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Research Article

TO DETERMINE THE SAFETY OF ANTI-EPILEPTIC DRUGS IN CHILDREN TREATED FOR SEIZURES¹Muhammad Irfan, ²Muhammad Adnan, ³Usman Hafeez, ⁴Moazzam Hussain¹.Muhammad Medical College Mirpurkhas.².Allama Iqbal medical College Lahore³.Allama Iqbal medical College Lahore.⁴Nishtar Medical University & Hospital Multan.

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Abstract:

Epilepsy is a neurological disorder in which recurring seizures occur in the person. It is most common childhood disorder in United State. The seizures in a children start with the changes in electrical as well as chemical changes in the brain. There are various types of seizures such as absence seizures, atonic seizures, myoclonic seizures, febrile seizures and tonic-clonic seizures. Age is major factor to determine the recurrence of seizures and types of seizures. The sign and symptoms of epilepsy are convulsion with no fever, anger, jerking arms, sudden blinking, sudden stiffness and so on. Some drugs are considered more safe in children for the treatment of seizures.

Objective: The objective of this study is to determine the safety of epileptic drugs used for treatment of epilepsy or seizures in children.

Methods:

A prospective study was conducted to determine the safety of epileptic drugs used for the treatment of epilepsy in children. The data was collected of almost 150 children who are epileptic patient whose treatment is going in the hospital and they follow their treatment plan carefully. The data was collected from the patient fulfilled the inclusion and exclusion criteria then findings are noted and recorded. The data was analyzed by computer software SPSS and data were assessed by statistical t-test.

Results: The results of this study shows that the drugs used in children for the treatment of seizures are safe. The side effects of these drugs are most commonly in males and thus the duration of seizures in first thirty minutes is worst. The prevalence of Status epilepticus is most commonly occurring at the age of 1-5 years. There are no severe side effects have been seen which shows that the drugs used are very safe to use in children

Conclusion: Epilepsy or seizures are known as the most common brain disorder in United States and if it is not treated at the time it becomes more severe. The treatment plan for the children is different from the adults and the drugs used for their treatment are safe and cause very less side effects. Thus it is concluded that the use of these drugs are safe in children is safe.

Keywords: Seizures, Children, Antiepileptic drugs, Safe drugs.

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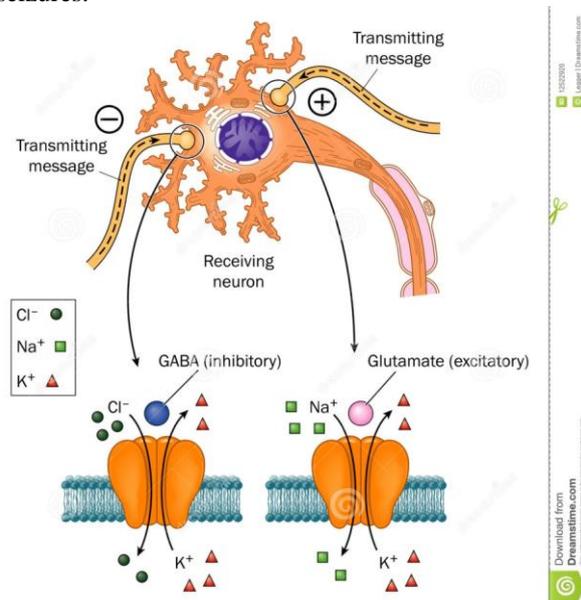
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INTRODUCTION:

Epilepsy is a neurological disorder in which recurrence of seizures done and these seizures are stimulated by the electrical as well as chemical changes in the brain or nervous system. There are various causes of seizures such as infection in brain like meningitis, encephalitis, abnormal level of sodium in blood, brain tumor, brain injury, epileptic shock and so on. The major sign and symptoms of epilepsy are staring, loss of consciousness, breathing problem, stiffening of the body, loss of bowel control, jerking movement in arms as well as legs, sudden stiffness, sudden falling, severe anger, particular changes in senses, loss of fear of anything, chewing and panic attacks (Jr, 2004). According to estimation almost out of 1000 children 1 child is died due to epilepsy. There are various types of epilepsy and the treatment of epilepsy is done according to type and duration of seizures.



There are various drugs used to treat seizures and epilepsy in children. For the treatment of tonic-clonic seizures carbamazepine, phenytoin and valproic acid is used. For the treatment of absence seizure ethosuximide is used. Mostly ethosuximide is used to treat seizures because it is mono therapy for children (M.D., 1984). There are some common side effects of these medications are double vision, nausea, rashes, dizziness, irresistibility and nausea. These drugs are most safe in the treatment of seizures in children. The epilepsy is treated by doing some lifestyle modifications such as ketogenic diet is provided to the patient because ketones present in ketogenic diet is helpful in seizures treatment (Curatolo, 2006).

Objective

The objective of this study is to check the safety of epileptic drugs in the treatment of seizures in the children.

