# Survey of Pediatric Status Epilepticus Treatment Practices and Adherence to Management Guidelines (Pedi-SPECTRUM e-Survey)

Renu Suthar<sup>10</sup>, Suresh Kumar Angurana<sup>20</sup>, Karthi Nallasamy<sup>30</sup>, Arun Bansal<sup>40</sup>, Jayashree Muralidharan<sup>50</sup>

Received on: 29 February 2024; Accepted on: 06 April 2024; Published on: 30 April 2024

# Abstract

Aim: Survey of treatment practices and adherence to pediatric status epilepticus (PSE) management guidelines in India.

Methods: This eSurvey was conducted over 35 days (15th October to 20th November 2023) and included questions related to hospital setting; antiseizure medications (ASMs); ancillary treatment; facilities available; etiology; and adherence to PSE management guidelines.

**Results:** A total of 170 respondents participated, majority of them were working in tertiary level hospitals (94.1%) as pediatric intensivists (56.5%) and pediatricians (19.4%), and were in clinical practice for 2–10 years (46.5%). Majority use intravenous (IV) midazolam and levetiracetam as first- and second-line ASMs (67.1 and 51.2%, respectively). In cases with refractory status epilepticus (RSE), the most commonly used ASM is midazolam infusion (92.4%). For super-refractory status epilepticus (SRSE), the commonly used third-line ASMs include midazolam infusion (34.1%), thiopentone infusion (26.5%), high dose phenobarbitone (18.2%), and ketamine infusion (15.3%). Overall, in cases with SRSE, 44.7% respondents use ketamine infusion, 42.5% use add-on oral topiramate, and 34.7% use high-dose phenobarbitone (1–3 mg/kg/hour) infusion. Most respondents targeted both clinical and EEG seizure control (48.8%). Ancillary treatment used for SRSE included IV pyridoxine (57.1%), methylprednisolone (45.3%), IVIG (42.4%), ketogenic diet (40.6%), and second-line immunomodulation (33.5%). Most common causes were febrile SE, viral encephalitis, and febrile illness-related epilepsy syndrome (60.6%, 52.4%, and 37.1%, respectively). Facilities available included pediatric intensive care units (PICU) (97.1%), mechanical ventilation (98.2%), pediatric neurologist (68.8%), MRI brain (86.5%), EEG (69.4%), and viral PCR (58.2%). The compliance with guidelines for timing of initiation of ASM ranged from 63.5 to 88.8%.

**Conclusion:** Intravenous midazolam bolus/es, levetiracetam, and midazolam infusion are commonly used first-, second-, and third-line ASMs, respectively. There were wide variations in use of ASMs for RSE and SRSE, ancillary treatment, and compliance to PSE management guidelines. **Keywords:** Antiseizure medications, Midazolam, Nonconvulsive status epilepticus, Status epilepticus, Thiopentone.

Indian Journal of Critical Care Medicine (2024): 10.5005/jp-journals-10071-24707

# HIGHLIGHTS

Intravenous levetiracetam is commonly used second-line antiseizure medication (ASM). In cases with refractory status epilepticus (RSE) and super-refractory status epilepticus (SRSE), there is wide variability in the use of ASMs and ancillary treatment. The compliance to pediatric status epilepticus (PSE) management guidelines is variable, especially in time-bound treatment decisions.

# INTRODUCTION

Pediatric status epilepticus (PSE) is a common neurological emergency associated with significant mortality and neuro-morbidity such as cognitive impairment and focal neurological deficits.<sup>1,2</sup> Goal of management of PSE is to stop seizure activity as quickly as possible to prevent neuronal injury, mortality, and to minimize short- and long-term neuro-morbidity.<sup>3,4</sup>

Management of PSE is a step-wise approach with first-line antiseizure medications (ASMs) typically benzodiazepines such as midazolam, lorazepam, or diazepam; followed by second-line ASMs including phenytoin/fosphenytoin, levetiracetam, or valproate.<sup>3–6</sup> Two recent randomized trials demonstrated that levetiracetam has similar efficacy to phenytoin as second-line ASM.<sup>7,8</sup> However, seizure recurrences between 1 and 24 hours and requirement mechanical ventilation were significantly higher with phenytoin as compared with levetiracetam.<sup>9</sup> In case of persistence of seizures

<sup>1</sup>Division of Pediatric Neurology, Department of Pediatrics, Advanced Pediatrics Centre, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India

<sup>2-5</sup>Division of Pediatric Critical Care, Department of Pediatrics, Advanced Pediatrics Centre, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India

**Corresponding Author:** Suresh Kumar Angurana, Division of Pediatric Critical Care, Department of Pediatrics, Advanced Pediatrics Centre, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India, Phone: +91 9855373969, e-mail: sureshangurana@gmail.com

How to cite this article: Suthar R, Angurana SK, Nallasamy K, Bansal A, Muralidharan J. Survey of Pediatric Status Epilepticus Treatment Practices and Adherence to Management Guidelines (Pedi-SPECTRUM e-Survey). Indian J Crit Care Med 2024;28(5):504–510.

