■ Original article

Epileptic Disord 2022; 24 (4): 667-676

Epileptic Disorders

Enteral lorazepam is a promising weaning strategy for midazolam-responsive febrile infection-related epilepsy syndrome (FIRES): a case series

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Received December 6, 2021;
Accepted March 24, 2022

ABSTRACT

Objective. Prolonged and repetitive cycles of pharmacological coma, with midazolam or other general anaesthetics, is often the mainstay for seizure control in febrile infection-related epilepsy syndrome (FIRES). Here we present our experience of enteral lorazepam as an effective weaning substitute in midazolam-dependent patients.

Methods. This was a retrospective study based on a review of medical records of all FIRES patients who had received enteral lorazepam as a weaning substitute for midazolam, between January 2020 and July 2021. The patients were divided into an *early* group (lorazepam initiated after one failed attempt to wean off midazolam) and *late* group (lorazepam initiated after two or more failed attempts). The conversion from intravenous midazolam to enteral lorazepam was also calculated, and epilepsy outcome at follow-up was also assessed.

Results. Seven patients (five males) were eligible. The median age at onset of FIRES was seven years (range: 4-14). A median of six (range: 6-8) anti-seizure medications (ASMs) had failed (including clobazam in two and clonazepam in one) to control seizures. The *early* and *late* lorazepam groups were comparable regarding the maximum midazolam dose for seizure control, total ASMs tried and days to wean off midazolam. The median (range) duration of hospital stay was 27 days (22-46) in the *early* group, compared to 51 days (40-78) in the *late* group. The *early* group patients were also on fewer ASMs (median: 3; range: 3-5) compared to the *late* group (median: 5; range: 4-6) at discharge. Five patients were sedated with initial lorazepam dose, but this side effect resolved on dosage reduction. On follow-up, all seven patients had seizure recurrence. In four, seizures recurred on reducing lorazepam, however, in three of these patients, this was resolved by escalating the dose.

Significance. Enteral lorazepam can be an effective weaning substitute for midazolam-dependent children with FIRES. Early introduction of enteral lorazepam was associated with reduced duration of hospital stay.

Key words: pharmacological coma, midazolam-dependent, enteral, lorazepam, FIRES

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doi:10.1684/epd.2022.1438

Febrile infection-related epilepsy syndrome (FIRES) is a subcategory of new-onset refractory status epilepticus (NORSE), characterized by prior febrile infection, between two weeks and 24 hours before the onset of seizures [1]. FIRES is one of the most devastating forms of epilepsies with difficult-to-control seizures in the acute phase, can require prolonged periods of intensive care unit (ICU) stay, and often leads to drug-resistant epilepsy [2, 3].

As the pathophysiological mechanism of this entity is still unclear, a targeted treatment protocol remains unavailable. Conventional antiseizure medications (ASMs) usually fail to control repetitive seizures [2]. Other modalities such as high-dose phenobarbitone, cannabidiol, the ketogenic diet, and immunotherapy (including anakinra) have been tried with variable results [2, 4-9]. More often though, prolonged periods of pharmacological coma is the mainstay for sustained seizure control [10].

This protracted period in hospital is a significant financial and emotional burden for families. Long intensive care stay, especially for ventilated patients, is also associated with other intervention-related secondary health complications [11]. In resource-limited settings, such as ours, this puts extra pressure on already strained healthcare infrastructure (especially with limited availability of paediatric intensive care beds) [12]. Hence, the need to wean off anaesthetic agents more rapidly cannot be overemphasized. Lorazepam has been successfully used both as an intravenous and enteral alternative for prolonged midazolam sedation in paediatric intensive care units [13, 14]. The conversion formula between the two medications is also well established [14].

In our first-ever case report, we were able to successfully wean off midazolam in a child with FIRES who was dependent on midazolam pharmacological coma (for seizure control) by adding enteral lorazepam. This significantly reduced the child's subsequent intensive care and hospital stay [15]. After this initial success, we have used a similar strategy in all our midazolam-dependent FIRES patients.

Based on a retrospective observational cohort study from three tertiary care paediatric neurology centres in India, we report the use of enteral lorazepam as a weaning substitute for midazolam-dependent children with FIRES.

