Original Research Article

A Study to Record & Assess the Incidence of Adverse Drug Reactions in Pediatric Patients on Antiepileptic Drugs Reporting in a Tertiary Health Care Center of Central India

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Abstract

Objective: To record & assess the incidence of Adverse drug reactions(ADRs) in pediatric patients on antiepileptic drugs(AEDs) reporting in a tertiary health care center of central India.

Method: A prospective observational study was undertaken for a period of 6 months between February 2019 to August 2019 to analyze adverse drug reactions due to antiepileptic drugs in pediatric department of a tertiary care hospital. Pediatric patients upto18years old were enrolled. Other parameters like most common class of drug causing ADR, common types of ADRs, commonly involved systems, comparison of ADRs in patients on monotherapy versus polypharmacy were studied. Two patients were discontinued from therapy due to ADRs and in 2 patients, dose had to be reduced.

Result: A total of 83patients were studied in the study duration where in a Total of 646 ADRs were reported. 6 various types of antiepileptic drugs were prescribed among which most frequently prescribed drugs were Midazolam (34.93%), Phenytoin (31.32%), Sodium Valproate (25.30%), Levetiracetam (7.22%). Patients on monotherapy were 34%,dual therapy 38%,triple therapy 21% and on polytherapy 7%. Most frequently reported ADRs with Monotherapy were fatigue & drowsiness. Central nervous system was most commonly affected followed by gastrointestinal system, skin &mucosa, urogenital system and miscellaneous ones like weight gain, rise in transaminase level and hematological changes.

Incidence of Slow thinking and decreased concentration was reported less with levetiracetam than valproic acid.2 patients were Discontinued from therapy due to ADRs and in 2 patients, dose had to be reduced.

Conclusion: AED-related adverse effects have high impact on the overall functioning and quality of life of children and affect their physical and psychosocial aspects of life. These factors need to be important considerations in selecting appropriate drug, dosage, dosage schedule, changes in dosages and schedules appropriately accordingly so that normal routine and quality of life is affected as minimal as possible. Also, If ADRs occur, appropriate actions are taken accordingly.

Keywords: ADR, AED, Pediatric Patients, Dual therapy

Introduction

Most children with new-onset epilepsy, especially those with idiopathic generalized epilepsies, achieve seizure freedom with appropriate antiepileptic drugs (AEDs). About 20 % of children with epilepsy will only experience a few seizures in the context of an idiopathic focal syndrome before spontaneous epilepsy remission [1].

However, nearly 20 % of the pediatric epilepsy population will continue to experience seizures despite AEDs, as either monotherapy or in combination [2].

As per WHO epilepsy is defined as occurrence of transient paroxysm of excessive or uncontrolled discharge of neuron which may be due to number of causes leading to epileptic seizures [3].

More than 50 million people worldwide are affected with epilepsy, making it one of the most common neurological diseases globally. It is estimated that there are more than 10 million cases of epilepsy in India [4]. Around 4-10% of children suffer at least one seizure in the first 16 years of life. The incidence is highest in children below 3 years of age, with a decreasing frequency in older children [5]. Treatment with AEDs is the most widely and commonly approachable choice for the management of epilepsy and different types of seizures irrespective of age and gender. The selection of therapy and drug of choice varies from Centre of healthcare as it is based upon the group of patients being treated, standard treatment guidelines that are followed and availability of drugs designed in the hospital formulary by the drug and therapeutic committee on the governing body [6].

Alongside its significant beneficial effects, evidence also indicates that AEDs may have varied adverse effects that may predominantly affect the cognitive functions, emotional well-being, as well as the motor and somatic functions [7].

There is a prevailing opinion that numerous developmental, psychological, behavioral, educational, and social disabilities among children and adolescents, who are being treated for epilepsy, could be partially explained by the adverse effects of AEDs [8,9].

This opinion garners particular credence when one considers that adverse events occur in up to 32% of the treated pediatric patients according to some studies [10].

The age of onset of epilepsy, the severity of seizures, the worry/concerns of the family and the psychological impact on them, as well as the cognitive impairment prevailing in children who are suffering from epilepsy, may all influence the quality of life in pediatric epilepsy. A recent review summarizing various studies related to this field has shown that AEDs may also have a negative impact on the child's well-being and daily functioning [11].

