Status Epilepticus in Neonates and Infants

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Abstract

Status epilepticus (SE) is a common neurological emergency in childhood associated with high mortality and morbidity. Acute management of seizures along with aggressive evaluation for establishing the underlying cause are crucial determinants of outcome. Neonatal status epilepticus carries the burden of poor neurological outcomes and may lead to global developmental delay as well as persistent seizures. The aetiology and pathophysiological mechanisms of SE in neonates and young infants differ compared to older children and adults. The most common causes of SE in neonates includes hypoxic sequelae, ischemic stroke and intracranial haemorrhage. In infants, febrile status epilepticus and acute symptomatic seizures are more common than remote symptomatic causes. Recent advances in neuroimaging modalities and molecular diagnostic techniques have facilitated better diagnostic precision. There is deplorable lack of evidence evaluating management strategies of SE in this age group. In addition to prompt initiation of antiseizure medications, vitamin supplementation needs to be empirically added. Simultaneously, meticulous evaluation to determine cause must also be conducted. In this review, we discuss challenges and an algorithmic approach to the diagnosis and management of SE in neonates and infants.

Keywords: Neonatal encephalopathy, refractory seizures, seizures in newborn

INTRODUCTION

Status epilepticus (SE) is one of the most common neurological emergencies in childhood, even more so in the neonatal period and infancy because of the propensity of the immature brain for continued seizure activity.[1,2] SE is not to be considered a disorder in itself; instead, it should be looked upon as the manifestation of an underlying aetiology. It necessitates prompt attention, not only for cessation of ongoing seizures but also demands aggressive evaluation to establish the cause.

Incidence estimates of SE among neonates range between 16% and 25%[3,4] and among infants, these approximate 12 to 25%.[1,5] In population-based studies, the incidence among infants has been reported to be around 50/100,000 per year.[6,7] The most common causes of SE in neonates include hypoxic ischemic injury, ischemic stroke, and intracranial haemorrhage. Cortical malformations, central nervous system (CNS) infections, inherited metabolic disorders, and epilepsy syndromes are less common.[4] In infants, febrile status epilepticus and acute symptomatic problems, e.g. CNS infections and dyselectrolytemia are more common[5,8] than remote symptomatic causes secondary to old CNS insult, structural or metabolic disorders or epilepsy syndromes.

Although recent advances in neuroimaging and molecular diagnostic techniques have improved the etiological yield of SE in neonates and infants, a cause can be identified in only half of the patients.[1] The outcome of SE in neonates and infants is worse as compared with older children and adults. Differences between children and neonates are elucidated in Table 1. Adverse neurological outcomes may occur in up to 66% of neonates with status including cerebral palsy and developmental delay.[4] Among infants affected by SE, only 48–53% recover completely, 36–54% develop neuro-developmental sequelae and 10–16% die during the acute episode.[8-10] Key features are highlighted in the summary table.

DEFINITION AND CLASSIFICATION

Convulsive status epilepticus (CSE) has been defined as continuous seizure activity lasting 30 min or more, or two or more seizures within this duration without recovery of consciousness between events.[11] The operational definition that guides the time after which treatment should be initiated is ≥5 min or two or more episodes without recovery.[12]

The International League Against Epilepsy (ILAE) Task Force has recently described the conceptual definition of SE in terms of two time points, t1 and t2. The time beyond which the seizure is considered prolonged is 5 min (t1) and the time beyond which there is risk of long-term sequelae such as neuronal injury and death, as well as alteration of neuronal circuits (t2) is 30 min for generalized tonic clonic seizures.[13] The classification

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system consists of four axes which provide a framework for diagnosis and treatment. The four axes are: (1) Semiology, (2) Aetiology, (3) Electroencephalography (EEG) and (4) Age. Semiological classification includes convulsive (with prominent motor manifestations) and non-convulsive (without prominent motor symptoms) types. Convulsive SE can be further subdivided into tonic-clonic, myoclonic, focal motor, tonic status, and hyperkinetic types. Non convulsive SE (NCSE) is grouped into NCSE with coma ("subtle" SE) and NCSE without coma. As per ILAE, the same descriptors should be used for neonatal seizures as other seizures.