Source of support: Nil Conflict of interest: None

(refractory status epilepticus, RSE), drugs to induce anesthesia are required.<sup>3,5,10</sup> However, beyond second-line ASMs, the evidence related to the efficacy of third-line agent for RSE is lacking. Commonly used therapies for RSE and SRSE are midazolam, thiopentone/ pentobarbital, high-dose phenobarbitone, propofol, ketamine, and

<sup>©</sup> The Author(s). 2024 Open Access. This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (https://creativecommons. org/licenses/by-nc/4.0/), which permits unrestricted use, distribution, and non-commercial reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated.

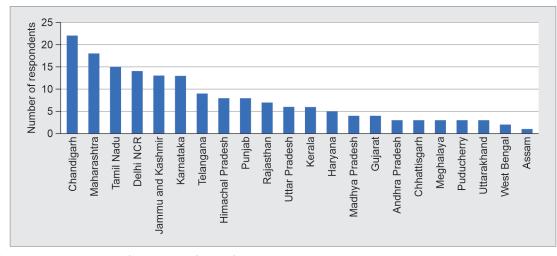


Fig. 1: Bar diagram showing number of respondents from different states and union territories

magnesium sulphate infusion; inhalational anesthetics; steroids; immunotherapy; and ketogenic diet.<sup>3,5,11,12</sup>

Several guidelines are available to guide the management of PSE in a time-bound fashion.<sup>3–5</sup> However, several studies and surveys demonstrated that there is wide variability in treatment modalities among treating physicians and poor adherence to PSE management guidelines, particularly in time-dependent decisions.<sup>13–16</sup> The information about variability in treatment practices and adherence to PSE management guidelines is limited from India. Therefore, we planned this survey in India to assess current treatment practices and adherence to PSE management guidelines among healthcare providers.

#### METHODS

This prospective eSurvey was developed by three investigators (Renu Suthar, Suresh Kumar Angurana, and Karthi Nallasamy) working in a tertiary care teaching hospital in North India. There were 7 sections including 54 questions. First section included demographic details of respondents including level of the healthcare facility, qualification and designation, years of practice, and load of PSE in their respective healthcare setting. Second and third sections included details about first- and second-line ASMs (type and doses). Fourth section included details about third-line ASMs and management of SRSE including intravenous anesthetic agents, EEG monitoring, and treatment end-points. Fifth section included ancillary treatment and usage of immunomodulation. Sixth section includes availability of facilities [Pediatric intensive care unit (PICU), mechanical ventilation, neurologist, etc.]; diagnostic work-up (brain imaging, EEG, PCR, and autoimmune testing); and etiology of PSE. Seventh section included details about guidelines being followed and compliance with these guidelines.

The responses to these questions were in the form of yes or no; multiple choices (to be ticked as per their practice); or short descriptives answers. The survey questions so framed were transported to Google form and the link of which was circulated in relevant WhatsApp groups of pediatric postgraduate fellows (MD/DNB), pediatric senior residents, pediatric critical care fellows (DNB/DM/Fellowships), pediatricians, and pediatric intensivists working PERs and PICUs in different healthcare settings in different parts in India. The survey was open for participation for 35 days (15th October to 20th November 2023). Participants were able to complete the survey only once and their identity remained anonymous unless they voluntarily provided their e-mail address. The responses recorded were transferred to Excel sheets and SPSS for further analysis.

There was no formal consent obtained from the participants as the survey does not include any patient's data and identity of the participants was not revealed. At beginning of the survey, it was mentioned that "by proceeding with the survey, it was assumed that the participants have consented to take part in the survey." The protocol was approved by the Institute Ethics Committee (IEC) along with waiver of the consent.

The primary outcome of this study was to assess current treatment practices and secondary outcome was to determine the adherence to PSE management guidelines among healthcare providers in India.

#### **Data Entry and Statistical Analysis**

The responses recorded were transferred to the Microsoft Excel 2010 (Microsoft, Redmond, WA, USA). Data analysis was done by using SPSS software version 20 (SPSS, Inc., Chicago, IL, USA). Descriptive statistics (number, percentages) were used for data representation.

#### RESULTS

In this eSurvey, 170 respondents participated from 22 states and Union Territories (UTs) of India. More than half (55.9%, n = 95) of the respondents were from 6 states and UTs (Chandigarh, Maharashtra, Tamil Nadu, Delhi NCR, Jammu and Kashmir, and Karnataka) (Fig. 1). Majority of respondents are working in tertiary level hospitals (94.1%) in capacity of pediatric intensivists (56.5%) and pediatricians (19.4%). Nearly half of them (46.5%) were in pediatric/pediatric critical care practice for 2–10 years. Majority (68.3%) manage PSE cases at frequency of 1–5 cases per month (Table 1).

