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Comparison of intranasal midazolam versus intravenous lorazepam for seizure termination and prevention of seizure clusters in the adult epilepsy monitoring unit

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ABSTRACT

Objective: The objective of the study was to compare the performance of intravenous (IV) lorazepam (IVL) and intranasal midazolam (INM) for seizure termination and prevention of seizure clusters in adults admitted to the epilepsy monitoring unit (EMU) in whom seizures were captured on continuous video-electroencephalogram.
Methods: Retrospective cohort of consecutive adults (≥18 years) with epilepsy admitted to the EMU at a single tertiary academic center, who experienced epileptic seizures (confirmed electroencephalographically) and required rescue therapy. The study spanned from January 2015 until December 2016, which included one year before and one year after transitioning from IVL to INM as the standard rescue therapy at our institution.
Results: A total of 50 subjects received rescue therapy and were included in the analysis. In the first year, out of 216 patients with epilepsy admitted to the EMU, 27 (13%) received IVL; in the second year, 23/217 (11%) received INM. There were no differences in baseline characteristics and markers of epilepsy severity, the median duration of index seizure (1.7 min [interquartile range (IQR): 1.1–2.7] in IVL vs. 2.0 min [IQR: 1.5–2.6] in INM group, $p = 0.20$), or in the number of subjects requiring repeat benzodiazepine administrations (IVL 8/27 [29.6%] vs. INM 7/23 [30.4%], $p = 0.95$). There were no differences in the median number of recurrent seizures in 24 h (1 [IQR: 1–3] in IVL vs. 2 [IQR: 1–4] in INM, $p = 0.27$), occurrence of status epilepticus (IVL 4/27 [14.8%] subjects vs. INM 1/23 [4.3%] subjects, $p = 0.36$), incidence of seizure clusters (IVL 8/27 [29.6%] subjects vs. INM 7/23 [30.4%] subjects, $p = 0.95$), need for transfer to an intensive care unit (ICU), or other adverse events.
Significance: In our retrospective study, INM was comparable with IVL for seizure termination and prevention of seizure clusters in the adult EMU. Intranasal midazolam circumvents the need for IV access to be maintained throughout hospitalization and is an attractive alternative to IVL as a rescue therapy in this setting. Ideally, future large, prospective, randomized, and double blind studies are needed to confirm these findings.

1. Introduction

Epilepsy is a neurological disorder affecting nearly 3 million adults in the United States, with a prevalence of approximately 1.2% in the general population [1,2]. The evaluation of patients with medically refractory epilepsy includes the characterization of seizure focus with continuous audio-visual-electroencephalography (EEG) monitoring in the adult epilepsy monitoring unit (EMU), which often requires tapering of antiseizure drugs (ASDs) to allow seizures to occur. While seizure occurrence is a necessary step for the precise identification of the seizure focus, those patients are at risk for prolonged seizures, seizure clusters, and status epilepticus [3]. The prompt management of prolonged seizures or clusters is of paramount importance for maintaining patient

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safety in this setting. This usually requires a rapid, safe, and easy administration of a rescue ASD; parenteral benzodiazepines are commonly utilized in this setting.

Rapid penetration into the central nervous system (CNS) is a critical feature for the efficacy of ASDs for seizure cessation. The intranasal (IN) route of administration is an attractive option because of the rich concentration of vascular tissue in the nares facilitating rapid absorption and subsequent CNS drug delivery [4]. In the event of seizures, the oral route of administration is rarely an option as swallowing is transiently impaired during a seizure or in the postictal state, and patients are prone to nausea and vomiting posing a high aspiration risk. The most frequently used alternative—intravenous (IV) administration—requires that a secured IV access be available at all times, which may affect patient comfort and does not guarantee that the access is patent when drug administration is needed. Midazolam, a lipophilic benzodiazepine at physiologic pH, has rapid entry in the CNS [5,6]. A pharmacokinetic evaluation of the IN route of midazolam administration (INM) demonstrated a time to maximum concentration (tmax) of 12 min, though time to minimum effective concentration is much faster at 2.5 min [7]. This attractive alternative to IV drug administration for seizure termination has been proven effective in the pediatric setting, including in convulsive status epilepticus [6].

