ISSN Print: 2394-7500
ISSN Online: 2394-5869
Impact Factor: 3.4
IJAR 2014; 1(1): 590-593
www.allresearchjournal.com
Received: 26-04-2014
Accepted: 30-05-2014

Dr. S Satyanarayanan
Assistant Professor, Department of Community Medicine, Aarupadai Veedu Medical College & Hospital, Puducherry, India

Dr. Kolati Naveen
Assistant Professor, Department of Paediatrics, Madha Medical College and Research Institute, Chennai, India

Correspondence
Dr. Kolati Naveen
Assistant Professor, Department of Paediatrics, Madha Medical College and Research Institute, Chennai, India

A randomized controlled trial examining clobazam vs. intermittent oral levetiracetam for the prevention of febrile seizures in children

Dr. S Satyanarayanan and Dr. Kolati Naveen

Abstract
Introduction: A simple febrile seizure is defined as a generalized seizure lasting less than fifteen minutes in a child between the ages of six months and five years, that does not repeat within twenty-four hours, and that is not preceded by or associated with an acute neurological illness. The most prevalent form of epilepsy in children is febrile seizures.
Methods: Children examined at an outpatient pediatric clinic who have experienced febrile seizures in the past. The identity of this randomized controlled experiment was disclosed to the participants. From January 2013 to December 2013, the study was conducted at the pediatric department at Madha Medical College and Research Institute in Chennai, India. Using simplified random sampling, the study participants were selected. The computer will do the randomization procedure.
Results: Children with a history of febrile seizures, defined as two or more episodes of febrile seizures in the preceding six months and at least one seizure recurrence in the preceding two weeks, ranging in age from six months to five years, were the subjects. This study's main goals are to assess the efficacy of oral levetiracetam and clobazam in treating febrile seizures in children and to ascertain how frequently these seizures recur following a 48-week follow-up period.
Conclusion: The study discovered that levetiracetam was much more beneficial than clobazam in lowering the frequency of recurrent febrile seizures, despite the effectiveness of both medications in this regard.

Keywords: Randomised controlled trial, levetiracetam, clobazam, febrile seizure

Introduction
A simple febrile seizure is defined as a generalized seizure lasting less than fifteen minutes in a child between the ages of six months and five years, that does not repeat within twenty-four hours, and that is not preceded by or associated with an acute neurological illness [1, 2]. The most prevalent form of epilepsy in children is febrile seizures. Approximately 2-3% of children report having them, and about 1/3 of those kids say they are well now. Complex febrile seizures (CFS) are characterized as seizures that last more than 15 minutes, happen more than once in a 24-hour period, and/or are linked to postictal neurologic abnormalities, most frequently a postictal palsy, or to prior neurologic impairments [3-5].
Most likely, a number of variables work together to trigger febrile seizures. Under the strain of a fever, a growing nervous system is particularly vulnerable to the negative effects of some vaccinations, infections, and genetic predispositions [6]. Additional risk factors include developmental delay, hospitalization in the neonatal critical care unit for longer than 28 days, and a family history of febrile seizures. These genes and other associated factors with a higher incidence of familial epilepsy syndromes may also raise the chance of febrile seizures, and underlying genetic abnormalities may make a person more vulnerable to environmental risk factors. The size of the temperature increase rather than the pace of increase is often connected with the seizure threshold, however it varies with age and vulnerability [7-9].
Therefore, the aim of this study was to assess the efficacy of clobazam and oral levetiracetamin treating febrile seizures in children and to ascertain the frequency of seizure recurrence throughout a 48-week follow-up period [10].
This study aims to assess the efficacy of clobazam and oral levetiracetam in treating febrile

seizures in children and to ascertain the frequency of seizure recurrence during a 48-week follow-up [11–13]. This study aims to evaluate the effectiveness of two treatment groups: levetiracetam and clobazam, in preventing febrile seizures and lowering the frequency of recurrent febrile seizures. In particular, we're interested in determining the relationship between the events and variables like family history.