Majority of respondents (67.1%) use intravenous midazolam as first-line ASM, 77.6% use 2 doses of midazolam before going to second-line ASM, and 78.2% reported the use of intermittent doses of benzodiazepine while managing RSE. More than half of the respondents (51.2%) use levetiracetam as second-line ASM in a loading dose on 40 mg/kg (48.5%). Majority (60.6%) use mini bolus/es of second-line ASM in cases with non-responding PSE. Approximately 95.3% respondents prefer to use alternative

Table 1: Demographic profile of the respondents and their healthcare
setting

setting	
Characteristics	Total respondents (n = 170)
Level of care provided	
Tertiary	160 (94.1)
Secondary	9 (5.3)
Primary	1 (0.6)
Designation	
Pediatric intensivist	96 (56.5)
Pediatrician	33 (19.4)
DM pediatric critical care fellow	17 (10)
MD pediatric fellow	8 (4.7)
IAP PCC fellow (IDPCCM)	7 (4.1)
Other	9 (5.3)
Duration of pediatric or pediatric critical care practice (in years)?	
<2	25 (14.7)
2–5	36 (21.2)
5–10	43 (25.3)
10–15	31 (18.2)
>15	35 (20.6)
How frequently you manage PSE (cases per month)	
Rarely	9 (5.3)
1–2	55 (32.4)
2–5	61 (35.9)
5–10	26 (15.3)
>10	19 (11.2)

Data represented as n (%)

Table 2: Details about usage of first- and second-line antiseizure medications

	Total respondents
Characteristics	(n = 170)
Which drug do you use as first-line ASM for management of PSE?	
IV Midazolam	114 (67.1)
IV Lorazepam	56 (32.9)
How many dosage/s of first-line ASM you give before proceeding to second-line ASM?	
1	31 (18.2)
2	132 (77.6)
3	7 (4.1)
Use intermittent doses of benzodiazepines while managing ongoing RSE	133 (78.2)
Which second-line ASM do you use for management of PSE?	
IV Levetiracetam	87 (51.2)
IV Phenytoin	70 (41.2)
IV Fosphenytoin	10 (5.9)
IV Valproate	3 (1.8)
Use mini-bolus/es of second-line ASM in cases with non-responding PSE?	103 (60.6)
	(Contd.)

(Contd...)

	Total respondents
Characteristics	(n = 170)
Use further alternative second-line ASM in cases with non-responding PSE (e.g., phenytoin followed by levetiracetam or phenobarbitone or valproate)?	162 (95.3)
Which further alternative second-line ASM do you use in cases with non-responding PSE?	
Levetiracetam	78 (45.9)
Valproate	62 (36.5)
Fosphenytoin	38 (22.4)
Phenytoin	37 (21.8)
Phenobarbitone	32 (18.8)
Lacosamide	9 (5.3)
What is the dose of IV levetiracetam used by you as second-line ASM during management of PSE?	
30 mg/kg	35 (20.6)
40 mg/kg	82 (48.5)
50 mg/kg	4 (2.4)
60 mg/kg	39 (22.9)
Other	10 (5.9)

second-line ASM in cases with non-responding PSE before going to third-line ASMs including levetiracetam (45.9%), phenytoin or fosphenytoin (44.2), valproate (36.5%), or phenobarbitone (18.8%) (Table 2).

In cases with RSE, majority of respondents use intravenous midazolam infusion (92.4%) at dose of 10-20 µg/kg/min (48.8%). If seizures continue despite midazolam infusion, 34.1% respondents continue with midazolam infusion, 26.5% use thiopentone infusion, 18.2% high-dose phenobarbitone, 15.3% ketamine infusion, and 5.9% propofol infusion. Overall, in cases with SRSE, 44.7% respondents use ketamine infusion, 42.5% use add-on oral topiramate, and 34.7% use high-dose phenobarbitone (1-3 mg/ kg/hour) infusion. Most respondents target both clinical and EEG seizure control (48.8%) for 12-48 hours (85.3%). After reasonable seizure control on third-line ASMs, majority of respondents slowly taper (46.5%) or continue all second-line ASM (Table 3).

