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ANTIEPILEPTIC DRUGS USED IN DIFFERENT TYPES OF EPILEPSY IN CHILDHOOD EPILEPTIC PATIENTS IN CHILDREN HOSPITAL AND INSTITUTE OF CHILD HEALTH LAHORE AND ITS COMPARISON WITH INTERNATIONAL STUDIES

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Objective: This study was under taken for the evaluation of pediatric epileptic patients and to determine the antiepileptic drugs used in treatment of different epilepsy types and its comparison with other studies. **Method:** This prospective study was conducted in the Neurology Department of the Children Hospital Lahore. A questionnaire was developed for collection of data. Three hundred patient's upto fifteen years of age with uncomplicated epileptic seizures were included in study. Data was analyzed by routine statistical methods. **Results:** Commonly encountered cases were of tonic clonic seizures 39%, myoclonic 12%, petitmal 11% and complex partial seizures 9%. Results shows that most commonly prescribed drug was valproic acid used in 67% cases. Valproate was also administered in combination with Topiramate, Lamotrigene, Clonazepam and Phenobarbitone.Carbamazepine was also found to be administered along with valproate, topiramate, Phenobarbitonea and Lamotrigene. Patients stable on monotherapy were 57 % and those stable on combination therapy are 43%. **Conclusion:** The tonic clonic seizure is most common in pediatric epileptic patients and for its treatment most recommended medicine is valproate. A study conducted in Iran reveals that phenobarbitone is the commonest antiepileptic drug (33.7%) because of its broad antiepileptic action and economical price. So it is concluded that proper selection of economical antiepileptic drug must be done for the proper treatment of epileptic patient and monotherapy should be encouraged as compare to combination therapy.

Key words: Epilepsy, Tonic clonic seizures, Monotherapy, Valproate

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INTRODUCTION

Epilepsy is a complex symptom caused by a variety of pathologic processes in the brain. It is characterized by occasional (paroxymal), excessive, and disorderly discharging of neurons, which can be detected by clinical manifestations, electroencephalographic recording or both **[1]**. Epilepsy is the third most common neurological disorder, following stroke and Alzheimers disease. The incidence is higher in first two decades of life but falls over the next few decades, only to increase again in late life, owing mainly to cerebrovascular diseases **[2, 3]**. This study was under taken for the evaluation of pediatric epileptic patients and to determine the occurrence of epileptic seizures,

antiepileptic drugs used in treatment of different epilepsy types and its comparison with other studies, and to determine the percentage of patients on monotherapy to emphasize its importance.

The particular symptoms produced in epilepsy depend on the function of the region of the brain that is affected. Thus involvement of the motor cortex causes convulsions; involvement of the hypothalamus causes peripheral autonomic discharge, and involvement of the reticular formation in the upper brainstem leads to loss of consciousness **[4, 5]**.

INTERNATIONAL CLASSIFICATION OF EPILEPTIC SEIZURES [6].

Partial (Focal, Local) Seizures

Some common forms of partial epilepsy arise months to years after cortical injury sustained as a consequence of stroke, trauma, or other factors. An effective prophylaxis administered to patients at high risk would be highly desirable. The drug inhibits seizures in patient with epilepsy **[7]**.

Selective inhibition of neuronal firing would be expected to reduce seizures with minimal unwanted effects. Carbamazepine, lamotrigine, phenytoin, and valproic acid inhibit high-frequency firing at concentrations known to be effective at limiting seizures in humans **[8]**.

Simple Partial Seizures (SPS)

Simple partial seizures are caused by a local cortical discharge that results in seizure symptoms appropriate to the function of the discharging area of brain, without impairment of consciousness.The distinguishing characteristic of SPS is that the patient remains conscious **[9]**.

Complex Partial Seizures (CPS)

The central features of CPSS are impairment of consciousness. A CPS may begin with a simple partial seizure with or with out aura, followed by impaired consciousness. The average duration of a CPS is 1-2 min, which is considerably longer than an SPS or an absence seizure.

Secondarily Generalized Seizures

These are partial seizures, either simple or complex, in which the focal discharge spreads to the entire brain. The involvement of the entire brain leads to a convulsive attack with the same characteristics as a generalized tonic-clonic convulsion explained below in detail **[10]**.

Generalized Seizures

In contrast to partial seizures, which arise from localized regions of the cerebral cortex, generalized-onset seizure arises from the reciprocal firing of the thalamus and cerebral cortex.