However, among neonates, application of the conventional definition of SE is contentious and variable definitions have been used. Using a duration of 5 min seems logical in neonates, as most seizures abort in 2–3 min.[14,15] Various definitions use the occurrence of continuous ictal activity lasting 30 min or more to define neonatal SE, or even any seizure with a duration of 5 min or more. Hence, an electrographic definition has been proposed in neonatal SE as seizure activity greater than 50% of the length of recording time in any electrographic record.[4,16] There are several reasons why challenges arise in defining neonatal status. This is because of uncertainty in identifying ongoing ictal activity as seizures are largely subtle, migratory or multifocal in neonates. The other is in establishing recovery of consciousness in between seizures which may be confounded by underlying encephalopathy. In addition, the vast majority of electrographically identifiable neonatal seizures lack clinical ictal correlate and necessitate a continuous EEG which may not be possible in resource-limited settings.[17] Antiseizure medications may convert clinically overt seizures into non-convulsive events, again identified only on continuous EEG.

DEVELOPMENTAL PREDISPOSITION TO SE IN NEONATES AND INFANTS

The pathophysiological mechanism which makes the neonatal brain more vulnerable to SE is the shift of balance towards CNS excitation than inhibition.[18,19] The predilection of the immature brain towards excitation is due to developmental receptor modulation and ion channel expression in the neonatal brain. There is relative overexpression of N-methyl-D-Aspartate (NMDA)[20] and α-amino-3-hydroxy-5-methyl-4-isoxazolepropionicacid(AMPA) receptors[21] which are excitatory receptors in the immature brain. NR2B, NR2D and NR3A subunits of NMDA are overexpressed and GluR2 receptor on AMPA is under expressed making both these receptors more permeable to calcium and hence, causing excitation. In addition, there is paradoxical excitation at gamma-amino butyric acid (GABA) receptors[22] rather than inhibition due to excess development of depolarising Na–K–Cl cotransporter (NKCC1) causing elevated intra-neuronal chloride levels.[23] As the brain matures, NKCC1 declines and NKCC2 increases thus causing a shift towards inhibition. NKCC1 has highest expression in the term neonate and NKCC2 starts getting expressed only towards the middle of the first year of life.[24]

Hyperpolarization-activated cyclic nucleotide-gated (HCN) channels maintain the resting membrane potential of brain and dendritic excitability. In the immature brain, there is reduced expression of HCN1 channel isoform, which gradually increases with age and leads to reduced excitability. Kv7.2 (KCNQ2), Kca 4.1 (KCNT1) potassium channels are implicated in early infantile epileptic encephalopathy (EIEE). Mutation in voltage gated Na channel (Nav1.1, Nav1.2, Nav1.3, Nav1.6) by sodium voltage-gated channels SCN1A, SCN2A, SCN 3A, SCN8A, have been associated with many epilepsy syndromes like generalized epilepsy with febrile seizure plus (GEFS+) and Dravet syndrome.

Summary Table. Key features of neonatal and infantile status epilepticus
Common aetiologies of neonatal SE hypoxic ischemic injury, ischemic stroke and intracranial haemorrhage. In infants, febrile status epilepticus and acute symptomatic problems, e.g., CNS infections and dyselectrolytemia are more common.
Outcome of SE in neonates and infants is worse as compared to older children and adults.
In neonates, many nonepileptic movements may resemble seizures, hence, electrographic correlation of the same will improve recognition and management.
Careful evaluation must be done to determine aetiology of SE, particularly to assess reversible causes and vitamin-responsive epilepsies.
Phenobarbitone forms the first line agent for management of neonatal SE.

Table 1: Characteristics of status epilepticus in Infants compared to children

Characteristics	Infants	Children (Overall)
Incidence	51-52/100,000/year	17-35/100,000/year
Aetiology	Febrile status epilepticus and acute symptomatic (80%)	Remote symptomatic and cryptogenic
Prior abnormal neurologic status[5]	21%	55%
Prior history of seizures[5]	20%	64%
Outcome[8-10]		
Recovery	48-53%	67-71% [9,26]
Mortality	10-16%	27%
Neurodevelopmental sequelae (long term follow-up)	36-54%	24.7% epilepsy
		8.8% intellectual disability
		2.1% motor disability

In the neonatal brain, although the cortical structure is similar to older children and adults, dendritic connections and arborisation, as well as synaptic structure are underdeveloped. Myelination is also immature and rapid spread of ictal discharges is hampered, hence, generalized tonicclonic SE does not usually occur. In addition, the presence of subtle seizures such as apnoea and orobuccolingual seizures suggest that these arise from a subcortical source rather than a cortical generator as in adults and older children.

AETIOLOGY

The ILAE classification for status epilepticus describes the aetiology of SE under following headings:[13,25]

1. **Known** (i.e. symptomatic): SE caused by a known disorder, which can be structural, metabolic, inflammatory, infectious, toxic, or genetic.