Historically, intravenous lorazepam (IVL) has been used for this indication in most institutions, including ours. In January 2016, our epilepsy center transitioned our preferred pharmacological agent for seizure termination in the EMU from IVL to INM. The rationale behind this transition was multifactorial: 1) promising performance of INM in aborting and preventing seizures as suggested by the pediatric literature [4,8,9]; 2) complications and discomfort of IV administration likely outweighed their benefit since they were used infrequently (~13% of admitted patients based on our institution experience; unpublished data); 3) improved patient safety in the event of loss of peripheral IV access, or difficulty using a peripheral IV due to ictal motor activity; 4) shorter half-life of midazolam (2.4 ± 0.8 h) might allow capturing additional seizures (often necessary) more readily than after lorazepam use (elimination half-life of 21 ± 7 h) [5]. However, the efficacy and safety of INM in the adult EMU has not been determined.

We sought to compare the performance of two distinct approaches to seizure termination and prevention of seizure clusters in adult patients admitted to the EMU who had epileptic seizures captured during EEG monitoring: IVL and INM. We hypothesized that INM would have a similar time to administration and time to seizure termination, as well as a similar performance to IVL in the prevention of seizure clusters and status epilepticus.

2. Methods

2.1. Study design

A retrospective chart review was performed for all adults (≥18 years) with epilepsy admitted to the EMU at the Yale New Haven Hospital from January 2015 to December 2016. All subjects with electroencephalographic confirmation of epileptic seizures who received either INM or IVL were included in the analyses. Informed consent was obtained at the time of admission, and the study was approved by the Yale Institutional Review Board.

2.2. Standard of care in the adult EMU

The Yale New Haven Hospital Comprehensive Epilepsy Center, a certified level 4 epilepsy center by the National Association of Epilepsy Centers, admits patients for medical and surgical evaluation and treatment of complex patients with medically refractory epilepsy. The EMU staff nurses undergo training in safety measures in the event of a seizure. The admitted patients are continuously observed on video by 24-hour personnel who monitor for any clinical events to notify the nurses promptly. Criteria for administration of rescue medication included in an as-needed (PRN) order, was either a single convulsive seizure lasting longer than 5 min, 3 seizures occurring within a 30-minute time period, or 3 convulsive seizures occurring within an 8-hour time period. Until December 2015, all patients had IV access secured and maintained for the duration of the hospitalization, and 1–2 mg IVL was used as the default seizure rescue medication if needed. Providers could select either 1 or 2 mg of IVL as the abortive order, but not both. In January 2016, 3 mg INM was instituted as the default first-line rescue therapy, and routine IV placement was discontinued, although the default treatment could be revised at the discretion of the admitting team of physicians at all timepoints. Similarly, ASD taper and other seizure induction procedures are initiated by decision of the epileptologists on a case-by-case basis, not per protocol. Intranasal midazolam was administered using the most concentrated formulation commercially available at the time of the study (injectable 5 mg/ml) via a nasal atomizer (0.1 ml/spray); 3 sprays in each nostril were administered totaling 3 mg.

2.3. Clinical variables and outcomes

The following clinical variables were abstracted from the electronic medical record: age, sex, race, reason for admission (seizure characterization, presurgical evaluation, intracranial study), and severity of epilepsy as evidenced by the number of ASDs on admission. Seizures were classified according to the 2017 International League Against Epilepsy (ILAE) consensus: focal with impaired awareness, focal aware, bilateral tonic–clonic, and absence [10]. Those without any apparent clinical signs were classified as electrographic seizures only. The initial event leading to the administration of rescue benzodiazepine (IVL or INM) was labeled as the index seizure. The following variables were collected: the ILAE classification and duration of index seizure determined by EEG recording, time to administration of rescue benzodiazepine from EEG seizure onset, number of seizures prior to index seizure, number of ASD discontinued and undergoing wean at the time of index seizure, time to recurrent seizures within 24 h after initial rescue drug administration, the number and type of additional rescue drugs required for the termination of subsequent seizures within 24 h of the index seizure, time to seizure cessation upon administration of rescue medication, duration of any seizure, occurrence of seizure clusters (at least 2 seizures within 6 h), occurrence of status epilepticus (>5 min of motor activity with loss of consciousness or >10 min of any seizure type, including electrographic seizures) [11], need for transfer to an intensive care unit (ICU) and reason for transfer, and other adverse effects. Seizure cluster was defined as occurrence of ≥2 seizures within 6 h and was measured for the first dose of benzodiazepine [12]. The occurrence of adverse events including hypotension (systolic blood pressure <90 mm Hg within 1 h of rescue medication administration), respiratory depression (decreased oxygen saturation requiring intervention within 1 h of rescue medication administration), aspiration pneumonia (evidenced by radiographic imaging or documentation in electronic medical record), and seizure-related physical or neuropsychiatric adverse events (tongue bite, confusion, post ictal agitation/psychosis, shoulder dislocation) were reported. Variables pertaining to the tolerability of either route of drug administration were recorded, including the frequency of IV changes, any adverse event related to IV access (e.g., burning at site, IV infiltration, phlebitis), and adverse events related to IN route (e.g., burning or stinging sensation, bad taste).

