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PRESCRIBING PATTERN AND ADVERSE DRUG REACTION MONITORING OF ANTIEPILEPTIC DRUGS IN CHILDREN IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Analyse the prescribing pattern of antiepileptic drugs and evaluate the adverse drug reactions. The study was commenced with institutional ethical committee approval and patients were enrolled according to the study protocol after obtaining written informed consent. Prescriptions of all children with epilepsy were analysed. Adverse drug reactions were monitored by interviewing with parents, by physical examination and by necessary lab investigations in children. Causality assessment was done using WHO UMC (World Health Organisation and Uppsala Monitoring Centre) scoring system. Most of the epileptic patients were effectively managed with conventional AEDS. The highly used AED was sodium valproate. Clobazam was mainly used as adjuvant. Mono therapy was prescribed in 71% of patients. Multiple drug therapy was used in 29% patients. Phenytoin and Sodium Valproate contributed equally to the ADRs. Transient increase in liver enzymes, sedation and gastritis were the common adverse reactions and for all the ADRs, the causality assessment was "probable". The treatment with AEDS was continued in all patients inspite of ADRs because the seizures were well controlled and the adverse effects did not significantly disrupt the normal activities. Since adverse drug reaction is the determining factor in drug selection due to similar efficacy of most antiepileptic drugs, our study gives an insight to promote rational drug use and reduce the adverse reactions by optimal drug selection, utilizing mono therapy and avoiding poly therapy whenever possible.

Keywords: Epileptic children, Prescribing pattern, Antiepileptics, Adverse reactions.

INTRODUCTION

Seizure is a transient occurrence of signs and symptoms resulting from abnormal excessive or synchronous neuronal activity in brain[1]. Epilepsy is defined as recurrent seizures unrelated to fever or to an acute cerebral insult[1].

Worldwide prevalence of active epilepsy ranges from 4 -5per1000 and in India it is 4.15-7.03per 1000 population[2]. Febrile seizure is the most common type in children followed by grandmal seizures. More than half of children with epilepsy will outgrow their seizure as they mature, while others(30%) may have seizure that continues into adulthood. So overall aim in treating epilepsy should be complete control of seizures without any untoward reactions due to medications[2,3].

Large numbers of drugs are currently available for epilepsy treatment. Old and conventional drugs are commonly used as first line drugs. They are less expensive and have more adverse effects. Newer drugs are used as add on therapy[3]. Seizure control may be achieved by monotherapy in about 80% of patients while other 20% requiring two or three drugs[4].

Some side effects may be common with above mentioned drugs. They are sedation, poor scholastic behaviours, ataxia, gum swelling, dermatological reactions and hepatotoxicity. They can be diverse as well ranging from idiosyncratic reactions (bone marrow depression) to acute myopia and glaucoma[5-7]. The aim of the study is to get an insight into the prescribing pattern of antiepileptic drugs for children and adverse drugs reactions caused by the drugs.

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Objective

❖ To analyse the prescribing pattern of antiepileptic drugs.

❖ To evaluate the adverse drug reactions caused by antiepileptic drugs.

MATERIALS AND METHODS

Study Population: 100 out patients

Study Design: prospective observational study

Study Duration: Three months

Study Place: Paediatric neurology outpatient department, Tirunelveli Medical College Hospital, Tirunelveli

Inclusion Criteria

❖ All children from 1year of age upto 13 years of age, both male and female with epilepsy getting antiepileptic drugs.

Exclusion Criteria

❖ Adults and children above 13 years of age.

❖ Patients with uncertain diagnosis.

❖ First episode of seizure.

❖ Seizure with acute conditions and other neurological illness.

❖ Children having pathological liver disease and renal disorders.

After obtaining institutional ethical committee approval, the study was commenced. Written informed consent was obtained from all the parents accompanying the children in their own vernacular language.

Prescriptions of all children with epilepsy were analysed and categorised to know the most common drugs used and the poly pharmacy.

Adverse drug reactions were monitored by interviewing with parents, by physical examination and also by necessary lab investigations in children. Suspected adverse drug reactions were documented in predesigned reporting form. Causality assessment of adverse drug reactions was done using WHO UMC (World Health Organisation and Uppsala Monitoring Centre) scoring system.

RESULTS

Patient Indicators

a)Sex Distribution

b)AGE DISTRIBUTION

Cause of Seizure

Most common cause of seizure was fever.

Prescription Indicators

a) Average no. of AEDs/patient=1.29

b) All antiepileptic drugs were prescribed in Generic name.

C) Types of Seizures and Drugs Prescribed

TYPE OF THERAPY

Monotherapy

Sodium valproate was most commonly prescribed as monotherapy.

