

Comparison of Buccal Midazolam with Rectal diazepam in Status Epilepticus in Terms of Recurrence of Seizures and Risk for Treatment Failure

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Abstract

Background: To compare buccal midazolam with rectal diazepam in status epilepticus in terms of recurrence of seizures and risk for treatment failure

Methods: In this randomized controlled study a total of 410 children with status epilepticus irrespective of cause were included. Patients were randomly divided into two groups. Patients in group A (n=205) were treated with buccal midazolam 0.3 mg/kg/dose and patients in group B (n=205) were treated with rectal diazepam 0.3 mg/kg/dose. Both groups were observed for duration of controlling of seizures within 10 minutes to see the risk for treatment failure and to check for recurrence of seizure within one hour after initial control of seizure.

Results: The average age of the patients was 4.66±2.95 years. Mean age was not significant between groups while mean duration of control of seizure was significant between groups. Recurrence was significantly high in group B as compared to group A. Group A was more effective than group B because the recurrence rate was low and treatment was significantly effective (p=0.002).

Conclusion: - Buccal midazolam offers a promising alternative to rectal diazepam for the treatment of seizures in children.

Key Words: Seizures, Buccal midazolam, Rectal diazepam, Status Epilepticus

Introduction

Transient occurrence of signs and symptoms resulting from abnormal neuronal activity in the brain is seizure. Status epilepticus (SE) is defined as a persistent epileptic seizure lasting 30 minutes or longer that is either continuous or intermittent without recovery of consciousness between seizures.¹ Seizures continuing beyond 5 minutes have the potential of progressing into full blown SE.² The estimated incidence of childhood SE is between 17 to 23

episodes per 100,000 per year.³ The highest incidence is in the first year of life.

Among types of SE, convulsive SE is the most fatal type. Non convulsive SE is less severe but early intervention may prevent bad outcome and secondary complications.⁴ The outcome of SE depends upon the underlying cause, the duration of the seizure and the age of the child. The reported mortality rate of SE in children varies between 3 and 9 percent.^{5,6} Recurrent SE occurred in 16 to 17 percent in the first year of follow-up. Recurrent SE occurred primarily in neurologically abnormal children.⁷ Refractory SE, defined as persistent seizure activity despite appropriate therapy, is associated with high mortality and morbidity.⁸

Causes of SE include central nervous system infections, acute hypoxic ischemic insult, metabolic causes (e.g hypoglycemia, inborn errors of metabolism), electrolyte imbalance, traumatic brain injury, drugs, intoxication, poisoning and cerebrovascular event.⁹ Febrile SE is the most common etiology.¹⁰

Duration of seizure activity impacts morbidity and mortality, effective methods for seizure control should be instituted as soon as possible preferably at home. The value of early treatment in seizures in reducing seizure-related morbidity has been established.¹¹ It has also been shown that prompt treatment of episodes of seizure at home results in need of fewer drugs at hospital and quicker control of the seizure.¹² Stoppage of seizure was 80 % when first-line antiepileptic drug was started less than 2 hours and was 40 % when treatment was started after 2 hours.¹³ Traditionally, benzodiazepines or other anticonvulsants have been given intravenously. The main problem in the management of the child actively showing seizure is the delay in reaching hospital and gaining an intravenous access. Rectal diazepam offers an alternative method of delivery. The long term prognosis for seizure cessation tends to be better in children than adults, particularly those who are neurologically intact.¹⁴

Patients and Methods

It is a randomized controlled study which was conducted in Paediatric Department of Holy Family Hospital Rawalpindi for one year from January 2014 to December 2014. Patients included were of age 3 months to 12 years of both sexes with documented SE. The patients having documented evidence of receiving intravenous antiepileptic drug before presentation were not included in the study. A total of 410 patients with SE irrespective of cause were included in this study. They were randomly divided into two groups, A and B. Group A (n=205) was given buccal midazolam 0.3 mg /kg/dose. Group B (n=205) was given rectal diazepam 0.3 mg/kg/dose. Both groups were observed for duration of controlling of seizures within 10 minutes to see the risk for treatment failure and to check for occurrence of seizure within 1 hour after initial control of seizure.

Results

Majority of the children were in age group 1 to 6 years (Table 1). The average age of the patients was 4.66 ± 2.95 years. Mean age was not significant between groups while mean duration of control of seizure was significant between groups (Table 2). Out of 410 patients, 52% (213/410) were male. The recurrence of seizures in subsequent hour after initial control of seizure was 20% (41/205) with rectal diazepam and 9.3% (19/205) with buccal midazolam. Recurrence was significantly high in group B as compared to group A (Table 3). According to operational definition of efficacy, group A was more effective than group B because its recurrence rate was low and treatment was significantly effective (p=0.002) (Table 4).

