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Assessment of Anti -Epileptic Drugs in Pediatrics Department in Tertiary Care Hospital, Baptist Hospital, Bangalore

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Abstract

Prescription audit is one of the important component of clinical pharmacy, where clinical pharmacist plays important role in optimization of medication use, minimizing number of medication-related problems and improving medication therapy. The main objective of present study is to find out the loose links between medication prescribing and its utilization in pediatric department especially with drugs belongs to Antiepileptic medication category. This prospective observational study carried out for a period of 6 months in the Department of Pharmacy practice, Karnataka College of pharmacy, Bangalore Baptist Hospital, Bangalore. The study was conducted on 100 patient receiving Antiepileptic Medication. The study showed that the maximum number of patient receiving antiepileptic medication belongs to age group of 2 to 6 years, while comparing the prevalence of ADR Levetiracetam, phenytoin and clobazam was identified which are associated with ADR, the highly prescribed drug was Valproic acid and carbamazepine. The ADRs documented was Loss of appetite, vomiting, anemia and Steven-Johnson syndrome. Evaluation of prescription was performed as which is major factor in drug related ADRs. In the discussion part various methods of improvement in prevention of ADRs due to prescription error has been suggested which can improve the drug utilization and precaution. An economic study is done in the end to put a light on the cost effective treatment therapy which might improve patient adherence.

Key words: Antiepileptic, epilepsy, pediatric, Prescription

Introduction

In the last two decades, several new anti-epileptic drugs (AEDs) have been approved for the treatment of epilepsy. While the use of these new-generation drugs is growing, some of the old-generation drugs are still preferred because of cost and availability. Similar efficacy and safety have been reported for both generations of AED (Weijenberg et al., 2010); however, there are differences between specific drugs.(Marson et al., 2007) Patient-specific factors such as age, gender, the type of epilepsy and the availability of monitoring also influence the choice of AEDs. The increasing utilization of the new AEDs presents a fresh challenge of identifying new toxicities and drug interactions. For example, the increasing use of lamotrigine in Sweden resulted in an increase in the reports of adverse reactions to the drug.(Kimland et al., 1987).

It is estimated that 0.5-1% of children have epilepsy. (Zupanc, 1996) In spite of the recent advances in pharmacologic therapy and the development of an improved classification system, 25% of children who are diagnosed with epilepsy remain refractory to traditional therapy. [5] Pediatric epilepsy differs from adult epilepsy in terms of the etiologies, response to treatment and the level of impact of the illness on the patient and the family. Antiepileptic drugs (AEDs) as well as seizures are known to affect learning, schooling, social development and behavior. Twenty to thirty percent of children with epilepsy have learning difficulties. A careful and detailed assessment is required to tailor the treatment and educational programs. Seizures affect the personality and interfere with schooling and choice of career. Overall support for the child is an important aspect of management.(Aicardi & Arzimanoglou, 1996).

In clinical practice, it is well known that many children with epilepsy have cognitive problems, ranging from mild learning and school problems to mental retardation or even mental decline. Although these problems are also encountered in adults with epilepsy, the impact of epilepsy on developing cognitive processes is likely to be morepromiment. The proportion of children with cognitive problems is higher in refractory epilepsy. This already points to the possible deleterious effect of the epileptic process itself on cognitive

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development. In recent paper, it was shown that 16% of the children with refractory epilepsy, a normal IQ was found.(Weijenberg et al., 2010)

Epilepsy is one of the most common neurological conditions which occurs in about 5 to 8 cases per 1000 people per annum in developed countries (Ngug et al., 2010)

Epilepsy affects people of all ages and although treatable, often requires lifelong medication and sometimes surgery to control seizure. The high health care costs related to assessment and treatment, surgery and hospitalization for seizures, as well as lost employment, income, and household work, are well recognized. These costs vary according to the severity of the condition, response to treatment, length of time since diagnosis, and the perspective examined (e.g. health systems, societal or individuals and families). (Zupanc,1996)

Drug treatment forms one of the most important forms of therapy for a vast majority of epilepsy patients. Clinical experience has shown that AEDs can control high proportion of cases of epilepsy. However, there are certain general principles or guidelines should be followed to get the best results of medical management. Clinical practice has shown that a precise diagnosis when combined with better understanding of the mechanisms of action of AEDs gives the most effective use of drug treatment. Various factors like age of onset, seizure type and frequency, electroencephalography (EEG) and imaging results, etc. enable the neurologist to reach a precise syndromic diagnosis and to select the most appropriate AEDs for individual patient. Treatment is a reasonable compromise between benefits and toxicity, i.e., between control of seizures and side effects. It is important to explain to the patient and family members that various drugs may have to be used at various dosages to reach the best possible drug with appropriate dose. This will increase their cooperation during this chronic treatment. Whenever possible, the initial drug choice must be based on a specific syndromic diagnosis. (Aicardi & Arzimanoglou, 1996)

Childhood epilepsy poses unique challenges to the threading physician First of all, and more than in adults, epilepsy should be considered as a symptom of an underlying brain dysfunction and a thorough diagnostic work-up to be done in many children presenting with epileptic seizures. (Reynolds & Shorvon, 1981; Matricardi et al., 1989) This includes detailed neuroimaging genetic and tailored metabolic workup. Not uncommonly, this diagnostic workup together with the uncertainly about seizure type, delays the exact epileptic syndrome diagnosis. The purpose of the present review is to assessment of anti -epileptic drugs in pediatrics department in tertiary care hospital.