The level of well-being and functioning may be predicted by the actual number of AEDs being given as well as by the AED-related adverse effects [12][13].

Adverse effects are frequently reported in pediatric epilepsy; and, the higher the number of AEDs taken, more is the likelihood that adverse effects would occur [14].

Methodology

A prospective observational study was undertaken for a period of 6 months between February 2019 to August 2019 to analyze adverse drug reactions due to AEDs in pediatric department of a tertiary care hospital wherein, ADRs were diagnosed by Pediatrician. Pediatric patients upto18years old were enrolled.83 patients were included in the study data. 2 patients were discontinued from therapy due to ADRs and in 2 patients, dose had to be reduced. The data was recorded as per recent version of standard ADR form

obtained from Central Drug Standard Control Organization (CDSCO) website.

Other parameters like most common class of drugs causing ADR, common types of ADRs, commonly involved systems, comparison of ADRs in patients on monotherapy versus polypharmacy were studied.

Results and Discussions

A total of 83patients were studied in the study duration where in a Total of 646 ADRs were reported.

As shown in figure -1, 6 various types of antiepileptic drugs were prescribed among which most frequently prescribed drugs were Midazolam (34.93%), Phenytoin (31.32%), Sodium Valproate (25.30%), Levetiracetam (7.22%).

Patients on monotherapy were 34%, dual therapy 38%, triple therapy 21% and on polytherapy 7% as shown in figure -2.

