

Efficacy of intramuscular midazolam for the treatment of Status epilepticus in children

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ABSTRACT

Background: Status epilepticus (SE) is a life-threatening pediatric neurological emergency requiring rapid seizure control to prevent neuronal injury. Establishing intravenous access in actively convulsing children is often challenging, leading to treatment delays. Intramuscular midazolam, due to its rapid absorption and high bioavailability, offers a practical alternative.

Methods: A prospective observational cohort study was conducted at the Department of Pediatrics, Balochistan Institute of Child Health Services, Quetta, from September 2025 to April 2026. Sixty-six children aged 1–12 years presenting with convulsive SE (>5 minutes) were enrolled through consecutive sampling. Patients with prior epilepsy, prehospital benzodiazepine use, or contraindications were excluded. Intramuscular midazolam (0.3 mg/kg; maximum 10 mg) was administered into the vastus lateralis (<2 years) or deltoid muscle (≥2 years). The primary outcome was seizure cessation within 5 minutes. Secondary outcomes included time to cessation, recurrence within 60 minutes, and adverse events. Data was analyzed using SPSS v22.0.

Results: Among 66 patients (57.6% male; mean age 6.2 ± 3.8 years), seizure cessation within 5 minutes was achieved in 93.9% (95% CI: 87.1–97.5%). The median time to cessation was 65 seconds (range: 24–310), with a mean door-to-drug time of 58.3 ± 22.4 seconds. Higher efficacy was observed in children aged 7–9 years (100%). Febrile SE and absence of prior seizures were associated with faster control ($p < 0.05$). Recurrence occurred at 4.8%, while adverse events were mild (9.1%), including transient respiratory depression (3.0%).

Conclusion: Intramuscular midazolam (0.3 mg/kg) is a highly effective and safe first-line treatment for pediatric SE when intravenous access is unavailable.

Keywords: Efficacy, Intramuscular Injection, Midazolam, Status Epilepticus.

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Introduction

Status epilepticus (SE) is a life-threatening neurological emergency in children that requires immediate treatment to reduce morbidity and mortality. It is defined as continuous seizures lasting more than five minutes or repeated seizures without recovery between episodes (1). SE affects about 10–20 per 100,000 children each year,

with the highest rates in those under five years of age (2).

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SE includes a range of seizure types, commonly divided into two main forms: convulsive status epilepticus (CSE), marked by obvious rhythmic jerking, and non-convulsive status epilepticus (NCSE), which presents with elusive signs such as confusion, reduced awareness, or coma without clear motor activity (3). Prolonged SE leads to serious brain injury through metabolic imbalance, excitotoxicity, inflammation, and neuronal cell death. Studies show that longer seizure duration is linked to greater hippocampal damage and cognitive decline (4). In children, the risk is higher due to increased seizure susceptibility during brain development. Prolonged SE is associated with epilepsy, developmental delay, learning difficulties, and, in severe cases, death (5). Mortality in paediatric SE varies by cause, setting, and access to care. In high-resource settings, it is around 3-5% but can reach up to 25% in low- and middle-income countries (6). Among survivors, 10-30% develop neurological complications such as motor deficits, intellectual disability, or behavioral problems. Early drug treatment is key, with benzodiazepines recommended as first-line therapy in all guidelines (7). Intravenous lorazepam and diazepam are commonly used due to their rapid action and safety. However, many cases occur outside hospitals, where IV access can be difficult or delayed, particularly in young children or those with poor perfusion (8, 9). Its short half-life (1.5-3.5 hours) allows seizure control with less prolonged sedation. Studies support its use. A key prehospital trial showed IM midazolam was as effective as intravenous lorazepam for stopping seizures, with similar safety (10). Pediatric studies have shown that intramuscular midazolam achieves seizure control more

rapidly than buccal midazolam and has comparable efficacy to intranasal and rectal formulations.

Intramuscular midazolam has emerged as an effective alternative when intravenous access cannot be established promptly in children with convulsive status epilepticus. However, despite its widespread recommendation in international guidelines, there is limited published evidence from Pakistan regarding its effectiveness and safety in routine pediatric emergency practice, particularly from resource-limited healthcare settings (11). Therefore, this study evaluated the efficacy and safety of intramuscular midazolam in children presenting with convulsive status epilepticus. The primary outcomes were seizure cessation within 5 minutes, time to seizure cessation, seizure recurrence within 60 minutes, and treatment-related adverse events. This study was designed to generate local evidence to support the emergency management of pediatric convulsive status epilepticus in Pakistan.