Methodology

Children examined at an outpatient pediatric clinic who have experienced febrile seizures in the past. The identity of this randomized controlled experiment was disclosed to the participants. From January 2013 to December 2013, the study was conducted at the pediatric department at Madha Medical College and Research Institute in Chennai, India. Using simplified random sampling, the study participants were selected. The computer will do the randomization procedure. A random sequence created by a computer will be used for randomization.

Inclusion Criteria

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

Exclusion Criteria

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

Statistical Methods

Numerical data, including age, age at first seizure, duration of seizure, and fever episodes, are represented by means of the mean, median, mode, and standard deviation. Gender and family history are examples of categorical qualities that are represented using percentages and frequencies. When needed, graphs like pie charts and bar charts are used. When there is a category variable specified, data can be displayed using both tables and bar charts. The statistical significance is established using the chi-square test. Fisher's exact test is used when the expected value of more than 20% of the cells is less than 5. We discovered a relationship between the groups' total number of feverish episodes and frequency of febrile seizures using Fischer's exact test. An independent t test revealed relationships between continuous variables such age and seizure onset age and the recurrence of febrile seizures. Statistics were considered to be statistically significant at p-values less than 0.05. Data was entered into a Microsoft Excel spreadsheet, and SPSS 16 was used for analysis.

Results

The following categories comprise the study's findings: classification based on epilepsy subtype, age, gender, and duration of seizures. Relationships between cluster members for the frequency of febrile episodes, recurrent febrile seizures, family history, and onset age.

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

Variables (in months)	
Mean	32.5
Median	34.3
Mode	36.4
Standard deviation(SD)	11.1
Minimum	13.8
Maximum	50.0

The table above displays the contestants' ages. The individuals' average age (standard deviation) was 32.5 months.

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

Variables (in months)	Levetiracetam	clobazam
Mean	32.75	33.24
Median	34.09	31.09
Mode	34.80	34.98
Standard deviation (SD)	12.00	9.72
Minimum	17.89	15.20
Maximum	50.00	47.00

The table above displays the age distribution among the groupings. The results showed that the levetiracetam group's mean treatment duration was 32.75 months, while the clobazam group's mean treatment length was 33.24 months. The minimum and highest durations of levetiracetam were 17 and 50 months, respectively. The range for the clobazam group was 13 and 47 months, correspondingly.

Table 3: Distribution of gender in the population

Variable	Frequency
Male	30
Female	20

The table above displays the subjects' gender distribution. There were 30 men and 20 women among the subjects.

Table 4: Distribution of gender within the Groups

	Levetiracetam	clobazam
Male	29	27
Female	21	23

The table above displays the gender distribution among the categories. In the levetiracetam group, 29 males and 21 females were present. The clobazam group consisted of 23 women and 27 males.

Table 5: Weight distribution in the population based on group

Variables	Levetiracetam	clobazam
Mean	13.21	13.43
Median	11.00	11.00
Mode	13.00	11
Standard deviation(SD)	1.38	2.35
Minimum	9.21	4.00
Maximum	15.00	16.00

The table above displays the subjects' weight distribution. The levetiracetam group's mean (SD) weight in kilograms was 13.21 kg, whereas the clobazam group's weight was 13.43 kg. The lowest and maximum weights in the levetiracetam group were 9.21 and 15 kg, respectively. The minimum and maximum weights for the clobazam group were 4 and 16 kg, respectively.

Table 6: The distribution of seizure types among the Groups

	Levetiracetam	clobazam
Focal	8	6
Generalized	42	44

The above table displays the reported seizure types among the subjects, broken down by group. Forty-two people in both groups experienced generalized seizures, while eight participants experienced focal 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 table above displays the population's distribution of seizure duration. The mean duration of group seizures with levetiracetam was 8.39 minutes, whereas the average group seizures with clobazam was 9.10 minutes. The shortest seizure lasted six minutes in both groups. The longest duration for the Levetiracetam group was 21 minutes, whereas the Clobazam group's maximum duration was 31 minutes.

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

	Levetiracetam	Clobazam
Normal	47	46
Abnormal	3	4

The table above displays the developmental history dispersion among the categories. In the levetiracetam group, there were 3 abnormal subjects and 46 normal subjects. In the clobazam group, there were 4 aberrant subjects and 45 normal subjects.

