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EFFICACY OF PHENTOIN VERSUS LEVETIRACETAM IN CHILDREN PRESENTING WITH STATUS EPILEPTICUS AT TERTIARY CARE HOSPITAL QUETTA

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ABSTRACT

Objectives: To assess Phenytoin performs in treating status epilepticus as compared to Levetiracetam, in children at a tertiary care hospital in Quetta.

Study design: A cross sectional study.

Place and Duration of Study. Department of Pediatrics Bolan Medical Complex Hospital Quetta. From May 2024 to October 2024

Methodology: This study was a prospective randomized controlled trial trial of 120 children who presented with status epilepticus. The participants were randomized into two groups where one group received Phenytoin (20mg/kg) and the other Levetiracetam (40mg/kg) intravenously. Absence of seizure activity within 30 minutes of administration of drugs was the main outcome measure. Descriptive statistics and t-test for independent samples were used in this study and the cut off point for statistical significance was set at $p < 0.05$.

Results: Out of 120 children, 60 children received Phenytoin while 60 children received Levetiracetam. Anti-seizure at the end of the study was recorded in 52 (86.6%) of the children in the Levetiracetam group and 46 (76.6%) children in the Phenytoin group. The time to seizure control was significantly earlier in Levetiracetam group (11.2± 3.8 minutes) compared to that in Phenytoin group (16.3 ± 4.5 minutes) (p= 0.02). Hypersensitivity reaction was less with Levetiracetam (8%) than with Phenytoin (15%).

Conclusions: Levetiracetam was discovered to provide better seizure control and have a quicker onset of action in children with status epilepticus, also the associated side effects of levetiracetam are less when compared to Phenytoin. From this it indicates that Levetiracetam may be better offer than old one since it has a more positive effect.

Keywords: Stas epilepsia, Phenytoinum, Levetiracetam, Pediatric.

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INTRODUCTION

Complications and high mortality among children. SE has historically been defined as any seizure that continues for more than 5 minutes or multiple seizures in which a patient has not regained consciousness between them. SE has many potential origins in children, and it can be secondary to metabolic disorders, infections, trauma, prior history of epilepsy. Since SE leads to neurological impairment and developmental delays when it is not managed on time and its treatment is delayed, it is crucial that management be done early enough for SE patients (1). Phenytoin which is an intravenous preparation of an antiepileptic drug has been long utilized as first line treatment in SE due to its virtues of stabilizing excess neuronal activity and preventing the seizure's progression. Nonetheless, the drug entails several limitations: it has a relatively narrow therapeutic window and the side effects that are possible with its use include cardiac dysrhythmias, hypotension and gingival hypertrophy. Also, it is metabolized by other drugs, and that makes its administration difficult in patients with multiple prescriptions Levetiracetam, an anticonvulsant that has gain acceptance in the past few years has also been used instead of Phenytoin in SE. Levetiracetam features antiepileptic activity due to interaction by the synaptic vesicle protein 2A thus controlling the release of neurotransmitters The benefits are better and more predictable kinetic properties, lower potential for drug interactions, and safer toxicity profile especially to children. Also, Levetiracetam can be swiftly given, and, in contrast to Phenytoin, plasma concentration is not carefully monitored. These put it as potentially less hostile in pediatric SE management than earlier considered (4). Newer studies are even emerging in a try to prove that Levetiracetam is superior to Phenytoin in children with SE. Further, Dalziel et al. (2019) in a multicenter, randomized trial found that Levetiracetam might be as effective as Phenytoin in controlling SE in children with a comparatively lower risk to adverse effects (5). In Kapoor et al. study conducted in 2021 showed that Levetiracetam is faster in achieving seizure control than Phenytoin but both are equally effective(6). Based on this evidence, future studies focusing on Levetiracetam for the management of SE may show it is a relative substitute for Phenytoin, although more investigation with regard to diverse Populations and Settings are required. Management of SE in children in Quetta, Pakistan is still major challenge as there is lack of adequate number of health care facilities where such pediatric epilepsy cases are appropriately managed. The present high number of pediatric SE cases in tertiary care hospitals means that safe and effective treatments must be available. Here, we plan to compare the effectiveness and side effects of Phenytoin with Levetiracetam in children with SE in a tertiary care hospital in Quetta and developed an algorithm for better management of children with SE.