The ancillary treatment used by the respondents in cases with SRSE include intravenous pyridoxine (57.1%), methylprednisolone (45.3%), intravenous immunoglobulin (42.4%), ketogenic diet (40.6%), second-line immunomodulation (tocilizumab, anakinra, or rituximab) (33.5%), magnesium sulphate (23.5%), plasma exchange (18.8%), therapeutic hypothermia (7.1%), and inhalational anesthetics (5.9%) (Table 4). Majority of respondents have facilities at their hospital including availability of PICU (97.1%), mechanical ventilation (98.2%), CT head (95.3%), brain MRI (86.5%), EEG (69.4%), pediatric neurologist (68.8%), and viral PCR testing (58.2%). Majority of respondents (88.2%) do work-up for autoimmune encephalitis in cases with RSE/SRSE without apparent etiology (Table 4).

The most common etiology of PSE reported by respondents was febrile status epileptics (60.6%), viral encephalitis (52.4%), febrile illness-related epilepsy syndrome (FIRES) (37.1%), pre-existing epilepsy (30%), autoimmune encephalitis (27.6%), metabolic



Table 3: Details about usage of third-line antiseizure medications in cases with refractory and super-refractory status epilepticus

Table 4: Details about usage of ancillary treatment for super-refractory status epilepticus and facilities available

	Total respondents
Characteristics	(n = 170)
Which is the preferred third-line ASM do you use in cases with RSE?	
IV Midazolam infusion	157 (92.4)
IV High-dose phenobarbitone infusion	5 (2.9)
IV Thiopentone infusion	4 (2.4)
IV Propofol or ketamine infusion	4 (2.4)
Which is the next third-line ASM do you use in non-responding RSE or SRSE?	
IV Midazolam infusion	58 (34.1)
IV Thiopentone infusion	45 (26.5)
IV High-dose phenobarbitone	31 (18.2)
IV Ketamine infusion	26 (15.3)
IV Propofol infusion	10 (5.9)
What is the maximum dose of IV Midazolam infusion do you use?	
2–10 μg/kg/min	39 (22.9)
10–15 μg/kg/min	25 (14.7)
15–20 μg/kg/min	58 (34.1)
20–30 μg/kg/min	40 (23.5)
>30 µg/kg/min	8 (4.7)
Use intravenous ketamine infusion in cases with SRSE	76 (44.7)
Use add-on oral topiramate in cases with SRSE	72 (42.4)
Use intravenous high dose phenobarbitone in cases with SRSE	59 (34.7)
What is the threshold used by you for tapering third-line ASM?	
Clinical seizure control	68 (40)
EEG showing burst suppression	19 (11.2)
Both	83 (48.8)
When do you consider tapering third-line ASM once seizures are controlled?	
6–12 hours seizure free period	10 (5.9)
12–24 hours seizure free period	70 (41.2)
24–48 hours seizure free period	75 (44.1)
>48 hours seizure free period	15 (8.8)
How do you handle second-line ASMs after achieving reasonable seizure control with third-line ASMs?	
Slowly taper over days	79 (46.5)
Continue all	55 (32.4)
Stop all except the first addition	13 (7.6)
Stop all except the last addition	12 (7.1)
Other practice	11 (6.5)
Data represented as $n$ (%)	

Data represented as n (%)

(14.1%), bacterial meningitis (13.5%), tropical infections (12.4%), and traumatic (10%) (Fig. 2).

The compliance with guidelines as far as timing of initiation of ASM is concerned ranged from 63.5 to 88.8%. Majority of the respondents (61.2%) felt that the timeline suggested by management guidelines are too strict to follow in actual clinical

Characteristics	Total respondent (n = 170)
Ancillary treatments used by respondents	(11 - 170)
Pyridoxine	97 (57.1)
Methylprednisolone	77 (45.3)
IVIG	77 (43.3) 72 (42.4)
Ketogenic diet	69 (40.6)
5	
Use second-line immunomodulation (e.g., tocilizumab, anakinra, or rituximab) in cases with SRSE	57 (33.5)
Which is the preferred second-line immunomodulation you use in cases with SRSE?	
Rituximab	30 (17.6)
Tocilizumab	20 (11.8)
Anakinra	7 (4.1)
Use magnesium sulphate in cases with SRSE	40 (23.5)
Use plasma exchange in cases with SRSE	32 (18.8)
Use therapeutic hypothermia in cases with SRSE	12 (7.1)
Use inhalational anesthetic in cases with SRSE	10 (5.9)
Use vagal nerve stimulation in cases with SRSE	4 (2.4)
Facilities available	
PICU	165 (97.1)
Mechanical ventilation	167 (98.2)
CT head	162 (95.3)
MRI brain	147 (86.5)
EEG monitoring	118 (69.4)
Type of EEG available	
Routine 20 channel EEG for 30 min	47 (29.4)
Continuous 20 channel EEG monitoring	41 (25.9)
Continuous video EEG	18 (11.3)
Amplitude integrated EEG	10 (6.3)
Compressed spectral array	11 (6.9)
Pediatric neurologist	117 (68.8)
CSF viral multiplex PCR	99 (58.2)
Invasive intracranial pressure monitoring	63 (37.1)
Work-up for autoimmune encephalitis in cases with RSE/SRSE without apparent etiology	150 (88.2)
Work-up for NMO and MOG antibodies in cases with RSE/SRSE with suspected acute disseminated encephalomyelitis	142 (83.5)
Data represented as n (%)	

practice. Nearly half (48.8%) of respondents' report using local/unit specific protocols for management of PSE. Other reported following international guidelines (47.4%), national guidelines (35.3%), and individual practice (17.3%) (Table 5).