Materials and Methods

The patient demographics and all medically relevant information was noted in a predefined data collection form. Alternatively, these case charts were reviewed for potential drug interactions, drugs involved in interactions (dose, route, frequency, therapy duration, indication), laboratory investigations, followed up for assessing observed adverse drug interaction and pharmacist's intervention. The Micromedex, Medscape and references books were used as tools to review the prescription and case charts. The clinical pharmacist's intervention was done by suggesting physician about the drug related problems.

The study consisted of the following procedure:

- ✓ Selection of the topic.
- ✓ Literature survey.
- ✓ Approval from the institutional ethics committee and permission from the hospital was obtained before starting the study.
- ✓ The data consisted of drug names, dispensing dates, prescribing wards.
- ✓ Awareness about Drug-Drug interaction and spontaneous reporting to the concern authority.
- ✓ Case analyzed based on criteria for usage pattern of anti-conversant in pediatric patient and identify inappropriateness of medication in geriatric.
- ✓ The ages were classified as 4 class)
- ✓ Patients was classified in 2 groups rural area and urban area
- ✓ Drug-Drug interaction were detected using previously developed online interaction checker (Micromedex) database and Shockley's drug interaction book.
- ✓ Communicated with patient or attainder related to history of patients, herbal medicine, and nutraceutical
- ✓ Categorizing common drugs used in patient
- ✓ Categorizing common disease in male and females.

Result and Discusion

The present study was conducted in pediatric department and the sample size was 100, Out of 100 patients, 34(34%) of patients recruited were female and 66(66%) were male patients, 14(14%)of the patient were of the age group New born <1month and out of this age group 4(4%) was females and 10(10%)was males, 20(20%) were of 1month-2 years age group and out of this age group 6(6%)was females and 14(14%) was males.42(42%)were of 2-6 years age group and out of this age group16(16%)was females and 26(26%) was males , 24(24%) were of 6-12 years age group and out of this age group8(8%) was females and 16(16%) was males.

The study shows different type of seizure cases which was, out of 100 patients 60(60%) suffer from generalized seizure, 48(48%)were of generalized tonic-clonic seizuresgroup,7(7%)were of generalized tonic seizures group, 5(5%) were of Akinetic , absence and myoclonic seizures group, 40(40%) suffer from partial seizure, 10(10%) were of Simple partial seizures group,25(25%) were of Complex partial seizures group,3(3%) were of Temporal lobe seizures group,2(2%) were of Partial to general ,breath holding attacks and unclassified. TABLE1

Table 1: Distribution Of Diffrent Seizure Type Among 100 Patients

General seizures	No. in each group	(%) in each group
Generalized tonic-clonic seizures	48	48%
Generalized tonic seizures	7	7%
Akinetic,absence and myoclonic seizures	5	5%
Total generalized seizures	60	60%
Partial seizures	No. in each group	(%) in each group
Simple partial seizures	10	10%
Complex partial seizures	25	25%
Temporal lobe seizures	3	3%
Partial to general ,breath holding attacks and unclassified	2	2%
Total partial seizures	40	40%
Grand total seizures	100	100%

The average duration of hospital stay was about 3 days, minimum was 1 day and maximum was 5 days. Out of 100 patients ,16(16%)patient had stay on 1 day and out of this 10(15%) was male and 6(17%)was female, 26(26%) patient had stay on 2 days and out of this 18(27.2%) was males and 8 (23%) was females.31 (31%) patient had stay on 3days and out of this 11 (32. %) was females and 20 (30%) was males.15 (15%) patient had stay on 4 days and out of this 10 (15%) was males and 5 (14.7%) was females.12(12%) patients had stay on 5 days and out of this 8(2.12%)was females and4(12%) was males.

The study shows that the drug which was highly prescribed was Valproic acid followedby carbamazepine. Valproic acid is highly prescribed drug which is about 43(36.7%) followed by Carbamazepine 20(17.1%), Lamotrigin 11(9.4%), Phenobarbital10(7.7%), Topiramate 10 (8.5%), Phenytoin 8 (6.8%), Clobazam 5 (4.3%), Levetiracetam 5 (4.3%), and Vigabatrin 3(2.6%). TABLE 2