Two AEDS

Sodium valproate and clobazam was most commonly prescribed as combination therapy.

Three AEDS

Sodium valproate,phenytoin and clobazam combination was most commonly used.

Adverse Drug Reactions

Table 1. GTCS was the most common seizure type and sodium valproate was the most commonly prescribed drug

Seizure type	%	Most Commonly Prescribed Drugs	%	Second Most Commonly Prescribed Drugs	%	Others	%
GTCS	56	Sodium valproate	39	Phenytoin Carbamazepine	8 5	Bct Clobazam Phenobarbitone Mvt Risperidone Diazepam	22 9 9 2 1 1
Complex partial seizure	20	Sodium valproate	16	Carbamazepine Phenobarbitone	5 4	Bct Clobazam Folic acid Risperidone Lamotrigene	6 3 1 1 1
Simple focal seizure	15	Carbamazepine	9	Valproate Phenobarbitone Phenytoin	5 4 1	Bct Clobazam	3 1
Absence seizure	9	Phenobarbitone	4	Valproate Carbamazepine	3 2	Bct	2

Table 2. Increase in liver enzymes was the most commonly reported ADR which was transient

No: of Patients	ADR Reported	Suspected Drug	Causality
16	Transient Increase In Liver Enzymes	Sodium Valproate	Probable
8	Sedation	Clobazam, Carbamazepine, Sodium valproate	Probable
6	GI Upset	sodium valproate, Phenytoin	Probable
3	Headache	Sodium valproate, Phenytoin	Probable
3	Weight Gain	Sodium Valproate	Probable
2	Anaemia	Sodium valproate	Probable
1	Lymphadenopathy	Phenytoin	Probable
1	Ataxia	Sodium valproate	Probable
1	Gum Hypertrophy	Phenytoin	Probable

Table 3. WHO-UMC Causality Categories

Certain	• Event or laboratory test abnormality, with plausible time relationship to drug intake • Cannot be explained by disease or other drugs • Response to withdrawal plausible (pharmacologically, pathologically) • Event definitive pharmacologically or phenomenologically (i.e. anobjective and specific medical disorder or a recognised pharmacological phenomenon) • Rechallenge satisfactory, if necessary
Probable/ Likely	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • Unlikely to be attributed to disease or other drugs • Response to withdrawal clinically reasonable • Rechallenge not required
Possible	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • Could also be explained by disease or other drugs • Information on drug withdrawal may be lacking or unclear
Unlikely	• Event or laboratory test abnormality, with a time to drug intake that makes a relationship improbable (but not impossible) • Disease or other drugs provide plausible explanations
Conditional/ Unclassified	• Event or laboratory test abnormality • More data for proper assessment needed, or • Additional data under examination
Unassessable/ Unclassifiable	• Report suggesting an adverse reaction • Cannot be judged because information is insufficient or contradictory • Data cannot be supplemented or verified

Fig 1. Among 100 patients,62 were male and 38 were female

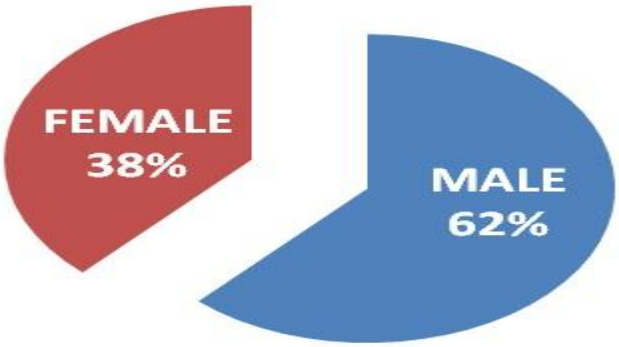

Fig 2. There were more number of patients in age group less than 5years and more than 10years