2.4. Statistical methods

We compared the patients who received IVL to those who received INM for several measures. Baseline characteristics were compared using Student's t-test or nonparametric Wilcoxon rank sum test for continuous variables and the Chi-square or Fisher's exact test for categorical variables. Seizure-related variable comparisons were performed using a

random-effects logistic regression model to account for clustering within patients. Time-to-event outcomes included time-to-drug administration (IVL or INM) following initial seizure, time-to-first repeat dose of benzodiazepine following the initial administration of intervention (IVL or INM), and time-to-recurrent-seizure following the initial administration of rescue benzodiazepine (IVL or INM). These outcomes were compared using the Kaplan–Meier method and the log-rank test. All tests were two-sided, with p-values <0.05 considered to be statistically significant. Analyses were completed using SAS 9.4 (SAS Institute, Cary, NC). All continuous variables were reported as means with standard deviations and categorical variables as medians with interquartile ranges (IQRs).

3. Results

3.1. Patients

A total of 484 patients admitted to the EMU during the study time frame were identified and reviewed for eligibility. The IVL cohort comprised 216 patients with definite epilepsy admitted from January to December 2015 with an admission order for as-needed (PRN) IVL, and the INM included 217 patients from January to December 2016 with an admission order for PRN INM. Of these, 50 patients received rescue medication for an electrographically confirmed seizure and were included in the final analysis: 27/216 (13%) in the IVL and 23/217 (11%) patients in the INM groups. Of 27 patients in IVL group, 19 received 1 mg and 8 received 2 mg; review of documentation did not yield rationale for dose selection. Baseline demographics were well-matched with respect to age, gender, ethnicity, reason for admission, and severity of epilepsy as described by the number of prescribed ASDs prior to admission, number of ASDs completely discontinued at the time of index seizure, number of ASDs undergoing wean and completely discontinued at the time of index seizure, and number of seizures prior to index seizure requiring rescue medication (Table 1).

3.2. Index seizure and rescue benzodiazepine administrations

There were no differences between the number of patients requiring repeat rescue benzodiazepine administration within 24 h of the index seizure between IVL (8/27, 29.6%) and INM groups (7/23, 30.4%; p = 0.95). There were no differences in the number of repeat benzodiazepine administration within 6 h of index seizure (IVL 0.4 ± 0.7 vs. INM 0.2 ± 0.4; p = 0.24). There were no differences between the median number of seizures within 24 h of index seizure: 1 (IQR: 1–3) in IVL vs. 2 (IQR: 1–4) in INM groups (p = 0.24) or in the median duration of initial seizures: 1.7 min (IQR: 1.1–2.7) in IVL vs. 2.0 min (IQR: 1.5–2.6) in INM group (p = 0.20). There were no differences between IVL and INM groups with respect to the median time to seizure cessation after administration of benzodiazepine (IVL 3.3 min [IQR: 1.2–62.4] vs. INM 3.2 min [IQR 0.1–28.5]; p = 0.86) or in the number of subjects who were still seizing at the time of drug administration (4 patients in the IVL group vs. 3 in the INM group). Table 1 summarizes the semiologic characteristics of index seizure and Table 2 the duration of index seizure and other details of rescue therapy administration between groups.

No differences were observed between groups with respect to time-to-drug administration following initial seizure (log-rank p = 0.15; Fig. 1) or in time-to-next-drug administration after initial rescue medication (log-rank p = 0.90; Fig. 2). The median time-to-drug administration after initial seizure was 0.35 h (95% CI: 0.17 to 0.77) in the IVL group and 0.31 h (95% CI: 0.10 to 0.41) in the INM group. Additionally, there were no differences seen between time-to-recurrent-seizure after administration of IVL or INM. The median time-to-seizure-recurrence was 13.14 h (95% CI: 4.49, NA) for INM group (log-rank p = 0.31; Fig. 3); no recurrence occurred in the IVL group.

