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Original Article

Comparative Study of Buccal Midazolam and I.V Diazepam for Acute Treatment of Seizure in Pediatrics Age Group

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Abstract
Background: *Seizure episode is a common pediatrics neurological emergency requiring hospitalization. Urgent treatment of seizure results in favorable prognosis. Buccal Midazolam can be better drugs than intravenous (I/V) diazepam as first choice in situation where there is difficulty in accessing the i. v line urgently or in remote area where availability of trained person to control seizure is limited.*
Materials and Methods: *Total 50 (29 boys, 21 girls) patients were enrolled in the study. In the study group A, patients received buccal Midazolam (0.3 mg/kg/ dose) and in control group B, patient received I.V Diazepam (0.2 mg/kg/dose).*
Results: *In 24 cases (96%) of both group A and B, seizures were aborted by giving buccal Midazolam and i.v Diazepam respectively (P > 0.05). The mean time needed for cessation of seizures in group A was 90 ± 150 seconds (1.68 min) with the lowest time being 32 seconds and highest being 289 seconds while it was 80 ± 130 seconds (1.4 minutes) in group B with the lowest being 31 seconds and the highest being 299 seconds. The difference in time taken to control seizures between two groups was statistically insignificant (P = 0.641). No significant side effects were seen in either group.*
Conclusions: *Buccal Midazolam is quite safe drugs, equally effective than I.V Diazepam in controlling the prolonged seizure in children and can be given easily.*
Keywords: *prolonged seizure, Buccal Midazolam, i.v Diazepam, Efficacy.*

INTRODUCTION

Seizure episode is a common pediatric neurological emergency requiring hospitalization. Although the status epileptic is defined as seizure activity lasting for 30 minutes or more, or a series of seizures without recovery of consciousness in between them, it is well known that seizure activity should be terminated at the earliest. The longer the duration of seizure, the more likely the development of pharmacoresistance [1] and animal studies suggest a greater likelihood of neuronal damage [2]. Therefore the seizure or intermittent seizures without full recovery of consciousness lasting more than 5 minutes is used as a guide for intervention [3].

The major problem in the management of a child with active seizure is the wastage of time prior to drug administration that occur in reaching a hospital and gaining an intravenous (I/V) access. It is also known that prompt treatment of episodes of seizure at home results in need of fewer drugs at hospital and quicker control of the seizure episodes. Rectal diazepam (DZ) offers an alternate route of drug administration but has a slower onset of action, much lower peak concentration, socially unacceptable routes, placing themselves at risk of allegations of sexual abuse.

The buccal mucosa is highly vascularized, with a large surface area and lower degree of enzyme leading to less drug degradation prior to absorption; and also drug get direct access to systemic circulation, bypassing the first-pass metabolism by liver. Also the buccal route can be used by any person like patients- caregivers, emergency care workers as this route easily accessible and non-invasive. The intranasal route is of limited use because nasal cavity of child is of relatively small capacity (gets flooded by small volumes of drug), and is often congested by mucus, which may affect absorption. Midazolam contains an imidazole ring which is highly water soluble so gets rapidly absorbed from rectal, nasal and buccal mucosa, and is also highly lipophilic at central nervous system [4]. So considering the benefit of buccal route,

The aim of this study was to compare the efficacy of buccal Midazolam and intravenous diazepam in children aged 1 month and above to control seizures lasting more than 5 minute.

MATERIALS AND METHODS

This prospective study was conducted in the Department of Pediatrics, indira Gandhi institute of medical sciences Patna, during the period March 2015 to December 2015. Informed written consent from the parent/guardian was obtained. Efficacy of drugs was defined as cessation of seizures within 5 minutes of administration of the drug and no recurrence of seizure in the next one hour.

Inclusion Criteria

- Prolonged seizures of more than 5 minutes duration
- In children aged 1 month and over.

Exclusion Criteria

- Patients who have already received i.v benzodiazepine/barbiturates in last 24 hour.

A total 50 (29 male and 21 female) patients were enrolled in the study. The detailed clinical history and clinical examination was done. The patients was randomized in two groups-

Study Group A- patients received buccal Midazolam (0.3 mg/kg/dose) and

Control Group B- patient received Intravenous (i.v) Diazepam (0.2 mg/kg/dose).

To control seizure, the required amount of drug was withdrawn from, the Midazolam vial (1 mg/ml), into the syringe. The needle was removed. The child was placed in the supine position and any saliva if present was sucked out. Mouth was opened gently by holding chin and applying downward pressure on the lower lip. The nozzle of the syringe was placed between the lower gum and cheek on one side of the mouth (the buccal cavity). The dose was given slowly into the mouth; syringe was removed, lips were closed together, the cheeks were rubbed from outside. Midazolam can be given on either side of buccal cavity. Midazolam was given slowly to avoid choking or swallowing it. The time taken to control the seizures was noted. The control group (B) with the same indication was given Diazepam at the dose of 0.2 mg/kg/dose @ 1 mg/minute intravenously.