## DISCUSSION

Convulsive SE (CSE) is defined as a convulsive seizure that continues for a prolonged period (longer than 5 minutes), or repeated convulsive seizures with no recovery in between.<sup>3,5,17</sup> Prolonged seizures can lead to irreversible neuronal damage; short- and longterm neurological, cognitive, and behavioral impairments; and poor quality of life.<sup>1,2</sup> Two important factors which determine the

Survey of Pediatric Status Epilepticus Treatment Practices

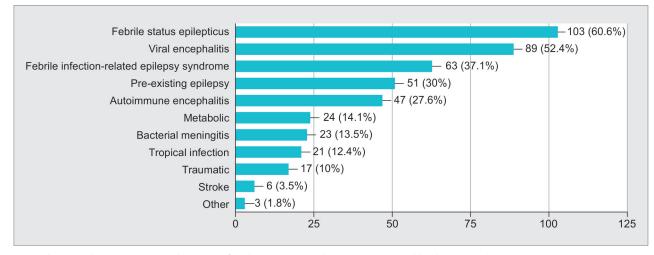


Fig. 2: Bar diagram showing common diagnosis of pediatric status epilepticus as reported by the respondents

 Table 5: Details regarding compliance to the guidelines for management of pediatric status epilepticus

Compliance and adherence to the SE management guidelines	Total respondents (n = 170)
Able to administer repeat doses of benzodiazepine within first 5–15 minutes as recommended by PSE management guidelines	151 (88.8)
Able to initiate second-line ASM within 15–30 minutes as recommended by the PSE management guidelines	138 (81.2)
Able to initiate third-line ASM within 60 minutes as recommended by the PSE management guidelines	108 (63.5)
The timeline suggested by the PSE management guidelines is too strict to follow in actual clinical practice	104 (61.2)
Unit have local protocol for management of PSE If no local protocol, guidelines followed for management of PSE	82 (48.8)
International guidelines	63 (47.4)
National guidelines	47 (35.3)
Individual practice	23 (17.3)
Data represented as $n$ (%)	

Data represented as n (%)

timing of initiation of treatment are the duration of seizure activity which makes it unlikely to self-terminate and, therefore, requires treatment; and the duration of seizure after which neurological harm becomes significant if seizures continue. Seizures lasting for >5 minutes tend to become prolonged and need treatment for termination. Therefore, any seizure activity lasting for >5 minutes is classified as SE and interventions are recommended.<sup>3,18</sup> With appropriate management, the outcome of children with SE without previous neurological problems is generally good.<sup>19</sup>

As per current guidelines, the pharmacological management of PSE include first-line ASM which include benzodiazepines (midazolam, diazepam, or lorazepam) (5–20 minutes) followed by second-line ASM (fosphenytoin/phenytoin, valproate, levetiracetam, or phenobarbitone) (20–40 min), and in nonresponsive cases (RSE), repeat dose of second-line ASM or anesthetic drugs (midazolam, thiopentone, pentobarbital, or propofol) (40–60 min) along with intubation and mechanical ventilation.<sup>3–5</sup> However, there is wide variability in management of PSE and poor compliance to guidelines.<sup>3–5,13–17</sup>

Regarding the first-line ASM, midazolam was the most preferred agent and most respondents use 2 doses. Until recently phenytoin was commonly used second-line ASM.<sup>3,5,13,14</sup> However, two recent large randomized controlled trials (RCTs) compared the efficacy of levetiracetam and phenytoin as second-line ASM in PSE and noted that levetiracetam is equally effective and safe second-line ASM.<sup>7, 8</sup> However, due to safety profile and comparative ease of administration, it was suggested that levetiracetam could be an appropriate alternative to phenytoin as second-line ASM in PSE.<sup>7</sup> Angurana and Suthar in a meta-analysis (12 RCTs, 2,293 children with SE) comparing levetiracetam and phenytoin as second-line ASM demonstrated that there was similar rate of seizure cessation within 5–60 minutes (82 vs 77.5%, respectively, p = 0.30); and higher seizure recurrences within 1–24 hour (16.6 vs 9.7%, p = 0.01) and higher need of mechanical ventilation (21.4 vs 14.2%, p = 0.04) in phenytoin group.<sup>9</sup> Tyson et al. conducted an online survey of clinicians across 55 PERs and 29 PICUs in the United Kingdom and Ireland and demonstrated that most clinicians use phenytoin (76.4% in PER and 60.9% in PICU) as second-line ASM, however, they seek greater flexibility in choice of second-line ASM, with levetiracetam (60.9%) being preferred alternative to phenytoin.<sup>17</sup> Few other surveys also demonstrated preference toward levetiracetam as second-line ASM.<sup>14,15</sup>