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

	Levetiracetam	clobazam
Yes	7	4
No	43	46

The above table displays the distribution of people who have experienced seizures in the past. Positive family histories were reported by 4 individuals in the clobazam group and 7 individuals in the levetiracetam group.

Discussion

To evaluate the effectiveness of clobazam and oral levetiracetam in treating febrile seizures in children, as well as the likelihood of seizures returning after a 48-week period of observation. There were 47 women and 50 men among the participants overall. Seizures frequently started between months and a year later in the groups that received levetiracetam and clobazam. The occurrence of repeated febrile seizures did not correlate with the onset of febrile seizures at a younger age, being a female, or having a family history of seizures.

Although the majority of epilepsy cases manifest between birth and age two, recent study by Margriet *et al*. indicates that the likelihood of seizures declines with age. Additional research supported the pattern of male dominance. Based on the data that is currently available, generalized seizures are by far the most common form. Strong correlations have been shown between the following conditions: fever lasting more than an hour, having a family history of seizures, and experiencing a seizure for the first time before the age of 18 months [14].

The study found that the average number of febrile episodes was 3.48 for those on clobazam and 3.61 for those receiving levetiracetam. Levetiracetam users experienced no more than six occurrences. The number of occurrences in the clobazam group ranged from 0 to 8. In the levetiracetam group, there was one recurrence of febrile seizures, but in the clobazam group, there were fifteen cases. The same individual experienced two distinct bouts of febrile seizures in each group. There are no appreciable differences in the frequency of fever episodes or the recurrence of febrile seizures between the groups. Compared to those who received levetiracetam, those who received clobazam saw a decreased rate of febrile seizure recurrence [15].

A 2016 study by Chaudhary *et al*. found that among the 98 febrile episodes in the LEV-treated group, 12 cases of FS were noted. Of the 25 children getting CLB, 66 developed fever, and 9 of them had FS. The frequency of febrile seizures varied significantly between the two groups. Seizures recurred less frequently in the CLB group than in the LEV group. Rose *et al*. (2005) found that the average number of febrile episodes was 2.56 in the placebo group and 3.1 in the clobazam group. A recurrence of seizures was reported by six of the 48 participants in the placebo group and one of the 60 participants in the clobazam group (1.7% each). In addition to causing fatigue and drowsiness, clobazam users also reported ataxia [16].

In a 2004 study, Bajaj *et al*. discovered that 23 patients receiving clobazam and 24 patients receiving a placebo had generalized seizures, while 3 patients receiving clobazam and 6 patients receiving a placebo had partial seizures. Generalized seizures were reported by seven clobazam patients and two placebo patients, whereas partial seizures were reported by twenty-three placebo patients and two placebo patients [17]. In 31% of patients on clobazam and 83% of individuals on a placebo, there were recurrences of febrile seizures. Following therapy, the frequency of seizures decreased from 0.139 per febrile episode in the clobazam group to 0.820 in the placebo group. In the clobazam group, the average number of seizures during the previous six

months dropped from 4.33 2.78 to 0.7 1.37, but in the placebo group, there was no change [18].

In a 2014 study by Lin Han Yu *et al*., the efficacy of levetiracetam in preventing more seizures was compared to a placebo. Eleven of the 148 children in the levetiracetam group experienced an FS relapse [19]. In the control group, 37 children had fever, and 19 of them experienced febrile seizures once again. The two groups' rates of fever and febrile seizure recurrence differed significantly. In comparison to the control group, the LEV group incurred a lower total cost of preventing the recurrence of febrile seizures. Significant fatigue was noted by one patient in the LEV group during the 48-week follow-up period. to evaluate the effectiveness of clobazam and oral levetiracetam in treating febrile seizures in children, as well as the likelihood of seizures returning after a 48-week period of observation.

Conclusion

Children with febrile seizures who had at least one seizure recurrence in the previous two weeks and an onset age between six months and five years were included in the open-label randomised controlled trial. There was no discernible link seen between fever bouts and febrile seizure recurrence. Levetiracetam caused more febrile seizures than clobazam. The recurrence of febrile seizures was not significantly impacted by age of onset, gender, or family history of seizures. The study found that clobazam reduced the recurrence of febrile seizures less than levetiracetam.