Literature review

Puneet et al. conducted a study to determine the safety of vaporate and phenytoin in patient having status epilepticus. The study is conducted to check that which drug is more suitable, safe and cause less side effects in children and treat the seizures in a best way. During his study he collected the data from two groups of patients one who take phenytoin and one other group take valporate for the treatment of seizures. The data was revealed that some patients are not treated with single drug and use two or more drugs to prevent the recurrence of seizures. The results of this study concluded that the use of phenytoin is safer in children and the side effects produced by phenytoin are very less and minute because phenytoin give immediate treatment and thus the seizures prevent at that time (PuneetAgarwal, 2007).

Roshan et al. conducted a study to determine the outcomes of Midazolam infusion in the management of childhood status epilepticus. In this study he collected the data of almost 68 children from 2 months to 14 years old range group and then conducted a study on them. It was determined by Roshan that almost 30 children had stable status epilepticus whereas the 38 children had refractory status epilepticus. For the treatment of refractory epilepticus patients administered Phenobarbital before giving them medizolam whereas the patients have stable status epilepticus just administer medizolam and the condition of one child is very severe which is not be treated by these medications (Roshan Koul, 2002).

Elizabeth et al. conducted a study to determine that how diet is used as a treatment of epilepsy and reduce the chances of seizures in patient. This study determines that there are different types of diet used in treatment of epilepsy such as ketogenic diet. Ketogenic diet minimizes the metabolism of fasting recommended by modern physicians for the treatment of epilepsy. This study concluded that ketogenic diet is very useful in the treatment of seizures as ketones present in this diet helps to fight against seizures (Elizabeth E.Bailey, 2005).

F B Gibberd et al. conducted a study to determine the aspects of neurological disease such as epilepsy in children. This study determines that epilepsy is a serious neurological disorder in which recurrence seizures occurs. It is an abnormal proximal discharge of neurons due to which seizures happened. The severity of seizures is mostly depending upon the age. The most common and safe treatment use for the prevention of epilepsy is carbamazepine, phenytoin and ethosuximide. (Gibberd, 1975)

Anna Edelvik *et al.* conducted a study to determine the long-term effects of epilepsy surgery. In this study data was collected of almost 300 patients whose surgery has been done and these patients follow the Swedish National Epilepsy Surgery treatment. The result of this study shows that most of the children have seizures can be completely cured after surgery and thus they stop the drugs they use for treatment (Anna Edelvik, 2013).

N.W *et al.* conducted a study to determine the utilization of drugs in children and compare that which drug is safest to use in children. In this study the data was collected from the children having age of 0-19 years until they received only one prescription from the physician. It was concluded that almost 4 out of 1000 children has diagnosed epilepsy every year. Valporic acid is considered as the safest drug to used in treatment of seizures in children (N. W. van de Vrie-Hoekstra, 2008).

Anannit Visudtihan *et al.* conducted a study to determine the pharmacokinetic as well as clinical application of valporate to treat epilepsy in children. This study is about the role of IV valporate to treat seizures and determination of its pharmacokinetic parameters to obtain the optimum therapeutic level. A cross sectional study is done and data was collected from 7 patients and administer the valporate by measuring the exact ratio of the dose that has to be administered and thus the therapeutic level is measured. The results of this study concluded that occurrence of seizures minimized after 20 minutes of administration of initial dose and the recurrence of seizures occur after 44-5 hours of administration of the drug (Anannit Visudtibhan, 2011).

METHODOLOGY:

Study design

Prospective observational study

Study duration

3 months

Sampling technique

Convenient sampling technique

Sample size

150

Inclusion criteria

The inclusions criteria of the patients to take participate in this study are following

- Neurological disorder
- Status Epilepticus
- Seizures
- Severity of disease
- Treatment plan of the patient
- Patients have age from 2 to 19 years

Exclusion criteria

The exclusion criteria of the patients that don't take participate in this study are following

- People having direct as well as indirect restorations in military regions
- People having hypertension
- People having some other acute or chronic disease

Statistical Tool

SPSS version 19

T test

ETHICAL CONSIDERATION

- Written informed consent was taken from all the patients.
- All informed and collected data will be kept confidential.
- Data will be saved in personal laptop and hard copies from data will be in locker.
- Participants will remain anonymous throughout the study
- The subject was informed there are no disadvantages or risk on the procedure of study.
- They were also informed that they are free to withdraw at any time during the process of the study

DATA COLLECTION

- The data was collected y using data collection sheets.
- The data was collected from different age groups people having different activities.
- Demographics data should be collected from all participants of research.

DATA ANALYSIS

The statistical analysis of data is done by using SPSS new version.

T test was applied in statistical P-value<0.5 is analyzed.

RESULTS:

Safety of drugs

Safety	Group A	Group B	P-value
Yes	150(100%)	146(97.3%)	0.12
No	0(0.0%)	4(2.7%)	0.12
Total	150(100%)	150(100%)	

The results about the safety of drug shows that the phenytoin is given to the group A and their results show that this drug is completely safe in the patient and all the patients who take this drug are safe. The group B takes carbamazepine and the result of this group shows that this drug is safer in the children but due to some reasons such as dose related factors or patient related factors this drug is not be safe in 4 children but overall results shows that both drugs are safe but phenytoin is safer as compare to carbamazepine. These results are analyzed by using statistical t-test.