Patient's vitals (heart rate, respiratory rate, blood pressure, and SpO2) were monitored continuously and recorded at every 5 minutes interval. Besides this, the required life support was provided to every patient. If seizures were not controlled within 5 minute of using the drug (buccal Midazolam or i.v diazepam), or seizures recurred within 1 hour, then other anticonvulsant drugs (I/V phenobarbitone or phenytoin as per the

protocol) were used to control seizures. These patient were called non –responders.

STATISTICS

The results were averaged (mean + standard deviation) for continuous data and the number and percentage of dichotomous data. The proportions were compared using Chi-square ($\chi 2$) test of significance. The proportion of cases belonging to a specific group of the parameter or having a particular problem was expressed in absolute number and percentage. The Student's *t*-test was used to determine whether there was a statistical difference between groups in the parameters measured if the data is normal.

RESULTS

Table (a)

PARAMETER	Group A (Buccal Midazolam)	Group (B) i.v Diazepam
Age mean (std deviation) In month	34.2 ± 33.2	41.8 ± 40.8
Mean duration of seizure (minute)	12 ± 4	11.5 ± 4
No. of seizure aborted	24	24
Time to control seizure. Mean (std dev.) in seconds	90 ± 150	80 ± 130

In this study the mean age of patients in group (A) was 34.2 ± 33.2months while in group B was 41.8 ± 40.8 months. 80% children were having seizures before the age of 5 years, and 20% were having seizures in age group of 5 years and above. Both groups were comparable with respect to the mean age of cases ($P > 0.281$). There were 15 males (60%) and 10 females (40%) in group A and 12 males (48 %) and 13 females (52%) were present. On applying statistical test (Chi-square) both the groups were comparable with respect to sex distribution ($P > 0.05$). Patients in group A presented with seizures of mean duration 12 ± 4 minutes while in group B, it was 11.5 ± 4 minutes. The difference between them was statistically not significant ($P > 0.05$). (Table- a)

About 40 cases (19 in group A and 21 in group B)had generalized tonic-clonic seizures, 6 cases (4 in group A and 2 in group B) had clonic seizures, 2 cases (1 in group A and 1 in group B) cases had partial seizures, and 2 case (1 in group A , and 1 in group B) had tonic seizures . The cause of seizure was febrile seizure (case 7 Vs case 5) , seizure disorder (case 5 Vs case 4) , Meningoencephalitis (case 7 Vs case 10), Neurocysticercosis (case 2 Vs case 1), cerebral palsy (case 2 Vs case 4) , other cause (case 2 Vs case 1) in group A and group B respectively. The difference between the distribution of cases according to the type of seizures and cause of seizure among two groups was statistically not significant.

In group A, 24 cases (96%) of seizures were controlled by giving buccal Midazolam and in group B 48 cases (96%) of seizures were aborted by giving i.v Diazepam ($P > 0.05$) figure -(a).

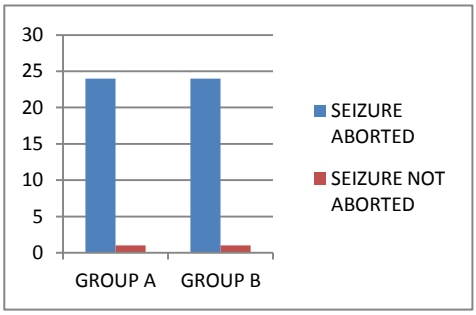

Figure (a) -- Distribution of cases according to seizures aborted.

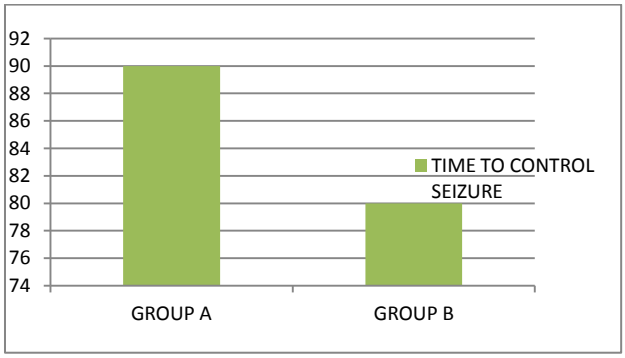

Figure (b) Comparison of mean time taken for control of seizures after drug administration.

