Status Epilepticus in Children: Management and Outcomes

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KEY POINTS

1. Early recognition and intervention: Immediate treatment initiation at 5 minutes (t1) to prevent neurological damage starting at 30 minutes (t2).
2. Systematic ABCDE assessment: Prioritizing airway protection, adequate oxygenation (>94%), lateral positioning, and intravenous access.
3. First-Line therapy: Benzodiazepines (lorazepam, diazepam, midazolam) constitute the cornerstone of initial treatment, demonstrating rapid therapeutic onset within 5 minutes.
4. Sequential treatment escalation: Second-line agents (fosphenytoin, levetiracetam, valproic acid) if seizures persist beyond 20-30 minutes despite benzodiazepine; third-line anesthetics for refractory cases.
5. EEG Monitoring: 48% of patients continue experiencing electrographic seizures after clinical cessation, necessitating continuous EEG monitoring within 60 minutes.
6. Prognosis: Clinical outcomes are predominantly determined by underlying causes. While mortality remains low (0-3%); structural or metabolic abnormalities have the highest recurrence risk.
7. Refractory status epilepticus management: Require aggressive multimodal treatment strategies including immunotherapy and alternative approaches such as ketogenic diet.

POINTS CLÉS

1. Reconnaissance et intervention précoces : Initiation immédiate du traitement à 5 minutes (t1) pour prévenir les lésions neurologiques débutant à 30 minutes (t2).
2. Évaluation systématique ABCDE : Priorisant la protection des voies aériennes, l'oxygénation adéquate (>94%), le positionnement latéral et l'accès intraveineux.
3. Traitement de première ligne : Les benzodiazépines (lorazépam, diazépam, midazolam) constituent la pierre angulaire du traitement initial, démontrant un début d'action rapide en moins de 5 minutes.
4. Escalade thérapeutique séquentielle : Agents de deuxième ligne (fosphénytoïne, lévétiracétam, acide valproïque) si les crises persistent au-delà de 20-30 minutes malgré les benzodiazépines ; traitement de troisième ligne pour les cas réfractaires.
5. Surveillance EEG : 48% des patients continuent de présenter des crises électrographiques après la cessation clinique ; nécessitant une surveillance EEG continue dans les 60 minutes.
6. Pronostic : Les résultats cliniques sont principalement déterminés par les causes sous-jacentes. Bien que la mortalité reste faible (0-3%) ; les anomalies structurelles ou métaboliques présentent le risque de récurrence le plus élevé.
7. Prise en charge de l'état de mal épileptique réfractaire : Nécessite des stratégies thérapeutiques multimodales agressives incluant l'immunothérapie et des approches alternatives telles que le régime cétogène.

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INTRODUCTION

A seizure is defined as an acute, temporary disturbance of central nervous system function characterized by abnormal excessive and hypersynchronous neuronal discharge in the cortical gray matter, resulting in a change in neurological function and observable signs or symptoms. It represents a frequent neurological condition within the pediatric age group, affecting approximately 5% to 8% of children, especially during infancy and early childhood. Clinical differentiation of seizures from other paroxysmal disorders is essential, as these events may mimic various conditions including syncope and movement disorders [1].

DEFINITION OF STATUS EPILEPTICUS

Status epilepticus (SE) constitutes a critical neurological condition defined by excessively extended seizure activity or successive epileptic episodes without recovery of consciousness [2].

Over the past decades, the definition of SE has undergone significant revisions.

Previously, it was defined as a seizure with a duration equal to or greater than 30 minutes or a series of seizures in which the patient does not regain normal mental status between seizures. Recent definitions such as the one from the International League Against Epilepsy (ILAE) include a shorter duration of seizure activity.

The development of SE occurs through two primary pathways: dysfunction of seizure termination processes or triggering mechanisms that perpetuate pathologically prolonged convulsive activity (after t1). This condition carries significant long-term implications (post-t2), including cellular death, neuronal damage, and structural neural network modifications, influenced by seizure type and temporal duration [3].

T1 (Treatment initiation): 5 minutes, **T2 (Risk of long-term consequences):** 30 minutes.

Within this conceptual model, t1 serves as the critical decision point for commencing treatment, whereas t2 indicates when aggressive therapeutic measures become essential to avoid long-term complications [1].

This definition accounts for the natural resolution of most generalized tonic-clonic seizures within 5 minutes without treatment [4].