Tonic - Clonic (Grand Mal) Seizures

Tonic-clonic seizures consist of an initial increase in tone of certain muscles (tonic phase) followed by bilateral symmetric jerking of the extremities (clonic phase). Tonic-clonic seizures most often occur as part of localization-related/symptomatic (partial, focal) epilepsy.

Absence (Petit Mal) Seizures

Simple (typical) absence (petit mal) seizures are characterized by a sudden cessation of motor activity or speech with a blank facial expression and flickering of the eye lids **[11]**.

Myoclonic Seizures

Myoclonic seizures are characterized by sudden, brief (less than 350 μsec), shock like contractions that may be generalized or confined to the face and trunk, or to one or more extremities, or even to individual muscles or groups of muscles **[12]**.

Tonic and Atonic Seizures

Tonic seizures are brief seizures consisting of the sudden onset of increased tone in the extensor muscle. If standing, the patient typically falls to the ground. The duration of these seizures is longer than Myoclonic seizures **[13]**.

Clonic Seizures

Clonic seizures occur almost exclusively in neonates and young children. The attack begins with loss or impairment of consciousness, associated with sudden hypotonia or a brief, generalized tonic spasm.

Infantile Spasms (West Syndrome)

Infantile spasms are an age specific disorder occurring only in children during the first 2 years of life. The peak age of onset is between 4 and 6 months, and approximately 90% of infantile spasms begin before 12 months of age **[14, 15]**.

Status Epilepticus

Status epilepticus is defined as a continuous convulsion lasting longer than 30 min or the occurrence of serial convulsions between which there is no return of consciousness **[16]**.

MATERIALS AND METHODS

The Study Area

The study was conducted in the Neurology Department of The Children's Hospital, Lahore.

Inclusion Criteria

Patients up to fifteen years of age visiting neurology department of the children hospital Lahore during the period of seven months, having an uncomplicated epileptic seizures like tonic clonic, tonic, clonic, atonic, petitmal, simple and complex partial seizures etc, declared through clinical examination and specialized diagnostic procedures including EEG and serum electrolyte test, under the supervision of neurologists were included in the study.

Exclusion Criteria

Patients with other under lying complications like T.B of brain, meningitis, or cases of neurosurgery like hydrocephalous were excluded from the study. Moreover patient having critical condition (Shock) were also excluded.

Study Design

This prospective study involves the detailed interview of patient / parent about his epileptic seizures, antiepileptic drugs administer to him on specially design Performa in out door of neurology department **[17, 18]**.

RESULTS

Occurrence of Epileptic Seizures

Demographic data on disease occurrence in epileptic patients of Children's Hospital Lahore, is shown in Table 1. The table indicates occurrence of simple partial, complex partial and secondary generalize seizures is 3, 9 and 7 percent respectively. While occurrence of tonic clonic, tonic, clonic, myoclonic, petitmal, atonic, infantile spasm, is 39, 6, 3, 12, 11, 6, 4 percent respectively.

Different Treatments used in Generalize Seizures

Different treatments used in tonic clonic, tonic and clonic seizures are given in Table 2. Graphical representation of these treatments is given in Figure 1. While table 3 shows different treatments used in myoclonic, petitaml, atonic and infantile spasm and its graphical representation is given in figure 2.

Different Treatments used in Partial Seizures

In this clinical study of pediatric epileptic patients different treatments used in partial seizures like simple partial seizures (SPS), complex partial seizures (CPS) and secondary generalize (Sec generalize) seizures, are given in Table 4 and graphical representation is given in Figure 3.

Monotherapy and Combination Therapy

In different epileptic seizures percentage of patients taking monotherapy and combination therapy were shown in Figure 4 and 5 respectively. Mean of percentage of patients on monotherapy and combination was 57 ± 31 and 43 ± 31 respectively.

DISCUSSION

In our prospective study partial seizures were found 19% and generalized seizures were found in 77% patients and infantile spasm in 4 % cases. The most common type of epilepsy was tonic clonic seizure 39%, complex partial seizure are 9% myoclonic seizure were 12% and peptit mal seizure were 11 % as shown in table No 1. In a study by koul et al conducted in rural Kashmir partial seizures were found 12% and generalized seizures were 79% **[19]**.