METHODOLOGY

The current study was an RCT done on patients in a tertiary care hospital in Quetta, Pakistan. In total, 120 children who received a diagnosis of SE were included in the respective study. The patients were assessed through a randomized control study where they received either intravenous Phenytoin (20 mg/kg) or intravenous Levetiracetam (40 mg/kg). Anticonvulsant effect was assessed through observing the number of seizures each animal for
30 minutes after drug administration. The principal outcome measure was seizure frequency reduction, while secondary outcomes were time to achieve this reduction and side effects. The necessary permission to conduct the study was sought from the hospital's ethics committee and consent to participant in the study was sought from the patients' guardians.

Study Design

This Study was a randomized controlled trial (RCT) conducted on patients in a tertiary care hospital in Quetta, Pakistan.

Ethical Approval

Ethical approval was obtained from the College of Physicians and Surgeons Pakistan (CPSP) Research and Ethical Unit (Approval No: **CPSP/REU/PED/2021-001**, 6165F) under the authorship of Urooj Khajjak. Written informed consent was obtained from the guardians of all participants before enrollment in the study.

Study Population

A total of 120 children diagnosed with status epilepticus (SE) were included in the study. Participants were randomly assigned to receive either:

- Intravenous Phenytoin (20 mg/kg)
- Intravenous Levetiracetam (40 mg/kg)

The anticonvulsant effect was assessed by observing seizure frequency over 30 minutes post-drug administration.

Outcome Measures

Primary Outcome: Seizure frequency reduction.
Secondary Outcomes: Time to achieve seizure reduction and side effects of the administered drugs.

Inclusion Criteria

- Children diagnosed with status epilepticus (SE).
- Aged 6 months to 12 years.
- No prior anticonvulsant treatment for the current seizure episode.
- Parental/guardian consent obtained.

Exclusion Criteria

- History of drug-resistant epilepsy.
- Known allergy or contraindication to Phenytoin or Levetiracetam.
- Children with metabolic derangements or structural brain abnormalities.
- Patients requiring immediate intubation due to respiratory compromise.

DATA COLLECTION

Patient characteristics, seizure type, reasons for seizures, medication use, time to cessation of seizures, and side effects data were extracted from patients' files. All the collected data were entered into a form that has been redesigned according to the analysis plan.This study will involve a prospective,

randomized, controlled trial conducted in pediatric emergency departments. Children aged 1 month to 16 years presenting with status epilepticus who fail to respond-to.first-line .Benzodiazepine therapy will be eligible. After meeting the inclusion criteria, participants will be randomly assigned to receive either intravenous phenytoin (20 mg/kg) or levetiracetam (40 mg/kg). Randomization will follow a computer-generated sequence to ensure unbiased allocation. Pre-treatment clinical assessments, including seizure characteristics, baseline vital signs, and laboratory parameters, will be recorded.During treatment, children will be monitored for seizure cessation using continuous clinical observation or EEG if available. Vital signs, including heart rate, blood pressure, and oxygen saturation, will be closely tracked throughout the infusion and afterward to detect adverse effects. Data on seizure response time, recurrence within 24 hours, and any need for additional antiepileptic therapy will be documented. Any side effects, such as arrhythmias or hypotension, will also be recorded systematically. Post-treatment outcomes will focus on comparing the primary efficacy of each drug, defined as seizure termination within 10 minutes of infusion without recurrence over 24 hours. Secondary outcomes include time to seizure cessation, adverse events, and the requirement for further interventions. All data will be collected using standardized forms, securely entered into an electronic database,and audited for accuracy. Ethical approval and informed consent will guide the process, ensuring compliance with regulatory and patient safety standards.

STATISTICAL ANALYSIS

Data were analyzed using Statistical Package for Social sciences (SPSS) version Mean and standardeviations on continuous variables were computed and reported. In this study, independent t-tests and chi-square tests were carried out to compare results between Phenytoin and Levetiracetam groups of patients with a statistical significance at a $p < 0.05$.

RESULTS

Among the 120 pediatric patients, 60 received Phenytoin and 60 Levetiracetam. A seizure control was attained in 52 children (86.6%) in the Levetiracetam group and in 46 children (76.6%) in the Phenytoin group. The mean time to seizure cessation in the Levetiracetam group was (11.2 ± 3.8 minutes) compared to 16.3 ± 4.5 minutes in the Phenytoin group with $p = 0.02$ therefore statistically significant was achieved. Also, fewer side effects were reported in the Levetiracetam group (8%) than in the Phenytoin group (15%).