Refractory status epilepticus (RSE) is characterized by persistent seizure activity, beyond 1 hour, that fails to respond to multiple first- and second-line antiseizure medications with distinct mechanisms of action, such as benzodiazepines, fosphenytoin or phenytoin, and phenobarbital [5].

Super-refractory status epilepticus (SRSE) is characterized by seizures that persist for 24 hours or longer following the initiation of anesthetic treatment, or SE that recurs during the tapering or discontinuation of anesthetic agents.

Nonconvulsive status epilepticus (NCSE) is characterized by continuous seizure activity with minimal or absent clinical manifestations, commonly observed in PICU patients, particularly as a sequela of prolonged convulsive SE.

New-Onset Refractory Status Epilepticus (NORSE) represents a rare, yet catastrophic syndrome characterized by the abrupt development of intractable seizures without identifiable acute structural, toxic, or metabolic precipitants. Febrile Infection-Related Epilepsy Syndrome (FIRES) is considered a phenotypic variant of NORSE, distinguished by a preceding febrile illness occurring within 2 weeks to 24 hours prior to refractory status epilepticus onset [6].

ETIOLOGIES OF STATUS EPILEPTICUS IN CHILDREN

Etiological classification of status epilepticus includes symptomatic cases, defined by the presence of a known structural or metabolic cause, which are further categorized as either acute or remote symptomatic.

Acute symptomatic seizures are temporally linked (within 7 days) to systemic metabolic disturbances, toxic exposures, or acute neurological insults. Remote symptomatic seizures arise from pre-existing CNS pathology established more than one week prior, including sequelae of infections, traumatic brain injury, cerebrovascular disease, or congenital cortical malformations that have created permanent structural abnormalities. Remote symptomatic status epilepticus frequently occurs in patients with chronic epilepsy or established neurological disorders. Idiopathic status epilepticus represents cases of unknown etiology despite thorough investigation [1]. SE encompasses multiple etiological pathways, with acute precipitating causes categorized as follows [5,7-9]:

Infectious Causes: Central nervous system infections, including bacterial and viral meningitis, encephalitis, and space-occupying lesions such as intracranial abscesses.

Metabolic Disorders: Systemic metabolic disturbances such as hypoglycemia, electrolyte abnormalities (hyponatremia, hypocalcemia), hepatic dysfunction with encephalopathy, and inborn errors of metabolism.

Vascular and Traumatic Causes: Acute cerebrovascular accidents and head trauma, whether associated with intracranial bleeding or not.

Toxicological Causes: Drug-induced seizures and withdrawal syndromes, particularly from alcohol, benzodiazepines, and barbiturates.

Other Acute Conditions: Hypoxic events, hypertensive emergencies, and autoimmune inflammatory disorders.

Table 1: Common etiologies of pediatric status epilepticus by age group [7-9]

Age Group	Most Common Etiologies	Clinical Considerations
Neonates	Hypoxic-ischemic encephalopathy, CNS infections, Inborn errors of metabolism, Intracranial hemorrhage	High suspicion for metabolic disorders
Infants (1-24 months)	Febrile seizures, CNS infections, Metabolic disorders, Developmental abnormalities	Peak age for febrile SE
Children (2-12 years)	Febrile SE, Acute symptomatic (infections, trauma), Remote symptomatic (epilepsy), Idiopathic	Consider autoimmune encephalitis
Adolescents (>12 years)	Remote symptomatic (epilepsy), Drug withdrawal/toxicity, CNS infections, Autoimmune encephalitis	Consider NORSE/FIRES

DIAGNOSTIC WORK-UP

A systematic diagnostic approach is essential for identifying treatable causes and guiding management decisions [10].

Initial Assessment include capillary blood glucose testing, vital signs monitoring (heart rate, blood pressure, oxygen saturation, temperature), a brief neurological examination and assessment for trauma or toxic ingestion.

Essential initial laboratory testing should include serum glucose and electrolytes (sodium, calcium, magnesium), complete blood count, blood gas analysis, and antiseizure medication levels in patients with known epilepsy. Additional investigations may be required based on clinical context, including liver and kidney function tests, ammonia levels, toxicology screening when toxic ingestion is suspected, blood cultures if systemic infection is a concern, and lactate and pyruvate levels when inborn errors of metabolism are considered.

Brain imaging (CT or MRI) should be performed after stabilization and seizure control. The American Academy of Neurology recommends neuroimaging after the child is stabilized and SE is controlled.

Lumbar puncture (LP) is indicated when CNS infection is suspected.