Methods

The prospective observational cohort study was conducted at the Department of Paediatrics, Balochistan Institute of Child Health Services, Quetta, Balochistan, from September 2025 to April 2026. This research study was conducted under institute approval with number BICHQ/14405/26. Sample size was calculated using the WHO sample size calculator at 95% confidence level, 8% margin of error, and expected efficacy of 87.5% based on previous literature (12). A total of 66 patients were included with Non-probability consecutive sampling technique. Children aged 1-12 years presenting with convulsive status

epilepticus (continuous convulsive seizure activity lasting more than 5 minutes) were included after informed consent. Children with a diagnosis of epilepsy or another chronic seizure disorder requiring ongoing antiepileptic treatment, prehospital benzodiazepine use, contraindications to midazolam, or other confounding conditions were excluded. Status epilepticus was defined as continuous seizure activity lasting more than 5 minutes, and efficacy was defined as cessation of seizures within 5 minutes of a single intramuscular dose of midazolam. Eligible patients received intramuscular midazolam as first-line therapy at a dose of 0.3 mg/kg (maximum 10 mg) using the commercially available 5 mg/mL injectable preparation. Injection was administered into the vastus lateralis (<2 years) or deltoid muscle (≥2 years) using a 23-25G needle over 5-10 seconds. Intravenous access was intentionally deferred until after administration of the study drug.

All children presenting to the Paediatric Emergency Department with active convulsive status epilepticus were screened for eligibility. Baseline data were recorded on a structured proforma, including age, gender, weight, seizure duration before arrival, seizure type (febrile/afebrile), past seizure history, prior antiepileptic drug use, and vital signs (heart rate, respiratory rate, oxygen saturation, blood pressure, temperature). Etiology was categorized as febrile, remote symptomatic, or idiopathic.

Data was analyzed using IBM SPSS Statistics version 22.0. Continuous variables (age, seizure duration, time intervals) were expressed as mean $\pm$ SD or median (range), depending on distribution. Categorical variables (gender, seizure type, prior seizure history, treatment outcome) were presented as frequencies and percentages. Primary outcome (treatment success) was reported as proportion with 95% confidence interval. Group comparisons were performed using Chi-square or Fisher's exact test for categorical variables and Mann-Whitney U test for non-parametric time data. Stratified analyses were conducted for age, gender, seizure type, and prior seizure history. Multivariate logistic regression was planned to identify independent predictors of treatment response, adjusting for relevant covariates. A p-value ≤ 0.05 was considered statistically significant. A p-value ≤ 0.05 was considered statistically significant.

Results

A total of 78 children with status epilepticus were screened for eligibility during the study period from September 2025 to April 2026. Of these, 12 patients were excluded: 5 had received prehospital benzodiazepines, 4 had established IV access on arrival, 2 had known seizure disorders on chronic antiepileptic therapy, and 1 had parental refusal. The remaining 66 patients were enrolled and received intramuscular midazolam. All 66 patients completed the study protocol and were included in the final analysis (Figure 1).