Methods

Patient selection

Our retrospective cohort included all children with a diagnosis of FIRES who were dependent on midazolam for seizure control and were subsequently treated with enteral lorazepam as a weaning substitute. These patients were seen between January 2020 and July 2021 at three paediatric neurology centres in India (Jaipur, Hyderabad, and Pune).

The inclusion criteria for FIRES in our study were: (1) acute onset of the first seizure, two weeks to 24 hours after antecedent febrile illness in a previously healthy child; (2) frequent seizures evolving into refractory status epilepticus; and (3) absence of an identified pathogen in cerebrospinal fluid (CSF) [1]. Those children with a previous history of unprovoked seizures, seizures due to a known neurological disease, and/or with a structural lesion on magnetic resonance imaging (MRI) were excluded from the study.

Data collection

Data were extracted from medical case records, including clinical details and management during hospital admission. The infectious (seasonal, herpes simplex virus, and common bacterial), autoimmune (N-methyl-D-aspartate [NMDA], anti-myelin oligodendrocyte glycoprotein [MOG]) and basic metabolic workup (blood sugar, calcium, lactate, and serum ammonia) were performed in all patients. Serum contactin-associated protein 2 and leucine-rich glioma-inactivated 1(LG1) were also evaluated in most of the patients.

Patients were monitored for electroclinical and electrographic seizures with continuous 21-channel video-EEG monitoring (Nihon Koden or Nicolet) until there was seizure cessation for 24 hours. Afterwards, one four-hour epoch of EEG was performed daily to monitor for electrographic/electroclinical seizures.

3-tesla (T) brain MRI was performed in the first week of the hospital stay. If MRI had already been performed before admission to our department (1.5 or 3 T), it was only repeated if standard imaging protocols were not followed. Follow-up MRI was performed only if clinically indicated.

From medical records, follow-up disability status (using Modified Rankin Score) and epilepsy outcome were confirmed. If any of the above information was not available, it was sought via the families by the treating paediatric neurologist by telephone.

FIRES treatment protocol

All patients with FIRES at the three participating centres were managed according to proposed protocols for the management of FIRES [8, 16]. Intravenous (IV) aesthetic infusions were started when two or three ASMs failed to control seizures, with midazolam being the most widely used anaesthetic across the centres. Typically, midazolam coma induction was

initiated at 3-5 µg/kg/minute and titrated (up to a maximum of 25 µg/kg/minute) in order to achieve complete clinical and electrographic seizure control. When midazolam was ineffective or partially effective at maximum dosage, other anaesthetic agents were used including ketamine, thiopentone, and/or propofol.
Along with pharmacological coma, the ketogenic diet and immunomodulation (methylprednisolone [MPS] and intravenous immunoglobulin [IVIG]) were also tried in the initial weeks. Subsequent immunomodulation with cyclophosphamide or rituximab was used at the discretion of the treating paediatric neurologist but was not uniform across the centres.

Enteral lorazepam protocol for midazolam-responsive patients

In all patients whose seizures had responded to midazolam, the weaning of midazolam was attempted for the first time after 48-72 hours during the clinical and electrographic seizure-free period. If the first attempt to wean off midazolam was successful, lorazepam was not added and ongoing ASMs were continued. If there was seizure (electrographic/electroclinical) recurrence during this initial attempt at weaning off midazolam, then midazolam infusion was escalated back to a minimum dose required for seizure control. Enteral lorazepam was then initiated during one of these subsequent attempts to wean off midazolam. Based on the formula adapted from a study by Warrington *et al*. [14], the dose of lorazepam was calculated from the minimum intravenous midazolam dosage required for seizure (electrographic) control (see *figure 1* with an example for a 10 kg child). After initiation of enteral lorazepam, midazolam infusion was concomitantly weaned off over the next four to seven days, with continuous EEG monitoring. Tablet lorazepam (two milligrams) was crushed and given in four divided doses via nasogastric route initially and later when feasible/at discharge orally in three divided doses. If a child developed side effects (especially sedation) to lorazepam, a minimal tolerated dose was obtained.
The data on maximum dosage of intravenous midazolam infusion to control seizures, midazolam infusion rate at the time of lorazepam introduction, and dose of lorazepam at initiation and discharge were retrieved. Any documented side effect of lorazepam was also noted.

