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Research Article

STUDY OF UTILIZATION PATTERN AND DRUG INTERACTIONS OF ANTI-EPILEPTIC DRUGS IN A PRIVATE HOSPITAL

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ABSTRACT

Objective: This study attempts to get an insight into the utilization pattern of anti-epileptic drugs (AEDs) and their drug interactions in cases collected from the neurology department in a private hospital. **Methods:** In a prospective study spanning 6 months (February-August 2013), we have analyzed the prescription data of 38 patients with seizures. We retrieved prescription data from patient profile forms and documented essential data in a patient profile form, designed for our study. The demographic data, AEDs prescribed and their drug interactions were recorded. **Results:** Of 38 cases, 32 (84.21%) were males and 6 (15.78%) were females. The mean age of patients was 40 years, and 50% of them belongs to an age group of above 40 and 45% belongs to age group below 40. Above the age group of 40, 95% were males and 5% were females. Below the age group of 40, 72.22% were males and 27.77% were females. From the 38 prescriptions analyzed, phenytoin was the most common drug prescribed (92.10%) for the treatment, followed by diazepam (36.84%) and sodium valproate (7.89%). Monotherapy was given in 57.89% of patients. The overall incidence of drug interactions was 13 out of 38 cases. In this study, milder drug interaction (phenytoin with ranitidine) was found to be 52.63%, and moderate drug interaction (phenytoin with diazepam) was found to be 39.47%. **Conclusion:** This study revealed that phenytoin, diazepam, and ranitidine accounted for most of the drug interactions. This study concludes that patient education and observation were necessary for proper utilization of drugs.

Keywords: Anti-epileptic drugs, Prescription, Drug interactions, Patient education.

INTRODUCTION

Epilepsy is a common neurological disorder which demands immediate medical attention and often long-term therapy. The overall aim in treating epilepsy should be complete control of seizures, without causing any untoward reaction due to the medication. A recent study in Bangalore, India, reported that the problem is nearly 2½ times higher in rural areas as compared to urban areas [1,2], where they are not receiving any treatment. Monotherapy is the usual dictum, but polytherapy is needed for patients with multiple seizure types or refractory 18 diseases.

An epileptic seizure is a transient paroxysm of uncontrolled discharges in neurons causing an event that is discernible by the person experiencing the seizure and/or observer. Epilepsy is a medical condition with recurrent, unprovoked seizures [3,4].

Epileptic seizures have many causes, including a genetic predisposition for certain seizures, head trauma, stroke, brain tumors, alcohol or drug withdrawal, and other [4,5] conditions. The interest in drug utilization studies began in the early 1960s, and its importance has increased since then due to increase in marketing of new drugs, wide variation in the pattern of drug prescribing and consumption, growing concern about delayed adverse effects and the increasing [6] concern regarding the cost of drugs.

Drugs such as gabapentin, lamotrigine, vigabatrin, topiramate, tiagabine, and zonisamide are the newer ones and currently used as ad-donor alternative therapy. They have lesser adverse effects and have few, if any, drug interactions [7-9].

Some side effects may be common with the above-mentioned drugs and include sedation and ataxia. They can be diverse as well, ranging from idiosyncratic reactions like bone marrow depression (carbamazepine) to acute myopia and glaucoma (topiramate). Monotherapy is the usual dictum, but polytherapy is needed for patients with multiple seizure types or refractory disease [10-12]. In contrast to other studies, our study revealed frequent use of newer anti-epileptic drug (AED) namely topiramate as an adjuvant [12,13].

Epilepsy is the most common serious neurological disorder affecting an estimated 50 million people worldwide. Particular focus should be placed on a safe diagnosis, seizure and syndrome classification, and choice of pharmacological and surgical options for a range of patient populations with different health-care requirements [14]. Epilepsy is not a disease, but it is a syndrome of different cerebral disorders of the central nervous system which is characterized by excessive discharges of large numbers of neurons [15-17]. It is very disabling condition, rendered especially disturbing because of its unpredictability and it is being a common neurological disorder worldwide [18]. Serious adverse events have been associated with felbamate and lamotrigine, however, and more experience is needed with many of the other newer AEDs to better define their safety profiles. Monotherapy should be the goal when AED treatment is instituted for the adult with epilepsy.