3.3. Semiology of seizures

A total of 107 seizures were captured in 50 patients within 24 h of index seizure (53 seizures in 27 patients for IVL group and 54 seizures

Table 1
Baseline characteristics and seizure semiology.

	Lorazepam (N = 27)	Midazolam (N = 23)	p-Value
Age			
Mean (SD)	38.6 (14.0)	40.0 (12.1)	0.71
Gender			0.74
Female	13 (48.1%)	10 (43.5%)	
Male	14 (51.9%)	13 (56.5%)	
Race/ethnicity			0.47
White/Caucasian	15 (55.6%)	14 (60.9%)	
Black/African-American	4 (14.8%)	3 (13.0%)	
Hispanic/Latino	8 (29.6%)	4 (17.4%)	
Other	0 (0.0%)	2 (8.7%)	
Reason for admission			0.63
Seizure characterization	18 (66.7%)	18 (78.3%)	
Pre-/surgical evaluation	3 (11.1%)	5 (21.7%)	
Intracranial study	6 (22.2%)	0 (0.0%)	
Number of ASD at baseline			
Mean (SD)	2.6 (0.9)	2.4 (0.8)	0.48
Number of ASDs discontinued at time of index seizure, median (IQR)	1 (1–2)	1 (1–3)	0.24
Number of ASDs undergoing wean and/or completely discontinued at time of index seizure, median (IQR)	2 (1–2)	2 (2–3)	0.09
Number of seizures prior to index seizure, median (IQR)	2 (1–4)	2 (1–5)	0.92

	Lorazepam (N = 53)	Midazolam (N = 54)
Types of seizure		
Focal onset with impaired awareness	24 (45.3%)	17 (31.5%)
Focal with secondary generalization	20 (37.7%)	28 (51.8%)
Electrographic only	6 (11.3%)	4 (7.4%)
Focal with preservation of awareness	3 (5.7%)	4 (7.4%)
Absence	0 (0.0%)	1 (1.9%)

All values expressed as frequency (%) unless otherwise indicated. Index seizure is the seizure prompting benzodiazepine rescue administration.
ASD = antiseizure drugs, SD = standard deviation.
Tests are chi-square or Fisher's exact test for categorical variables, t-test (parametric) or Wilcoxon rank sum test (nonparametric) for continuous variables.

Table 2
Efficacy: seizure response.

	Lorazepam (N = 27)	Midazolam (N = 23)	p-Value
Repeat benzodiazepine administered (within 24 h, # of patients)	8 (29.6%)	7 (30.4%)	0.95
# of repeat benzodiazepine (within 6 h), mean (SD)	0.4 (0.7)	0.2 (0.4)	0.24
Total # of seizures per patient including index seizure within 24 h of index seizure, median (IQR)	1 (1–3)	2 (1–4)	0.24
Duration of index seizure (min), median (IQR)	1.7 (1.1–2.7)	2.0 (1.5–2.6)	0.20
Time to seizure cessation after benzodiazepine administration (min)[a], median (IQR)	3.3 (1.2–62.4)	3.2 (0.1–28.5)	0.86
Seizure cluster, n (%)	8 (29.6)	7 (30.4)	0.95
Status epilepticus, n (%)	4 (14.8)	1 (4.3)	0.36

All values expressed as frequency (%) unless otherwise indicated.
[a] In patients still experiencing seizures when benzodiazepine administered.