Early versus late group (initiation of lorazepam)

We compared the outcomes between patients who received lorazepam *early* (initiated after one failed attempt at weaning off midazolam) *versus* those who received it *late* (initiated after two or more failed attempts). The outcomes compared corresponded to time taken to wean off midazolam, duration of hospital stay, and number of other ASMs (in addition to lorazepam) at the time of discharge.

***Total Intravenous midazolam (mg/day) X 0.3 = Total enteral Lorazepam (mg/day)**
---------- = ...mg enteral lorazepam/ 6 hourly
4

Agent	Potency	Half life (Hrs)	Bioavailability
Midazolam (IV)	1	8.2	100%
Lorazepam (Enteral)	2	14.2	90%

Example:

Wt-10 kg, Minimum dose of intravenous midazolam controlling seizures-4 microgram (mcg) /kg/mnt

Total dose of Midazolam (mg)/day given = 4 x 10 x 60x24 = 57600 microgram = 57.6 mg/day

57.6 mg x 0.3 = 17.2 mg enteral lorazepam/day
---------- = 4.3 mg (Approx. 4 mg)/ every 6 hours
4

**This Figure is adapted from [14]Warrington SE, Collier HK, Himebauch AS, et al. Evaluation of intravenous to enteral benzodiazepine conversion calculations in a Pediatric intensive care setting. Pediatr Crit Care med 2018;19: e569-75. Copyright © 2018 by the society of Critical Care medicine and the World federation of Pediatric intensive care and Critical Care Societies.*

■ **Figure 1.** The conversion formula for intravenous midazolam and enteral lorazepam (with an example for a 10-kg child).

Statistics

The data collected from medical records were compiled on a Microsoft Excel spreadsheet. The variables were then summarized and descriptive statistics applied. The central tendencies (median [range]) for outcome variables in the *early* and *late* lorazepam groups were calculated and tabulated for comparison.

Ethics

The ethical approval for this study was obtained from the institutional ethics committee (IEC/2021/47). All information about patients was kept strictly confidential.

Results

Patient characteristics

A total of 19 FIRES patients were seen during the study period, with a median age of eight years (range: 4-15; M: F ratio: 1.7:1], at the three centres. Of these 19, in 11, either midazolam was ineffective or multiple pharmacological coma medications were required for seizure control. In the remaining eight midazolam-responsive patients, the initial attempt at weaning off midazolam itself was successful in one child, hence, this child did not subsequently receive enteral lorazepam. The remaining seven children (7/19; 37%) were included in this study (status epilepticus initially responded to midazolam infusion but this could not be weaned off on at least one occasion, hence weaning with enteral lorazepam was attempted). In these seven patients, the median age at onset of the disorder was seven years (range: 4-14) and five were males.

All seven patients had normal development before the onset of FIRES. Seizure onset occurred at a mean of 4.5 (±1.8) days from the start of febrile illness. The most common type of seizure was focal oro-motor in six and multifocal in one.

Investigations

The infectious, basic metabolic and autoimmune workup was non-contributory. All patients underwent a CSF examination, the results of which were largely unremarkable, except for mild pleocytosis in four and raised protein in three (*supplementary table S1*).

EEG on admission showed diffuse slowing in all patients. Predominantly right frontotemporal-onset ictal activity with a migrating focus was the most common EEG finding, seen in five patients (representative EEGs of one of the patients are presented in *figure 2A-E*).

Three of the seven patients had abnormal initial brain MRI, showing left mesial temporal hyperintensity, bilateral hippocampal hyperintensity and diffuse leptomeningeal enhancement in each of the patients, respectively. Follow-up brain MRI was subsequently performed in three patients, which was normal in one and showed diffuse cortical atrophy in the other two.