Based on its temporal relationship, it can be subdivided into:

a. Acute symptomatic: SE during acute neurologic insult (e.g. CNS infection, trauma, hypoxia) or metabolic alterations (hypoglycemia, hypocalcemia, hypo/hypernatremia etc.).

b. Remote symptomatic: Known history of previous insult (e.g. posttraumatic, postencephalitic, poststroke).

c. Progressive: SE in progressive neurologic disease (e.g. malignancy, neurodegenerative disease).

d. SE in defined electroclinical syndromes.

Neonates:
1. Self-limited neonatal seizures (Benign neonatal epilepsy, BNE).
2. Self-limited familial neonatal epilepsy (Benign familial neonatal epilepsy, BFNE).
3. Ohtahara syndrome.
4. Early myoclonic encephalopathy (EME).

Infancy:
1. Generalised epilepsy febrile seizure plus (GEFS+)
2. Dravet syndrome
3. West syndrome
4. Myoclonic epilepsy of infancy
5. Myoclonic encephalopathy in non-progressive disorders
6. Epilepsy of infancy with migratory focal seizures (Migratory partial seizure of infancy (MPSI))

2. **Unknown** (i.e. cryptogenic)

Neonatal status epilepticus is a manifestation of the underlying brain dysfunction due to diverse causes. In a case series of 26 neonates, most common causes were hypoxic ischemic encephalopathy (HIE) in 31%; intracranial haemorrhage 31% and others (38%) included infections, cerebral malformations, ischemic stroke, metabolic and unknown causes.[4]Seizures due to HIE are noted in the first 12-24 h of life. Vascular cause, leading to either arterial of venous strokes, result in seizures of focal nature beyond the first 24 h of life. Preterm neonates are particularly predisposed to intraventricular haemorrhage.[26]In infants, the most common aetiology is febrile status epilepticus

30-41%.[5,8] This is followed by acute symptomatic causes of which CNS infection and transient metabolic abnormality are most common. Remote symptomatic, inherited metabolic, genetic constitute around 6-7% each. As advanced investigation techniques have emerged, the aetiological spectrum has expanded [Table 2].

EVALUATION

Status epilepticus at any age demands urgent intervention, as well as evaluation for aetiology. The aim is to identify associated symptomatic causes with the target of directed intervention to halt SE and thereby prevent neurologic injury. Evaluation begins from history and examination followed by relevant individualized investigations. Foremost, it is essential to recognize the presence of seizures, which as aforementioned, may be challenging to identify, especially if subtle.[27]In addition, myoclonic seizures as well as subtle

Table 2: Aetiology of status epilepticus in neonates and infants[26]

Category	Aetiology
Structural	Hypoxic ischemic encephalopathy (40-60%)
	Ischemic stroke: Arterial, venous (6-17%)
	Intracranial haemorrhage (7-18%)
	Malformations of cortical development (3-17%)
	Intrauterine viral infections sequelae (CMV, Toxoplasmosis)
Infectious	Meningitis, Encephalitis, brain abscess (2-14%)
	Bacterial, viral, fungal, protozoal
Genetic	Channelopathies: Early infantile epileptic encephalopathy
	Na channel (SCN1A, SCN1B, SCN2A, SCN8A) and GABA receptor (GABRG2) in GEFS+and Dravet syndrome
	K channel (KCNQ2, KCNT1) in BNE, Ohtahara syndrome and MPSI
	STX BP1, ARX, KCNQ2, SCN2A in Ohtahara ERBB4, SLC25A22 in EME
Metabolic	*Transient metabolic*- (3-5%)
	Hypoglycemia, Hypocalcemia, Hyponatremia, Hypophosphatemia
	Local anaesthetic intoxication in neonates
	Inherited metabolic- (1-4%)
	Aminoacidopathy- Non ketotic hypoglycinemia (NKH), Maple syrup urine disease (MSUD)
	Organic academia
	Biotinidase deficiency
	Sulphite oxidase deficiency
	Mitochondrial disorders (pyruvate dehydrogenase, cytochrome C oxidase deficiency)
	Hyperammonemia (Urea cycle defects)
	Glucose transporter deficiency (GLUT1)
	Peroxisomal disorders
	Vitamin responsive seizures (Pyridoxine deficiency, Pyridoxal-5-phosphate deficiency, Folinic acid responsive seizures)
Immune	Autoimmune encephalitis
Unknown	Cause is not known; previously called cryptogenic (2%)

CMV Cytomegalovirus; MSUD Maple Syrup Urine Disease; NKH Non ketotic hyperglycinemia

seizures do not have good EEG correlation. Certain epileptic events in neonates that are ictal but may be erroneously missed or not considered ictal include diaphragmatic myoclonic jerks resembling hiccups, as seen in glycine encephalopathy, focal tonic posturing with autonomic features etc.[27]Movements which may resemble seizures but are less likely to be ictal include cycling or pedalling movements, sucking or puckering, blinking without tonic eye deviation. Certain non-epileptic movements mimicking seizures include jitteriness, benign sleep myoclonus, tremors, dystonia and startle response.