Table 2: Utilization Of Antiepileptic Drug In Pediatric Ward

Drug	Gender				Total	
	Male		Female			
	N	%	N	%	N	%
Carbamazepine	11	9.4%	9	7.7%	20	17.1%
Clobazam	3	2.6%	2	1.7%	5	4.3%
Clonazepam	2	1.7%	1	0.9%	3	2.6%
Lamotrigine	6	5.1%	5	4.3%	11	9.4%
Levetiracetam	3	2.6%	2	1.7%	5	4.3%
Phenytoin	5	4.3%	3	2.6%	8	6.8%
Phenobarbital	5	4.3%	4	3.4%	9	7.7%
Topiramate	5	4.3%	5	4.3%	10	8.5%
Valproic acid	28	23.9%	15	12.8%	43	36.7%
vigabatrin	2	1.7%	1	0.9%	3	2.6%
Total	70	59.8%	47	40.2%	117	100%

As the prescription error plays a major role in incidence of harm to the patient it become important to generated a prescription related error report, which shows that 31% prescription contains drugs without generic name, 27% contains inappropriate abbreviation, 15% prescription not legible, 10% mislabeling, 9% frequency not defined, 9% variation in dose, 4% route not mentioned, 3% not in capital letter, 3% without signature or name of physician.

The study shows that in 100 prescriptions 52 drug interaction was there out of which 15(28.8%) was Major, 20 (38.5%) was moderate, and 17 (32.7%) minor. Further drug interaction was categories as Pharmacokinetic and pharmacodynamics interaction it was found that there was 28 pharmacokinetic and 26 pharmacodynamics interactions. It was noted that there was major interaction drugs Clonazepam, Phenytoin, Phenobarbital, Clobazam with Carbamazepine. TABLE 3, 4. The study has shown there was 5% incidence of ADR which includes drugs Levetiracetam causing Loss of appetite, Phenytoin causing anemia and Clobazam causing Steven Jonson syndrome.

Table 3: Severity And Mechanism Of Drug Interaction

Drug-drug interaction	Type of interaction	Total	(%) Total
Severity	Major	15	28.8%
	Moderate	20	38.5%
	Minor	17	32.7%
	Total	52	100%
Pharmacokinetic Interaction	Absorption	9	32.2%
	Distribution	5	17.8%
	Metabolism	13	46.5%
	Excretion	1	3.5%
	Total	28	100%
Pharmacodynamic Interaction	Synergism	18	70%
	Antagonism	8	30%
	Neutralization	0	0
Total		26	100%

Table 4: Effect Of Some Important Drug-Drug Interaction

Drug-drug interaction	Interaction effect	Severity	Management
Carbamazepine+ clonazepam	Reducing plasma levels of clonazepam	Major	Monitoring clonazepam plasma level
Carbamazepine+ phenytoin	Decreasing phenytoin and carbamazepinconcentration	Major	Monitor both dosage
Clonazepam + phenobarbital	Additive respiratory depression	Major	Reduction in dose of one or both drugs
Phenobarbital+ clobzam	Additive respiratory depression	Major	Monitor both dosage
Carbamazepine+ Ehosuximide	Loss of efficacy of ethosuximide	Moderate	Monitor, dose adjustment
Carbamazepine+ levetiracetam	Carbamazepine toxicity	Moderate	Monitoring
Carbamazepine+ phenobarbital	Decreased carbamazepine exposure	Moderate	Monitoring
Carbamazepine+ Valproate acid	Carbamazepine toxicity	Moderate	Monitoring for carbamazepine
Ethosuximide+ phenobarbital	Decreased ethosuximide serum concentration	Moderate	Monitoring
Ethosuximide+ Valproate acid	Increased risk of ethosuximide toxicity	Moderate	Monitoring

Phenobarbital+ Valproate acid	Phenobarbital toxicity	Moderate	Monitoring for phenobarbital toxicity
Phenytoin+ clobazam	Increased risk of phenytoin toxicity	Moderate	Monitoring for phenytoin toxicity
Phenytoin+ Valproate acid	Altered valproate acid	Moderate	Monitoring

While doing drugs economic behavior study it was concluded that Phenytoin, Levetiracetam and Valproic acid was very costly drug compare to Phenobarbital and Carbamazepine though the drugs have low side effect but was 10 times as much costlier than regular drugs.

Conclusion

This study is an attempt to evaluate the Antiepileptic drug prescribing and usage in pediatric ward of tertiary care hospital. The study result shows that majority seizures cases was in male patient which may be because of higher male is to female ratio. And the age group was highly affected was between 2to 6 year-old children's. Generalized tonic clonic seizures was almost half of the diagnosis and complex partial seizures account one fourth of total diagnosis. It was concluded that Valproic acid was highly prescribed drug and Carbamazepine was second highly prescribed drug. It was found that majority of prescription was without generic name and with inappropriate abbreviations. Study shows that carbamazepine was interacting with Phenytoin, Phenobarbital, clonazepam and clobazam and those were major interactions. In the study it was noted that adverse drug reactions were due to drug interaction and drugs involved were levetiracetam, phenytoin and clobazam. While doing economic analysis it was concluded that that Phenytoin, Levetiracetam and Valproic acid was most costly drugs used in treatment of similar kind of seizure disorder even though the cheaper alternative phenobarbital and carbamazepine was available for the treatment.

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