Treatment of FIRES

- ***Conventional antiseizure medications (ASMs)***

Each of the seven patients had failed multiple ASMs, and hence required pharmacological coma for seizure control (*figure 3*, a representative case). A median of six (range: 6-8) ASMs (excluding lorazepam) were tried to control seizures. Benzodiazepines other than lorazepam were also used in three of these seven patients (clobazam in two and clonazepam in one). Six patients also received supratherapeutic doses of phenobarbitone, but this was ineffective in all of the patients.

- ***Ancillary treatment***

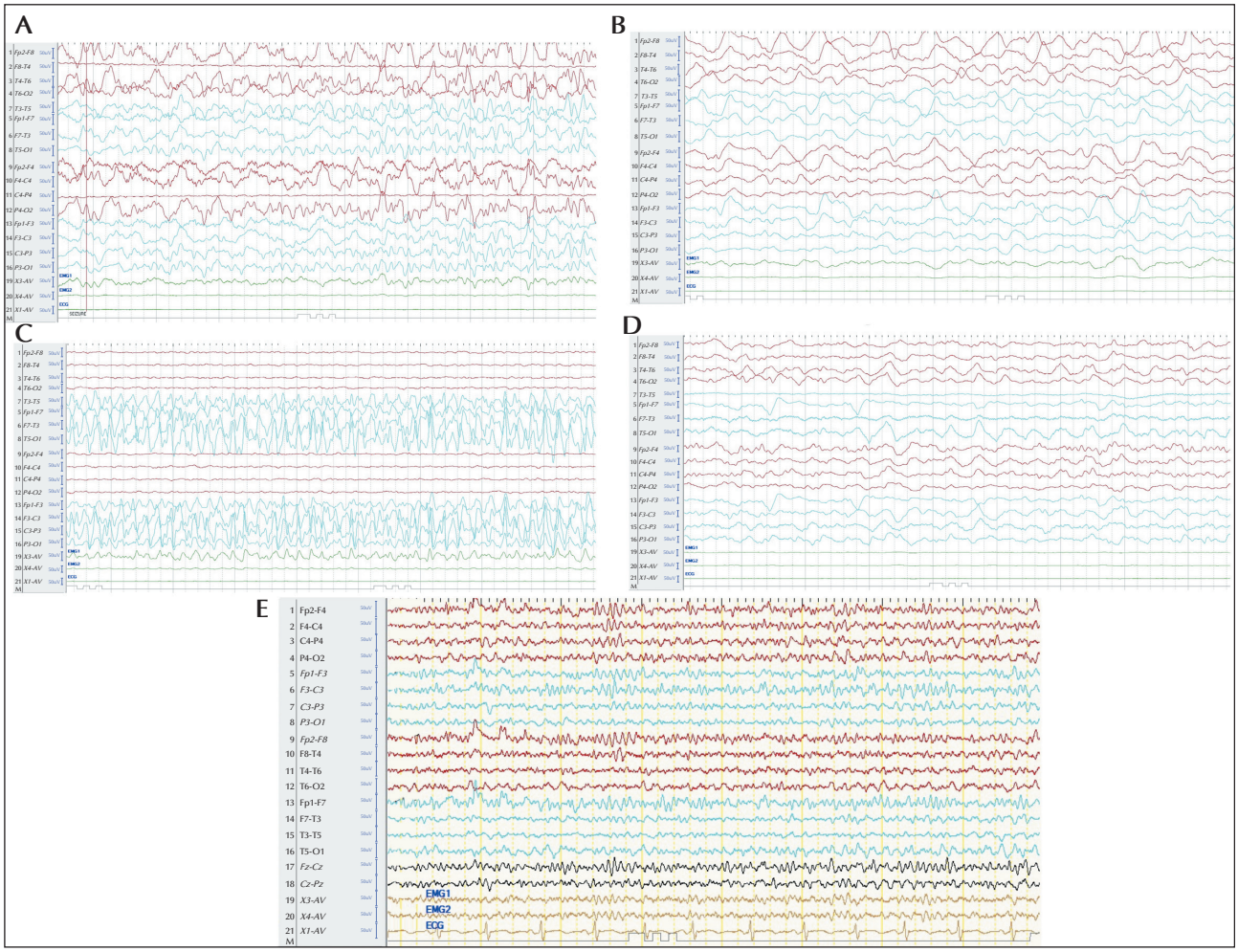
The ketogenic diet was used in all patients at a median of 10 days (range: 4-27 days) from onset and continued for a median duration of 10 days (range: 6-13 days). In six patients, the ketogenic diet was ineffective, and in the remaining patient, it was felt to be partially effective, and so was continued at discharge.