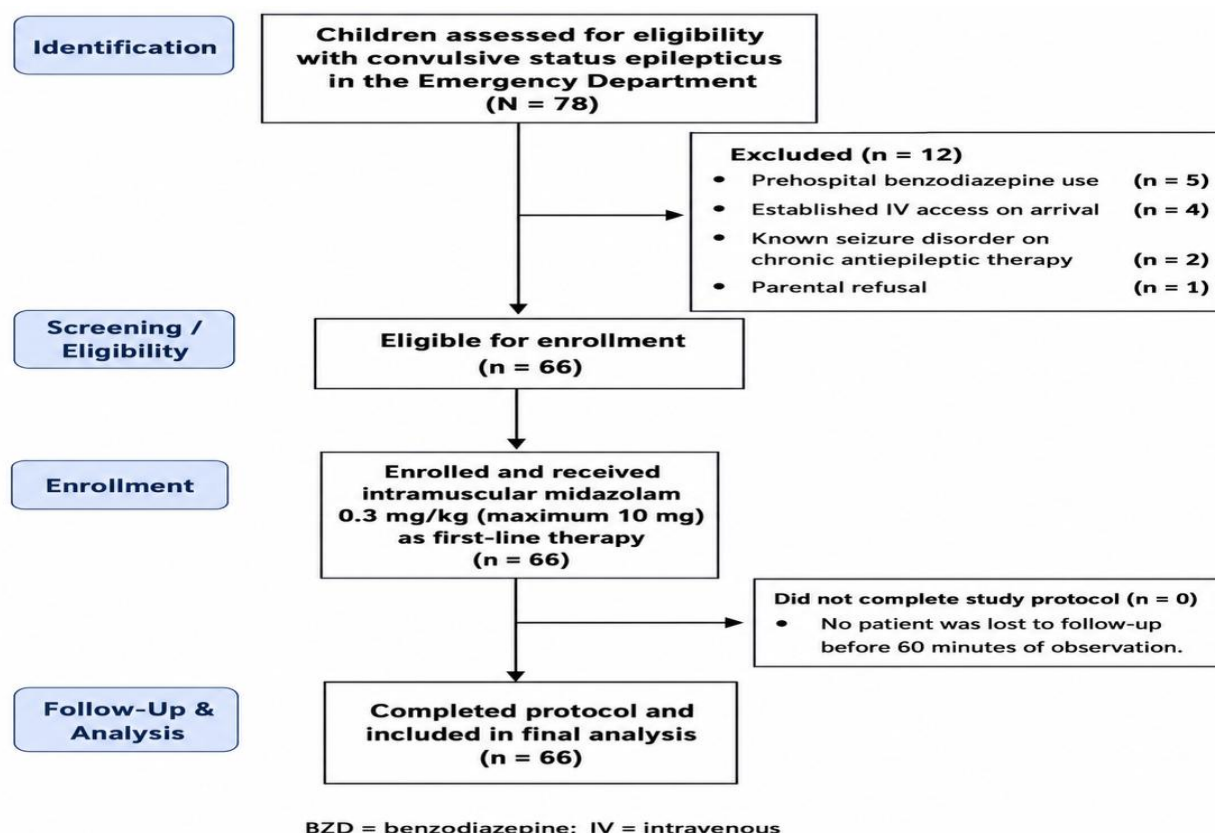


Figure 1: sketch of the overall samples used in the study.

A total of 66 children were included in the study. Among them, 38(57.6%) were male and 28(42.4%) were female. The mean age of the study population was 6.2 ± 3.8 years. According to the age groups, 22 children (33.3%) were between 1-3 years, 16 (24.2%) between 4–6 years, and 14 (21.2%) each in the 7–9 years and 10–12 years groups. The mean body weight was 19.4 ± 8.2 kg. The median duration of seizures before arrival at the hospital was 12 minutes, with a range of 6 to 45 minutes. Regarding seizure type, febrile SE was observed in 35 patients (53.0%), while 31

patients (47.0%) presented with afebrile SE. In terms of etiology, febrile causes were identified in 35 cases (53.0%), followed by remote symptomatic causes in 18 cases (27.3%), and idiopathic causes in 13 cases (19.7%). A previous history of seizures was reported in 18 patients (27.3%), whereas 48 patients (72.7%) had no such history. Prior use of antiepileptic drugs was reported in 8 patients (12.1%), while the majority, 58 patients (87.9%), had not received any antiepileptic treatment before presentation.

Table 1: Baseline Characteristics of Study Population (N = 66)

Parameters		Values
Gender, n (%)	Male	38 (57.6%)
	Female	28 (42.4%)
Age groups, n (%)	Age (years), mean $\pm$ SD	6.2 ± 3.8
	1–3 years	22 (33.3%)
	4–6 years	16 (24.2%)