Table 1: Occurrence of epileptic seizures

Type of Seizure	Percent prevalence
Simple partial seizure	3
Complex partial seizures	9
Sec generalized seizures	7
Tonic clonic seizures	39
Tonic seizures	6
Clonic seizures	3
Myoclonic seizures	12
Petit mal seizures	11
Atonic seizures	6
Infantile spasm	4

In tonic clonic seizures valproate was used in 39% cases and carbamazepine was used in 15.4% cases. The combination of valproate with topiramate and lamotrigene was used in 15 and 13 % cases respectively. In tonic seizures valproate carbamazepine and phenobarbitone were used in 33, 17 and 17% cases respectively, while the combination of carbamazepine +clobazam was used in 33 % cases. In clonic seizures valproate was used in 33% cases and combination of valproate and lamotrigene was used in 67% cases as shown in table No 2.

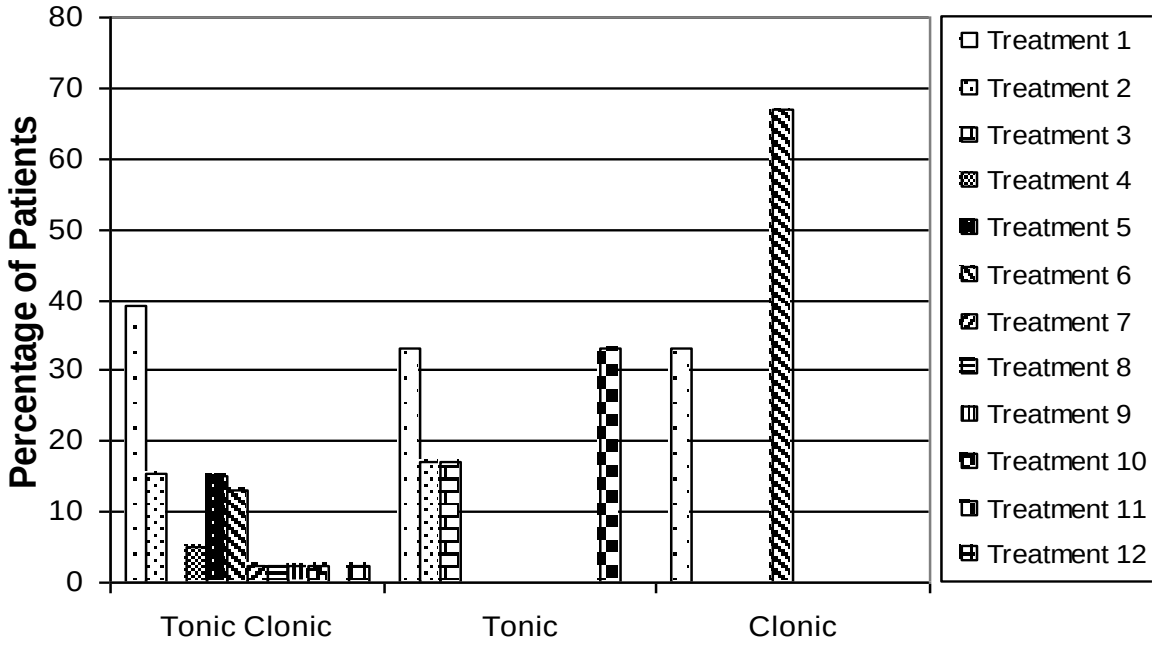

Figure 1: Different treatments used in tonic clonic, tonic and clonic seizures

Table 2: Various treatments used in tonic clonic, tonic and clonic seizures

Treatments	Drugs used	Tonic Clonic	Tonic	Clonic
Treatment 1	Valproate	39	33	33
Treatment 2	Carbamazepine	15.4	17	0
Treatment 3	Phenobarbitone	0	17	0
Treatment 4	Topiramate	5	0	0
Treatment 5	Valproate+Topiramate	15	0	0
Treatment 6	Valproate+Lamotrigene	13	0	67
Treatment 7	Valproate+Phenobarbitone	2.5	0	0
Treatment 8	Carbamazepine+Valproate	2.5	0	0
Treatment 9	Carbamazepine +Topiramate	2.5	0	0
Treatment 10	Carbamazepine +Phenobarbitone	2.5	0	0
Treatment 11	Carbamazepine+Clobazam	0	33	0
Treatment 12	Phenobarbitone+Clonazepam	2.5	0	0

In myoclonic seizures valproate was used in 42% cases. Combination of valproate + clonazepam and combination of phenobarbitone + clonazepam were used in 25, 25% cases. For petit mal seizures valproate was used in 82 % cases and for atonic seizures valproate was used in 83% cases. In infantile spasm combination of valporate + clonazepam was used in 25% cases, combination of valporate + clonazepam + prednisolone was used in 25% cases and combination of phenobarbitone + clonazepam was used in 50% cases as shown in table No 3.

