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Original Research Article

Oral clobazam compared with diazepam in recurrent febrile seizures in pediatric patients: compliance and effectiveness

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ABSTRACT

Background: Febrile seizures (FS), affecting 2–5% of children under five, often recur and impact families emotionally. This study aims to assess the compliance and effectiveness of oral Clobazam versus Diazepam in treating recurrent FS in children. The aim of the study was to evaluate the compliance and effectiveness of oral Clobazam compared to Diazepam in pediatric patients with recurrent FS.
Methods: This comparative observational study was conducted at the Department of Pediatrics, Sir Salimullah Medical College Mitford Hospital (SSMCMH), Dhaka, over a 12 months period. One hundred children aged 6 months to 5 years with FS were randomized into Group A (oral Diazepam) with 51 children and Group B (oral Clobazam) with 49 children. The study was ethically approved and data were analyzed using SPSS 20 and Excel 2007 with t-Tests at p=0.05.
Results: In a study of 100 pediatric patients (Group A: 51, Group B: 49), males were more common in both groups (32.79% in Diazepam, 26.23% in Clobazam) and most children were aged 6–24 months (29.5% vs. 32.78%). Seizures occurred in 3.92% (Diazepam) and 8.16% (Clobazam), with no significant difference (p>0.05). Non-compliance and recurrent seizures were slightly higher in the Clobazam group. Side effects included irritability (Diazepam) and vomiting, drowsiness and irritability (Clobazam).
Conclusions: This study found that oral Clobazam and Diazepam have similar efficacy and compliance, with Clobazam showing a slightly higher incidence of recurrent seizures and side effects.

Keywords: Compliance, Diazepam, Effectiveness, Oral clobazam, Pediatric patients, Recurrent febrile seizures

INTRODUCTION

Febrile seizures (FS) are the most common seizure disorder in children, with a prevalence of 2–5% in those under five years old, occurring in an age-specific pattern.[1] FS are defined as seizures occurring between 6 and 60 months of age, associated with a body temperature of 38°C or higher and without evidence of intracranial infection, metabolic disturbances or a history of prior a FS.[2,3] They primarily affect children aged 3 months to 5 years, with a peak incidence between 14 and 18 months. FS make up roughly 25% of all childhood seizures, including cases of status epilepticus.[4-6] These seizures often recur, with a recurrence rate of 50% in children who experience their first seizure before 12 months of age, decreasing to 30% in older children.[7] Risk factors for recurrence include an initial FS before 12 months of age,

a family history of FS in first-degree relatives, seizures triggered by low-grade fever and a short interval between fever onset and seizure occurrence. The recurrent nature of FS significantly impacts families, with approximately 50% of recurrences occurring within the first year and 90% within two years of the initial episode.[8] About one-third of children experience a second seizure following another febrile illness and up to 10% may have three or more episodes.[9] These repeated occurrences can adversely affect the quality of life for both children and their families, underscoring the need for effective management strategies. Implementing appropriate prophylactic treatments can reduce the risk of recurrence, alleviating the emotional and psychological stress on families while improving long-term outcomes for affected children. Clobazam with significant anxiolytic and anticonvulsant effects, functions as a partial agonist on the gamma-aminobutyric acid (GABA) receptor complex.[10] Unlike Diazepam, it preferentially binds to the α-2 subunit, resulting in reduced sedation and cognitive side effects, thereby offering a more favorable side effect profile.[11] In contrast, Diazepam, a commonly used benzodiazepine for FS prophylaxis, is administered orally or as suppositories but is often discontinued due to side effects such as dizziness, drowsiness and imbalance.[12,13] Clobazam has gained attention as an effective option for intermittent FS prophylaxis, with studies indicating fewer side effects compared to Diazepam, making it a preferred choice for managing FS in children.[14,15]

Despite its advantages, significant gaps persist in understanding the comparative effectiveness and adherence to Clobazam versus Diazepam, especially in pediatric populations. The prominent adverse effects of Diazepam, including sedation and ataxia, underscore the necessity for alternatives like Clobazam.[16] However, studies evaluating Clobazam's efficacy for FS remain limited. Moreover, little research has explored Clobazam's potential to alleviate parental anxiety associated with seizure recurrence. Bridging these gaps is crucial to inform clinical decision-making and enhance the quality of care for children with FS. The purpose of the study was to assess the compliance and effectiveness of oral Clobazam compared to oral Diazepam in pediatric patients with recurrent FS.

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METHODS

This comparative observational study was conducted at the Department of Pediatrics, Sir Salimullah Medical College Mitford (SSMCMH), Dhaka, over a 12 months period. A total of 100 children (aged 6 months to 5 years) with a history of single or multiple episodes of simple or complex FS, who were admitted to the pediatric ward, were purposively selected for this study. The children were randomly divided into two groups: Group A (51 children) and Group B (49 children).

