HHS Public Access

Author manuscript

Seizure. Author manuscript; available in PMC 2018 November 01.

Published in final edited form as:

Seizure. 2017 November ; 52: 76–80. doi:10.1016/j.seizure.2017.09.019.

Safety of intravenous lacosamide in critically ill children

Sarah S. Welsh, MD[a], **Nan Lin, MD**[b], **Alexis A. Topjian, MD, MSCE**[a], and **Nicholas S. Abend, MD, MSCE**[b]

[a]Division of Critical Care Medicine, Children's Hospital of Philadelphia, Department of Anesthesia and Critical Care Medicine, The University of Pennsylvania

[b]Division of Neurology, Children's Hospital of Philadelphia, Departments of Neurology and Pediatrics, The University of Pennsylvania

Abstract

PURPOSE—Acute seizures are common in critically ill children. These patients would benefit from intravenous anti-seizure medications with few adverse effects. We reviewed the usage and effects of intravenous lacosamide in critically ill children.

METHODS—This retrospective series included consecutive patients who received at least one dose of intravenous lacosamide from April 2011 to February 2016 in the pediatric intensive care unit of a quaternary care children's hospital, including patients with new lacosamide initiation and continuation of outpatient oral lacosamide. Dosing and prescribing practices were reviewed. Adverse effects were defined by predefined criteria, and most were evaluated during the full admission.

RESULTS—We identified 51 intensive care unit admissions (47 unique patients) with intravenous lacosamide administration. Lacosamide was utilized as a third or fourth-line anti-seizure medication for acute seizures or status epilepticus in the lacosamide-naïve cohort. One patient experienced bradycardia and one patient experienced a rash that were considered potentially related to lacosamide. No other adverse effects were identified, including no evidence of PR interval prolongation.

CONCLUSIONS—Lacosamide was well tolerated in critically ill children. Further study is warranted to evaluate the effectiveness of earlier lacosamide use for pediatric status epilepticus and acute seizures.

Communicating Author: Nicholas Abend, abend@email.chop.edu, 215-590-1719.

Disclosures

The study was supported by an Investigator Initiated Grant from UCB Pharma. The investigators designed the study and performed the analyses without any involvement from the company.

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Dr. Abend has performed expert testimony unrelated to this study.

Dr. Abend receives royalties for a textbook published by Demos.

Keywords

Seizure; status epilepticus; lacosamide; pediatric

Introduction

Seizures are the most common reason for neurology consultation in the pediatric intensive care unit (PICU).[1; 2] Additionally, with increasing use of continuous electroencephalographic (EEG) monitoring in critically ill children with acute encephalopathy,[3; 4] electrographic seizures are often identified.[5; 6] Since electrographic seizures are associated with unfavorable neurobehavioral outcomes,[5–8] most physicians aim to terminate them by administering anti-seizure medications.[9; 10] However, few data are available to guide evidence-based seizure management in critically ill children, particularly for seizures that are refractory to initial medications.[10; 11] Critically ill children often have multi-system organ dysfunction and receive numerous medications. Thus, these patients would therefore benefit from intravenous anti-seizure medication options with few adverse effects or drug-drug interactions, leading to increasing use of newer anti-seizure medications such as lacosamide. Lacosamide has a novel mechanism of action involving augmentation of slow inactivation of voltage-gated sodium channels. Lacosamide was introduced in 2008 for epilepsy management in adults and is still not approved in children, although it is used for pediatric epilepsy management.[12] While case series have described lacosamide as safe and sometimes effective in terminating or reducing seizures and status epilepticus in critically ill adults[13–28] only very limited data are available regarding the use of lacosamide for seizures and status epilepticus in critically ill children.[29–31] We aimed to evaluate the safety of intravenous lacosamide in critically ill children with seizures and status epilepticus.