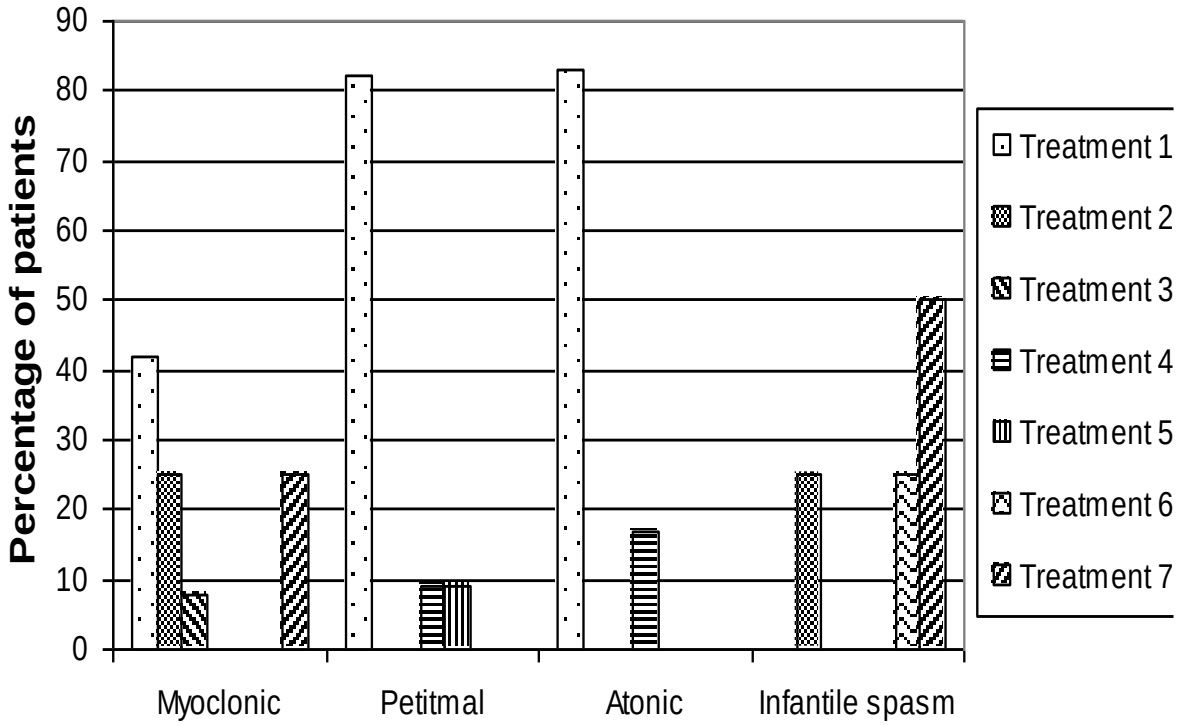

Figure 2: Different treatments used in myoclonic, petitmal, atonic, and infantile spasm

Table 3: Various treatments used in myoclonic, petitmal, atonic, and infantile spasm

Treatments	Drugs used	Myoclonic	Petitmal	Atonic	Infantile spasm
Treatment 1	Valproate	42	82	83	0
Treatment 2	Valproate+Clonazepam	25	0	0	25
Treatment 3	Valproate+Phenobarbitone	8	0	0	0
Treatment 4	Valproate+Lamotrigene	0	9	17	0
Treatment 5	Valproate+Carbamazepine	0	9	0	0
Treatment 6	Valproate+Clonazepam+Prednisolone	0	0	0	25
Treatment 7	Phenobarbitone+Clonazepam	25	0	0	50

For simple partial seizures carbamazepine was used in 67% cases and phenobarbitone was used in 33 % cases. For complex partial seizures carbamazepine was used in 78% cases while combination of carbamazepine and topiramate was used in 11% cases. In secondary generalize seizures carbamazepine and phenobarbitone was used in 14, 14% cases, while combination of valporate + topiramate was used in 29% cases as shown in table No 4.