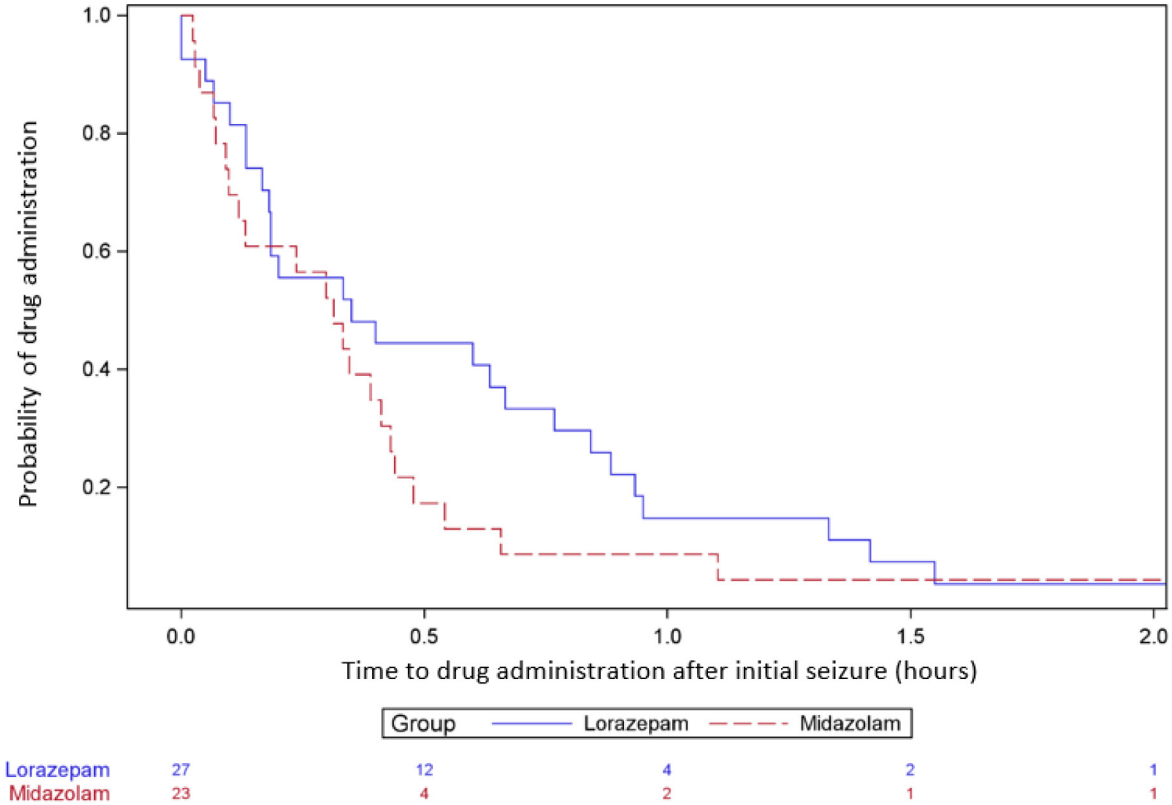
in 23 patients for INM group; Table 1). In the IVL group, seizures were more often focal with impaired awareness (24/53, 45.3%), followed by focal with secondary generalization (20/53, 37.7%), electrographic only (6/53, 11.3%), and focal with preserved awareness (3/53, 5.7%). In the INM group, focal with secondary generalization were more commonly seen (28/54, 51.8%), followed by focal with impaired awareness (17/54, 31.5%), electrographic only (4/54, 7.4%), and focal with preserved awareness (4/54, 7.4%). One patient in the entire cohort experienced absence seizures, who was in the INM group (1/54, 1.9%).

3.4. Prevalence of status epilepticus and seizure clusters

Five patients experienced status epilepticus: 1/23 (4.3%) in INM group and 4/27 (14.8%) in IVL group, p = 0.36. Of the 5 patients, 4 had focal nonconvulsive status epilepticus with impairment of awareness and 1 had electrographic nonconvulsive status epilepticus without impairment of awareness. None had refractory status epilepticus; all responded to either benzodiazepine alone (n = 1) or benzodiazepine and 1 ASD (n = 4). There was no difference in the number of patients with seizure clusters (at least 2 seizures within 6 h) in the two groups: 7/23 (30.4%) in INM vs. 8/27 (29.6%) IVL, p = 0.95.

3.5. Safety and tolerability

A summary of the safety and tolerability endpoints is shown in Table 3. There were no episodes of hypotension or respiratory depression observed after the administration of either IVL or INM. No patients required urgent or unplanned transfer to the ICU. Similar incidences of seizure-related adverse events were observed among IVL and INM groups. Seven patients in the midazolam group (30.4%) had fatigue or



	Estimate [95% CI]
Lorazepam	0.35 [0.17, 0.77]
Midazolam	0.31 [0.10, 0.41]

Fig. 1. Time-to-drug administration following initial seizure.