The mean time to control seizures in group A was 90 ± 150 seconds (1.68 min) with the lowest time being 32 seconds and highest being 289 seconds while it was 80 ± 130 seconds (1.4 minutes) in group B with the lowest being 31 seconds and the highest being 299 seconds. The difference in time taken to control seizures between two groups was statistically insignificant (P = 0.641). (Figure b).

No any seizures recurred in patient of either group in the subsequent 1 hour. Seizures were not controlled within 5 minutes of drug administration in one patient of each group so other anticonvulsant was given to control seizures

DISCUSSION

This study show seizure in 24 cases (96%) in both group A and B were controlled by buccal Midazolam and i.v Diazepam respectively. Talukdar *et al.*,[5] selected 60 cases in each group, 51 out of 60 cases (85%) seizures were aborted by buccal Midazolam and 56 out of 60 cases (93.3%) by IV diazepam. Kutlu *et al.* [6] studied 19 patients, 84.2% seizures were aborted by buccal Midazolam. In a randomized clinical trial by Tonekaboni *et al.* [7] 92 patients with acute seizures, ranging from 6 months to 14 years, were randomly assigned to receive either buccal Midazolam (32 cases) or I/V Diazepam (60 cases) at the emergency department of a children's hospital. In the Midazolam group, 22 (68.8%) patients were relieved from seizures in 10 min. Meanwhile, Diazepam controlled the episodes of 42 (70%) patients within 10 min. The difference was, however, not statistically significant (P=0.9). Tonekaboni *et al.* [7] also proved that buccal Midazolam is as effective as and safer than I/V DZ in control of seizures.

In our study, mean time taken by drug, from its administration to cessation of seizures in group A was 90.00 ± 150 seconds (168 min), and it was 80 ± 130 seconds (1.4 min) in group B. In the study by Talukdar *et al.*[5] mean time for control of seizures after starting treatment in Midazolam group was 1.69 minutes and 1.13 minutes in Diazepam , not counting the time to insert the I/V line. These shows buccal Midazolam was as safe and effective as i.v Diazepam.

In this study, it was observed that the mean time taken from receiving patient at hospital to starting treatment was shorter in Midazolam group while it was longer in Diazepam group as the time spent in accessing the i. v route for diazepam was curtailed.

Buccal Midazolam was used in a dose of 0.3 mg/kg in the study. Muchohi *et al.*[8] used Midazolam at the currently recommended dose (0.3 mg/kg). It was found out that buccal Midazolam was quite safe, no any significant side effects especially cardio-respiratory was observed in both groups. Both Kutlu *et al.* [6] and Melendez *et al.* [9] reported no adverse cardio-respiratory effects in their series of patients. There was no recurrence of seizures in the subsequent 1 hour in both the group.

CONCLUSION

Buccal Midazolam is quite safe drugs and is equally effective than I.V Diazepam in controlling the prolonged seizure in children. This is a promising drugs in situation where there is difficulty in accessing the i. v line urgently and in remote area where availability of trained person to control seizure is limited.

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REFERNCES

1. Chin RF, Neville BG, Peckham C, Wade A, et al. Treatment of community-onset, childhood convulsive status epileptics: A prospective, population-based study. Lancet Neurol 2008; 7: 696-703.
2. Scantlebury MH, Heida JG, Hasson HJ, Velísková J, *et al.* Age-dependent consequences of status epilepticus: Animal models. Epilepsia 2007; 48: 75-82.

3. Anderson M. Benzodiazepines for prolonged seizures. Arch Dis Child Educ Pract Ed 2010; 95: 183-9.
4. Schwagmeier R, Alincic S, Striebel HW. Midazolam pharmacokinetics following intravenous and buccal administration. Br J Clin Pharmacol 1998; 46: 203-6.
5. Talukdar B, Chakrabarty B. Efficacy of buccal Midazolam compared to intravenous diazepam in controlling convulsions in children: A randomized controlled trial. Brain Dev 2009; 31: 744-9.
6. Kutlu NO, Dogrul M, Yakinci C, Soylu H. Buccal Midazolam for treatment of prolonged seizures in children. Brain Dev 2003; 25: 275-8.
7. Tonekaboni SH, Shamsabadi FM, Anvari SS, Mazrooei A, et al . A comparison of buccal Midazolam and intravenous diazepam for the acute treatment of seizures in children. Iran J Pediatr 2012; 22:303-8.
8. Muchohi SN, Kokwaro GO, Ogutu BR, Edwards G, et al Pharmacokinetics and clinical efficacy of Midazolam in children with severe malaria and convulsions. Br J Clin Pharmacol 2008;66: 529-38.
9. Melendez R, Batista D, Font D, Bausà T, *et al.* Prolonged convulsions treated with buccal Midazolam in a setting of mentally retarded patients with refractory epilepsy. Neurologia 2006;21: 411-3.