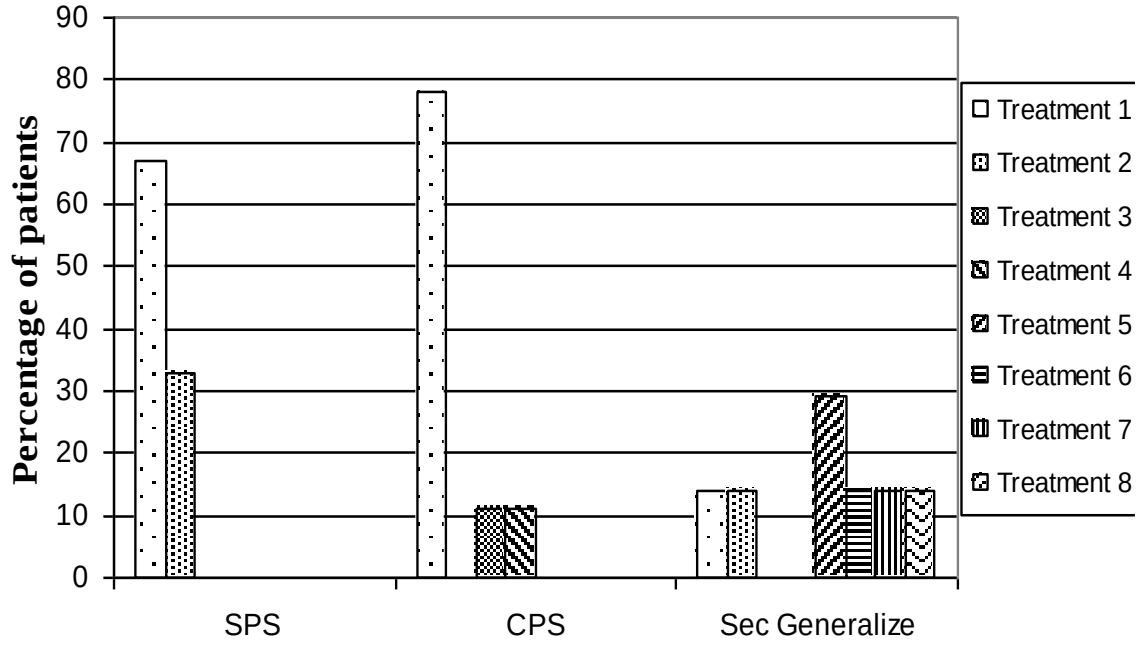

Figure 3: Different treatments used in simple partial, complex partial and secondary generalize seizures

Table 4: Various treatments used in simple partial, complex partial and secondary generalize seizures

Treatments	Drugs used	Simple partial seizure (SPS)	Complex partial seizure (CPS)	Secondary generalize seizure
Treatment 1	Carbamazepine	67	78	14
Treatment 2	Phenobarbitone	33	0	14
Treatment 3	Carbamazepine+Topiramate	0	11	0
Treatment 4	Carbamazepine +Valproate+Topiramate	0	11	0
Treatment 5	Valproate+Topiramate	0	0	29
Treatment 6	Valproate+Lamotrigene	0	0	14
Treatment 7	Valproate+Phenobarbitone	0	0	14
Treatment 8	Carbamazepine+Lamotrigene	0	0	14

Regional office of world health organization in New Delhi published a manual for physician for the treatment of epilepsy **[20]** and another WHO manual for medical and clinical officers in Africa **[21]**, recommend phenobarbitone, phenytoin, valproic acid and carbamazepine for all major types of epilepsy. Phenobarbitone and phenytoin are the cheapest antiepileptic drugs. Study by us indicates that only in 12 percent cases these drugs were used. The most commonly prescribed drug either in monotherapy or in multiple therapy was valproic acid 67% as evaluated from Table No. 2 - 4 and shown in Figure No. 2 - 4. In contrast to other countries this percentage was very high. A study conducted in Iran reveals that phenobarbitone is the commonest antiepileptic drug (33.7%) because of its broad antiepileptic action and economical price **[22]**. Similarly another study conducted in north west India reveals that most of their epilepsy patients were on phenytoin due to its simple dosing schedule and economical price **[23]**.