Side effects

Side effects	Group A	Group B
Drop in Glasgow coma scale	0(0.0%)	0(0.0%)
Drop in blood pressure	0(0.0%)	0(0.0%)
Cardiac depression	0(0.0%)	1(0.7%)
Respiratory depression	0(0.0%)	3(2.0%)
Total	0(0.0%)	4(2.7%)

The table shows that there are different types of severe side effects of antiepileptic drugs some are serious such as respiratory depression and cardiac depression. The results show that there is no any side effects in group A who takes phenytoin for the treatment of epilepsy in children but the patients who take carbamazepine of group B show some side effects in 4 patients. In 1 patient this drug shows respiratory depression due to which has difficulty breathing occurs and in 3 patients side effect of cardiac depression seen. Thus, results show that phenytoin is safer in patients as compare to carbamazepine.

Duration of Status Epilepticus

Duration (minutes)	Group A	Group B
11-30	136(90.7%)	1443(95.3%)
31-60	14(9.3%)	7(44.7%)
Total	150(100%)	150(100%)

The above results show the duration of epilepsy after the administration of drugs which means that the how much time a drug take to reduce these seizures. The analysis and results of the data show that in group A which take phenytoin majority of the people overcome the seizures in first thirty minutes but there are some patients who show less effects so almost 14 patient overcome these seizures have chances of recurrent or overcome the seizures within one hour. The results of second group which takes carbamazepine show that almost majority of the people show immediate response and thus show their effects within 30 minutes due to which the occurrence of seizures overcome within 30 minutes whereas almost 7 children don't show immediate reaction and thus overall results of

the above data show that most of the patients show immediate results but some patients didn't show immediate response after the administration of antiepileptic drugs.

Risk factors

Diagnosis	Group A	Group B
Meningitis	71(47.3%)	57(38.0%)
CP and epilepsy	40(26.7%)	55(36.6%)
Complex and febrile fits	8(5.3%)	10(6.7%)
Encephalitis	4(2.7%)	3(2.0%)
Epilepsy	27(18.0%)	25(16.7%)
Total	150(100%)	150(100%)

There are some risks factors which also determine the seizures in patients such as group A who take phenytoin have meningitis have more chances of seizures, in the same way CP and epilepsy and seizures in epilepsy are also very common but the use of these drugs in treatment of encephalitis and complex and febrile fits is very rare. The group B who takes carbamazepine are mostly use in treatment of patients who has seizures due to meningitis, CP and epilepsy, seizures due to epilepsy and it use rarely in the treatment of seizures due to encephalitis and complex and febrile fits.

DISCUSSION:

The study was conducted to check the safety of antiepileptic drugs in patients having age group 2 years to 18 years. The drugs used mostly in the treatment of seizures in children are phenytoin, carbamazepine, ethosuximide and valproate. This study was conducted on 300 patients and divided them into two groups each of 150 patients. One group takes phenytoin and other group takes carbamazepine. The analysis of data by t-test shows that the phenytoin is safer drug as compare to carbamazepine and these results are similar to the study conducted by Anannt. Aninnt *et al.* conducted a study to determine the efficacy and safety of anti-epileptic drugs in children and the results of this study shows that phenytoin is safest drug as compare to other anti-epileptic drugs thus phenytoin can be used more widely. There are various side effects of the anti-epileptic drugs and the incidence of these side effects is more in the patients who takes carbamazepine as compare to phenytoin as there are no any side effects seen in the patients of group A who takes phenytoin while some serious side effects such as respiratory depression as well as cardiac depression seen in 4 patients out of 150 patients are seen in the patients who take carbamazepine which determine that phenytoin is safer drug as it doesn't cause any serious side effects in the patients.

The seizures in epilepsy are also treated with some lifestyle modifications such as taking fresh air and taking ketogenic diet. Ketogenic diet plays an important role in the treatment of epilepsy such as ketones present in the ketogenic diet is very helpful in the prevention of seizures in epileptic patients. Elizabeth *et al.* conducted a study to determine the prevalence of seizures in the patients who take ketogenic diet and thus the study shows that ketogenic diet plays an important role in the cure of seizures.

CONCLUSION:

Epilepsy is a neurological disorder in which seizures occur due to abnormal changes in electrical and chemical alterations in the brain due to which seizures occur. There are various types of seizures in children such as tonic seizures, tonic seizures, absence seizures and tonic-clonic seizures. The signs and symptoms of epilepsy are staring, sudden fall and chewing without any reason. There are various drugs used in the treatment of seizures in children such as phenytoin, valproate, carbamazepine, ethosuximide and ethambutol. These drugs are safe in children for the treatment of seizures. The results of this study show that phenytoin is the safest drug to use in the treatment of epilepsy and thus there are no side effects seen in the patients who use phenytoin but the patients who take carbamazepine show some side effects in some patients thus due to these reasons phenytoin is a safer drug considered for the children. Ethosuximide is most commonly used when the patient requires mono drug therapy. Thus it is concluded that phenytoin is the safest drug in children for the treatment of seizures.

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