Methods

We performed a single-center retrospective study of consecutive patients admitted to the PICU from April 2011 until February 2016 who received at least one dose of intravenous lacosamide. Lacosamide was introduced in the United States in 2008 for epilepsy management in adults, but we selected a start date after electronic medical record implementation at our site to ensure we could identify and collect data on consecutive patients. The study was approved by the institutional review board, and consent was not required since it was a retrospective study.

Data were abstracted from the electronic medical record and entered directly into the Research Electronic Data Capture (REDCap) system.[32] Two members of the study team reviewed patient demographics, prior medical history, pre-admission diagnoses, primary and additional problems at admission, functional scores at admission and hospital discharge, pre-admission medications, lacosamide data, specific predefined adverse events, in-hospital mortality, and EEG data. Lacosamide data included the use of lacosamide prior to admission, timing of administration relative to other anti-seizure medications, loading dose, whether maintenance dosing was initiated, the maximum total daily dose, whether the patient was discharged from the hospital on lacosamide, and the reasons for lacosamide

discontinuation. We evaluated for predefined adverse events by reviewing all physician notes, nursing notes, vital sign documentation, laboratory tests, and electrocardiogram (ECG) results. Adverse event categories included cardiopulmonary events, laboratory abnormalities, and other adverse events. EEG data included the EEG background at the time of lacosamide administration, presence or absence of seizures, seizure characteristics prior to and after lacosamide administration, and the impact of lacosamide on seizures. Seizure improvement was defined as comments in progress notes or EEG reports that lacosamide had improved, reduced, or terminated seizures. The Pediatric Cerebral Performance Category (PCPC) score, a validated six-point scale categorizing degrees of functional impairment, was used to estimate pre-admission and discharge function. PCPC categories are (1) normal, (2) mild disability, (3) moderate disability, (4) severe disability, (5) coma and vegetative state, and (6) death.[33; 34]

Descriptive statistics are presented including means (standard deviation) and medians (interquartile ranges, IQR). Two sub-groups were delineated for analysis: (1) patients who had not received lacosamide prior to PICU admission, and (2) patients who were receiving oral lacosamide prior to PICU admission.

Results

Review of the pharmacy electronic medical record established a cohort of 51 PICU admissions with 47 unique patients who received intravenous lacosamide. The cohort separated into 29 patients (62%) who had not received lacosamide prior to PICU admission and 18 patients (38%) who were receiving oral lacosamide prior to PICU admission. Table 1 provides demographic and clinical characteristics. The cohort was predominantly male (65%), and there was a large age range that included infants (median admission age 5 years and 8 months; IQR 1 year 10 months,11 years 3 months). Most patients (67%) had underlying neurodevelopmental diagnoses prior to PICU admission including pre-existing epilepsy (63%). Most patients (86%) were admitted or transferred to the PICU on the first hospital day. EEG data were available for 75% of the patients. Seizures were ongoing at the time of lacosamide administration in 73% of admissions and included electrographically confirmed status epilepticus in 42% of admissions.

Among the 29 patients who had not received lacosamide prior to PICU admission, lacosamide was never selected as the first or second non-benzodiazepine anti-seizure medication. Lacosamide was administered as the third-line, fourth-line, or later non-benzodiazepine anti-seizure medication in 6 of 29 (21%), 12 of 29 (41%), and 11 of 29 (38%) of patients, respectively. Twenty-eight of 29 patients (97%) received an intravenous lacosamide loading doses with a median loading dose of 2 mg/kg (IQR 1.9, 2.7); the remaining patient was started on maintenance intravenous lacosamide without an initial loading dose. Local hospital practice recommends infusion of lacosamide over 30–60 minutes yielding a maximum infusion rate of 0.2 mg/kg/min. The maximum total daily dose ranged from 1–6.5 mg/kg divided twice daily. Twenty-five patients (86%) had maintenance dosing initiated, and 17 patients (58%) were discharged on oral lacosamide. Among the 12 patients who were not discharged on lacosamide, 11 patients had lacosamide discontinuation since it was not considered beneficial. One patient had lacosamide discontinued because the

primary team was concerned about QTc (not PR) prolongation, although the pre- and post-lacosamide QTc measurements were 520 milliseconds and 359 milliseconds, respectively, with no documented evidence of QTc prolongation.