Immunomodulation with MPS and IVIG was attempted in all seven patients but had no beneficial effect. In four patients, rituximab was also given but was ineffective.

- ***Midazolam coma induction***

Midazolam coma induction was initiated at a median of two days (range: 2-6 days) from the onset of seizures. The median maximum midazolam infusion rate required to control seizures was 15 µg/kg/minute (range: 4-25 µg/kg/minute). In five patients, ketamine was also later added in an attempt to decrease the dose and duration of midazolam infusion but was unsuccessful in all. In one other patient, due to mild hepatic dysfunction at the onset of illness, thiopentone and ketamine were initially tried. However, as both were ineffective, finally midazolam was initiated (with close monitoring of liver function), resulting in seizure cessation.

The median dose of midazolam infusion when lorazepam was initiated was 4 µg/kg/minute (range: 4-10 µg/kg/minute). After starting enteral lorazepam, a median of five days (range: 4-7 days) was required to wean off midazolam (*table 1*). The median duration of midazolam coma induction was 22 days (range: 12-66 days).



■ **Figure 2.** Representative EEG recordings of one of the patients (settings- sensitivity: 10 µV/mm; low filter: 1 Hz; high filter: 70 Hz; paper speed: 30 mm/sec). (A) Day 1 of admission showing an electrographic seizure with right hemispheric onset. (B) Day 6 of admission showing diffuse slowing of EEG rhythms with 1-2-Hz delta activity on midazolam infusion (20 µg/kg/minute). (C) Day 12 of admission showing recurrence of an electrographic seizure, this time left hemispheric in the form of a high-amplitude fast rhythm upon weaning midazolam infusion to 2 µg/kg/minute. (D) Day 40 of admission showing diffuse 2-3-Hz slow rhythm on enteral lorazepam, after completely weaning off midazolam infusion (no electrographic seizures were recorded in this prolonged EEG recording). (E) At three months of follow-up, sleep EEG showed well-modulated sleep rhythms with symmetric sleep spindles with a diffusely fast rhythm (on oral lorazepam at 2 mg/kg/d).