Table 1: Paediatric Status Epilepticus- Age distribution

Age (years)	Group A (No(%))	Group B(No(%))
< 1	21 (10.24)	44 (21.46)
1 -6	131(63.90)	106(51.71)
7-12	53 (25.85)	55 (26.83)

Table 2: Comparison of characteristics between groups

Variables	Group A(n=205)	Group B(n=205)	p-Value
Age (Years)	4.85±2.78	4.47±3.11	0.18
Duration of control of seizure(minutes)	7.54±6.29	9.96±8.71	0.001

Table 3: Recurrence of Seizures

	Group A No(%)	Group B No(%)
Yes	19(9.3)	41(20.0)
No	186(90.7)	164 (8.0)

According to gender stratification, for male cases, efficacy was high in group A than B but statistically not significant (p=0.125) (Table 5), while in female cases efficacy was significantly high in group A than group B (p=0.005)(Table 6).

Table 4: Comparison of efficacy between groups

Efficacy	Group A n=205	Group B n=205	Total	P-Value
Yes	186(90.7%)	164(80%)	350(85.4%)	0.002
No	19(9.3%)	41(20%)	60(14.6%)	

Chi-Square = 9.45

Table 5: Comparison of efficacy between groups for male patients

Efficacy	Group A n=109	Group B n=104	Total	P-Value
Yes	98(89.9%)	86(82.7%)	184(86.4%)	0.125
No	11(10.1%)	18(17.3%)	29(13.6%)	

Chi-Square = 2.35

Table 6: Comparison of efficacy between groups for female patients

Efficacy	Group A (n=96)	Group B (n=101)	Total	P-Value
Yes	88(91.7%)	78(77.2%)	166(84.3%)	0.005
No	8(8.3%)	23(22.8%)	31(15.7%)	

Chi-Square = 7.73

Discussion

Seizures lie among prevalent diseases of childhood and occur in 10% of children.¹⁵ In the emergency setting, the intravenous route is considered as the most suitable method, delivering adequate quantities of benzodiazepines in a short time. When intravenous administration is not available, other forms of benzodiazepine administration such as rectal diazepam or buccal midazolam may offer an alternative way of drug administration.¹⁶ Midazolam, an inexpensive benzodiazepine with anticonvulsive activity, can be administered via multiple routes, including topical application in the buccal cavity.¹⁷ Buccal midazolam has been found to be as effective and safe as rectal diazepam in control of seizures in developed countries.¹⁸ Potential advantages of buccal midazolam over rectal diazepam include improved efficacy, at least in developed countries, ease of administration, and safety.¹⁹

In the present study the average age of the patients was 4.66 ± 2.95 years. Out of 410 patients, 52% (213/410) were male and 48% (197/410) were female. In a study conducted by Tonekaboni et al, fifty-one (55.4%) out of 92 patients were male and forty one (44.6%) were female.²⁰ In our study, the recurrence of

seizures in subsequent hour after initial control of seizure was 20% (41/205) with rectal diazepam and 9.3% (19/205) with buccal midazolam. Similar result was also observed in a study conducted by Mpimbaza A et al, where the recurrence of seizures in subsequent hour after initial control of seizure was 17.5% with rectal diazepam and 8% with buccal midazolam.²¹

According to operational definition of efficacy, Group A was more effective than group B because the recurrence rate was low and treatment was significantly effective ($p=0.002$). In the study conducted by Thomas Marshal, buccal midazolam was found effective in seizure attacks.²² In a study conducted in China, comparison of midazolam was done with diazepam that showed different results and there was no significant difference in between two drugs in controlling seizures.²³ In a study conducted in India comparison of buccal midazolam was done with diazepam via another route that proved buccal midazolam can be used as an alternative to rectal or intravenous diazepam.²⁴ In one study conducted in Iran, efficacy of buccal midazolam was studied that showed it is more effective than rectal diazepam and easy to use as a buccal route.²⁵

Conclusions

1. Buccal midazolam offers a promising alternative to rectal diazepam for the treatment of seizures in children. Midazolam offers benefits over diazepam in ease of use, improved efficacy over 1 hour, and a more prolonged anticonvulsive effect.

2. Buccal midazolam may be a more effective bridge to long-acting agents in children who need prolonged anticonvulsant therapy.

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