Considering the recent evidence about the efficacy of levetiracetam,<sup>7-9</sup> ready to use preparation, ease and speed of administration, and better safety profile, many clinicians have already incorporated levetiracetam as an alternative second-line ASM in their practice awaiting changes in national and international guidelines.<sup>14,15,17</sup> In index eSurvey, we also noted a trend towards preference in using levetiracetam as second-line ASM (51.2% respondents).

Regarding the third-line ASM (for RSE), there is no clear evidence to guide therapy.<sup>3,5</sup> However, most clinicians typically use midazolam infusion, and in cases with no response, thiopentone/barbiturate infusion.<sup>20,21</sup> A recent survey from Turkey (334 participants including 136 pediatric neurologists, 102 pediatric emergency medicine specialists, and 96 pediatric intensive care specialists) demonstrated that for RSE, the common drugs preferred were midazolam

infusion by emergency specialists (76.5%) and barbiturate infusion by intensive care specialists (49%). For the treatment of SRSE, about half of intensive care specialists and neurologists preferred to use immunomodulation and 60% neurologists preferred ketogenic diet.<sup>14</sup> Another survey from Argentina (252 participants; 77% pediatricians and 16% intensive care specialists) demonstrated that most participants preferred midazolam infusion as third-line ASM (63%) and only 17% preferred thiopentone infusions.<sup>13</sup> The preference in use of midazolam infusion as third-line ASM in literature as well as in the index eSurvey is possibly due to lack of evidence for this stage of treatment, easily availability, and better adverse effect profile. The titration goals are variable among clinicians including clinical seizure control, burst suppression, or both.

There is lack of clear information about the duration of pharmacological coma and treatment end-points.<sup>3</sup> However, the manifestations of ongoing seizures become subtle over time, there is high risk of development of nonconvulsive SE (NCSE) after CSE, poorly controlled CSE and NCSE are associated with grave prognosis, and with time the response to ASMs is poor.<sup>3,22</sup> Therefore, continuous EEG (cEEG) monitoring is crucial in PSE. It has important diagnostic (to detect ongoing electrographic seizures [ES], particular patterns pointing toward diagnosis, and adjusting medications) and prognostic value.<sup>3</sup> Fung et al. performed a survey of cEEG monitoring in PICUs of 48 US and Canadian institutions.<sup>23</sup> The continuous EEG was almost always available at 86% of the US institutions and 18% of the Canadian institutions. The indications for cEEG were generally aligned with the American Clinical Neurophysiology Society indications (84-100%). All these centers had facility for neurological consultations. The neurologist's approval was always needed to initiate cEEG monitoring in 38% of the US institutions and 82% of the Canadian institutions; and the decision to end cEEG monitoring (100%). The usual duration of cEEG monitoring was 24 hours (70%) for ES screening in patients without EEG risk factors for seizures and longer in patients with EEG risk factors for seizures. Among children with ES, cEEG was usually continued for 24 hours after the last seizure (76%). Authors noted that the main limitations to performing additional cEEG were insufficient technologists (67%), equipment (52%), and electroencephalographers (19%). Majority of clinicians (65%) aimed to terminating all nonconvulsive seizures.<sup>23</sup> With increasing availability of cEEG as well as pediatric neurologists, the use of cEEG in PSE is increasing as demonstrated in index eSurvey where 70% respondents use cEEG while managing PSE and 85.3% respondents consider seizure free period of 12-48 hours before tapering third-line ASMs.

Early identification of etiology of PSE is important. FIRES and autoimmune encephalitis have been recognized as important causes of SRSE in children.<sup>3,24</sup> Therefore, immunotherapy has also used commonly in children with SRSE.<sup>24,25</sup> Early initiation of enteral ketogenic diet has been shown to be effective, safe, and well-tolerated in management of SRSE.<sup>24</sup> There is role of pyridoxine therapy in young children with SRSE even in absence of a significant deficiency in pyridoxine.<sup>26</sup> High rates of use of ancillary therapies in index eSurvey suggest heightened awareness about these etiologies of SRSE among respondents, support of pediatric neurologists, availability of diagnostic work-up and ancillary therapies, and more and more gain in experience with these treatment options. In addition to heterogeneity in treatment approaches, the compliance to PSE management guidelines is generally poor (15–20%) especially to time-dependent decisions.<sup>13,16,27</sup>

The strengths of this study include that this is the first survey that provided real world data concerning the current PSE treatment practices among pediatric intensivists and pediatricians throughout India. This study will serve as primer for future studies to record actual treatment practices, improvement in facilities and quality of care, and formulation of guidelines for Indian settings. The usual limitations of any online survey apply to this study as well. The treatment practices were not evaluated directly but based on survey. This survey has not evaluated the treatment practices followed by pediatric neurologists. The details about pre-hospital management, availability of ASMs, cost factors, and short- and long-term outcomes were not recorded.