Inclusion criteria

Children of both sexes, having one or more episodes of FS. Age between 6 months to 5 years. Both simple and complex FS were considered.

Exclusion criteria

Neurological disabilities, progressive neurological disease, afebrile seizure, acute CNS infection diagnosed clinically, symptomatic seizure of other nature, developmental delay, mental retardation, chromosomal abnormalities, getting long-term antiepileptic drug.

Informed consent was obtained from all parents/guardians, ensuring confidentiality and voluntary participation. Patients were randomly apportioned into Group-A and Group-B, with Group-A having 51 and Group-B having 49 children. Group-A received oral Diazepam (0.33 mg/kg every 8 hours for 72 hours, maximum 10 mg per dose) and Group-B received oral Clobazam (1 mg/kg as a single dose, maximum 20 mg) for febrile episodes. Each patient was followed up monthly for six months.

Data were collected after acceptance of the research protocol by the ethical review committee of SSMCMH and review by BCPSA, using a pretested questionnaire. The aim and objective of the study were explained to the guardians. Written informed consent was obtained from parents before enrollment. Parents were trained to recognize FS and drug toxicities. FS recurrence, drug safety, side effects, compliance and comparative efficacy of Clobazam and Diazepam were assessed over six months period. Ethical consideration was ensured by obtaining written approval from the ethical committee of SSMCMH and the protocol was submitted to BCPS and accepted by the reviewers. Collected data were processed and analyzed using SPSS 20 (Statistical Package for Social Science) and Microsoft Office Excel 2007, with Student's t-tests carried out at a significance level of $p=0.05$.

RESULTS

The age distribution shows that in group A (Oral Diazepam), 29.5% of children were aged 6–24 months, 18.03% were aged 25–48 months and 3.27% were aged 49–60 months. In Group B (Oral Clobazam), 32.78% of children were aged 6–24 months, 13.11% were aged 25–48 months and 3.27% were aged 49–60 months. The gender distribution shows that in Group A (Oral Diazepam), 32.79% of the total study population were male and 18.03% were female. In Group B (Oral Clobazam), 26.23% were male and 22.95% were female. A slight male predominance was observed in Group A,

while Group B showed a more balanced distribution between males and females.

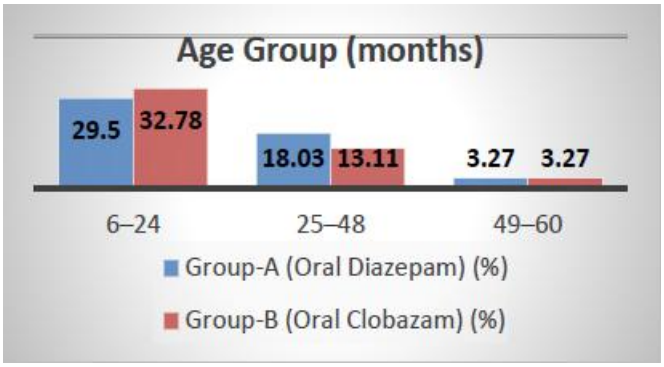

Figure 1: Age distribution of pediatric patients across study groups (n=100).

Seizures occurred in both study groups during the study period. In Group A, 2 (3.92%) patient experienced convulsions, while in Group B, 4 (8.16%) patients experienced convulsions. The two-tailed p value calculated was p=0.981166, which is greater than 0.05, providing evidence to accept the null hypothesis of equal means. This indicates no significant difference in the efficacy of the two drugs. Drug compliance for both groups is shown in Table 2. In group A, 2 (3.92%) patients missed their medication and in group B, 3 (6.12%) patients missed their medication. This difference was negligible. The calculated two-tailed p value was 0.982526, indicating no significant effect on the data analysis.

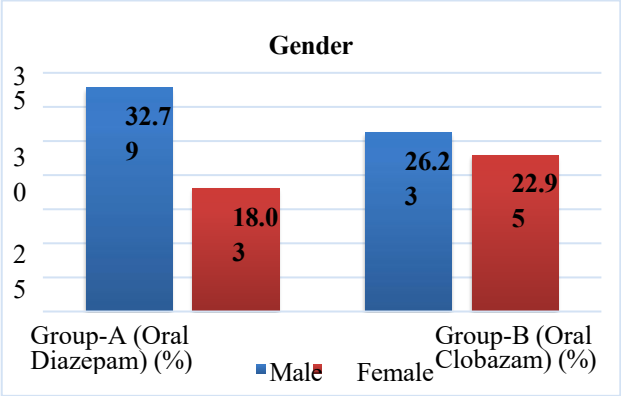

Figure 2: Sex Distribution of pediatric patients across study groups (n=100).

Table 1: Occurrence of seizures during febrile episodes in the study groups (n=100).