OUTCOME OF STATUS EPILEPTICUS

The prognosis of status epilepticus is primarily influenced by three key factors: the underlying cause, the timeliness of therapeutic intervention, and the degree of treatment resistance exhibited by the seizures [6]. Pediatric SE carries a relatively low mortality rate (0-3%), but survivors face significant long-term neurological consequence including an elevated risk of developing epilepsy (13-74%) and experiencing recurrent SE (20% within 4 years). The prognosis is mainly influenced by the underlying causative factors, where structural or metabolic disorders present the greatest risk for seizure recurrence [11].

ELECTROENCEPHALOGRAPHY IN STATUS EPILEPTICUS

During prolonged convulsive SE, seizure activity frequently evolves into subtle or nonconvulsive forms that lack overt clinical manifestations, necessitating continuous electroencephalographic (EEG) monitoring. Current evidence demonstrates that up to 48% of patients with generalized convulsive status epilepticus continue to exhibit electrographic seizures after cessation of clinical convulsions. Guidelines from the American Clinical Neurophysiology Society recommend initiating EEG monitoring within 60 minutes of ongoing convulsive SE, or immediately when nonconvulsive seizures are suspected following initial treatment. Delays in EEG implementation significantly compromise seizure recognition and appropriate therapeutic intervention, with substantially higher mortality rates compared to those without ongoing ictal activity [12].

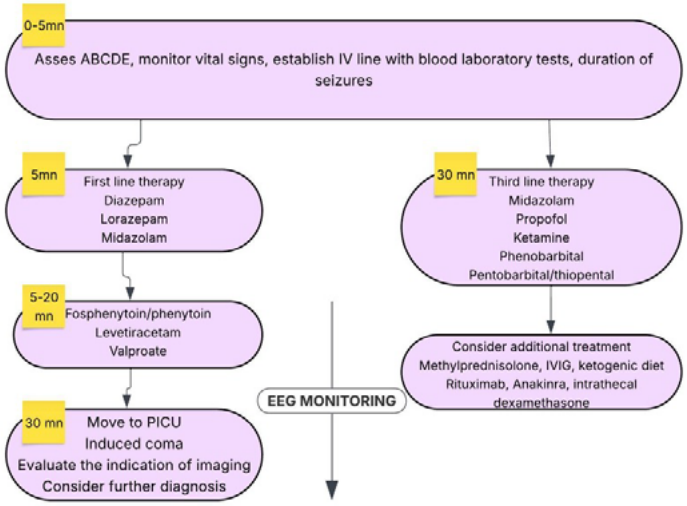
Continuous EEG monitoring should be implemented immediately following SE diagnosis to guide treatment decisions and monitor seizure control, generally continuing for a minimum of 24 hours after complete seizure cessation [12].

MANAGEMENT OF STATUS EPILEPTICUS

A summary of the treatment strategy is presented in Fig.1.

Emergency seizure management begins with sys tematic ABCDE assessment, emphasizing airway maintenance and breathing support before initiating antiepileptic therapy. Patients require lateral decubitus positioning to minimize aspiration hazard, with oxygen therapy administered to maintain arterial saturation above 94%. Establishing intravenous access and monitoring cardiorespiratory parameters are critical preliminary measures.

Figure 1 : Treatment approaches for pediatric status epilepticus



First- and Second-Line Pharmacotherapy (Table 2)

As a first-line treatment, benzodiazepines (diazepam, lorazepam, and midazolam) are recommended. If intravenous (IV) access is not available, alternative routes like buccal, rectal, intramuscular should be considered. All three benzodiazepine demonstrate quick action initiation under 5 minutes and enhance inhibitory neurotransmission via attachment to specific diazepine site on the GABAA receptor.

Second-line treatments include phenytoin, fosphenytoin, levetiracetam and valproic acid.

Table 2: The first and the second line possible treatments.