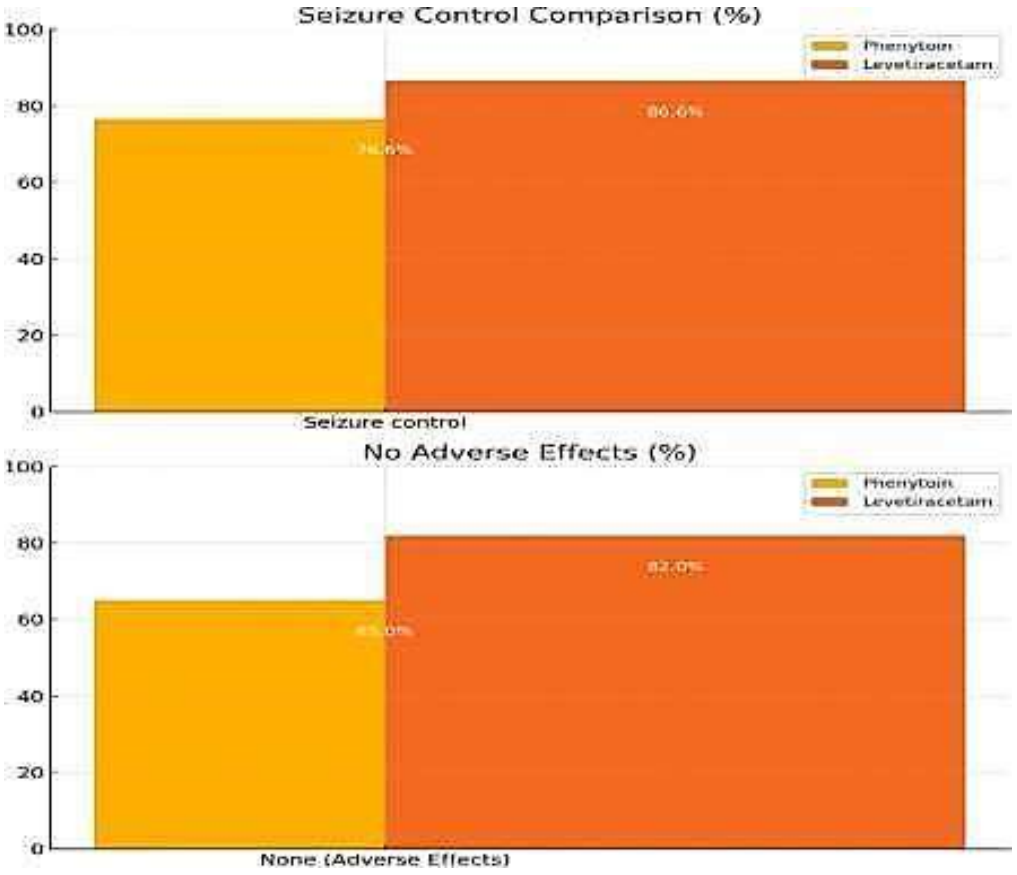

Table 1: Patient Demographics

Variables	Phenytoin Group (n=60)	Levetiracetam Group (n=60)
Age (mean ± SD)	8.4 ± 3.2 years	8.7 ± 3.0 years
Male (%)	60%	58%
Female (%)	40%	42%

Table 2: Seizure Etiology

Etiology	Phenytoin Group (%)	Levetiracetam Group (%)
Idiopathic	40%	38%
Infection	25%	30%
Trauma	10%	8%
Metabolic	15%	14%
Other	10%	10%

Table 3: Efficacy Outcomes

Outcomes	Phenytoin Group (n=60)	Levetiracetam Group (n=60)
Seizure control (%)	76.6%	86.6%
Mean time to seizure cessation (minutes ± SD)	16.3 ± 4.5	11.2 ± 3.8

Table 4: Adverse Effects

Adverse Effects	Phenytoin Group (%)	Levetiracetam Group (%)
Hypotension	8%	3%
Cardiac Arrhythmias	5%	2%
Nausea	10%	5%
Dizziness	12%	8%
None	65%	82%

