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ORIGINAL ARTICLE

Efficacy of Levetriacetam and Phenytoin as Combination Therapy in Infants Presented with Status Epilepticus

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ABSTRACT

Levetiracetam may be an effective and safer alternative to phenytoin as a second-line intravenous anticonvulsant for the treatment of juvenile convulsive status epilepticus. Objective of this study was to determine the efficacy of Levitriacetam and Phenytoin as combination therapy in infants presented with status epilepticus.

Material and Methods: In this cross observational sectional study (01-02-2020 to 31-07-2020) at department of pediatrics mayo hospital Lahore. study the infants were enrolled of either gender and age less than 1 year that were suffering from a seizure with 5 minutes or more of continuous clinical seizure activity or recurrent seizure activity without recovery between seizures.Then these cases were started with both Phenytoin (Loading: 15 - 20 mg/kg IV *Maintenance: 5 - 8 mg/kg/d) and Levitriacetam (Loading dose5 10 mg/kg IV and Maintenance dose 10 – 30 mg/kg/dose q12 hours) and were observed daily to look for fits. Efficacy was labelled as yes where there were no fits for 48 hours after the treatment.

Results: In this study there were total 120 cases and out of these 74 (61.67%) were males and 46 (38.33%) females. Mean age of the subjects was 4.57±3.97 months. Mean duration of symptoms was 2.23±1.47 days. Out of 120, tonic clonic seizures were noted in 78 (65%) of the cases and 30 (25%) of the cases had family history of epilepsy. Efficacy was noted in 84 (70%) of the cases.

Conclusion: Combination of Levetriacetam and Phenytoin is highly efficacious in infants presented with status epilepticus.

Keywords; Levetriacetam, Phenytoin, Status epilepticus, Fits, Infantile seizures

INTRODUCTION

Seizures are one of the most frightening symptoms that are rather common in children's populations and are seen on a regular basis in emergency rooms. Changes in the body's structure, function, and biochemistry can all contribute to seizure activity, and each of these factors can play a role. It is possible for it to be idiopathic in a considerable amount of cases. [1-2]

Rapid cerebral electrical discharge can result in neuronal injuries during seizures, and ongoing uninhibited activity can result in serious damage to the body, including rhabdomyolysis, electrolyte imbalance, renal failure, and also increases the risk of aspiration during these seizure activities. Both of these factors can increase the likelihood that a person will aspirate during seizure activities.[3-4]

There has been a variety of anti-epileptic medications researched and tested, each with a unique success rate and profile of adverse effects. These include benzodiazepines phenobarbital, phenytoin, primidone, carbamazepine, valproic acid, ethosuximide, gabapentin, lamotrigine, levitriacetam etc. [5]

The older medicines are still widely utilised; they produce more profound sedations and also provide synergistic effects when combined with one another. The newer drugs have showed fewer sedation and adverse effect profiles when compared to the older ones, but they lack the data, and the majority of the research are done in Western populations.[6]

Levetiracetam may be an effective and safer alternative to phenytoin as a second-line intravenous anticonvulsant for the treatment of juvenile convulsive status epilepticus in the United Kingdom, according to some data. The current recommended treatment is phenytoin. But studies are available which prove that Despite the lack of statistically significant superiority of levetiracetam over phenytoin, the known safety profile of levetiracetam and its relatively simple administration suggest that it may be a suitable alternative to phenytoin as the first-choice, second-line anticonvulsant in the treatment of paediatric convulsive status epilepticus.[7]

Still few studies have shown that in children who have status epilepticus with convulsions, levetiracetam does not perform any better than phenytoin.[8] As a result of this, it was decided to conduct a study to investigate whether or not an adjunct therapy consisting of one newer medicine (Leviteracitum) and one of the most well-known drugs (Phenytoin) is effective.

PATIENTS AND METHODS

This was a cross sectional observational study that was carried out, at department of pediatrics mayo hospital Lahore during 01-02-2020 to 31-07-2020. Objective of this study was to determine the efficacy of Levitriacetam and Phenytoin as combination therapy in infants presented with status epilepticus.

Infants of either gender or age less than one year old who were experiencing a seizure that lasted for five minutes or more of continuous clinical seizure activity or recurrent seizure activity without recovery in between seizures were enrolled in this study as participants. The infants had to have a history of epilepsy. After that, these patients were given phenytoin (Loading: 15 - 20 mg/kg IV *Maintenance: 5 - 8 mg/kg/d) and levetiracetam (Loading IV and Maintenance dose 10 - 30 mg/kg/dose q12 hours), and they were monitored every day to see if they experienced any fits. When there were no fits for forty-eight hours after receiving treatment, the researchers determined that the treatment was effective.

For the purpose of data analysis, SPSS version 22.0 was utilised. When dealing with categorical variables, we made use of frequency and percentages, and when dealing with quantitative variables, we displayed mean values together with standard deviations. For the purpose of data stratification, a Chi-square test was utilised, and a post-stratification p value of less than 0.05 was considered significant.