The drawback of polypharmacy is a higher incidence of adverse effects, drug interactions, and added costs. The latter constitutes an economic burden on the patients in addition to the existing psychological medical and social burden [19,20]. The liver is the primary organ for drug metabolism and elimination for many AEDs and thus is subjected to drug-induced toxicity. There is a wide range of hepatotoxic reactions, from mild and transient elevations of hepatic enzymes to fatal hepatic failure. There are two types of drug interactions between drugs such as pharmacokinetic and pharmacodynamic. For AEDs, pharmacokinetic interactions are the most notable type, but pharmacodynamic interactions involving reciprocal potentiation of pharmacological effects at the site of action are also important. By far the most important pharmacokinetic interactions are those involving cytochrome P450 isoenzymes in hepatic metabolism. Among old generation AEDs, carbamazepine, phenytoin, phenobarbital, and primidone induce the activity of several enzymes involved in drug metabolism, leading to decreased plasma concentration and reduced pharmacological effect of drugs, which are substrates of the same enzymes (e.g., tiagabine, valproic acid, lamotrigine, and topiramate). In contrast, the new AEDs gabapentin, lamotrigine, levetiracetam, tiagabine, topiramate, vigabatrin, and zonisamide do not induce the metabolism of other AEDs.

Interactions involving enzyme inhibition includes the increase in plasma concentrations of lamotrigine and phenobarbital caused by valproic acid. Among AEDs, the least potential interaction is associated with gabapentin and levetiracetam.

Individual AED interactions may be divided into three levels depending on the clinical consequences of alterations in serum concentrations. This approach may point to interactions of specific importance although it should be implemented with caution as it is not meant to oversimplify fact matters. Level 1 involves serious clinical consequences, and the combination should be avoided. Level 2, usually, implies cautiousness and possible dosage adjustments, as the combination may not be possible to avoid. Level 3 refers to interactions where dosage adjustments are, usually, not necessary. Updated knowledge regarding drug interactions is important to predict the potential for harmful or lacking effects involving AEDs.

METHODOLOGY

Study site
This study was conducted in Private Hospital, Erode, Tamil Nadu. It is an 800 bedded Tertiary Care Hospital, providing specialized health care services to all strata of people in and around erode and also the rural population.

Study design
This is a hospital-based prospective observational study conducted on in-patients to review the current prescribing pattern of AEDs and their drug interactions in patients with epilepsy admitted to the neurology department.

Sample size
A total of 38 cases was collected from the neurology department and the data were collected in a well-designed proforma.

Study period
A prospective study was conducted for a period of 6 months from February to August 2013.

Study criteria
Inclusion criteria
Patients with seizures, of both sex and all age groups, who are prescribed an AEDs, are included in the study.

Exclusion criteria
Patients with status epilepticus and seizures associated with acute conditions like paralytic stroke and coma are excluded.

Source of data

Data were collected using a well-designed patient data collection form.

By reviewing the patient's treatment chart and case sheets of the patients

Preparation of data collection form
Information extracted from the case files included: Demographic data, chief complaint, if he/she is a known case of epilepsy and etiology of seizure, habits (smoker/alcoholic/food habits), past medical history and past medication history, family history, laboratory details, diagnosis (provisional or confirmatory). Treatment: AEDs prescribed and prescription of the AEDs by generic names. The recommended dosages of the AEDs were obtained from the patient case files and discharge summary.

Statistical method
The data of each case file were collected and analyzed by a percentage method.

Prescribing indicators include
1. Most commonly prescribed AEDs in this study
2. Number of AEDs prescribed using generic names
3. Analysis of drug interactions in prescription.

Patient indicators include
1. Total number of male and female patient
2. Average age of male and female patients
3. Number of patients receiving monotherapy and multiple AEDs, respectively.

RESULTS AND FINDING

The study includes 38 epileptic patients on anti-epileptic among whom 32 (84.21%) patients were found to be male and 6 (15.78%) patients were females (Fig. 1).

The mean age of patients was 40 years, and 50% of them belongs to the age group above 40 and 45% belongs to age group below 40. Above the age group of 40, 95% were males and 5% were females (Fig. 2). Below the age group of 40, 72.22% were males and 27.77% were females. From the 38 prescriptions analyzed, phenytoin was the most common drug prescribed (92.10%) for the treatment, followed by diazepam (36.84%) and sodium valproate. (7.89%) (Fig. 3) Monotherapy was given in 57.89% of patients. The overall incidences of drug interactions were 13 out of 38 cases. In this study, milder drug interaction (phenytoin with ranitidine) was 52.63%, moderate drug interaction (phenytoin with diazepam) was 39.47% (Fig. 4).