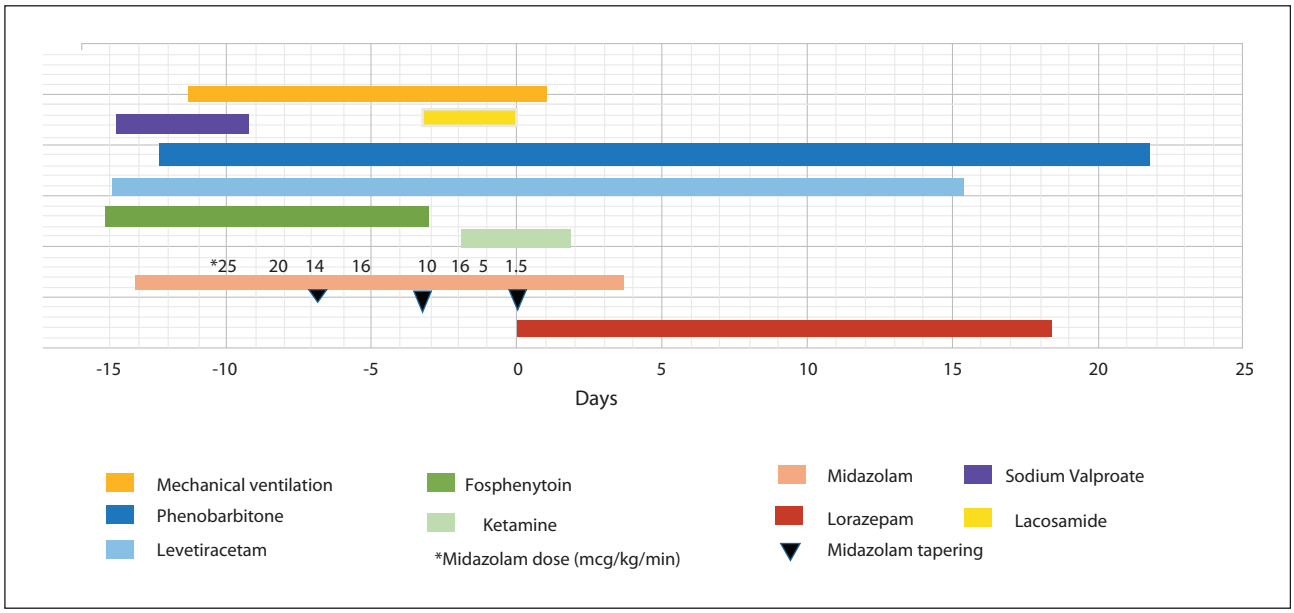
• ***Enteral lorazepam***

Patients received enteral lorazepam at a median of 13 days (range:7-61 days) from seizure onset (*table 1*). The median lorazepam dose at initiation was 3 mg/kg/d (range:1-3 mg/kg/d). The median total daily lorazepam dose was 40 mg/day (range: 32-60 mg/day).

Lorazepam was effective in six of the seven midazolam-dependent patients. In the remaining patient, it was felt to be partially effective, as the ketogenic diet was also concomitantly initiated.

Five patients were deeply sedated on the initial dose of enteral lorazepam, including one who was also ataxic. Sedation was resolved in all of them following dosage reduction, before discharge from hospital (*table 1*).

The median duration of hospital stay in the whole cohort was 40 days (range: 22-78 days). At discharge, patients were on a median lorazepam dose of 2.5 mg/kg/d (range: 0.4-3 mg/kg/d) and a median of four other ASMs (range: 3-6), in addition to lorazepam. One



■ **Figure 3.** Hospital course and antiseizure medications used in one of the patients, as a representative case.

patient was also taking the ketogenic diet. Following initiation of enteral lorazepam, none of the patients had recurrence of seizures in the hospital.

• ***Early versus late group (lorazepam initiation)***

In the first three of the seven patients (Patients 1-3; *table 1*), enteral lorazepam was initiated only after two or more unsuccessful attempts at weaning off midazolam *(*late group). In the subsequent four patients (Patients 4-7; *table 1*), lorazepam was introduced early, after the first unsuccessful attempt to wean off midazolam itself (early group).

The two groups were comparable regarding maximum midazolam dose required for seizure control, other ASMs tried, and days required to taper off midazolam infusion after adding enteral lorazepam (*table 2*).

In the late group, lorazepam was initiated later and at a lower median midazolam weaning dose, compared to the early group. In the early group, the median hospital stay was shorter (27 days), compared to the late group (51 days) (*table 2*).

• ***Follow-up outcome***

The median follow-up period was 10 months (range: 4-19 months). At the last follow-up visit, patients were taking a median of three ASMs (range: 3-5). One patient was also on the ketogenic diet. The median Modified Rankin Score in the whole cohort was 2 (range: 2-4) at the last follow-up contact.

At discharge, none of the patients had ongoing seizures, but all seven had seizure recurrence on follow-up. In four of these seven, seizures recurred when lorazepam was being weaned off after 12, 14, 71, and 68 days of discharge (3, 10, 2, and 60 days, respectively, from the day lorazepam reduction was started). In three of these four patients in whom seizures recurred upon weaning off lorazepam, escalating the dose back up stopped the seizures. In the fourth patient, clobazam was given instead of lorazepam, which helped to reduce the frequency of seizures, but complete control could not be achieved. In the remaining three of the seven patients, seizures recurred even while patients received a discharge dose of lorazepam. On follow-up, four of the seven patients (57%) continued to have drug-resistant seizures, though not severe enough to require readmission.

Discussion

FIRES is one of the most devastating forms of acute epilepsies. In these patients, prolonged periods of pharmacological coma to control electrographic and electroclinical seizures are often required [8]. Usually, gamma-aminobutyric acid (GABA) mimetic agents, such as midazolam, thiopentone and high-dose phenobarbitone, have been the more effective agents [17-20]. Among these, midazolam is usually the first

▼ **Table 1.** In-hospital treatment details of all seven patients.