Table 2 details the adverse event data for each of the two patient sub-groups. Most of the adverse events were attributed to other drugs or the underlying illness course since the adverse event documented after lacosamide administration had also been present prior to lacosamide administration. Only two adverse events were considered potentially attributable to lacosamide. One patient had bradycardia three hours post-lacosamide load (with a maximum infusion rate of 0.06 mg/kg/min); while occurrence at 3 hours was outside the monitoring parameters set by the study, the bradycardia was attributed by the primary clinical team to lacosamide in the physician notes. One patient had a drug rash attributed by the primary team to lacosamide which was described as briefly present, erythematous, and confined to the face.

Within the group who had not received lacosamide prior to PICU admission, 20 of 29 patients (69%) had an ECG prior to lacosamide initiation. The median PR interval was 120 milliseconds (IQR 112, 126). A post-lacosamide ECG was obtained in 90% of those patients, and the median PR interval was 132 milliseconds (IQR 120, 135). A 17 year old patient had a post-lacosamide PR interval that was higher than expected for pediatric data but within normal range for adult data (post initiation PR 190 milliseconds, normal range for adults 120–200 milliseconds).[35] ECGs were not regularly performed for patients already receiving lacosamide at admission. However, 13 patients who were already receiving lacosamide prior to PICU admission had an ECG performed during admission, and the median PR interval was 132 milliseconds (IQR 120, 148).

Seizures were ongoing when lacosamide was administered for 37 patients. Based on review of the clinical reports and EEG data, 7 patients (19%) had seizure improvement after lacosamide administration. These included 4 of 26 patients (15%) who had not received lacosamide prior to PICU admission and 3 of 11 patients (27%) who were already receiving lacosamide prior to PICU admission.

Discussion

This retrospective study of critically ill children who received intravenous lacosamide indicates that administration is safe and well-tolerated. Lacosamide augments slow inactivation of voltage-gated sodium channels, thereby impeding the conduction of action potentials and decreasing neuronal hyper-excitability. Given the mechanism of action, side effects such as PR interval prolongation and other ECG abnormalities, including heart block, have been reported. This study focused on systemic side effects that might limit lacosamide usage in the critically ill pediatric patient population. Key findings include lack of PR interval prolongation, only very rare bradycardia (possibly occurring in one patient) attributable to lacosamide, and the absence of hemodynamic instability. These are clinically meaningful considerations when selecting anti-seizure medications for critically ill patients as some anti-seizure medications decrease systemic vascular resistance or induce other cardiovascular complications. There was also no evidence of laboratory abnormalities

attributable to lacosamide. Finally, while the study was retrospective and therefore not prescriptive as to dosing, most practitioners administered a 2 mg/kg intravenous loading dose as a third, fourth, or later anti-seizure medication. Finally, although lacosamide was generally administered as a late anti-seizure medication indicating ongoing refractory seizures and loaded at a relatively low dose, 19% of patients with new initiation of lacosamide for ongoing seizures experienced seizure improvement after lacosamide initiation.

Three previous studies evaluated intravenous lacosamide usage, safety, and efficacy in children. Arkilo et al. published a retrospective case series of 47 children under 12 years of age who received intravenous lacosamide, including 32 who received intravenous lacosamide to treat acute seizures or status epilepticus. The initial dosing ranged from 1–11 mg/kg, and there were no reported significant adverse effects.[29] Grosso et al. published a retrospective case study of 11 pediatric patients with refractory status epilepticus in whom lacosamide was generally administered as a third or fourth line anti-seizure medication. There were no identified serious adverse effects, even with higher loading doses (mean dose of 8.6mg/kg) than in the current study.[30] Poddar et al. published a retrospective case series of 8 pediatric patients receiving intravenous lacosamide for treatment of status epilepticus. Loading dose ranged from 3–10 mg/kg with the majority of patients receiving a loading dose of 10 mg/kg. Bradycardia occurred in one patient within 24 hours of receiving lacosamide, but no other adverse effects were reported.[31] Our large retrospective study of consecutive patients with detailed assessment for predefined adverse effects support the conclusions of the prior studies that lacosamide is well tolerated in the critically ill pediatric population.