DISCUSSION

The advances in the therapeutically aspects of epilepsy and the efficacy of monotherapy versus combination therapy have not been extensively

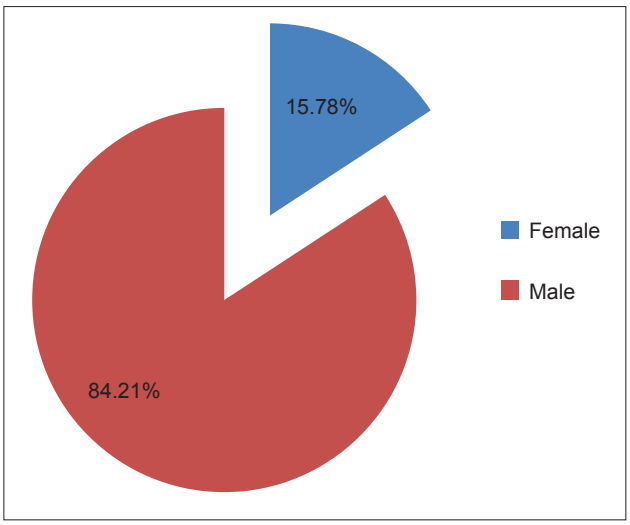

Fig. 1: Graphical representation of the distribution of 38 epileptic patients based on the gender

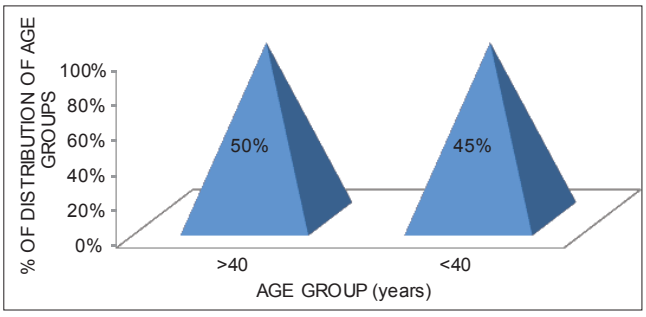

Fig. 2: Graphical representation of the distribution of age groups

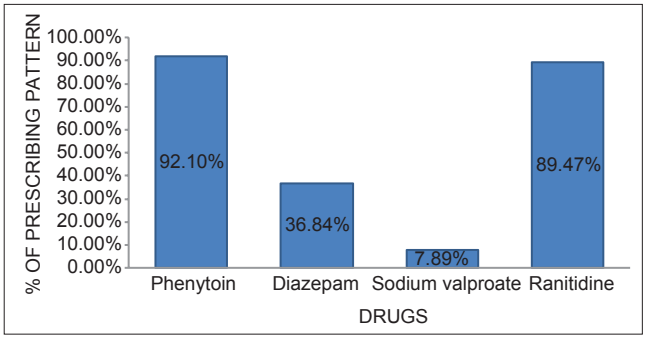

Fig. 3: Graphical representation of prescribing pattern of drugs in a private hospital

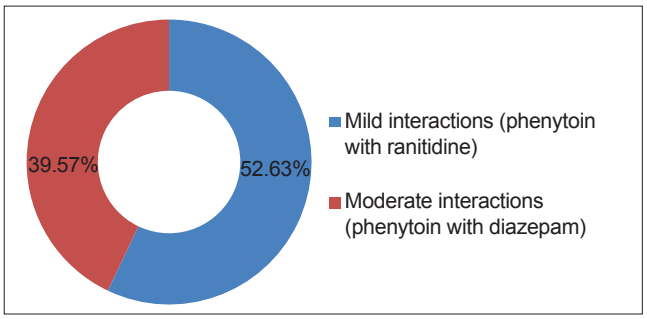

Fig. 4: Graphical representation of drug interactions among the 38 prescriptions

studied. In this study, we were able to make inferences with regard to the most commonly prescribed AEDs, the different age group distribution, drug interactions, and the gender most likely affected. A total of 38 epileptic patients was included. The incidence of epilepsy was found to be higher in male than in females and also the incidence of epilepsy increases with an increase in age. It was observed that phenytoin was the most frequently prescribed drug followed by diazepam and sodium valproate. phenytoin was widely prescribed in our study, unlike another South Indian study by Radhakrishnan, where it was underutilized, in spite of being less expensive [6,7]. The above studies justify the use of phenytoin because it was as equally effective as other AEDs when used in monotherapy with very less incidences of adverse drug reactions, and also the cost was least.

CONCLUSION

An epileptic episode occurs more in the age group of above 40 years. Monotherapy was preferred in most of the cases. Phenytoin was the most frequently prescribed AEDs followed by diazepam and sodium valproate. The milder drug interactions were more common than moderate drug interaction. Our study revealed that phenytoin, diazepam, and ranitidine accounted for most of the drug interactions. This study concludes that patient education and observation were necessary for proper utilization of drugs.

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