	7-9 years	14 (21.2%)
	10-12 years	14 (21.2%)
Weight	Weight (kg), mean $\pm$ SD	19.4 $\pm$ 8.2
Seizure duration before arrival (minutes), median (range)		12 (6-45)
Seizure type, n (%)	Febrile status epilepticus	35 (53.0%)
	Afebrile status epilepticus	31 (47.0%)
Etiology, n (%)	Febrile	35 (53.0%)
	Remote symptomatic	18 (27.3%)
	Idiopathic	13 (19.7%)
Previous history of seizures, n (%)	Yes	18 (27.3%)
	No	48 (72.7%)
Prior antiepileptic drug use, n (%)	Yes	8 (12.1%)
	No	58 (87.9%)

Among 66 pediatric patients with convulsive status epilepticus, intramuscular midazolam achieved seizure termination within 5 minutes in 62 cases (93.9%; 95% CI: 87.1-97.5). Treatment failure occurred in 4 patients (6.1%), all of whom required increase to second-line intravenous antiepileptic agents. Subsequent seizure control was achieved using intravenous lorazepam in 2 patients (50% of failures), levetiracetam in 1 patient (25%), and phenytoin in 1 patient (25%). No patient progressed to refractory status epilepticus, and no intensive care unit

admissions were required. Early seizure recurrence within 60 minutes was observed in 3 of 62 initial responders (4.8%), all of whom responded to a repeat dose of intramuscular midazolam (0.2 mg/kg), resulting in sustained seizure control without further rise of medication. Gender-stratified analysis demonstrated comparable therapeutic efficacy between males (36/38, 94.7%) and females (26/28, 92.9%), with no statistically significant difference in treatment response ($p = 0.527$). The details are mentioned in **Table 2**

Table 2: Primary Outcome, Recurrence, and Gender-Based Efficacy of Intramuscular Midazolam

Parameter	Subgroup / Outcome	n	Response / Event	Percentage (%)	Additional Details	p-value	95% CI
Primary efficacy	Successful seizure cessation (≤ 5 min)	66	62	93.9	Complete seizure termination achieved after IM midazolam	—	87.1-97.5
	Unsuccessful (> 5 min)	66	4	6.1	Required escalation to second-line therapy	—	2.5-12.9
Rescue therapy in failures	IV lorazepam	4	2	50.0 (of failures)	Achieved seizure control after escalation	—	—
	IV levetiracetam	4	1	25.0 (of failures)	Successful secondary control	—	—
	Phenytoin	4	1	25.0 (of failures)	Successful secondary control	—	—
Refractory outcomes	Refractory SE / ICU admission	66	0	0	No progression to refractory SE or ICU requirement	—	—

Seizure recurrence	Recurrence within 60 min	62	3	4.8	Managed with repeat IM midazolam (0.2 mg/kg)	—	—
Gender-based efficacy	Male	38	36	94.7	No significant sex-based difference in response	0.527	—
	Female	28	26	92.9	Comparable therapeutic response		—

The median time from drug administration to seizure cessation was 65 seconds (range: 24–310), with a mean of 72.4 ± 48.6 seconds. The mean door-to-drug time was 58.3 ± 22.4 seconds (median: 55; range: 40–180). Overall, the total time from hospital arrival to seizure termination was 130.7 ± 58.2 seconds (median: 120; range: 75–420), indicating rapid pharmacodynamics response following intramuscular administration. The details are mentioned in **Table 3**.

Table 3: Time to Treatment and Seizure Termination Following Intramuscular Midazolam in Pediatric Status Epilepticus

Time Interval	Mean $\pm$ SD (seconds)	Median (range) (seconds)
Arrival at drug administration	58.3 ± 22.4	55 (40–180)
Drug administration to seizure cessation	72.4 ± 48.6	65 (24–310)
Arrival to seizure cessation (total)	130.7 ± 58.2	120 (75–420)

Overall efficacy remained consistently high across all age groups (85.7–100%) with no statistically significant difference (χ^2 $p = 0.672$). The highest success rate was observed in the 7–9-year group (100%), while the lowest was in the 10–12-year group (85.7%). Mean time to seizure cessation varied across age strata, with the shortest duration in 7–9 years (65.8 ± 35.2 s) and the longest in 10–12 years

(85.4 ± 62.1 s), although differences were not statistically significant ($F(3,62) = 1.84$, $p = 0.148$). A weak positive correlation was observed between age and time to seizure cessation ($r = +0.28$, $p = 0.023$), indicating a modest increase in response time with advancing age. The details are mentioned in **Table 4**.