To improve the outcomes of PSE, there is need to improve the treatment practices for management of PSE, strengthening of healthcare settings, formulation and implementation of evidencebased and locally adaptable management protocols, and training programs for healthcare providers.

# CONCLUSION

Intravenous midazolam bolus/es, levetiracetam, and midazolam infusion are commonly used first, second, and third-line ASMs, respectively. For RSE and SRSE, there is wide variability in use of ASMs and ancillary treatment. There is wide variation is compliance to SE management guidelines and half of participants had their own protocols.

# **AUTHOR CONTRIBUTIONS**

Angurana SK, Suthar R, and Nallasamy K planned study and collected data, analyzed the data, and written manuscript. Bansal A and Muralidharan J reviewed manuscript and provided intellectual inputs. All authors reviewed and approved the final manuscript.

#### Ethical Approval

Institute Ethics Committee, PGIMER, Chandigarh (No.: INT/IEC/2023/ SPL-965 dated 8/9/2023).

## ORCID

Renu Suthar © https://orcid.org/0000-0003-4701-6168 Suresh Kumar Angurana © https://orcid.org/0000-0001-6370-8258 Karthi Nallasamy © https://orcid.org/0000-0002-6713-9846 Arun Bansal © https://orcid.org/0000-0001-6212-6889 Jayashree Muralidharan © https://orcid.org/0000-0002-6149-1355

#### REFERENCES

- 1. Chin RFM. The outcomes of childhood convulsive status epilepticus. Epilepsy Behav 2019;101(Pt B):106286. DOI: 10.1016/j. yebeh.2019.04.039.
- Kling R, Ritvanen J, Mustonen H, Kämppi L. Long-term outcome of convulsive status epilepticus: A 10-year follow-up. Epileptic Disord 2022;24(6):1046–1059. English. DOI: 10.1684/epd.2022.1482.
- Glauser T, Shinnar S, Gloss D, Alldredge B, Arya R, Bainbridge J, et al. Evidence-based guideline: Treatment of convulsive status epilepticus in children and adults: Report of the Guideline Committee of the American Epilepsy Society. Epilepsy Curr 2016;16(1):48–61. DOI: 10.5698/1535-7597-16.1.48.
- Van de Voorde P, Turner NM, Djakow J, de Lucas N, Martinez-Mejias A, Biarent D, et al. European Resuscitation Council Guidelines 2021: Paediatric life support. Resuscitation 2021;161:327–387. DOI: 10.1016/j. resuscitation.2021.02.015.

- Mishra D, Sharma S, Sankhyan N, Konanki R, Kamate M, Kanhere S, et al. Multi-disciplinary group on management of status epilepticus in children in India. Consensus guidelines on management of childhood convulsive status epilepticus. Indian Pediatr 2014;51(12):975–990. DOI: 10.1007/s13312-014-0543-4.
- Singhi S, Angurana SK. Principles of management of central nervous system infections. Indian J Pediatr 2019;86(1):52–59. DOI: 10.1007/ s12098-017-2583-y.
- Lyttle MD, Rainford NEA, Gamble C, Messahel S, Humphreys A, Hickey H, et al. Paediatric emergency research in the United Kingdom & Ireland (PERUKI) collaborative. Levetiracetam versus phenytoin for second-line treatment of paediatric convulsive status epilepticus (EcLiPSE): A multicentre, open-label, randomised trial. Lancet 2019;393(10186):2125–2134. DOI: 10.1016/S0140-6736(19) 30724-X.
- Dalziel SR, Borland ML, Furyk J, Bonisch M, Neutze J, Donath S, et al. Levetiracetam versus phenytoin for second-line treatment of convulsive status epilepticus in children (ConSEPT): An open-label, multicentre, randomised controlled trial. Lancet 2019;393(10186):2135–2145. DOI: 10.1016/S0140-6736(19)30722-6.
- 9. Angurana SK, Suthar R. Efficacy and safety of levetiracetam vs. phenytoin as second line antiseizure medication for pediatric convulsive status epilepticus: A systematic review and meta-analysis of randomized controlled trials. J Trop Pediatr 2021;67(2):fmab014. DOI: 10.1093/tropej/fmab014.
- McTague A, Martland T, Appleton R. Drug management for acute tonic-clonic convulsions including convulsive status epilepticus in children. Cochrane Database Syst Rev 2018;1(1):CD001905. DOI: 10.1002/14651858.CD001905.pub3.
- 11. Patten W, Naqvi SZ, Raszynski A, Totapally BR. Complications during the management of pediatric refractory status epilepticus with benzodiazepine and pentobarbital infusions. Indian J Crit Care Med 2015;19(5):275–277. DOI: 10.4103/0972-5229.156476.
- Masapu D, Gopala Krishna KN, Sanjib S, Chakrabarti D, Mundlamuri RC, Manohar N, et al. A comparative study of midazolam and targetcontrolled propofol infusion in the treatment of refractory status epilepticus. Indian J Crit Care Med 2018;22(6):441–448. DOI: 10.4103/ ijccm.IJCCM\_327\_17.
- Nuñez P, Hansen J, Aprea V, Álvarez Ricciardi MB, Oviedo S, Fustiñana A, et al. Management of status epilepticus in childhood: A survey conducted at pediatric hospitals in the City of Buenos Aires. Arch Argent Pediatr 2023;121(2):e202202696. DOI: 10.5546/aap.2022-02696.eng.
- Dedeoglu Ö, Akça H, Emeksiz S, Kartal A, Kurt NÇ. Management of status epilepticus by different pediatric Departments: Neurology, intensive care, and emergency medicine. Eur Neurol 2023;86(5): 315–324. DOI: 10.1159/000533191.

