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A Randomized Controlled Trial Comparing the Prevention of Febrile Seizures in Children with Intermittent Oral Levetiracetam Versus Clobazam

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Abstract

Background: When a kid between the ages of 6 months and 5 years old experiences a generalized seizure that lasts less than 15 minutes and does not recur within 24 hours but is not preceded by or related to an acute sickness of the neurological system, this is known as a simple febrile seizure. Febrile seizures are the most common type of epilepsy in youngsters. **Material and Methods:** Children having a previous episode of febrile seizures who are seen in an outpatient paediatric clinic. This randomised controlled experiment did not hide its identity from participants. The research was carried out in Department of Pediatrics, Bhaskar Medical College & General Hospital, Moinabad, Yenkapally, Telangana, India. Research was conducted from November 2021 to October 2022. Simplified random sampling was used to choose the study participants. The randomization process will be carried out by a computer. **Results:** Subjects were children aged 6 months to 5 years old who had a history of febrile seizures, defined as two or more episodes of febrile seizures in the previous 6 months, with at least one seizure recurrence in the previous 2 weeks. The primary purpose of this study is to compare the effectiveness of oral levetiracetam and clobazam in the treatment of febrile seizures in children, as well as to determine the frequency with which such seizures return after a follow-up period of 48 weeks. **Conclusion:** While both medicines were effective in reducing the frequency of repeat febrile seizures, the study found that clobazam was significantly less effective than levetiracetam.

Keywords: Randomised controlled trial, Levetiracetam, Clobazam, febrile seizure.

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Introduction

When a kid between the ages of 6 months and 5 years old experiences a generalized seizure that lasts less than 15 minutes and does not recur within 24 hours but is not preceded by or related to an acute sickness of the neurological system, this is known as a simple febrile seizure.[1,2] Febrile seizures are the most common type of epilepsy in youngsters. About 2–5% of all children experience them, and about 1/3 of those youngsters claim that they have recovered. Seizures that last longer than 15 minutes, occur more than once every 24 hours, and/or are associated with postictal neurologic abnormalities, most commonly a postictal palsy, or with previous neurologic deficits have been defined as complex febrile seizures (CFS). The condition is known as febrile status epilepticus if the CFS lasts for more than 30 minutes, or if there is a series of brief seizures with no recovery of consciousness during the interictal period.[3-5]

It's likely that a combination of factors causes febrile seizures. A young, developing neurological system under the stress of a fever is especially susceptible to the harmful effects of viruses, some vaccines, and genetic predisposition.[6] Having a family history of febrile seizures, developmental delay, and hospitalisation in the neonatal intensive care unit for

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longer than 28 days are further risk factors. Incidence factors for familial epilepsy syndromes, such as these genes, may also increase the risk of febrile seizures, and underlying genetic abnormalities may increase susceptibility to environmental risk factors. Seizure threshold varies with age and vulnerability, but is generally associated with the magnitude of the temperature increase rather than the rate of increase.[7-9]

Not many pharmacological studies evaluating their effectiveness in preventing or decreasing febrile seizure recurrence have been conducted in a paediatric context. Thus, the purpose of this study was to compare the effectiveness of oral levetiracetam and clobazam in the treatment of febrile seizures in children, as well as to determine the frequency with which such seizures recurred over a 48-week follow-up period.[10] The purpose of this study is to compare the effectiveness of oral levetiracetam and clobazam in the treatment of febrile seizures in children, as well as to determine the frequency with which such seizures return after a follow-up period of 48 weeks.[11-13] The goals of this study are to compare the efficacy of the levetiracetam group vs the clobazam group in preventing febrile seizures and reducing the frequency with which febrile seizures return. Specifically, we want to see how factors like family history are connected to the occurrences.

Methodology

Children having a previous episode of febrile seizures who are seen in an outpatient paediatric clinic. This randomised controlled experiment did not hide its identity from participants. The research was carried out in Department of Pediatrics, Bhaskar Medical College & General Hospital, Moinabad, Yenkapally, Telangana, India. Research was conducted from November 2021 to October 2022. Simplified random sampling was used to choose the study participants. The randomization process will be carried out by a computer. Randomization will be done by computer generated random sequence.