Group	Seizures in any episode		P value (Two tail)
	Yes, N (%)	No, N (%)	
Group-A, oral Diazepam n=51	2 (3.29)	49 (96.08)	0.98117
Group-B, Oral Clobazam n=49	4 (8.16)	45 (91.84)	
Total	6 (6.0)	94 (94.0)	

Table 2: Drug Compliance in Study Groups During Follow-Up (n=100).

Group	Drug compliance		P value (Two tail)
	Yes, N (%)	No, N (%)	
Group-A, Oral Diazepam n=51	49 (96.08)	2 (3.92)	0.982526
Group-B, Oral Clobazam n=49	46 (93.88)	3 (6.12)	
Total	95 (95.00)	5 (5.00)	

Table 3: Data of children with seizure recurrence during 6-month follow-up (n=4).

Cas	Group (Diazepam-A; Clobazam-B)	Age on enrollment (Month)	Sex (Male=M; Female=F)	Episode on enrollment (Initial=I; Recurrent=R)	Type of seizure on enrollment (Simple=S; Complex=(	No of febrile episode	No of seizure episode	No of seizure in same episode	Types of seizure (Simple=S; Complex=(	Compliance (Yes=Y; No=N)	Adverse effect
i	A	21	F	I	C	1	1	1	S	Y	Irritability
ii	B	22	M	R	S	2	1	1	S	N	
iii	B	30	F	R	S	1	1	1	S	Y	Vomiting, Drowsiness Irritability
iv	B	12	F	I	C	1	1	1	S	N	

Among the 100 samples, irrespective of age and sex, 1 patient (1.96%) from the Diazepam group and 3 patients (6.12%) from the Clobazam group experienced recurrent FS. During enrollment, 2 of these patients had simple

seizures and the other 2 had complex seizures. However, all recurrent seizures were identified as simple. Of the recurrent seizure cases, 1 patient in Group-A (Diazepam) showed compliance with the drug, while 2 of the 3 patients in Group-B (Clobazam) showed non-compliance. Among the recurrent cases, 1 patient in the Diazepam group became irritable, while 1 patient in the Clobazam group experienced vomiting, drowsiness and irritability.

DISCUSSION

Recurrent FS are common concern in pediatric patients, significantly impacting their health and quality of life. Management strategies often involve anticonvulsant medications such as oral Diazepam and Clobazam. While both drugs are widely used, their comparative effectiveness and patient compliance in managing recurrent FS remain underexplored. This observational study aimed to assess and compare the compliance and efficacy of oral Diazepam and oral Clobazam in pediatric patients with recurrent FS. A total of 100 children aged 6 months to 5 years were randomly assigned to either Diazepam or Clobazam groups and followed up for six months. The study was focused on seizure recurrence, drug safety, side effects and overall treatment compliance, with statistical analysis revealing no significant differences between the two medications in terms of efficacy or compliance.

In this study, the majority of children in Group-A (Diazepam) and Group-B (Clobazam) were aged 6-24 months, with a notable male predominance in both groups. These observations are consistent with the findings of Hossain et al, who reported a significant proportion of FS cases in children under two years of age and a higher prevalence among males.[17] This similarity underscores the importance of demographic factors such as age and gender in the incidence of FS. Understanding these patterns can aid in developing targeted interventions and improving management strategies for pediatric patients with FS.

In this study, FS occurred in 3.92% of patients in the Diazepam group and 8.16% of patients in the Clobazam group during the follow-up period. Although no significant difference in efficacy was found between the two drugs (p=0.981166), these results are consistent with the study by Khosroshahi et al where 1.7% of patients in the Clobazam group and 3.1% of patients in the Diazepam group developed FS during a 12-month follow-up.[18] Both studies observed a higher frequency of FS in the Clobazam group compared to the Diazepam group, though this difference was not that much significant. These findings suggest that while Clobazam may have a marginally higher incidence of recurrent FS, this difference is clinically negligible supporting the overall equivalence in efficacy between the two medications.

In this study, drug compliance showed that 2 patients (3.92%) in Group-A (Diazepam) missed their medication, while 3 patients (6.12%) in Group-B (Clobazam) missed theirs. This difference was negligible, with a calculated two-tailed p-value of 0.982526, indicating no significant effect on the data analysis. Similar findings were observed in the study by Khosroshahi et al where compliance rates were similarly high and the incidence of FS were slightly higher in the Clobazam group compared to the Diazepam group, but this difference was also statistically insignificant.[18] The consistent results across these studies support the conclusion that both Diazepam and Clobazam are effective for intermittent prophylaxis of FS, with comparable compliance rates and no significant differences in their efficacy.