- 15. Kowoll CM, Klein M, Salih F, Fink GR, Stetefeld HR, Onur OA, et al. IGNITE status epilepticus survey: A nationwide interrogation about the current management of status epilepticus in Germany. J Clin Med 2022;11(5):1171. DOI: 10.3390/jcm11051171.
- 16. Philpott NG, Dante SA, Philpott D, Perin J, Bhatia P, Henderson E, et al. Treatment guideline nonadherence pretransport associated with need for higher level of care in children transferred to a pediatric tertiary care center for status epilepticus. Pediatr Emerg Care 2023;39(10):780–785. DOI: 10.1097/PEC.00000000002952.
- Tyson M, Trenear R, Skellett S, Maconochie I, Mullen N. Survey about second-line agents for pediatric convulsive status epilepticus. Pediatr Emerg Care 2023;39(4):247–252. DOI: 10.1097/PEC.000000000002745.
- Trinka E, Cock H, Hesdorffer D, Rossetti AO, Scheffer IE, Shinnar S, et al. A definition and classification of status epilepticus – Report of the ILAE Task Force on Classification of Status Epilepticus. Epilepsia 2015;56(10):1515–1523. DOI: 10.1111/epi.13121.
- Pujar SS, Martinos MM, Cortina-Borja M, Chong WKK, De Haan M, Gillberg C, et al. Long-term prognosis after childhood convulsive status epilepticus: A prospective cohort study. Lancet Child Adolesc Health 2018;2(2):103–111. DOI: 10.1016/S2352-4642(17)30174-8.
- Vasquez A, Farias-Moeller R, Tatum W. Pediatric refractory and superrefractory status epilepticus. Seizure 2019;68:62–71. DOI: 10.1016/j. seizure.2018.05.012.
- 21. Crawshaw AA, Cock HR. Medical management of status epilepticus: Emergency room to intensive care unit. Seizure 2020;75:145–152. DOI: 10.1016/j.seizure.2019.10.006.
- 22. Payne ET, Zhao XY, Frndova H, McBain K, Sharma R, Hutchison JS, et al. Seizure burden is independently associated with short term outcome in critically ill children. Brain 2014;137(Pt 5):1429–1438. DOI: 10.1093/brain/awu042.
- 24. van Baalen A. Febrile infection-related epilepsy syndrome in childhood: A clinical review and practical approach. Seizure 2023;111:215–222. DOI: 10.1016/j.seizure.2023.09.008.
- 25. Barcia Aguilar C, Sánchez Fernández I, Loddenkemper T. Status epilepticus-work-up and management in children. Semin Neurol 2020;40(6):661–674. DOI: 10.1055/s-0040-1719076.
- 26. Ferlisi M, Shorvon S. The outcome of therapies in refractory and superrefractory convulsive status epilepticus and recommendations for therapy. Brain 2012;135(Pt 8):2314–2328. DOI: 10.1093/brain/aws091.
- AlMohaimeed BA, Hundallah KJ, Bashiri FA, AlMohaimeed SA, Tabarki BM. Evaluation of adherence to pediatric status epilepticus management guidelines in Saudi Arabia. Neurosciences (Riyadh) 2020;25(3):182–187. DOI: 10.17712/nsj.2020.3.20190106.