Conflict of Interest

None.

Funding

None.

References

1. Graves RC, Oehler K, Tingle LE. Febrile seizures: risks, evaluation, and prognosis. Am Fam. Physician. 2012 Jan;85(2):149-153.
2. Seizures SF. Febrile Seizures: Guideline for the Neurodiagnostic Evaluation of the Child with a Simple Febrile Seizure. Pediatrics. 2011 Feb 1;127(2):389 LP-394.
3. Verity CM, Butler NR, Golding J. Febrile convulsions in a national cohort followed up from birth. I--Prevalence and recurrence in the first five years of life. Br Med J (Clin Res Ed). 1985 May;290(6478):1307-1310.
4. Mani KS, Rangan G, Srinivas HV, Kalyanasundaram S, Narendran S, Reddy AK, *et al*. The Yelandur study: A community-based approach to epilepsy in rural South India--epidemiological aspects. Seizure. 1998 Aug;7(4):281-288.
5. Goel D, Agarwal A, Dhanai JS, Semval VD, Mehrotra V, Saxena V, *et al*. Comprehensive rural epilepsy surveillance programme in Uttarakhand state of India. Neurology India. 2009;57:355-356.
6. Hackett R, Hackett L, Bhakta P. Febrile seizures in a south Indian district: incidence and associations. Dev. Med Child Neurol. 1997 Jun;39(6):380-384.
7. Capovilla G, Mastrangelo M, Romeo A, Vigevano F. Recommendations for the management of febrile seizures: Ad Hoc Task Force of LICE Guidelines Commission. Epilepsia. 2009 Jan;50(1):2-6.
8. Berg AT, Shinnar S, Shapiro ED, Salomon ME, Crain EF, Hauser WA. Risk factors for a first febrile seizure: A matched case-control study. Epilepsia. 1995 Apr;36(4):334-341.
9. Hall CB, Long CE, Schnabel KC, Caserta MT, McIntyre KM, Costanzo MA, *et al*. Human herpesvirus-6 infection in children. A prospective study of complications and reactivation. N Eng. J Med. 1994 Aug;331(7):432-438.
10. Van Zeijl JH, Mullaart RA, Galama JMD. The pathogenesis of febrile seizures: Is there a role for specific infections? Rev Med Virol. 2002;12(2):93-106.
11. Ng YT, Conry JA, Drummond R, Stolle J, Weinberg MA. Randomized, phase III study results of clobazam in Lennox-Gastaut syndrome. Neurology. 2011 Oct;77(15):1473-1481.
12. Rose W, Kirubakaran C, Scott JX. Intermittent clobazam therapy in febrile seizures. Indian J Pediatr. 2005 Jan;72(1):31-33.
13. Khosroshahi N, Faramarzi F, Salamati P, Haghighi SMO, Kamrani K. Diazepam versus clobazam for intermittent prophylaxis of febrile seizures. Indian J Pediatr. 2011 Jan;78(1):38-40.
14. Sattar S, Saha SK, Parveen F, Banu LA, Momen A, Ahmed AU, *et al*.
15. Bajaj AS, Bajaj BK, Puri V, Tayal G. Intermittent clobazam in febrile seizures: An Indian experience. J Pediatr Neurol. 2005;3:19-23.
16. Hu L-Y, Zou L-P, Zhong J-M, Gao L, Zhao J-B, Xiao N, *et al*.
17. van Stuijvenberg M, Steyerberg EW, Derksen-Lubsen G, Moll HA. Temperature, Age, and Recurrence of Febrile Seizure. Arch Pediatr. Adolesc. Med. 1998 Dec 1;152(12):1170-1175.
18. Martindale JL, Goldstein JN, Pallin DJ. Emergency department seizure epidemiology. Emerg. Med Clin. North Am. 2011 Feb;29(1):15-27.
19. Chen C-Y, Chang Y-J, Wu H-P. New-onset seizures in pediatric emergency. Pediatr. Neonatol. 2010 Apr;51(2):103-111.