Inclusion Criteria

1. A history of two or more febrile seizure events within the previous six months
2. At least one seizure within the last two weeks,
3. Age at first of between six months and five years

Exclusion Criteria

1. Intracranial infections and past episodes of seizures without a fever
2. Brain injury
3. Currently taking medication to treat epilepsy

Statistical Methods

Mean, median, mode, and standard deviation are used to depict numerical data such as age, age at first seizure, seizure length, and febrile episodes. Frequencies and percentages are used to depict categorical characteristics such as gender and family history. Graphs such as pie charts and bar charts are employed as necessary. Both tables and bar charts can be used to display data when a category variable is included. The chi-square test is used to determine statistical significance. When the anticipated value of more than 20% of the cells is less than 5, Fisher's exact test is applied. Using Fischer's exact test, we found a correlation between the groups and their frequency of febrile seizures and overall number of feverish episodes. Independent t test found associations between recurrence of febrile seizure and continuous variables such age and seizure onset age. Values of p less than 0.05 were judged to be statistically significant. Information was recorded in a Microsoft Excel spreadsheet and analysed with SPSS 16.

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RESULTS

The study's findings are broken down into the following categories: Grouping according to age, gender, seizure length, and epilepsy subtype. Correlation between cluster members with respect to onset age, family history, number of febrile episodes, and number of recurrent febrile seizures.

Table 1: Statistical analysis of the population's age structure

Variables (in months)	
Mean	32.5
Median	35.1
Mode	37.1
Standard deviation (SD)	11.1
Minimum	13.8
Maximum	50.0

The ages of the participants are shown in the table above. As a group, the subjects had a mean (SD) age of 32.5 months.

Table 2: Group-based breakdown of the population's age distribution

Variables (in months)	**Levetiracetam**	**clobazam**
Mean	33.75	34.24
Median	35.09	32.09
Mode	35.80	35.98
Standard deviation (SD)	12.00	9.72
Minimum	17.89	15.20
Maximum	50.00	47.00

The distribution of ages between the groups is seen in the above table. According to the findings, the mean duration of treatment in the levetiracetam group was 33.75 months, while it was 34.24 months in the clobazam group. Levetiracetam had a minimum and maximum of 17 and 50 months, respectively. The clobazam group had a range of 13 and 47 months, respectively.

Table 3: Distribution of gender in the population

Variable	**Frequency**
Male	30
Female	20

The gender distribution of the subjects is shown in the above table. 20 women and 30 men made up the subjects.

Table 4: Distribution of gender within the Groups

	Levetiracetam	**clobazam**
Male	28	26
Female	22	24

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The distribution of gender between the groupings is shown in the above table. In the levetiracetam group, there were 22 females and 28 males. In the clobazam group, there were 26 men and 24 women.

Table 5: Weight distribution in the population based on group

Variables	Levetiracetam	clobazam
Mean	12.21	12.43
Median	11.00	11.00
Mode	12.00	10
Standard deviation (SD)	1.38	2.35
Minimum	9.41	4.00
Maximum	16.00	17.00

The weight distribution among the subjects is shown in the table above. The mean (SD) weight in kilo grams for the levetiracetam group was 12.21 kg, while the weight for the clobazam group was 12.43 kg. The levetiracetam group's minimum and maximum weights were 9.41 and 16 kg, respectively. The clobazam group's minimum and maximum weights were 4 and 17 kg, respectively.

Table 6: The distribution of seizure types among the Groups

	Levetiracetam	clobazam
Focal	5	6
Generalized	45	44

The reported types of seizures among the subjects, broken down by group, are shown in the above table. Five of the participants had focal seizures, and 45 of the subjects in both groups had generalized seizures.

Table 7: The distribution of seizure duration in the population by group

Variables (minutes)	Levetiracetam	Clobazam
Mean	8.39	9.10
Median	6.00	6.00
Mode	6	6
Standard deviation (SD)	6.13	6.23
Minimum	6	6
Maximum	21	31

The distribution of seizure duration in the population is shown in the table above. Levetiracetam group seizures lasted an average of 8.39 minutes, while clobazam group seizures lasted an average of 9.10 minutes. In both groups, the shortest seizure lasted six minutes. Levetiracetam group's maximum time was 21 minutes, while clobazam group's highest time was 31 minutes.

Table 8: Across the groups, the dispersion of developmental history

	Levetiracetam	Clobazam
Normal	47	45
Abnormal	3	5

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The distribution of developmental history among the groupings is shown in the above table. There were 3 aberrant subjects and 47 normal subjects in the levetiracetam group. There were 45 normal subjects and 5 aberrant subjects in the clobazam group.