Strengths of the study include evaluation of consecutive contemporary patients with detailed assessment for adverse events. ECG and EEG data were available for most patients, and all components of the patient electronic medical chart were screened for specific adverse effects which were rated as attributable or non-attributable. The duration of follow-up for many potential adverse events was the entirety of the hospital stay. The limitations of the study include the retrospective design, the lack of standardized lacosamide dosing, and the relatively low lacosamide loading doses.

In conclusion, given our data indicate lacosamide is well tolerated, further study is warranted to compare the effectiveness of lacosamide with other anti-seizure medications in critically ill children. Future studies should explore whether lacosamide may be more effective earlier in the treatment regimen and using higher initial dosing, a practice that may be supported by the favorable side effect profile.

References

1. Bell MJ, Carpenter J, Au AK, et al. Development of a pediatric neurocritical care service. Neurocrit Care. 2009; 10:4–10. [PubMed: 18256793]
2. LaRovere KL, Graham RJ, Tasker RC. Pediatric neurocritical care: a neurology consultation model and implication for education and training. Pediatr Neurol. 2013; 48:206–211. [PubMed: 23419471]
3. Herman ST, Abend NS, Bleck TP, et al. Consensus statement on continuous EEG in critically ill adults and children, part I: indications. J Clin Neurophysiol. 2015; 32:87–95. [PubMed: 25626778]