Patient No. (in the order they presented)	Number of ASMs used (excluding lorazepam)	Maximum dose of midazolam used (μg/kg/minute)	Number of unsuccessful attempts at midazolam taper before enteral lorazepam	No. days with FIRES before starting enteral lorazepam	Dose of midazolam infusion when lorazepam was started (μg/kg/minute)	Dose of enteral lorazepam at initiation (mg/kg/d)	Total days to taper midazolam after starting enteral lorazepam	Side effects of enteral lorazepam	Dose of lorazepam at discharge (mg/kg/d)
1	11 [a]	13	5	61	4	1.2	5	Sedation	0.9
2	5	25	2	15	1.5	1	4	Sedation	0.5
3	8	20	3	35	4	3	5	-	3
4	7 [b]	15	1	7	10	3	7	Sedation	1
5	7	25	1	8	10	3	4	-	3
6	6	20	1	12	8	3	6	Sedation	1
7	6[a]	4	1	13	4	6→3[*]	4	Sedation, Ataxia	2.5

ASM: antiseizure medication;
[a]Including clobazam (1 mg/kg/day);
[b]Including clonazepam (0.05 mg/kg/d);
[*]Inadvertently miscalculated and changed to correct dose after 48 hours.

▼ **Table 2.** Comparison between early and late group (lorazepam initiation).

	Early group (*n*=4) Median (range)	Late group (*n*=3) Median (range)
Max. dose of midazolam infusion (µg/kg/minute)	17.5 (4-25)	15 (13-25)
Dose of midazolam (µg/kg/minute) when lorazepam started	9 (4-10)	4 (1.5-4)
Total days to taper midazolam after starting lorazepam	4 (4-7)	5 (4-5)
No. days with FIRES before starting lorazepam	10 (7-13)	35 (15-61)
Duration (in days) of midazolam treatment	20 (12-39)	40 (19-66)
Total no. of ASMs tried (except lorazepam)	7 (7-8)	9 (6-12)
Duration (in days) of hospital stay	27 (22-46)	51 (40-78)
No. of ASMs at discharge	3 (3-5)	5 (4-6)
Modified Rankin Score	2 (2-4)	2 (2-2)
Follow-up duration (months)	8.5 (4-16)	11 (10-19)

ASM: antiseizure medication.

used anti-seizure medication for pharmacological coma, though with variable efficacy [17-19, 21].

Lorazepam remains the mainstay for initial acute seizure management of all forms of status epilepticus (including FIRES) due to its favourable pharmacokinetics and longer duration of action, as compared to midazolam [22-24]. However, during the early and maintenance phase of FIRES, most patients need prolonged periods of pharmacological coma for seizure suppression, for which midazolam with a shorter half-life is better suited than lorazepam. But even in these midazolam-responsive patients, seizures often tend to recur when midazolam infusion is being weaned off. Thus, midazolam needs to be continued for extended periods, sometimes for weeks to months, resulting in prolonged intensive care stay with its associated co-morbidities.

Previous papers have reported lorazepam as an effective alternative or weaning substitute for midazolam sedation in paediatric ICUs [13, 14]. We used the same calculations for conversion of midazolam to enteral lorazepam (*figure 1*) in one of our patients with FIRES with the aim of continuing seizure control, while weaning off midazolam [15]. After this successful experience, we used the same strategy in all our subsequent FIRES patients, whose seizures had responded but were dependent on ongoing intravenous midazolam infusion for seizure control.

Lorazepam has good oral bioavailability but has the drawback of a shorter half-life, compared to other benzodiazepines (clobazam and clonazepam) [25-27]. Theoretically, clobazam and clonazepam should have a similar effect during the maintenance phase, with the added advantage of less frequent daily dosing, compared to lorazepam. However, both clobazam and clonazepam were tried (before using lorazepam) in three patients and found to be ineffective in controlling seizures.