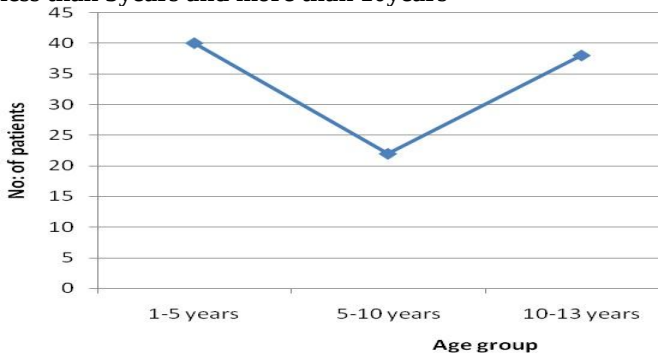

Fig 3. Monotherapy was commonly prescribed

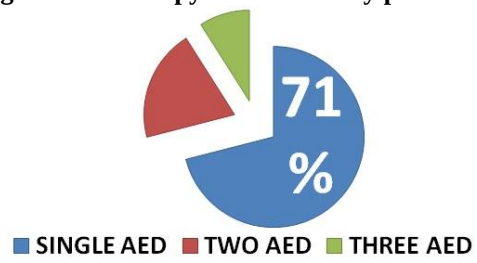

Fig 4. Suspected ADR reporting form

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

For VOLUNTARY reporting of Adverse Drug Reactions by healthcare professionals

CDSCO
Central Drugs Standard Control Organization
Directorate General of Health Services,
Ministry of Health & Family Welfare, Government of India,
FDA Bhavan, ITO, Kotla Road, New Delhi
www.cdsco.nic.in

(AMC/ NCC Use only
AMC Report No.
Worldwide Unique no.

A. Patient Information
1.Patient Initials _____
2.Age at time of Event or date of birth _____
3. Sex ☐M ☐ F
4. Weight ____Kgs
12. Relevant tests / laboratory data with dates

B .Suspected Adverse Reaction
5. Date of reaction stated (dd/mm/yyyy)
6. Date of recovery (dd/mm/yyyy)
7. Describe reaction or problem
13. Other relevant history including pre-existing medical conditions (e.g. allergies, race, pregnancy, smoking, alcohol use, hepatic/ renal dysfunction etc)
14. Seriousness of the reaction
☐ Death (dd/mm/yyy)____
☐ Life threatening
☐ Hospitalization-initial or prolonged
☐ Disability
☐ Congenital anomaly
☐ Required intervention to prevent permanent impairment / damage
☐ Other (specify)
15. Outcomes
☐ Fatal ☐ Recovering ☐ Unknown
☐ Continuing ☐ Recovered ☐ Other (specify)____

C.Suspected medication(s)

S.No	8. Name (brand and /or generic name)	Manufacturer (if known)	Batch No./ Lot No. (if known)	Exp. Date (if known)	Dose used	Route used	Frequency	Therapy dates (if known give duration) Date started	Date stopped	Reason for use of prescribed for
i.										
ii.										
iii.										
iv.										

Sl.No As per C	9. Reaction abated after drug stopped or dose reduced					10. Reaction reappeared after reintroduction				
	Yes	No	Unknown	NA	Reduced dose	Yes	No	Unknown	NA	If reintroduced dose
i.										
ii.										
iii.										
iv.										

11. Concomitant medical product including self medication and herbal remedies with therapy dates (exclude those used to treat reaction)

D. Reporter (see confidentiality section in first page)
16. Name and Professional Address : _____
Pin code : _____ E-mail _____
Tel. No. (with STD code): _____
Occupation Signature
17. Causality Assessment
18. Date of this report (dd/mm/yyyy)

DISCUSSION

The incidence of epilepsy has a bimodal distribution with a peak incidence in the first decade and second peak in the elderly[2]. In the present study the peak was observed at the age group of 1 to 13 years.

Various epidemiological studies on epilepsy are unable to explain a difference in gender distribution in their study population and some studies describe a female predominance[2]. In our study the least number of females may be due to poor understanding of disease and treatment, social stigma and the male relative has to give consent and accompany the females for hospital visit.

There was disproportionate large number of generalized seizures among our study group. This was likely due to incomplete clinical information, EEG and imaging. Most of the epileptic patients were effectively managed with conventional AEDS. The highly used AED

was sodium valproate because of its broad spectrum of activity. Clobazam was mainly used as add on therapy.

Mono therapy was prescribed in 71% of our patients, as in many previous studies with its many advantages [3, 4]. Multiple drug therapy was prescribed in some patients with dual therapy in 20% pateints and three AEDS in 9% patients. Un favourable combinations were used in two patients with phenytoin and phenobarbitone combination and with phenytoin and sodium valproate combination which can lead to bidirectional, complex and variable interactions.

Phenytoin and Sodium Valproate contributed equally to the occurrence of ADRs. Most of these correspond well with the known adverse effect profile of these drugs[5-8]. The treatment with AED was continued in all patients who reported adverse effects because the seizures were well controlled and the adverse effects did not significantly disrupt the normal activities of the patient.

LIMITATIONS

The study was single centered with small sample size and done only in pediatric age group. Recommends multi centric study in general population.

CONCLUSION

Since adverse drug reaction is the determining factor in drug selection due to similar efficacy of most antiepileptic drugs, our study gives an insight about prescription pattern to promote rational drug use and to reduce adverse reactions by optimal antiepileptic drug selection, utilizing mono therapy and elimination of poly therapy when feasible.

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None

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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