4. Sanchez SM, Carpenter J, Chapman KE, et al. Pediatric ICU EEG monitoring: current resources and practice in the United States and Canada. J Clin Neurophysiol. 2013; 30:156–160. [PubMed: 23545766]
5. Abend NS, Arndt DH, Carpenter JL, et al. Electrographic seizures in pediatric ICU patients: cohort study of risk factors and mortality. Neurology. 2013; 81:383–391. [PubMed: 23794680]
6. Payne ET, Zhao XY, Frndova H, et al. Seizure burden is independently associated with short term outcome in critically ill children. Brain. 2014; 137:1429–1438. [PubMed: 24595203]
7. Topjian AA, Gutierrez-Colina AM, Sanchez SM, et al. Electrographic Status Epilepticus is Associated with Mortality and Worse Short-Term Outcome in Critically Ill Children. Crit Care Med. 2013; 41:215–223. [PubMed: 23164815]
8. Wagenman KL, Blake TP, Sanchez SM, et al. Electrographic status epilepticus and long-term outcome in critically ill children. Neurology. 2014; 82:396–404. [PubMed: 24384638]
9. Abend NS, Hahn CD, Dlugos DJ, et al. Survey of EEG Monitoring and Non-Convulsive Seizure Management in Critically Ill Patients. American Epilepsy Society (abstract). 2009
10. Abend NS, Sanchez SM, Berg RA, et al. Treatment of electrographic seizures and status epilepticus in critically ill children: A single center experience. Seizure. 2013; 22:467–471. [PubMed: 23601851]
11. Sanchez Fernandez I, Abend NS, Agadi S, et al. Gaps and opportunities in refractory status epilepticus research in children: a multi-center approach by the Pediatric Status Epilepticus Research Group (pSERG). Seizure. 2014; 23:87–97. [PubMed: 24183923]
12. McGinnis E, Kessler SK. Lacosamide use in children with epilepsy: Retention rate and effect of concomitant sodium channel blockers in a large cohort. Epilepsia. 2016; 57:1416–1425. [PubMed: 27430392]
13. Belcastro V, Vidale S, Pierguidi L, et al. Intravenous lacosamide as treatment option in post-stroke non convulsive status epilepticus in the elderly: a proof-of-concept, observational study. Seizure. 2013; 22:905–907. [PubMed: 23953988]
14. d'Orsi G, Pacillo F, Trivisano M, et al. Lacosamide in absence status epilepticus. Seizure. 2013
15. d'Orsi G, Pascarella MG, Martino T, et al. Intravenous lacosamide in seizure emergencies: Observations from a hospitalized in-patient adult population. Seizure. 2016; 42:20–28. [PubMed: 27693808]
16. Goodwin H, Hinson HE, Shermock KM, et al. The use of lacosamide in refractory status epilepticus. Neurocrit Care. 2011; 14:348–353. [PubMed: 21249530]
17. Guilhoto LM, Loddenkemper T, Gooty VD, et al. Experience with lacosamide in a series of children with drug-resistant focal epilepsy. Pediatr Neurol. 2011; 44:414–419. [PubMed: 21555051]
18. Hawkes MA, Fernandez Suarez M, Ugarnes G, et al. Single-dose oral lacosamide in refractory simple partial status epilepticus: case report and review. Clin Neuropharmacol. 2013; 36:138–140. [PubMed: 23860347]
19. Hofler J, Trinka E. Lacosamide as a new treatment option in status epilepticus. Epilepsia. 2013; 54:393–404. [PubMed: 23293881]
20. Hofler J, Unterberger I, Dobesberger J, et al. Intravenous lacosamide in status epilepticus and seizure clusters. Epilepsia. 2011; 52:e148–152. [PubMed: 21801171]
21. Jain V, Harvey AS. Treatment of refractory tonic status epilepticus with intravenous lacosamide. Epilepsia. 2012; 53:761–762. [PubMed: 22462573]
22. Kellinghaus C, Berning S, Immisch I, et al. Intravenous lacosamide for treatment of status epilepticus. Acta Neurol Scand. 2011; 123:137–141. [PubMed: 20868429]
23. Kellinghaus C, Berning S, Stogbauer F. Intravenous lacosamide or phenytoin for treatment of refractory status epilepticus. Acta Neurol Scand. 2014; 129:294–299. [PubMed: 23937330]
24. Koubeissi MZ, Mayor CL, Estephan B, et al. Efficacy and safety of intravenous lacosamide in refractory nonconvulsive status epilepticus. Acta Neurol Scand. 2011; 123:142–146. [PubMed: 21198444]
25. Miro J, Toledo M, Santamarina E, et al. Efficacy of intravenous lacosamide as an add-on treatment in refractory status epilepticus: a multicentric prospective study. Seizure. 2013; 22:77–79. [PubMed: 23127776]

26. Mnatsakanyan L, Chung JM, Tsimerinov EI, et al. Intravenous Lacosamide in refractory nonconvulsive status epilepticus. Seizure. 2012; 21:198–201. [PubMed: 22244046]
27. Santamarina E, Toledo M, Sueiras M, et al. Usefulness of intravenous lacosamide in status epilepticus. J Neurol. 2013; 260:3122–3128. [PubMed: 24122063]
28. Sutter R, Marsch S, Ruegg S. Safety and efficacy of intravenous lacosamide for adjunctive treatment of refractory status epilepticus: a comparative cohort study. CNS Drugs. 2013; 27:321–329. [PubMed: 23533010]
29. Arkilo D, Gustafson M, Ritter FJ. Clinical experience of intravenous lacosamide in infants and young children. Eur J Paediatr Neurol. 2016; 20:212–217. [PubMed: 26810009]
30. Grosso S, Zamponi N, Bartocci A, et al. Lacosamide in children with refractory status epilepticus. A multicenter Italian experience. Eur J Paediatr Neurol. 2014; 18:604–608. [PubMed: 24836405]
31. Poddar K, Sharma R, Ng YT. Intravenous Lacosamide in Pediatric Status Epilepticus: An Open-Label Efficacy and Safety Study. Pediatr Neurol. 2016; 61:83–86. [PubMed: 27241232]
32. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009; 42:377–381. [PubMed: 18929686]
33. Fiser DH. Assessing the outcome of pediatric intensive care. J Pediatr. 1992; 121:68–74. [PubMed: 1625096]
34. Fiser DH, Long N, Roberson PK, et al. Relationship of pediatric overall performance category and pediatric cerebral performance category scores at pediatric intensive care unit discharge with outcome measures collected at hospital discharge and 1- and 6-month follow-up assessments. Crit Care Med. 2000; 28:2616–2620. [PubMed: 10921604]
35. Rijnbeek PR, Witsenburg M, Schrama E, et al. New normal limits for the paediatric electrocardiogram. Eur Heart J. 2001; 22:702–711. [PubMed: 11286528]

