate	75(80)
Carbamazepine	9(10)
Phenytoin	6(7)
Overall AED utilisation (Total AED = 110)	
Valproate	81(74)
Carbamazepin	12(11)
Phenytoin	11(10)
Topiramate	2(2)
Lamotrigine	2(2)
Oxcarbamazepine	1(1)
Phenobarbitone	1(1)

Adverse drug reaction (ADR) profile: Five out of of 100 reported ADRs (incidence = 5%) as shown in the Table 4. Phenytoin and carbamazepine contributed equally to the occurrence of adverse effects (two cases each). None of the patients received any treatment for adverse effects.

Table 4: Adverse drug reactions.

No. of Patients ADR reported	Suspected drugs	Causality relationship	Whether treatment with AED continued/stopped
4 - Drowsiness, subtle imbalance	Phenytoin	Possible	Continued
1- Gum swelling	Phenytoin	Possible	Continued
2- Decreased memory and learning	Carbamazepine	Possible	Continued
2- Drowsiness	Topiramate	Possible	Continued

Efficacy profile of antiepileptic drugs: After 1 and 3 months of therapy with Valproate, Phenytoin and Carbamazepine there was significant reduction in epileptic event when compared to their respective baseline values (Table- 5).

Table 5: Efficacy of Valproate, Carbamazepine and Phenytoin in the prevention of Epileptic seizure.

Duration of therapy	No of epileptic seizures/month		
	Valproate(Mean ± SEM) [n=74]	Carbamazepine (Mean ± SEM) [n=14]	Phenytoin (Mean ± SEM) [n=11]
Baseline	4.99 ± 0.63.	4.14 ± 0.93	4.82 ± 0.91
After 1month	1.42 ± 0.49*	1.50 ± 0.25*	2.18 ± 0.55**
After 3month	0.07 ± 0.04*	0.57 ± 0.17*	1.00 ± 0.38*
After 6month	0.05 ± 0.01*	0.24 ± 0.09*	0.75 ± 0.15*

**p <0.001, **p<0.01 when compared to the respective control*

The current study attempts to analyze the pattern of drug utilization in different types of epilepsy. The majority of epileptic children received monotherapy and only a small percentage of patients required polytherapy for the control of seizures. This was in accordance with the standard text book knowledge of pharmacology which recommends monotherapy because of higher risk of adverse effects, drug interaction, teratogenicity and reduced patients compliance with polytherapy. It is also felt that India being a developing country, a large section of people live below the poverty line. Naturally the cost of treatment produces a substantial financial burden to the family. This financial constraint is one of the important causes for poor patient compliance with the antiepileptic drug therapy. It is therefore prudent to attach importance not only on efficacy and safety of the drugs, but also on daily or monthly cost of therapy. It would ultimately help to constitute an institutional Essential Drugs List and institutional treatment guideline of childhood epilepsy in terms of efficacy, safety, suitability and cost of antiepileptic drug therapy. It may be of immense help in the clinical management of epilepsy in the Government hospital of West Bengal. Valproate was the most commonly prescribed drug in GTCS, atonic, myoclonic and absence seizure. Carbamazepine was commonly prescribed drug in Partial seizure. The past decade had allowed the introduction of a number of newer AEDs for the treatment of epilepsy like felbamate,lamotrigine, topiramate and vigabatrin etc[7]. In our study, we observed 5% prescription of newer AEDs.The selection of 'P' drugs for various types of epilepsy should be based on efficacy, safety, suitability and cost. It was further observed that ma-

jority of epileptic children received the antiepileptic drugs in Brand or Proprietary name and in tablet form. The ultimate outcome of AED treatment in paediatric epilepsy is to attain no seizures and no side effects. Fortunately, this goal is often met by using an appropriate AED as monotherapy. Our data indicated that monotherapy was the therapy of choice in majority of patient with partial or generalized seizure. This finding correlated with the finding in other studies[8-11]. The reason for polytherapy may be attributed to higher incidence of refractory epilepsy in any study. Polytherapy increases the potential for drug drug interaction, can increase the risk of chronic toxicity and is associated with a higher cost of medication. However, in polytherapy there is improved seizure control. Among all the commonly prescribed antiepileptic drugs valproate, carbamazepine, phenytoin produced side effects which were mild; dose related and did not require withdrawal of therapy. Overall, drowsiness was the most frequent adverse effect in our study which is similar to the finding in a previous study[12]. Valproate achieved fastest seizure control in 95% of children within three months whereas Carbamazepine and Phenytoin required six months of therapy to achieve the same extent of seizure control. By comparing efficacy analysis among all the AEDs, it is observed that valproate is the most effective AED.

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CONCLUSION: Idiopathic Childhood Epilepsy was more common in male children of 1 to 5yr age. GTCS was the commonest type of epilepsy. The majority of epileptic children received monotherapy and older AED. Valproate was the commonly prescribed drug in all type of epilepsy other than Partial seizure. It was the most cost effective and safest AED.

The study was conducted in a very small number of patients and the demographic profile. Seizure recurrences after withdrawal of therapy could not be studied as the study was not conducted for 2 years and beyond that. If the study can be extended further by collecting the data for comparing the efficacy and the toxicity profile of the drugs from a sufficient number of patients from the aforesaid as well as the other tertiary care hospitals, it may be possible to resolve the long continued dispute of selecting the most appropriate drugs in a particular type of epilepsy.

REFERENCES:

1. White H. S. Mechanism of antiepileptic drugs. In: Porter R. J. Chadwick D. (1997) The epilepsies 2. Blue Books of Practical Neurology, *Boston Butterworth-Heinemann*, 1, 1-30.
2. McAbee G. N., Wark J. E. (2000) A practical approach to uncomplicated seizures in children, *Am Fam Physician*, 62, 1109-16.
3. Vining E. P. (1994) Pediatric seizures.Emerg Med Clin, *North Am*, 12, 973-88.
4. Powell-jackson P. R., et al (1984) Hepatotoxicity to sodium Valproate review, 25, 673-81.
5. Mc Namara, J. O. Pharmacotherapy of the epilepsies**.** Goodman &Gillman's The Pharmacological Basis of Therapeutics (2011) 11thed.McGraw-Hill, 19, 501-522.
6. Camfield P. R., Camfield C. S., Gordon K., Dooley J. M. (1997) If a first antiepileptic drug fails to control a child's epilepsy, what are the chances of success with the next drug?, *J. Pediatr*., 131, 821-4.
7. National Institute for Clinical Excellence. Newer drugs for epilepsy in children, technology appraisalal[online]. Available at: www.nice.org.uk/CG20.Accessed July 11, 2007.
8. Pellock J. M. (1994) Standard approach to antiepileptic drug treatmentin the United States, *Epilepsia*, 35(4), 11-18.
9. Chadwick D. (1994) Standard approach to antiepileptic drug treatmentin the United Kingdom, *Epilepsia*. 35(4), 3-10.
10. Mattson R. H. (1998) Medical management of epilepsy in adults.Neurology, 51 (suppl.4), S15-S20.
11. Reynolds E.H., Shorvon S.D. (1981) Monotherapy or Polytherapy forepilepsy?, *Epilepsia*, 22, 1-10.
12. Radhakrishnan K., Dinesh Nayak S., Pradeep Kumar S., SankaraSarma P. (1999) Profile of antiepileptic pharmacotherapy in a tertiaryreferral centre in South India: a pharmacoepidemiologic and pharmacoeconomic study, *Epilepsia*, 40, 179-85.