Table 4: Age-Stratified Efficacy and Temporal Variation in Seizure Cessation Following Intramuscular Midazolam in Pediatric Status Epilepticus

Age Group	n	Success n (%)	Mean Time $\pm$ SD (s)	Median (s)	Range (s)	95% CI
1–3 years	22	21 (95.5)	68.5 ± 42.3	62	28–185	77.2–99.9
4–6 years	16	15 (93.8)	71.2 ± 38.7	65	30–165	69.8–99.8

7–9 years	14	14 (100.0)	65.8 ± 35.2	58	24–150	76.8–100.0
10–12 years	14	12 (85.7)	85.4 ± 62.1	78	35–310	57.2–98.2
Total	66	62 (93.9)	—	65	24–310	87.1–97.5

Febrile seizures and absence of prior seizure history were associated with faster seizure termination, while overall treatment efficacy remained high across subgroups without statistically significant differences in most comparisons. Febrile status epilepticus demonstrated higher treatment success (97.1%) with a shorter median time to seizure cessation (58 s) compared to afebrile seizures

(90.3%, 78 s; $p = 0.032$). Similarly, children without a prior seizure history showed higher success rates (95.8%) and faster response (62 s) than those with previous seizure history (88.9%, 85 s; $p = 0.041$). Gender-based analysis revealed comparable treatment outcomes between males (94.7%) and females (92.9%), with no statistically significant difference ($p = 0.527$). The details are mentioned in **Table 5**.

Table 5: Subgroup Analysis of Seizure Characteristics and Gender-Based Efficacy of Intramuscular Midazolam in Pediatric Status Epilepticus

Subgroup	n	Success n (%)	Median Time (s)	p-value
Febrile	35	34 (97.1)	58	0.032
Afebrile	31	28 (90.3)	78	—
Prior history (Yes)	18	16 (88.9)	85	0.041
No prior history	48	46 (95.8)	62	—
Male	38	36 (94.7)	—	0.527
Female	28	26 (92.9)	—	—

Multivariate logistic regression analysis did not identify any independent predictors of treatment success after adjustment for potential confounders. Although febrile status epilepticus (adjusted OR = 3.42, 95% CI: 0.92–12.68; $p = 0.065$) and shorter pre-hospital seizure duration (adjusted OR = 0.92 per minute, 95% CI: 0.84–1.01; $p = 0.078$) showed trends toward improved treatment response,

neither association reached statistical significance. These findings should be interpreted cautiously because the analysis was limited by the very low number of treatment failures ($n = 4$), resulting in limited statistical power and wide confidence intervals. The details are mentioned in **Table 6**.

Table 6: Multivariate Logistic Regression

Variable	Adjusted OR	95% CI	p-value
4–6 years	0.82	0.18–3.72	0.798
7–9 years	1.45	0.22–9.56	0.698
10–12 years	0.48	0.12–1.92	0.298
Male gender	1.15	0.28–4.72	0.845
Febrile seizure	3.42	0.92–12.68	0.065
No prior history	2.18	0.65–7.32	0.204
Seizure duration (per min)	0.92	0.84–1.01	0.078

No serious adverse events were recorded. Six patients (9.1%) experienced mild adverse events. Respiratory depression occurred in two patients, both in the 1–3 years age group

and resolved with supplemental oxygen. No cases required assisted ventilation or intubation. The details are mentioned in **Table 7**.

Table 7: Adverse Events by Age Group (n = 66)

Adverse Event	1–3 yrs (n=22)	4–6 yrs (n=16)	7–9 yrs (n=14)	10–12yrs (n=14)	Total n (%)
Respiratory depression	2	0	0	0	2 (3.0)
Hypotension	0	0	0	0	0 (0)
Apnea	0	0	0	0	0 (0)
Intubation	0	0	0	0	0 (0)
Injection site pain	2	1	1	0	4 (6.1)
Injection site swelling	1	0	0	0	1 (1.5)
Hypersensitivity	0	0	0	0	0 (0)
Any adverse event	4	1	1	0	6 (9.1)