Highlights

- We reviewed the usage of intravenous lacosamide in critically ill children.
- Single-center retrospective study of 47 consecutive critically ill children.
- Potentially related adverse effects: 1 rash and 1 bradycardia.
- No evidence of PR interval prolongation.
- Overall, lacosamide was well tolerated in critically ill children.

Table 1

Patient Characteristics

Variable	Full Cohort (N=51) N (%)	Lacosamide initiated during PICU admission (N=29) N (%)	Taking lacosamide prior to PICU admission (N=22) N (%)
Age on admission (years)			
0–4	22 (43%)	14 (48%)	8 (36%)
4–12	17 (33%)	8 (28%)	9 (41%)
>12	12 (24%)	7 (24%)	5 (23%)
Gender Male	33 (65%)	17 (59%)	16 (73%)
Weight (kg)			
<5	1 (2%)	1 (3%)	0 (0%)
5–10	11 (22%)	7 (25%)	4 (18%)
10.1–40	26 (50%)	13 (45%)	13 (59%)
>40	13 (26%)	8 (27%)	5 (23%)
Neurodevelopmental problems prior to admission	34 (67%)	13 (45%)	21 (95%)
Diagnosis of epilepsy prior to admission	32 (63%)	12 (41%)	22 (100%)
Admitted to PICU on hospital day 1	44 (86%)	27 (93%)	18 (82%)
Admission PCPC score			
1 (Normal)	12 (23%)	12 (41%)	0 (0%)
2 (Mild Disability)	5 (10%)	2 (7%)	3 (14%)
3 (Moderate Disability)	9 (17%)	2 (7%)	7 (32%)
4 (Severe Disability)	22 (44%)	11 (38%)	11 (50%)
5 (Coma or Vegetative State)	3 (6%)	2 (7%)	1 (5%)
Discharge PCPC score			
1 (Normal)	0 (0%)	0 (0%)	0 (0%)
2 (Mild Disability)	6 (12%)	4 (14%)	2 (9%)
3 (Moderate Disability)	9 (18%)	2 (7%)	7 (32%)
4 (Severe Disability)	24 (47%)	15 (52%)	9 (41%)
5 (Coma or Vegetative State)	1 (2%)	1 (3%)	0 (0%)
6 (Death)	11 (22%)	7 (24%)	4 (18%)
Seizures (clinical and/or EEG) ongoing at Lacosamide Administration	37 (73%)	26 (90%)	11 (50%)
Seizure Characteristics at Lacosamide Administration			
Clinical Correlate			
Unknown	4 (11%)	0 (0%)	4 (36%)
All Clinical	5 (14%)	3 (12%)	2 (18%)
EEG-Only	13 (35%)	13 (50%)	0 (0%)