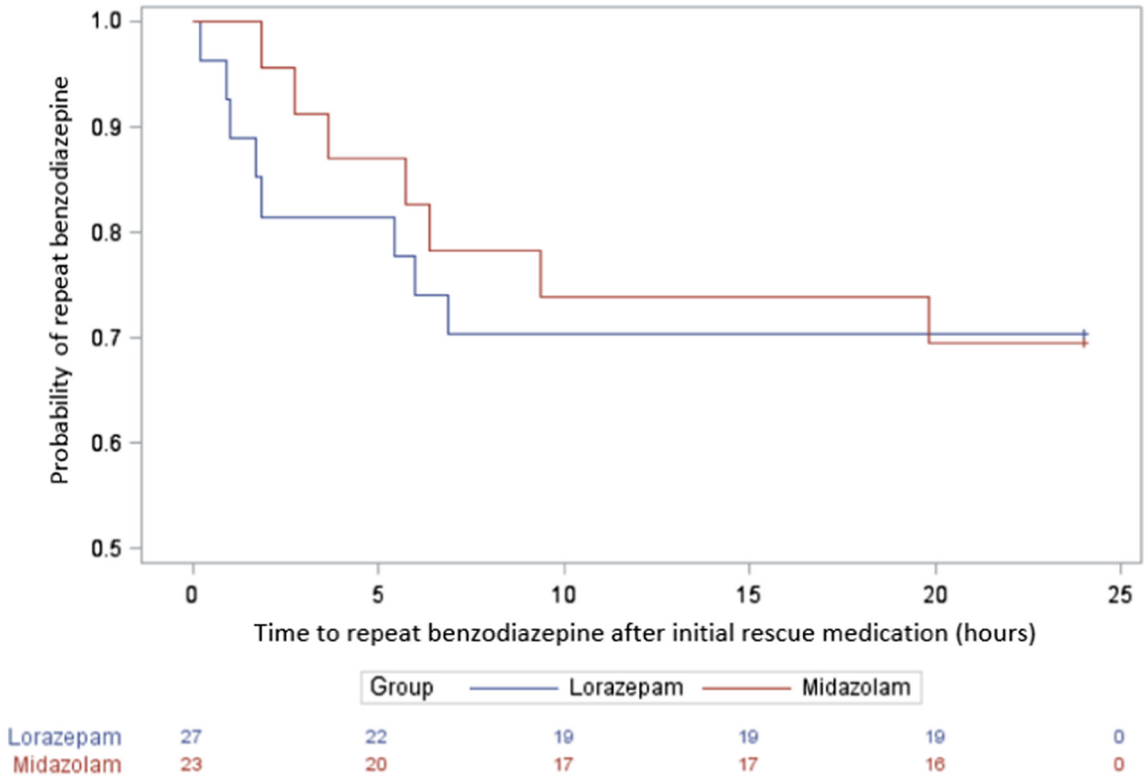


Fig. 2. Survival analysis: need for repeat benzodiazepine after administration of initial rescue medication. Log-rank p-value = 0.90. There is no difference between lorazepam and midazolam patients in time to repeated dose (p = 0.90).

felt tired, which contrasted to none reported in the IVL group (p = 0.002). There was a higher mean number of IV access changes in IVL compared with INM group (4 ± 2.9 vs. 0.6 ± 1, respectively, p < 0.001). Infiltration/extravasation of medications or phlebitis associated with IV access each occurred once in the IVL group (3.7%). All patients in the IVL and 8 patients in the INM had an IV catheter placed;