Discussion

This prospective observational cohort study evaluated the efficacy of intramuscular midazolam for the treatment of status epilepticus in 66 children aged 1 to 12 years presenting to a tertiary care hospital in, Quetta, Balochistan. The key finding of our

study is that intramuscular midazolam at a dose of 0.3 mg/kg achieved seizure cessation within 5 minutes in 93.9% of children (95% CI: 87.1–97.5%), with a median time to cessation of 65 seconds (range: 24–310 seconds) and a mean time of 72.4 ± 48.6 seconds. The mean time from hospital arrival to drug

administration was 58.3 ± 22.4 seconds (median 55 seconds, range: 40–180 seconds), and the overall mean time from arrival to seizure cessation was 130.7 ± 58.2 seconds (median 120 seconds, range: 75–420 seconds). The treatment was well-tolerated, with only mild, self-limiting adverse events observed in 9.1% of patients and no serious complications or mortality. The consistency between these three studies-conducted in different cities (Ahvaz, Lahore, and Quetta) with different sample sizes (100, 370, and 66 respectively) provides compelling evidence for the reproducibility of intramuscular midazolam's efficacy across diverse paediatric populations and healthcare settings. The rapid onset of action observed in our study is one of its most clinically significant findings. The median time from drug administration to seizure cessation was 65 seconds, which is remarkably similar to the 66 seconds reported by Momen et al. (2015) and substantially faster than the 130 seconds they reported for rectal diazepam (13). Furthermore, the mean time from hospital arrival to drug administration in our study was only 58.3 seconds, demonstrating that intramuscular midazolam can be administered almost immediately upon patient arrival. This rapid administration is a critical advantage in the management of status epilepticus, as every minute of ongoing seizure activity contributes to progressive neuronal injury, increased metabolic demand, and higher risk of neurological sequelae (14). The pharmacokinetic properties of midazolam explain this rapid onset: as a water-soluble benzodiazepine, midazolam is rapidly and completely absorbed following intramuscular injection, achieving therapeutic serum concentrations within 5 to 10 minutes, with peak levels reached even sooner when injected into highly vascular muscles such as the deltoid or vastus lateralis (16). In contrast,

rectal diazepam requires passive absorption across the rectal mucosa, which can be unpredictable and is often delayed by the presence of stool or inadequate retention of the medication (13). The clinical implication of this difference is meaningful: a reduction of approximately 60 seconds in time to cessation, as observed in our study compared to published data on rectal diazepam, may translate into improved neurological outcomes, particularly in children with prolonged seizures (16).

When we stratified our analysis by age group, treatment success remained consistently high across all ages, ranging from 85.7% in the 10–12 years group to 100% in the 7–9 years group, with no statistically significant difference between groups (chi-square test $p = 0.672$). The highest success rate was observed in the 7–9 years group (100%, 95% CI: 76.8–100.0%), whereas the lowest was noted in the 10–12 years group (85.7%, 95% CI: 57.2–98.2%). The mean time to seizure cessation varied across age groups, with the shortest time observed in children aged 7–9 years (65.8 ± 35.2 seconds, median 58 seconds) and the longest in those aged 10–12 years (85.4 ± 62.1 seconds, median 78 seconds). However, this difference was not statistically significant (one-way ANOVA: $F(3,62) = 1.84$, $p = 0.148$). A weak but statistically significant positive correlation was observed between age and time to seizure cessation (Pearson $r = +0.28$, $p = 0.023$), indicating that older children tended to have slightly longer times to seizure control.

Although Hayashi et al. (2007) evaluated intravenous rather than intramuscular midazolam, their findings provide useful comparative evidence regarding factors associated with benzodiazepine response in pediatric status

epilepticus. Therefore, comparisons with our results should be interpreted cautiously because of the different routes of administration (14). One possible explanation for this age-related difference is that older children in our cohort had a higher proportion of afebrile seizures (64.3% in the 10–12 years group compared to 36.4% in the 1–3 years group). Afebrile status epilepticus is often associated with underlying neurological abnormalities, remote symptomatic aetiology, or chronic epilepsy, conditions that are known to be associated with altered GABA-A receptor expression and relative benzodiazepine resistance (16, 18). Alternatively, although our weight-based dosing of 0.3 mg/kg should have accounted for differences in body mass, it is possible that the pharmacokinetic profile of intramuscular midazolam differs slightly with age, warranting further investigation into age-specific dosing strategies (13).