Variable	Full Cohort (N=51) N (%)	Lacosamide initiated during PICU admission (N=29) N (%)	Taking lacosamide prior to PICU admission (N=22) N (%)
Clinical and EEG-Only	15 (41%)	10 (38%)	5 (45%)
Seizure Type			
Unknown	4 (11%)	0 (0%)	4 (36%)
Independent Recurrent Seizures	15 (41%)	11 (41%)	4 (36%)
Continuous Seizure	9 (24%)	8 (31%)	1 (9%)
Ictal-Interictal Continuum	9 (24%)	7 (27%)	2 (18%)
EEG Category at Lacosamide Administration (N=38 with EEG data available)			
Ongoing status epilepticus	16 (42%)	15 (54%)	1 (10%)
Slow-Disorganized	15 (39%)	11 (39%)	4 (40%)
Discontinuous	2 (5%)	1 (4%)	1 (10%)
Attenuated	2 (5%)	0 (0%)	2 (20%)
Epileptic Encephalopathy	3 (8%)	1 (4%)	2 (20%)
Seizures Improvement after Lacosamide Initiation among Patients Experiencing Seizures at Time of Administration (N=37)	7 (19%)	4 (15%)	3 (27%)

EEG, electroencephalogram; PCPC, Pediatric Cerebral Performance Category; PICU, pediatric intensive care unit.

Table 2

Adverse event criteria and occurrence.

Adverse Event	Criteria and Assessment Duration		Cohort	
	Definition	**Assessment Duration**	**Lacosamide initiated during PICU admission (n=29)**	**Taking lacosamide prior to PICU admission (n=22)**
Cardiopulmonary events				
Bradycardia	AHA guidelines.[a]	1 Hour [d]	2 (7%) **	0 (0%) *
Systolic hypotension	AHA guidelines.[b]	1 Hour [d]	2 (7%) *	2 (9%) *
Respiratory depression	ADA guidelines.[c] OR Any increased in fraction of inspired oxygen (FiO2) or liter flow of oxygen, increase in ventilator settings, increase in level of non-invasive positive pressure support, or initiation of any new respiratory support mode.	1 Hour [d]	4 (14%) *	1 (5%) *
Arrhythmia	ECG documented PR interval prolongation OR Arrhythmia documented by ECG or referenced in any consult/progress note.	Anytime[e]	4 (14%) *	3 (14%) *
Laboratory abnormalities				
Neutropenia	Absolute neutrophil count less than 1000/uL.	Anytime[e]	4 (14%) *	2 (9%) *
Thrombocytopenia	Platelet count less than 100 K/uL.	Anytime[e]	9 (41%) *	2 (9%) *
Transaminitis	Any increase in aspartate aminotransferase (AST) or alanine aminotransferase (ALT) over institutional laboratory- defined normal range for age.	Anytime[e]	22 (76%) *	11 (50%) *
Other				
Skin rash	Review of vascular access and skin integrity flowsheet data, progress notes, nursing notes, and wound/skin care notes.	Anytime[e]	5 (17%) ***	0 (0%) *
Peripheral IV infiltrate	Review of vascular access and skin integrity flowsheet data, progress notes, nursing notes, and wound/skin care notes.	Anytime[e]	5 (17%) *	1 (5%) *

AHA, American Heart Association; bpm, beats per minute; ECG, electrocardiogram; IV intravenous; SBP, systolic blood pressure.

[a] Bradycardia as defined by AHA guidelines: neonate – 3 months (<80 bpm), 3 months – 2 years (<75 bpm), 2 years – 10 years (<60 bpm), and >10 years (<50 bpm).

[b] Systolic hypotenstion as defined by AHA guidelines: 0–28 days (<60 mg Hg), 1–12 months (<70 mm Hg), 1–10 years (<70 + (age in years x 2) mm Hg), and > 10 years (>90 mm Hg).

[c] Decrease in respiratory rate as defined by AHA guidelines: 0–12 months (<30 breaths per minute), 1–3 years (<24 breaths per minute), 3–5 years (<22 breaths per minute), 5–12 years (<18 breaths per minute), and >12 years (<12 breaths per minute).

[d] Adverse event occurred within 1 hour of IV lacosamide dose.

[e] Adverse event occurred at any time during hospital admission post IV lacosamide dose.

* Not attributable to lacosamide.

** One patient had bradycardia outside the window of observation (3 hours post-lacosamide initiation), but it was attributed by primary team to lacosamide.

*** One patient with rash attributed to lacosamide by the primary team.