Drug	Initial Dose	Maximum Single Dose	Half-Life	Main Side Effects
Lorazepam	0.05–0.1 mg/kg IV	4 mg	10 h	Somnolence, hypotension, bradycardia, respiratory depression
Diazepam	0.05–0.3 mg/kg IV	<5 y: 5 mg ≥5 y: 10 mg	40–50 h (Infants) 15–20h (Children)	Same adverse effects as mentioned above, thrombotic complications
Midazolam	0.1mg/kg (IV,IO) 0.2mg/kg (IM) 0.5mg/kg (Buccal) 0.2mg/kg (Intranasal)	5mg 10mg 10mg 10mg	1.5-2.5 h	Hypotension, respiratory depression, sedation
Phenytoin	15–20 mg/kg IV	1 g	7–42 h	Dysarthria, ataxia, somnolence, hypotension, arrhythmia, thrombophlebitis, purple glove syndrome
Fosphenytoin	15–20 mg PE/kg IV	1 g PE	12–29 h	Dysarthria, ataxia, sedation, hypotension, bradycardia, tachycardia
Levetiracetam	60 mg/kg	3000 mg	6-8 h	Behavioral changes, irritability; psychosis (low risk)
Valproic acid	10–30 mg/kg IV	30 mg/kg	7–13h (Children >2 months) 3.5–20h (Children 2–14 y)	Hypotension, arrhythmia, hepatitis, pancreatitis

Third line therapy in RSE (Table 3)

Third-line therapy include continuous infusions of anesthetizing ASMs such as high-dose benzodiazepines, ketamine, pentobarbital (PTB), or propofol (PRO) to help avoid complications of RSE and phenobarbital (except for neonates)[1,13,14].

Table 3: Third line treatments.

Drug	Loading dose	Maintenance dose	Adverse effects
Phenobarbital	15-20mg/kg	Additional 5-10 mg/kg boluses	Hypotension, respiratory depression, prolonged sedation
Ketamine	0.5-5mg/kg	1-10mg/kg/h	Tachycardia, arrythmia, hypertension
Midazolam	0.2mg/kg	0.05-2mg/kg/h	Hypotension, respiratory depression, sedation
Propofol	1-2mg/kg	1-5mg/kg/h (Only 24h)	PRIS, cardiorespiratory depression
Thiopental	2-7mg/kg	0.5-12mg/kg/h	Cardiorespiratory depression,illeus,hypernatriemia

Propofol use should be limited to a maximum of 24-48 hours due to the risk of Propofol Infusion Syndrome (PRIS), characterized by metabolic acidosis, rhabdomyolysis, cardiac failure, hyperkalemia, hypertriglyceridemia, and potentially fatal outcomes. Continuous monitoring of triglycerides, creatine kinase, lactate, and cardiac function is mandatory. PRIS risk is higher with prolonged use, high doses (>5 mg/kg/h), and concomitant catecholamine or corticosteroid administration [14,15]

EMERGING AND ADJUNCTIVE THERAPIES FOR RSE

When conventional antiseizure medications and anesthetic agents fail to control seizures, several emerging therapeutic options should be considered, particularly in cases of super-refractory SE.

Immunotherapy: For suspected autoimmune or inflammatory etiologies (particularly in NORSE/FIRES), early immunomodulatory therapy should be initiated and includes:

- High-dose corticosteroids (methylprednisolone 20-30 mg/kg/day for 3-5 days)
- Intravenous immunoglobulin (IVIG) (2 g/kg divided over 2-5 days)
- Plasma exchange - 5-7 exchanges over 10-14 days
- Rituximab (anti-CD20 monoclonal antibody, 375 mg/m²/week for 4 weeks) or tocilizumab (IL-6 receptor antagonist, 8 mg/kg every 2 weeks)

Early initiation of immunotherapy (within the first week) may improve outcomes in immune-mediated SE, particularly in NORSE/FIRES cases [14].

Ketogenic Diet: Has demonstrated efficacy in super-refractory SE, particularly in children, with seizure control achieved in 50-70% of cases. The diet induces metabolic changes that enhance GABAergic inhibition and provide alternative energy substrates for the brain [4,10,16].

Neurostimulation: Is an emerging treatment of RSE that may control seizures when other treatments fail. It includes Vagus nerve stimulation (VNS), Electroconvulsive therapy (ECT) and Deep brain stimulation (DBS): Experimental in acute SE; more established for chronic refractory epilepsy [17].

Therapeutic Hypothermia: Mild therapeutic hypothermia (32-34°C for 24-48 hours) may reduce cerebral metabolic demands, decrease excitotoxicity, and protect against neuronal injury. Clinical evidence in pediatric SE remains limited, and routine use is not currently recommended outside research protocols. Potential complications include coagulopathy, infection risk, and arrhythmias [14].

Surgical intervention: Hemispherectomy or focal resection may be considered in selected cases with identifiable focal structural lesions causing RSE, particularly when conventional therapies fail.