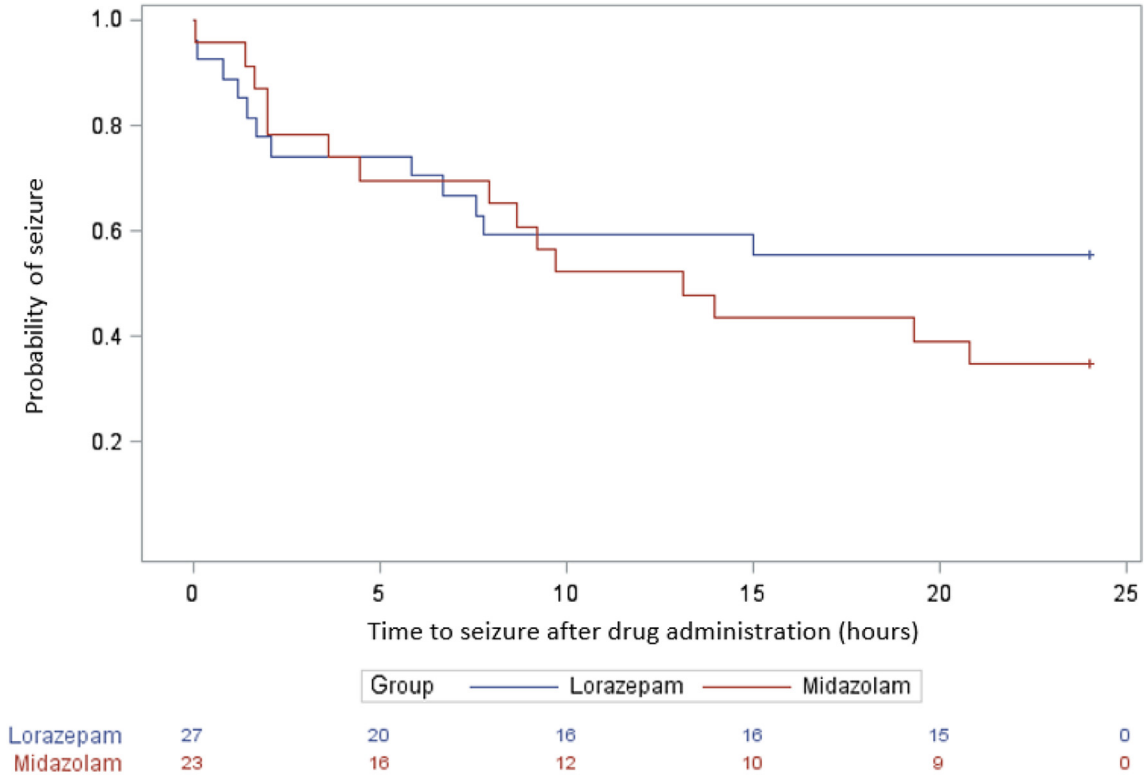


Fig. 3. Survival analysis: seizure recurrence after administration of initial rescue benzodiazepine.

Table 3
Safety endpoints.

	Lorazepam (N = 27)	Midazolam (N = 23)	p-Value
Any adverse event	15 (55.6%)	14 (60.9%)	0.70
Aspiration pneumonia	1 (3.7%)	0 (0.0%)	1.00
Transfer to ICU*	4 (14.8%)	0 (0.0%)	0.11
Hypotension	0 (0.0%)	0 (0.0%)	–
Respiratory depression	0 (0.0%)	0 (0.0%)	–
No seizure-related adverse events	13 (48.2%)	9 (39.1%)	0.52
Tongue bite	2 (7.4%)	5 (21.7%)	0.23
Postictal agitation/psychosis	4 (14.8%)	0 (0.0%)	0.11
Fatigue/tired	0 (0.0%)	7 (30.4%)	0.002
Confusion	10 (37.0%)	4 (17.4%)	0.12
Shoulder dislocation	1 (3.7%)	0 (0.0%)	1.00
Tolerability of IV			
Phlebitis	1 (3.7%)	0 (0.0%)	
Infiltration/extravasation	1 (3.7%)	0 (0.0%)	
Tolerated well	25 (92.6%)	6/8 (75.0%)	

All values expressed as frequency (%) unless otherwise indicated.
ICU = intensive care unit (*related to explantation of intracranial grid), RRT = rapid response team, IV = intravenous, SD = standard deviation.

twenty-five (92.6%) patients in the IVL and 6 (75%) patients in the INM group tolerated the IV catheter well (no documented phlebitis, infiltration, or extravasation).

4. Discussion

In this retrospective study of adult patients admitted to a single center EMU, no significant differences were found between INM and IVL regarding time-to-drug administration, time to next seizure, duration of index seizure, occurrence of seizure clusters, incidence of status epilepticus, or significant adverse effects. Thus, in our cohort, the performance of INM and IVL was comparable regarding seizure termination and prevention of SE and seizure clusters. The different intervention cohorts represented a cross-sectional analysis of a change in practice in our center when IVL was replaced by INM as preferred agent for rescue therapy in December 2015.

While the duration of index seizure was similar in both groups, a potential clinically significant difference (but not statistically significant) was noted in the risk of status epilepticus (4 in the IVL and 1 in the INM groups); given the small sample size, our findings are subjected to type II error and additional studies with larger dataset should explore this further. There was no difference in the number of patients developing seizure clusters in the two groups, or in time for seizure cessation after rescue medication was given.