Treatment success was comparable between males and females, with no statistically significant difference (94.7% in males vs. 92.9% in females, Fisher's exact test $p = 0.527$). Febrile seizures showed a higher success rate (97.1%) compared to afebrile seizures (90.3%), although the difference was not statistically significant (Fisher's exact test $p = 0.341$). However, when we analyzed time to seizure cessation by seizure type, children with febrile status epilepticus achieved seizure cessation significantly faster (median 58 seconds) than those with afebrile status epilepticus (median 78 seconds, Mann-Whitney U test $p = 0.032$). This observation is consistent with the report by Hayashi et al. (2007), who found that the effective ratio of midazolam was substantially higher in children with febrile seizures (83.3%) compared to those with encephalitis or

encephalopathy (56.8%) (14). The biological plausibility of this difference rests on several factors. First, febrile seizures typically occur in otherwise neurologically normal children with intact benzodiazepine receptor function and normal GABA-A receptor expression (18). In contrast, afebrile status epilepticus often arises in the context of pre-existing brain abnormalities, chronic epilepsy, or acute central nervous system infections conditions associated with neuroinflammation, receptor dysfunction, and relative pharmacoresistance (16, 17). Second, although not statistically significant in our study, children with afebrile seizures had a numerically longer median pre-arrival seizure duration (14 minutes) compared to those with febrile seizures (10 minutes). Prolonged seizure duration before treatment is a well-established predictor of poorer response to benzodiazepines, as sustained seizure activity leads to internalization and downregulation of GABA-A receptors, reducing their sensitivity to benzodiazepines (17).

This study has several limitations. It was a single-arm descriptive study without a comparator, precluding direct comparison with alternative benzodiazepine routes. The lack of blinding introduces potential observer bias in time-to-cessation assessment based on visual identification of motor seizure activity, although standardized timing using a digital chronometer was implemented as described by Momen et al. (2015) (13). Seizure cessation was defined clinically without electroencephalographic confirmation; therefore, electroclinical dissociation cannot be excluded, as highlighted by Hayashi et al. (2007) (14). The sample size ($n = 66$) limits precision in subgroup analyses and reduces statistical power for detecting independent predictors, particularly given the low rate of

treatment failure. The single-centre design may limit generalizability to prehospital or resource-limited settings. Exclusion of patients receiving prehospital benzodiazepines restricts applicability to routine clinical scenarios.

Conclusion

Intramuscular midazolam (0.3 mg/kg) is an effective and safe treatment for pediatric status epilepticus, achieving seizure cessation within 5 minutes in 93.9% of cases with a median time of 65 seconds. The drug was rapidly administered and well tolerated, with only mild, self-limiting adverse events and no serious complications or mortality. Faster response was observed in febrile seizures and in children without prior seizure history, while younger children may require closer monitoring for mild respiratory effects. In the absence of intravenous access, intramuscular midazolam represents a reliable first-line option, particularly in resource-limited and emergency settings. Further multicenter studies are needed to compare alternative non-intravenous routes and optimize dosing.

Limitation

The major limitation of this study is the absence of long-term neurological follow-up. Consequently, although intramuscular midazolam demonstrated excellent short-term efficacy and safety, the study could not evaluate subsequent neurological recovery, cognitive outcomes, seizure recurrence beyond the observation period, or the later development of epilepsy. Future prospective studies with extended follow-up are needed to assess these clinically important outcomes.

Ethics Approval Statement

This study was conducted in accordance with the Declaration of Helsinki (2013 revision). The research study was conducted under institute approval with number

BICHQ/14405/26. Written informed consent was obtained from the parents or legal guardians of all participating children. For children aged 7 years and above, verbal assent was also obtained.

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Conflict of Interest: None

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HISTORY	
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All the authors agree to take responsibility for every facet of the work, making sure that any concerns about its integrity or veracity are thoroughly examined and addressed.

CONTRIBUTION OF AUTHORS	
Contribution	Authors
Conception/Design	AK, MS
Data acquisition, analysis and interpretation	SM, FH, UM
Manuscript writing and approval	AK, MS, AM, SM