REGIONAL CONSIDERATIONS

Despite limited published data from the region, a Tunisian study on infantile status epilepticus reported higher mortality (15.8%) and neurological sequelae (36%) than western countries, reflecting challenges including delayed medical access, scarce EEG monitoring, and limited medication availability. This paucity of regional research highlights the need for both improved clinical resources and enhanced epidemiological surveillance in Tunisia and the Maghreb [18].

CONCLUSION

Status epilepticus management requires a time-sensitive, evidence-based approach where early intervention is paramount to prevent progression to refractory forms that become increasingly difficult to treat. This underscores the fundamental principle that in status epilepticus, time is brain, and rapid, systematic treatment implementation can be the difference between recovery and irreversible neurological compromise.

REFERENCES :

[1] Fuhrman BP, Zimmerman JJ, editors. Pediatric critical care. 6th ed. Philadelphia: Elsevier 2021.

[2] Abend NS, Loddenkemper T. Pediatric Status Epilepticus Management. Curr Opin Pediatr. déc 2014; 26(6):668-74.

[3] 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. oct 2015; 56(10): 1515-23.

[4] Shin JW. Management strategies for refractory status epilepticus. J Neurocrit Care. 19 déc 2023;16(2):59-68.

[5] DeLorenzo RJ, Garnett LK, Towne AR, Waterhouse EJ, Boggs JG, Morton L, et al. Comparison of status epilepticus with prolonged seizure episodes lasting from 10 to 29 minutes. Epilepsia. févr 1999; 40(2):164-9.

[6] Wylie T, Sandhu DS, Murr NI. Status epilepticus. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 [cited 2025 Jul 31]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK430686/

[7] Farmania R, Garg D, Sharma S. Status Epilepticus in Neonates and Infants. Ann Indian Acad Neurol. 2020;23(6) : 747-54

[8] Abend NS, Bearden D, Helbig I, McGuire J, Nariai H, Pak C, et al. Status Epilepticus and Refractory Status Epilepticus Management. Semin Pediatr Neurol. 2014;21(4):263-74.

[9] Specchio N, Pietrafusa N, Bellusci M, Trivisano M, Benvenga A, de Palma L, et al. Pediatric status epilepticus: Identification of prognostic factors using the new ILAE classification after 5 years of follow-up. Epilepsia. 2019; 60(12):2486-98.

[10] Riviello JJ Jr, Ashwal S, Hirtz D, Glauser T, Ballaban-Gil K, Kelley K, et al. Practice parameter: Diagnostic assessment of the child with status epilepticus (an evidence-based review): Report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. Neurology 2006; 67(9):1542-50

[11] Sidharth, Sharma S, Jain P, Mathur SB, Malhotra RK, Kumar V. Status epilepticus in pediatric patients severity score (STEPSS): a clinical score to predict the outcome of status epilepticus in children- a prospective cohort study. Seizure 2019; 71:328-32.

[12] Raspall-Chaure M, Chin RFM, Neville BG, Scott RC. Outcome of paediatric convulsive status epilepticus: a systematic review. Lancet Neurol. 2006; 5(9):769-79.

[13] Morgan LA, Sprigg BN, Barry D, Hrachovec JB, Novotny EJ, Akiyama LF, et al. Reducing time to electroencephalography in pediatric convulsive status epilepticus: a quality improvement initiative. Pediatric Neurology. 2024; 152:169-76.

[14] Vossler DG, Bainbridge JL, Boggs JG, Novotny EJ, Loddenkemper T, Faught E, et al. Treatment of refractory convulsive status epilepticus: a comprehensive review by the American Epilepsy Society Treatments Committee. Epilepsy Curr. 2020; 20(5):245-64.

[15] Becker LL, Gratopp A, Prager C, Elger CE, Kaindl AM. Treatment of pediatric convulsive status epilepticus. Front Neurol. 2023; 14:1175370.

[16] Nabbout R, Matricardi S, De Liso P, Dulac O, Oualha M. Ketogenic diet for super-refractory status epilepticus (SRSE) with NORSE and FIRES: Single tertiary center experience and literature data. Front Neurol. 2023; 14:1134827.

[17] Stavropoulos I, Khaw JH, Valentin A. Neuromodulation in new-onset refractory status epilepticus. Front Neurol. 2023; 14:1195844.

[18] Tabarki B, Yacoub M, Selmi H, Oubich F, Barsaoui S, Essoussi AS. Infantile status epilepticus in Tunisia. Clinical, etiological and prognostic aspects. Seizure. 2001; 10(5):365-69.