Previous pediatric literature assessing the efficacy of INM in the treatment of acute seizures demonstrated successful outcomes with a mean time to seizure control of 3.5 min and without return of seizures within 1 h [4,8,9]. A prospective study conducted to determine the efficacy of INM in convulsive seizures lasting more than 10 min in nine pediatric patients identified a success rate of 100% with respect to seizure termination with only one case requiring a second dose of INM [8]. The indication for employing a benzodiazepine rescue medication in our cohort was at the discretion of the treating epileptologist according to individual patient characteristics, although common criteria described in our methods were often employed. This is in contrast to different centers that may have more uniform parameters for the utilization of rescue benzodiazepine in this setting (e.g., two consecutive secondarily generalized seizures within 60 min or three or more focal seizures with impaired awareness within 24 h of monitoring) [13]. Not infrequently, patients prone to prolonged seizures are more likely to receive abortive rescue medication. In a multicenter retrospective cohort, seizures lasting 5 or more minutes comprised approximately 4% of all captured epileptic events in adults monitored in the EMU [3] and were even rarer in another single center cohort, occurring in only 2 of 428 patients [14]. Additionally, EMU patients with an increased tendency to progress to status epilepticus or those with frequent seizure clusters often require rescue benzodiazepine administration. Seizure clusters, defined here as occurrence of ≥2 seizures within 6 h similarly to other recent studies [15], have been reported in 23% to nearly half of patients in the EMU that undergo medication taper for medical and surgical evaluation of epilepsy [3,12–14]. Nonetheless, the administration of rescue medications is not consistently reported across studies, which limits our ability to interpret the discrepancy of seizure cluster incidence seen in our study with the available literature.

Several potentially relevant clinical differences in safety events of interest did not reach statistical significance, possibly due to small sample size. Tongue biting was more commonly seen in the INM group (5/23, or 21.7%) when compared with IVL (2/27, or 7.4%), which could be related to the higher proportion of bilateral tonic–clonic seizures in the INM group (51.8% or 28/54 seizures captured) versus the IVL (37.7% or 20/53 seizures). Notably, fatigue was reported in almost one-third of INM group (7/23, or 30.4%), but this was not reported by the patients receiving IVL; this was the only clinical symptom as safety endpoint that reached statistical significance. We speculate that this could be secondary to reporting bias related to our interest in asking patients about their experience with our new protocol of using INM, leading to increased documentation of sedation. Prospective studies should collect these data in a standardized fashion to confirm or refute differences in sedation between INM and IVL. As expected, patients in the IVL group experienced more IV-related complications; however, the vast majority of patients who had an IV access established tolerated it well.

While the limitations inherent to a retrospective study apply including the susceptibility to the effects of unmeasured confounders, no other significant change in our center occurred during the same time period, and the data are likely to represent the effect of the change in practice pertaining to type of benzodiazepine rescue. Our study has limitations in addition to the reduced external validity of results from a single center experience and its retrospective design. The small sample of patients that received rescue benzodiazepine following index seizure included in the final analyses precludes any meaningful subgroup analyses; this subjects the majority of our results to type II error. Differences that were of potential clinical importance, such as incidence of status epilepticus (less likely with INM) did not reach statistical difference. Further, the approach of medication withdrawal during the EMU evaluation was variable in this cohort as our institution does not have a uniform protocol for tapering of ASD, and these decisions are individualized to each case; this could have contributed to the variability of data seen in our study. Lastly, we could not ascertain reasoning behind IVL dose selection from available documentation, which led to nearly 30% of patients receiving a higher dose (2 mg), or perform subgroup analyses to identify differences between these regimens given the small sample size. The optimal IVL and INM dosing strategy remains subject for future prospective large studies in this population, in which recording of additional seizures is often necessary. In May 2019, the United States Food and Drug Administration approved the first INM commercially available formulation (5 mg/0.1 ml in one spray), which is 10 times more concentrated than the formulation used in our study and should allow easier administration and better absorption than the formulation we used in this study.

5. Conclusion

The results of our study suggest that INM is comparable with IVL for the treatment of prolonged seizures and for the prevention of SE and seizure clusters during medical and surgical evaluations in patients with epilepsy in an EMU. Given its ease of use and lack of need for IV access, it remains our rescue medication of choice in the EMU. However, our study was limited by its retrospective nature, single center experience, and its small sample size. Future prospective, multicenter,

double-blind, and randomized controlled trials comparing INM with IVL are needed to determine a preferred therapy in this setting.

Declaration of Competing Interest

Neither of the authors has any conflict of interest to disclose.

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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