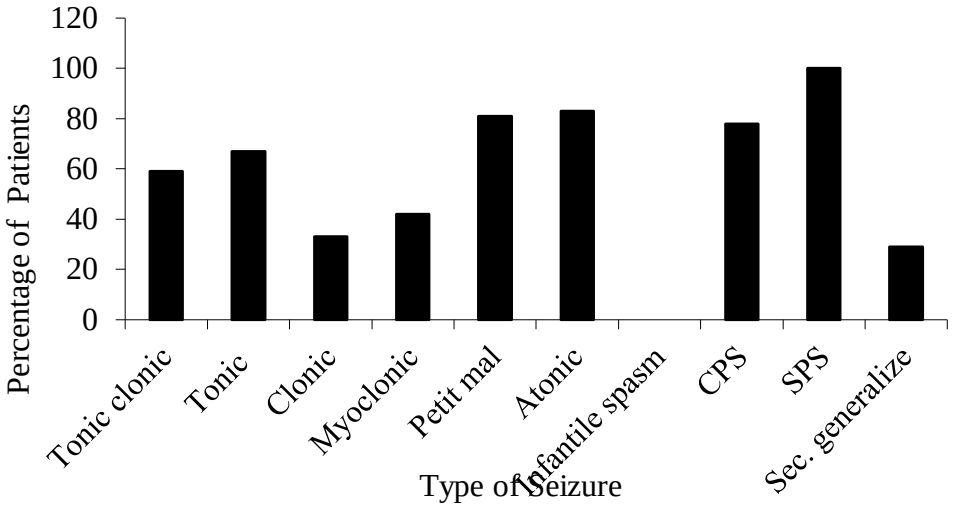

Figure 4: Percentage of patients on nonotherapy

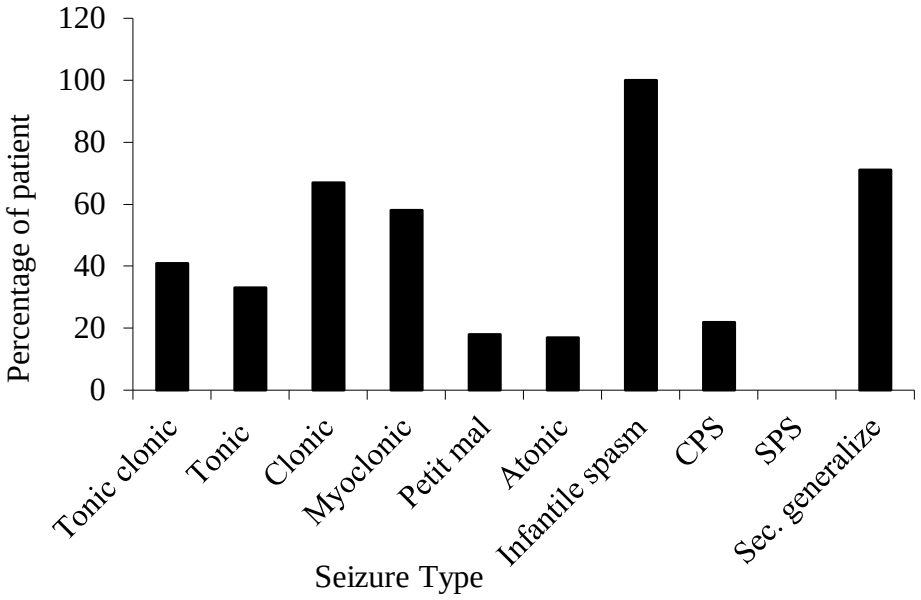

Figure 5: Percentage of patients on combination therapy

Valproate was administered in combination with Topiramate, Lamotrigene, Clonazepam and Phenobarbitone. Carbamazepine was also found to be administered along with valproate, topiramate, Phenobarbitonea and Lamotrigene.

The percentage of epileptic patients who were on combination therapy to control seizures has ranged in different studies from as high as 35% **[24]** to as low as 15% **[25]**. In this study percentage mean of patients on combination therapy were 43% ±31 as shown in Table 6 which indicates the need for proper dose increase in monotherapy i.e the dose should be increased in a well-controlled manner to get maximum benefits without unnecessarily exposing the patient to the risk of adverse reactions of these combination of drugs. Combination therapy was used for infantile spasm in 100% cases, while to treat secondary generalize seizures, myoclonic seizures, clonic seizures and tonic clonic seizures the percentage of combination therapy used was 71%, 58%, 67% and 41% respectively as shown in figure No 6

In our study it was found that simple partial seizures was treated by monotherapy in 100% cases. While complex partial seizures, petit mal seizures and atonic seizures were treated by monotherapy in 78%, 81% and 83% cases respectively as shown in table No 5.And the percentage mean of patients on monotherapy were 57 ± 31 which needs to be further improved as according to Schmidt **[26]** approximately 70 % patients when treated with single antileptic drug leads to complete seizure control without intolerable adverse effects.

CONCLUSION

It is concluded that proper selection of economical antiepileptic drug must be done for the proper treatment of epileptic patient. And monotherapy should be encouraged as compare to combination therapy.

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