As depicted in figure-3, most frequently reported ADRs with Monotherapy were fatigue, drowsiness, dizziness, gastrointestinal distress. Central nervous system was most commonly affected followed by gastrointestinal system, skin &mucosa, urogenital system and miscellaneous ones like weight gain, rise in transaminase level and hematological changes (microcytic anemia &leukocytosis). Incidence of Slow thinking and decreased concentration was reported less with levetiracetam than valproic acid. 2 patients were Discontinued from therapy due to ADRs and in 2 patients, dose had to be reduced.
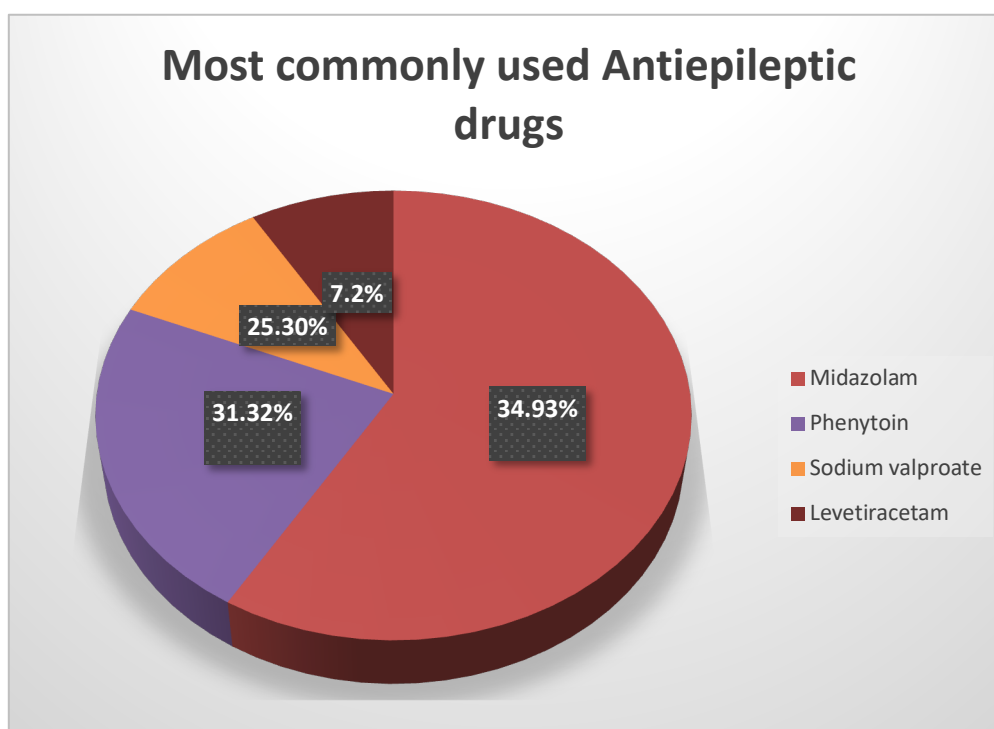
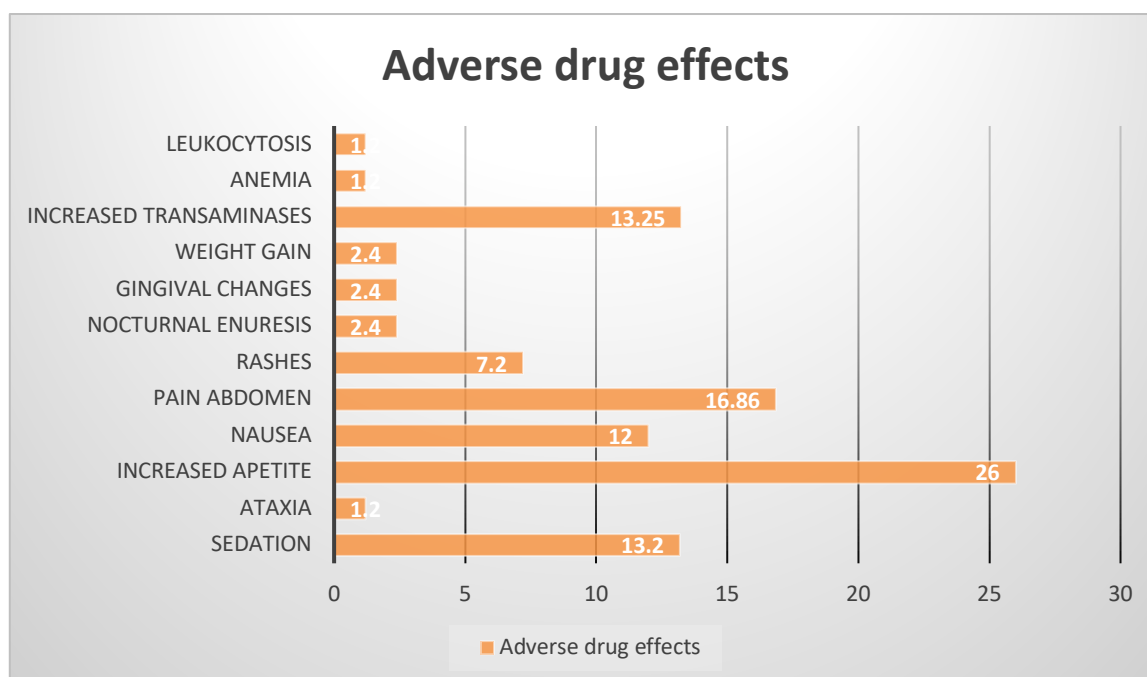**Figure 1: Most commonly used Antiepileptic drugs**