History taking needs to be meticulous and specific queries pertinent to aetiology need to be made. The presence of maternal fever with rash in the antenatal period points towards congenital infections. Details of birth history including gestational age at delivery, APGAR score, resuscitation details etc., will suggest hypoxic brain injury. The timing of onset of SE may also provide clues. SE due to HIE usually sets in within the first 24 h of life, whereas those due to vascular insult may occur beyond the first 24 h. Premature birth is a risk factor for intraventricular haemorrhage. The presence of focal SE points toward an underlying structural abnormality including cortical malformations, stroke etc., The presence of a rash or abnormal urinary odour may suggest inborn errors of metabolism. The presence of normal development in infant prior to the onset of SE could occur in febrile SE or any acute symptomatic cause. The presence of global developmental delay or regression may suggest genetic syndromes or epileptic encephalopathies. Similarly, clinical examination may exhibit revelatory clues. Some of these are summarized in Table 3.

Appropriate investigations need to be conducted based on the clinical setting. We have summarized these in Table 4.

Role of EEG in status epilepticus
As a rule, EEG is indicated in infants who have prolonged loss of consciousness after convulsive status epilepticus to evaluate the possibility of non-convulsive status epilepticus (NCSE). There is no defined role of continuous EEG to diagnose or treat convulsive status epilepticus.

In neonates, continuous EEG is a gold standard to diagnose and manage seizures.[18] It is a fundamental requirement for managing neonatal seizures and status epilepticus. This is because neonatal seizures are polymorphic and there is high inter-rater variability in their identification. Another issue is poor clinico-electrographic correlate in clinically suspected seizures, especially in subtle and generalized tonic seizure. Moreover, there are many electrographic seizures which do not have clinical correlate.[18] In addition, specific EEG patterns may sub serve pointers to the basal aetiology. For example,. periodic discharges are seen in herpes simplex encephalitis and hypoxia, hypsarrhythmia pattern is seen in West syndrome, burst-suppression pattern is seen in Ohtahara syndrome and early myoclonic epilepsy, and migrating focal discharges are observed in MPSI.[28]In an infant who develops status epilepticus superimposed on an underlying epileptic encephalopathy, the EEG may show ictal rhythms and electrographic seizures. An abbreviated-montage amplitude-integrated a EEG, is being increasingly used in neonatal ICUs.[29] This consists of one or two channel recordings on a semilogarithmic scale. The use of a EEG for detection of seizures is not considered ideal due to low sensitivity.

MANAGEMENT
The first step in management of SE is electrographic confirmation of seizure activity, especially in neonates. Continuous monitoring for diagnosis as well as treatment response is ideal. However, in resource-constrained settings, a short-term EEG initially for diagnosis and then after stoppage of convulsive seizure to confirm electrographic resolution of status epilepticus is probably more feasible.

Management algorithm is depicted in Figure 1. After securing airway, breathing and circulation, treatment and diagnostic evaluation must be conducted simultaneously. After collecting samples for routine blood tests, including electrolytes, intravenous glucose/calcium may be considered empirically, especially if there is no history of hypoxic ischemic insult. There are no specific evidence-based guidelines for

Table 3: Clinical clues on examination in neonatal and infantile status epilepticus

Clues in Examination	Diagnostic possibilities
Microcephaly/Macrocephaly	Structural malformation, hydrocephalus
Neurocutaneous markers	Genetic syndromes: Tuberous sclerosis, NF-1, Sturge Weber syndrome
Dysmorphism	Chromosomal anomalies
Single/Multiple congenital anomaly	Genetic syndromes, peroxisomal disorders
Eczematous rash/alopecia	Biotidinase deficiency
Abnormal urine odour	Inborn error metabolism
Neurologic examination:	Galactosemia, Hypoxic injury
Eye: cataract	
Fundus: Optic atrophy, RP, CRS	Mitochondrial disorders, storage disorders
Chorioretinitis	Congenital intrauterine infections
Tone: Hypotonia, spasticity, rigidity	Structural malformation, Hypoxic injury
Abnormal movements	Structural, Leigh's disease, Neurotransmitter disorders

