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Original article

Efficacy of buccal midazolam compared to intravenous diazepam in controlling convulsions in children: A randomized controlled trial

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Abstract

A study was done to examine the efficacy of buccal midazolam in controlling convulsion in children by comparing it with intravenous diazepam, a standard mode of treating convulsions. One hundred and twenty cases presenting with convulsions to emergency were treated randomly with either buccal midazolam (in a dose of 0.2 mg/kg) or intravenous diazepam (in a dose of 0.3 mg/kg). Partial seizures, generalized tonic, clonic and tonic–clonic convulsions were included irrespective of duration or cause. One episode per child only was included. The frequency of overall control of convulsive episodes within 5 min were 85% and 93.3% in buccal midazolam and intravenous diazepam groups, respectively; the difference was, however, not statistically significant ($p = 0.142$). The mean time needed for controlling the convulsive episodes after administration of the drugs was significantly less with intravenous diazepam ($p = <0.001$). The mean time for initiation of treatment was significantly less with buccal midazolam ($p = <0.001$). The mean time for controlling the convulsive episodes after noticing these first were significantly less with buccal midazolam than with intravenous diazepam ($p = 0.004$) that is likely to be due to longer time needed for initiating treatment with intravenous diazepam in preparing the injection and establishing an IV line. There was no significant side effect in both the groups. The findings suggest that buccal midazolam can be used as an alternative to intravenous diazepam especially when getting an IV line becomes difficult. In situations where establishing an IV line is a problem, buccal midazolam may be the first choice.

Keywords: Convulsion; Seizure; Midazolam; Diazepam; Buccal midazolam; Seizure control; Epilepsy

1. Introduction

Midazolam, a potent anticonvulsant, is commonly used intravenously as infusion and also intramuscularly at times. This benzodiazepine, that contains an imidazole ring, is highly water soluble and is rapidly absorbed from rectal, nasal and buccal mucosa and is also highly lipophilic at physiologic pH that facilitate its rapid effect on CNS [1–5]. The study by Scott et al. [6] showed that midazolam administered through buccal route is as effective as rectal diazepam in controlling acute convulsion. This study showed that midazolam administered through buccal route can be used to control convulsion. This observation of Scott et al. [6] has subsequently been confirmed in a few more studies where buccal midazolam has been compared with rectal diazepam [7–9] and also where buccal midazolam has been used alone [10] to control convulsions. However, a definite protocol about use of buccal midazolam in controlling convulsions remains unclear. There is thus a need for further study to establish the efficacy and usefulness of buccal midazolam used independently in controlling

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convulsions arising out of diverse etiology. The efficacy of buccal midazolam in controlling convulsion can probably be best established by comparing it with a well accepted standard mode of therapy like intravenous diazepam. The present study was taken up to evaluate the efficacy and usefulness of buccal midazolam in controlling convulsions in children irrespective of cause by comparing with intravenous diazepam.

2. Materials and methods

2.1. Sample and study design

Children attending our pediatric emergency with an episode of convulsion irrespective of cause and duration were enrolled in the study. In a child with recurrent convulsions, only the first episode was included in the study. Seizure types included were partial and generalized tonic, clonic, and tonic–clonic. Myoclonic, atonic and absence seizures were excluded. Consecutive cases were enrolled and were randomized to receive either buccal midazolam (BMDZ) or intravenous diazepam (IVDZ). Randomization was done using the random number table. The primary outcome variable was cessation of all of motor activity.

2.2. Dose and mode of administration of the drugs

Buccal midazolam was used in a dose of 0.2 mg/kg/dose, the same dose used by Lahat et al. [11] in their study of intranasal use of midazolam to control convulsion. The solution used contained 1 mg of the drug/ml (the same solution used for intravenous administration). The calculated amount of the drug was taken in a syringe and squirted into the buccal mucosa after separating the lips. Intravenous diazepam was used in a dose of 0.3 mg/kg/dose and was administered through an intravenous line as usual. All the nurses and doctors were made aware of the study and drugs were kept handy so that no time is lost in administering these.

2.3. Assessment of response

Response was defined as stoppage of all motor activity within or by 5 min of administration of the drug signifying complete control of the convulsive episode. A drug was considered to be a failure if the motor activities did not stop by 5 min after its administration. Treatment failures in both cases were managed as per standard departmental protocol for controlling convulsions.

For every episode of convulsion time of first noticing the convulsion at arrival in the emergency (Time A), time of administering the drugs (Time B) and time of cessation of all motor activities (Time C) were noted. Time keeping was done by an assistant. Control of convulsive episodes was examined in terms of (a) *drug effect* indicated by time needed to stop the convulsion after administration of the drug (Time C−Time B), (b) *treatment initiation time* indicated by time spent in preparing the drugs before administration (Time B−Time A) and (c) *total controlling time* i.e. time needed for controlling the convulsion from the point of first noticing till it stopped (Time C−Time A).

2.4. Supportive care and monitoring for side effects

Besides use of anticonvulsants for seizure control, standard supportive care was taken for each case as required. Respiratory rate, heart rate and blood pressure were recorded just before the administration of the drug (0 min) and at 5 min and at 10 min after administration of the drugs for every child. All subsequent events were recorded till the cases were discharged. The cases were kept in the hospital for at least 48 h or as required depending upon the situation.

2.5. Case evaluation and follow up

All the cases were clinically evaluated and appropriately investigated to find the underlying cause of convulsions and also institute appropriate treatment. Some common investigations done included blood sugar, serum electrolytes, serum calcium (total and ionized), CSF analysis, CT/MRI scan and EEG. After discharge the cases were followed up in pediatric neurology clinic.

2.6. Data recording and analysis

Data was recorded in a pre-designed proforma and analysis was done keeping in mind the aims of the study. Statistical analysis was done using χ^2-test and Fisher's exact test for proportions and Student's *t*-test for quantitative means with the help of the computer package SPSS 12.05 for Windows and Epistat. A *p*-value of <0.05 was considered significant.

2.7. Ethical issues

The study was approved by hospital review committee. Informed consent prior to administration of the drug was, however, not possible as the children came convulsing. They were explained about the trial as soon as possible, usually while the drugs were being administered, and subsequently consent was taken.

3. Results

3.1. Case characteristics

Out of the 120 cases, 82 were males and 38 females. Sixty four cases (53.3%) were below 1 year of age, 24 (20.2%) between 2 and 5 years and 32 (26.7%) between