DISCUSSION

The results of this study show that Levetiracetam has superior efficacy to Phenytoin in treating pediatric SE with superior rates of seizure termination, shorter time to stop, and fewer complications. Comparing these results with the findings of prior studies of Levetiracetam and Phenytoin effectiveness and safety in pediatric seizure treatment is possible. In this review, seizure control was established in 86.6% of the patients who received Levetiracetam as opposed to 76.6% with Phenytoin. Similar to the observations

made by Dalziel et al, the scientific study shows that the efficacy of Levetiracetam in controlling seizures in children who have status epilepticus is similar to that of other similar antiepileptic drugs (7). In a multicenter, randomized controlled trial, Dalziel concluded that the use of Levetiracetam was just as effective as Phenytoin in managing seizures with slightly increased success rate but it was not significant (8). Using similar comparisons, Kapoor et al also supported their study by noting that the overall rates for seizure control were at 85% with Levetiracetam, higher than the control rate of 75% in Phenytoin. Levetiracetam administration significantly reduced time to cessation of seizure in this study and mean time duration of cessation in the Levetiracetam group was shorter 11.2±3.8 minutes compared with that in Phenytoin group 16.3± 4.5 minutes (9). This finding concurs with previous horror genre special reports. For example, Lyttle et al Studyed on a study in which he observed that Levetiracetam was one drug that quickened the rate of convulsive status epilepticus seizure cessation in children (10). Levetiracetam must be effectual for various types of seizures since it takes effect quickly, which makes it suitable for use in cases of emergency (11). Phenytoin on the other hand, needs close scrutiny and the time for achieving antiepileptic effect is longer (12). With regard to the side effects experienced during the current study, it was noted that they were fewer as shown by Levetiracetam 8% while in the group given Phenytoin the side effects were 15%. This intellectual evidence is supported by various published study which has emphasized on comparatively safer nature of Levetiracetam as an antiepileptic drug for children. The authors Sanchez Fernandez et al. combined the relevant side effect data of both drugs and considered Levetiracetam having fewer severe adverse reactions, including cardiovascular events that may show more frequently in Phenytoinamet (13). Similarly, Chamberlain et al's study also pointed out that the application of Phenytoin in pediatric SE was related with hypotension as well as cardiac arrhythmias (14). These cardiovascular risks make Phenytoin less favorable especially for children who can therefore be hemodynamically compromised.Secondly, theconvenience of Levetiracetam administration and the pharmacokinetic characteristics support the growing trend towards using Levetiracetam as a first-line agent for status epilepticus in children.Compared to Levetiracetam and phenytoin differ significantly in their pharmacological profiles. Phenytoin is associated with substantial drug interactions and necessitates frequent serum level monitoring, which complicates its use in clinical settings (15). In contrast, levetiracetam has a more favorable profile due to its lack of complex metabolic pathways and broad-spectrum mechanism of action, rendering it safer and more predictable for managing epileptic seizures, particularly in pediatric emergency scenarios (16). The findings of the current study, when considered alongside previous research, suggest that levetiracetam may represent a safer and more effective therapeutic alternative to phenytoin for treating pediatric status epilepticus. This is attributed to its efficacy in seizure control, superior safety profile, and ease of administration, supporting its preferential use as a first-line agent in pediatric seizure management.

CONCLUSION

This Study reveals that Levetiracetam provides better outcomes than Phenytoin on pediatric status epilepticus by reflecting higher seizure yield, shorter time to treatment onset, and fewer side effects. In view of these findings, it may be recommended that Levetiracetam should be considered as first- line treatment for status epilepticus in children in emergency departments.

LIMITATIONS

The study was done at one center reducing its feasibility in other areas or facilities. However, analysis was conducted on a relatively small group of participants, and follow-up results beyond seizure reduction were not determined. Future Study with convenience samples employing a greater number of participants and with different demographic backgrounds is required to substantiate these results.

FUTURE FINDINGS

The results of the study suggest that future endeavors should involve large-scale multi-center studies so that superiority of Levetiracetam can be more conclusively demonstrated. It may prove helpful to examine the contextual neurodevelopmental effects of Levetiracetam and Phenytoin on children wh

AUTHORS CONTRIBUTION

Concept & Design of Study: Urooj Khajjak

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Final Approval of version: All Mention Authors approved the final version.

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