Table 9: Among the Groups, a history of seizures in the family

	Levetiracetam	**clobazam**
Yes	7	5
No	43	45

The distribution of participants with a history of seizures is shown in the table above. 7 people in the levetiracetam group and 5 people in the clobazam group had positive family histories, respectively.

DISCUSSION

To compare the efficacy of oral levetiracetam and clobazam in the treatment of febrile seizures in children, and to assess the recurrence rate of these seizures after 48 weeks of follow-up. Fifty men and forty-seven women made up the total number of participants. In the groups given levetiracetam and clobazam, seizures often began between months and a year later. There was no correlation between the commencement of febrile seizures at a younger age, being a female, or having a family history of seizures and the occurrence of subsequent febrile seizures.

While most cases of epilepsy appear between birth and the age of two, new research by Margriet et al. existing data suggests that the occurrence of seizures decreases with age. Other studies corroborated the male dominance trend. According to the available data, generalised seizures are by far the most prevalent type. Having a seizure for the first time before the age of 18 months, having a family history of seizures, and having a fever that lasts more than an hour are all strongly correlated with one another.[14-16]

The average number of febrile episodes was 3.61 for those using levetiracetam and 3.48 for those taking clobazam, according to the study. There were no more than six instances for those using levetiracetam. Between zero and eight events occurred in the clobazam group. There was a single recurrence of febrile seizures in 23 participants in the levetiracetam group and 15 patients in the clobazam group. Two different episodes of febrile seizures occurred in the same person across both groups. Fever occurrences and the recurrence of febrile seizures do not differ significantly between the groups. Those who were given clobazam had a lower rate of febrile seizure recurrence than those who were given levetiracetam.[17-19]

Out of a total of 98 febrile episodes in the LEV-treated group, 12 incidences of FS were observed in a study done in 2016 by Chaudhary et al. Fever occurred in 66 of the 25 children receiving CLB, and 9 of them had FS. There were significant distinctions in the frequency of febrile seizures between the two groups. Recurrence of seizures was less common in the CLB group compared to the LEV group. The average number of febrile episodes in the clobazam group was 3.1, while it was 2.56 in the placebo group, according to research by Rose et al. in 2005. Six of the 48 persons in the placebo group and one of the 60 people in the clobazam group (1.7% each) experienced a recurrence of seizures. Clobazam and placebo both caused sleepiness and weariness, but clobazam users also reported ataxia.[20-22]

In research done in 2004, Bajaj et al. found that 27 patients in the clobazam group and 24 patients in the placebo group experienced generalized seizures, whereas 3 patients in the clobazam group and 6 patients in the placebo group experienced partial seizures. Seven clobazam patients and two placebo patients experienced generalized seizures, while twenty-three placebo patients and two placebo patients experienced partial seizures.[23] Recurrences of febrile seizures occurred in 31% of patients receiving clobazam and 83% of patients

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receiving a placebo. Seizure frequency fell from 0.139 per febrile episode in the clobazam group to 0.820 in the placebo group after treatment. The average number of seizures in the past six months decreased from 4.33 2.78 to 0.7 1.37 in the clobazam group, whereas there was no change in the placebo group.[24-26]

The effectiveness of levetiracetam in avoiding future seizures was compared to that of a placebo in a 2014 study by Lin Han Yu et al. Among the 148 cases of fever in the levetiracetam group, 11 children had a relapse of FS.[27,28] Thirty-seven children in the control group experienced fever, and 19 of them had febrile seizures once again. There was a major difference in the recurrence of febrile seizures and fever between the two groups. The overall cost of preventing febrile seizure recurrence is lower in the LEV group compared to the control group. During the 48-week follow-up period, one patient in the LEV group reported significant fatigue. To compare the efficacy of oral levetiracetam and clobazam in the treatment of febrile seizures in children, and to assess the recurrence rate of these seizures after 48 weeks of follow-up.[29-31]

CONCLUSION

The study was an open-label randomised controlled trial of children with febrile seizures who had at least one seizure recurrence in the past two weeks and an onset age between 6 months and 5 years. No significant connection was seen between fever episodes and recurrence of febrile seizures. Clobazam had less febrile seizures than levetiracetam. Age of onset, gender, and family history of seizure did not significantly affect febrile seizure recurrence. Clobazam reduced febrile seizure recurrence less than levetiracetam, according to the study.

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