Among the 100 samples, 1 patient (1.96%) from the Diazepam group and 3 patients (6.12%) from the Clobazam group experienced recurrent FS, irrespective of age and sex. At the outset, 2 of these patients had simple FS. However, all recurrent seizures were identified as simple. Of the recurrent cases, 1 patient in Group-A (Diazepam) showed compliance with the drug, while 2 out of the 3 patients in Group B (Clobazam) were non-compliant. Among the recurrent cases, 1 patient in the Diazepam group became irritable, while I patient in the Clobazam group experienced vomiting, drowsiness and irritability. These findings indicate that while both medications were associated with recurrent FS, non-compliance seemed to play a role in the higher recurrence observed in the Clobazam group.

These results underscore the higher recurrence rate in the Clobazam group compared to the Diazepam group, despite similar compliance challenges across both groups. The observation that all recurrent seizures were simple, despite initial complexities in some cases, highlights the unpredictable nature of FS recurrence. The overall findings suggest that while both medications are effective, compliance remains a critical factor in managing recurrent FS.

This study had some limitations, conducted at a single center, limiting the generalizability of findings. Small sample size may affect the robustness of the results. Relied on interviewers' statements for data collection, introducing potential bias.

CONCLUSION

This study evaluated the compliance and effectiveness of oral Clobazam compared to Diazepam in pediatric patients with recurrent FS. The findings showed no significant difference in seizure occurrence between the two groups (p=0.981), suggesting both drugs have comparable efficacy. Drug compliance was also similar, except few negligible differences. However, the Clobazam group experienced a slightly higher incidence of recurrent seizures and reported more side effects, including irritability, vomiting and drowsiness.

Nevertheless, both medications were effective and well-compliant, with Clobazam exhibiting a marginally higher rate of recurrent seizures and side effects.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Engel Jr J. Report of the ILAE classification core group. Epilepsia. 2006;47(9):1558-68.
2. Mikati MA. Febrile seizures. In: Kliegman MR, Behrman RE, Schor NF, editors. Nelson textbook of pediatrics. 19th ed. Philadelphia: Saunders; 2011:2017-2018.
3. Karande S. Febrile seizures: a review for family physicians. Indian J Med Sci. 2007;61(3):648.
4. Sankar R, Koh S, Wu J, Menkes JH. Paroxysmal disorders. Child Neurol. 2006;7:919-22.
5. Mikati MA, Hani AJ. Seizures in childhood. In: Kliegman RM, Stanton BF, St. Geme JW, Schor NF, editors. Nelson textbook of pediatrics. 20th ed. Philadelphia: Elsevier; 2016: 2823-2857.
6. Talebian A, Vafaei S, Sharif MR, Akbari H, Sehat M, Kheirkhah D, et al. Comparison of the effects of clobazam and diazepam in prevention of recurrent febrile seizures. J Res Med Dental Sci. 2017;5(1):49.
7. Pavlidou E, Tzitiridou M, Kontopoulos E, Panteliadis CP. Which factors determine febrile seizure recurrence. A prospective study. Brain and Development. 2008;1;30(1):7-13.
8. Nakayama J, Arinami T. Molecular genetics of febrile seizures. Epilepsy research. 2006;1;70:190-8.
9. Shinnar S. Febrile seizures. In: Swaiman KF, Ashwal S, Ferriero DM, editors. Pediatric neurology: principles & practice. 4th ed. Philadelphia: Mosby; 2006: 1079-82.
10. Gastaut H, Low MD. Antiepileptic properties of clobazam, a 1–5 benzodiazepine, in man. Epilepsia. 1979;20(4):437-46.
11. Ng YT, Collins SD. Clobazam. Neurotherapeutics. 2007;4(1):138-44.
12. Verrotti A, Latini G, di Corcia G, Giannuzzi R, Salladini C, Trotta D, et al. Intermittent oral diazepam prophylaxis in febrile convulsions: its effectiveness for febrile seizure recurrence. European J Paed Neurol. 2004;8(3):131-4.
13. Pavlidou E, Tzitiridou M, Panteliadis C. Effectiveness of intermittent diazepam prophylaxis in febrile seizures: long-term prospective controlled study. J Child Neurol. 2006;21(12):1036-40.
14. Gupta S. Febrile seizures: an overview and use of clobazam as intermittent therapy. Pediatr Today. 2002;5:113-8.
15. Bajaj AS, Bajaj BK, Puri V, Tayal G. Intermittent clobazam in febrile seizures: an Indian experience. J Ped Neurol. 2005;3(1):19-23.
16. Akman ÇI. Febrile seizures: the role of intermittent prophylaxis. J Ped Neurol. 2005;3(01):001-3.
17. Hossain MM, Saha NC. Clinical review of febrile seizure and updates. Karnataka Paed J. 2021;36(1):3-12.
18. Khosroshahi N, Faramarzi F, Salamati P, Haghighi SM, Kamrani K. Diazepam versus clobazam for intermittent prophylaxis of febrile seizures. The Indian J Ped. 2011;78:38-40.

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