RESULTS

In this study there were total 120 cases and out of these 74 (61.67%) were males and 46 (38.33%) females. Mean age of the subjects was 4.57±3.97 months as shown in table I. Mean duration of symptoms was 2.23±1.47 days. Out of 120, tonic clonic seizures were noted in 78 (65%) of the cases and 30 (25%) of the cases had family history of epilepsy as in table II. Efficacy was noted in 84 (70%) of the cases (figure I).

Table 1: showing the detail of the various demographic variables of the patients enrolled (n= 120)

Variables	Mean ± SD	Range
Age (months)	4.57±3.97	0-12
Weight	3.31±0.54	2.5-5
Gender	N	%
Male	74	61.67%
Female	46	38.33%
Duration of symptoms	2.23±1.47	2.21±1.34
Type of seizure	N	%
Tonic clonic	78	65%
Myoclonic	42	35%
Family h/o epilepsy		
Yes	30	25%
No	90	75%

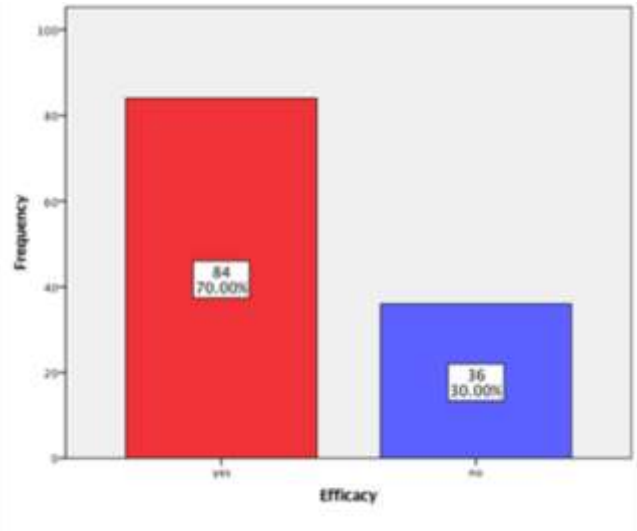

Figure 1: Efficacy of Levitriacetam and Phenytoin as combination therapy in infants presented with status epilepticus.

DISCUSSION

Seizures are very common emergency presentation in infants. In children, seizures are one of the most often experienced neurological symptoms. The average duration of a seizure is five minutes. Seizures that last more than five minutes are considered long. When a seizure lasts for more than 30 minutes or when two or more seizures happen in rapid succession without the patient regaining consciousness, the condition is known as status epilepticus, which can be fatal. There is wide array of underlying etiologies but that need prompt time to investigate and treat. During this active phase, the drugs with high degree of efficacy and minimal side effect profiles are required to overcome this situation. Levitriacetam and phenytoin has shown promising results where the former is newer one with better safety profile and latter is one of the oldest drugs. [9-10]

The efficacy of this treatment in preventing epileptic seizures was evaluated in the current study and found to be present in 70% of the cases. There was no such study identified using a combination of these two to control fits; rather, combinations of diverse regimens and randomized controlled were found to compare two or more medications. These trials have showed almost a close efficacy in their respective separate circumstances.

In a study conducted by Giri VP et al., the researchers evaluated the efficacy of valproic acid and lamotrigine. They found that efficacy with valproic acid was shown in 76.67% of the instances, but with lamotrigine, efficacy was seen in 56.67% of the cases.[11]

In another study done by Yilmaz U et al it was described that the antiepileptic drugs stopped seizure in 84.8% of the cases with multiple drugs and they did not find any significant difference among various drug groups and higher failure rates were noted with valproic acid alone seen in 16.7% as compared to Levitriacetam seen in 11.8% of the cases with p= 0.09.[12]

In a study carried out by Neubauer D et al., the researchers compared the effectiveness of single drug therapy and combination therapy with regard to seizure control and found that there was no significant difference between the various groups. However, combination therapy was found to be superior to single drug therapy.[13]

According to another study they compared 5 different drugs for fits controlsw2 in non syndromic epilepsy and it was noted that the most commonly prescribed and efficacious drug was Levitriacetam and was noted in 74% of the cases with p= 0.001.[14]

`Medical crises requiring immediate and proper anticonvulsant treatment include tonic-clonic convulsions and convulsive status epilepticus (now defined as a tonic-clonic convulsion lasting at least 30 minutes). Any tonic-clonic convulsion lasting more than five minutes should be treated with an anticonvulsant medicine, according to experts around the world. It is common practise to consider benzodiazepines to be first-line medications, while phenobarbital, phenytoin, and paraldehyde are considered to be second-line medications.[15] Multiple studies are conducted to examine the efficacy and safety of anticonvulsant medicines used to treat any acute tonicclonic convulsion of any duration, including established convulsive (tonic-clonic) status epilepticus in children who report to a hospital or emergency room.

CONCLUSION

Combination of Levetriacetam and Phenytoinis highly efficacious in controlling fits in infants.

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