Our present cohort of seven midazolam-responsive patients had failed multiple ASMs. Immunomodulation was also not effective in any of the patients, and the ketogenic diet was only partially useful in one. This reflects the explosive and refractory nature of this disorder and the difficulty in managing seizures with currently available therapeutic options.

In one of the larger and earliest series of FIRES, patients were mechanically ventilated for a median of 41 days [2]. Similarly, in 29 patients with FIRES reported by Sakuma *et al.*, a mean duration of 52.3 days of barbiturate coma was required [21]. Lee *et al.*, more recently, in their cohort of 29 patients, also reported a median hospitalization duration of 89 days (range: 24-220 days) [17]. Thus, despite the availability of better care and treatment modalities over the last decades, strategies to reduce ICU and hospital stay in children with FIRES remains a challenge. Even with newer therapies, such as anakinra (based on a recent multicentric study), the median period of hospitalization was significant (73.5 days) [9]. Against this backdrop, in our present cohort of midazolam-responsive FIRES patients, even though the numbers were small, enteral lorazepam was an effective weaning substitute. Lorazepam initiation was associated with early weaning of midazolam, within a week, in all our patients. Earlier introduction of lorazepam was also associated with reduced duration of hospital stay.

In our current study, we had selected those FIRES patients whose seizures had responded only to

midazolam infusion and had developed a dependency on midazolam for seizure control. In these midazolam-dependent patients, we initiated lorazepam only after at least one failed attempt at weaning off midazolam. This was to confirm whether other concomitant therapies, such as conventional ASMs, immunomodulation and/or the ketogenic diet, were efficacious.

A significant proportion of our FIRES patients seen during the same period (11/19; 58%) were not eligible for this study because they had failed coma induction with midazolam. These patients subsequently required ketamine, thiopentone, propofol, or gas inhalation, sequentially or in combination with midazolam. We did not use enteral lorazepam in these patients.

Enteral lorazepam though was not completely devoid of side effects. Most patients were sedated on the initiating dose of lorazepam. The frequent occurrence of sedation with the calculated lorazepam dosages raises the possibility of starting patients on a lower dose, although this needs to be confirmed in a future prospective study.

All seven patients had seizure recurrence on follow-up, which is not unusual in FIRES, as most patients are reported to develop drug-resistant epilepsy.[3] In most, seizures recurred when lorazepam was reduced, but control was again achieved with lorazepam escalation. The recurrence of seizures in all patients in whom lorazepam was withdrawn within three months of initiation creates a dilemma regarding the optimal timing to start weaning off the drug, and this should be addressed in the future using a larger cohort of patients.

In conclusion, we propose a promising therapeutic strategy for children with midazolam-dependent FIRES. In this subset, early introduction of enteral lorazepam could be a potentially effective and well-tolerated strategy to keep seizures under sustained control, thereby reducing the hospital stay and its associated complications. These early results on a limited number of patients are encouraging but need to be validated by conducting larger prospective studies. ■

Key points

- Enteral lorazepam is a potentially effective weaning strategy in a subset of FIRES patients who are midazolam-dependent.
- Early enteral lorazepam introduction may help to achieve sustained seizure control, thereby reducing hospital stay.
- Calculations for conversion of intravenous midazolam to an equivalent dose of enteral lorazepam are presented.

Supplementary material.
Supplementary table and summary slides accompanying the manuscript are available at www.epilepticdisorders.com.

Disclosures.
None of the authors have any conflicts of interest to declare.

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TEST YOURSELF

(1) Which is the most commonly used medication for pharmacological coma for FIRES?

A. High-dose phenobarbitone
B. Midazolam infusion
C. Thiopentone

(2) In which patients with FIRES was enteral lorazepam used?

A. Patients whose seizures were resistant to midazolam infusion
B. Patients who have responded to high-dose phenobarbitone
C. Patients who were responsive and dependent on midazolam infusion for seizure control

(3) What was the main benefit of using enteral lorazepam as a weaning strategy for midazolam-dependent FIRES patients?

A. A small amount of lorazepam was used to wean off midazolam infusion
B. Early use of lorazepam prevented seizure recurrence during follow-up
C. Early use of lorazepam was associated with a decrease in duration of hospital stay

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com.