Inference

Most commonly used drug was found to be Midazolam (34.93%), followed by Phenytoin (31.32%), sodium valproate (25.30%) and levetiracetam (7.2%).
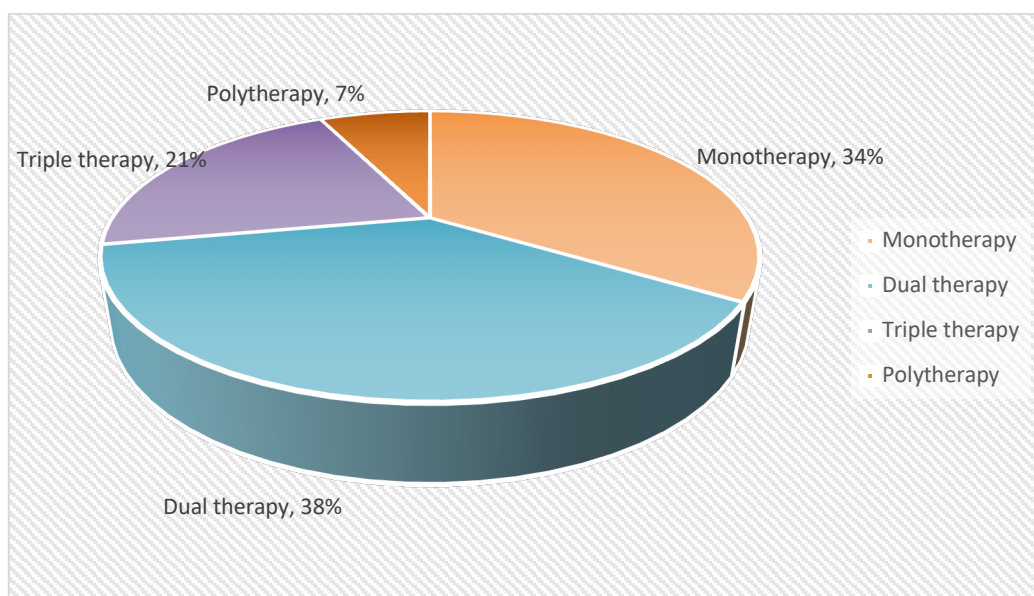
Figure 2: Distribution of various modes of therapy

Inference

Commonest mode is dual therapy (38%) followed by monotherapy (34%), triple therapy (21%), least common was polytherapy (7%

Figure 3: Frequency of various adverse effects

Discussion

In this study total 83 patients were included & in them 646 ADRs were reported in a period of 6 months.

In recent past some newer anticonvulsants (lamotrigine, topiramate, gabapentin) have been approved in several countries as "add on" drugs for control of refractory seizures but these medicines are very costly & inaccessible in most developing countries [15].

In developed countries more expensive AED like carbamazepine & valproic acid have become first line drugs due to lower risk of long-term side effects including cognitive impairment in children [15].

In our study midazolam (34.93%) was most commonly prescribed, this is in contrast to study of Lakshmi Prathyusha *et al*.where they reported valproate as commonest drug prescribed [16] whereas Dave *et al*.found it to be carbamazepine [17].

In our study phenytoin (31.32%) was next common drug prescribed, this finding is consistent with study of Lakshmi Prathyusha *et al*. [16].

In our study sodium valproate (25.30%) was third commonest drug prescribed followed by levetiracetam (7.22%) whereas Dave *et al*. reported sodium valproate second commonest drug prescribed [17].

About 75 -80% of people with epilepsy can be managed easily with one drug, this is known as monotherapy which checks interactions between drugs ensuring better compliance along with cost effectiveness [18].

In our study most common mode/ pattern of therapy was dual therapy (38%) which is in contrast to study of Lakshmi Prathyusha *et al* [16]. & Dave *et al*. [19] where they reported monotherapy as most common mode/pattern of prescription.

In our study monotherapy was second commonest mode (34%) followed by triple therapy (21%), polytherapy (7%) was least common mode, this finding is similar to finding of Lakshmi Prathyusha *et al*.[16]

In our study increased appetite (26%) was reported as most common ADR due to AED

Whereas Mudasir Maqbool *et al*. reported loss of appetite as most common ADR. [20], Anderson *et al*. reported behavioral problem & somnolence as commonest ADR [21].

Pain in abdomen was next common ADR reported in our study which is consistent with finding of Saurabh Nimesh [22].

Incidence of slow thinking & decreased concentration was reported less with levetiracetam than valproic acid, In two patients therapy was discontinued due to ADRs & in two patients dose was reduced

Conclusion

There is broad spectrum of ADRs due to antiepileptic drugs .The pediatric population is especially very sensitive to these ADRs because of immature metabolic machinery . These factors need to be important considerations in selecting appropriate drug, dosage, dosage schedule, changes in dosages and schedules appropriately accordingly so that normal routine and quality of life is affected as minimal as possible. It is the responsibility of clinician to keep update their knowledge about the possible ADRs due to antiepileptic drugs. Such pharmacovigilance studies are very essential in this regard. Clinician should honestly report ADRs & communicate to ADR monitoring centers . These information are very crucial for policy makers & to boost up national pharmacovigilance system.

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