NF-1, Neurofibromatosis type 1; RP, Retinitis pigmentosa; CRS, Cherry red spot

## Table 4: Evaluation of neonatal and infantile status epilepticus

Blood/urine/CSF investigations	Disease entities
Sepsis screen, leucocyte count	Presence of fever
Electrolytes, blood sugar	Metabolic abnormalities
Serum ammonia	UCD
Urine:	
Reducing substances	Galactosemia
Ketones	OA, MSUD
Gas chromatography	Aminoacidurias
CSF:	
Elevated CSF lactate	Meningitis and mitochondrial disorders
CSF: blood glucose ratio <0.5	GLUT1 deficiency
CSF: plasma glycine ratio >0.08	NKH
Arterial blood gas:	
Acidosis	OA
Alkalosis	UCD
Elevated lactate level	OA and mitochondrial disorders
Biotinidase enzyme assay	Biotinidase deficiency
Tandem mass spectrometry	OA, fatty acid oxidation defects and aminoacidurias
Genetic tests:	
MLPA	Single gene disorders
Karyotyping and array CGH	Dysmorphic features
Whole exome sequencing or next generation sequencing	Specific epilepsy syndromes
Radiological findings	
CT head: Periventricular calcification	CMV encephalitis
Diffuse calcification	Toxoplasmosis
MRI Brain: Meningeal enhancement, hydrocephalus, focal lesions	CNS infections: Meningitis, encephalitis, brain abscess
Periventricular leukomalacia, cystic encephalomalacia, thalamic hyperintensity	Preterm and term hypoxic brain injury
Agyria pachygyria complex	
Focal cortical dysplasia	Malformations of cortical development
Isolated globus or putamen hyperintensity	Organic acidemia, Mitochondrial disorder
Elevated signal intensity with restricted diffusion in thalamus, internal capsule, pons and cerebellum	MSUD

CGH, Comparative Genomic Hybridisation; CMV, cytomegalovirus; CSF, cerebrospinal fluid; CRS, cherry red spot; EME, early myoclonic epilepsy; FAOD, Fatty acid oxidation defect; GLUT, Glucose transporter deficiency; MSUD, Maple syrup urine disease; MLPA, Multiplex ligation dependent probe amplification, NGS, Next generation sequencing, NF-1, Neurofibromatosis-1; NKH, Non ketotic hyperglycinemia; OA, Organic acidemia; RP, Retinitis Pigmentosa; UCD, urea cycle defect

management and randomized controlled trials are lacking. The efficacy of a single antiseizure drug is 50% and of multiple drugs 60-70% in controlling SE.[30]Phenobarbitone is the drug of choice for status epilepticus in newborns (loading dose 15-20 mg/kg followed by maintenance 3-5 mg/kg/day. Loading may be repeated).[30,31] This is followed by phenytoin (loading dose 15-20 mg/kg intravenously followed by maintenance 5-8 mg/kg/day) or fosphenytoin (loading dose 15-20 mg/kg phenytoin equivalent intravenously followed by maintenance 5-8 mg/kg/day).[32]Following this, benzodiazepines are used. Lorazepam (loading dose of 0.05–0.10 mg/kg) or even midazolam infusion may be initiated. Other newer antiepileptic drugs such as levetiracetam (loading dose 20-30 mg/kg followed by initial maintenance 5-10 mg/kg/day) may be used next. Other alternatives include lidocaine and oral topiramate. Levetiracetam in neonatal SE has limited safety as well as efficacy data but is finding widening use due to favourable side effect profile among older children and adult patients.[33] It was approved in 2011 by the US Food and Drug Administration (FDA) for use among infants above the age of one month. Levetiracetam, unlike phenobarbitone, has not been associated with neuronal apoptosis.[34] Control over SE may be achieved in up to 86% of neonatal SE in the first hour of administration.[34]Another option which may be used in neonates with mild to moderate HIE with seizures is therapeutic hypothermia. This has been shown to decrease seizure load.[35]Another drug which fell into disrepute was bumetanide. This was used as an adjuvant drug to phenobarbitone in post-HIE neonatal seizures. The drug trial, NEMO (treatment of Neonatal seizures using Medication Off-patent trial) showed the occurrence of serious adverse effects such as hearing loss and had to be terminated prematurely.[36] Standardized protocols for SE management should be used as much as possible as these improve outcomes.[37]

One special feature in neonatal and infantile SE is the occurrence of inherited metabolic vitamin responsive seizures presenting as SE.[38] Vitamin trials are hence warranted in cases of presumed unknown aetiology and refractory epilepsy. In
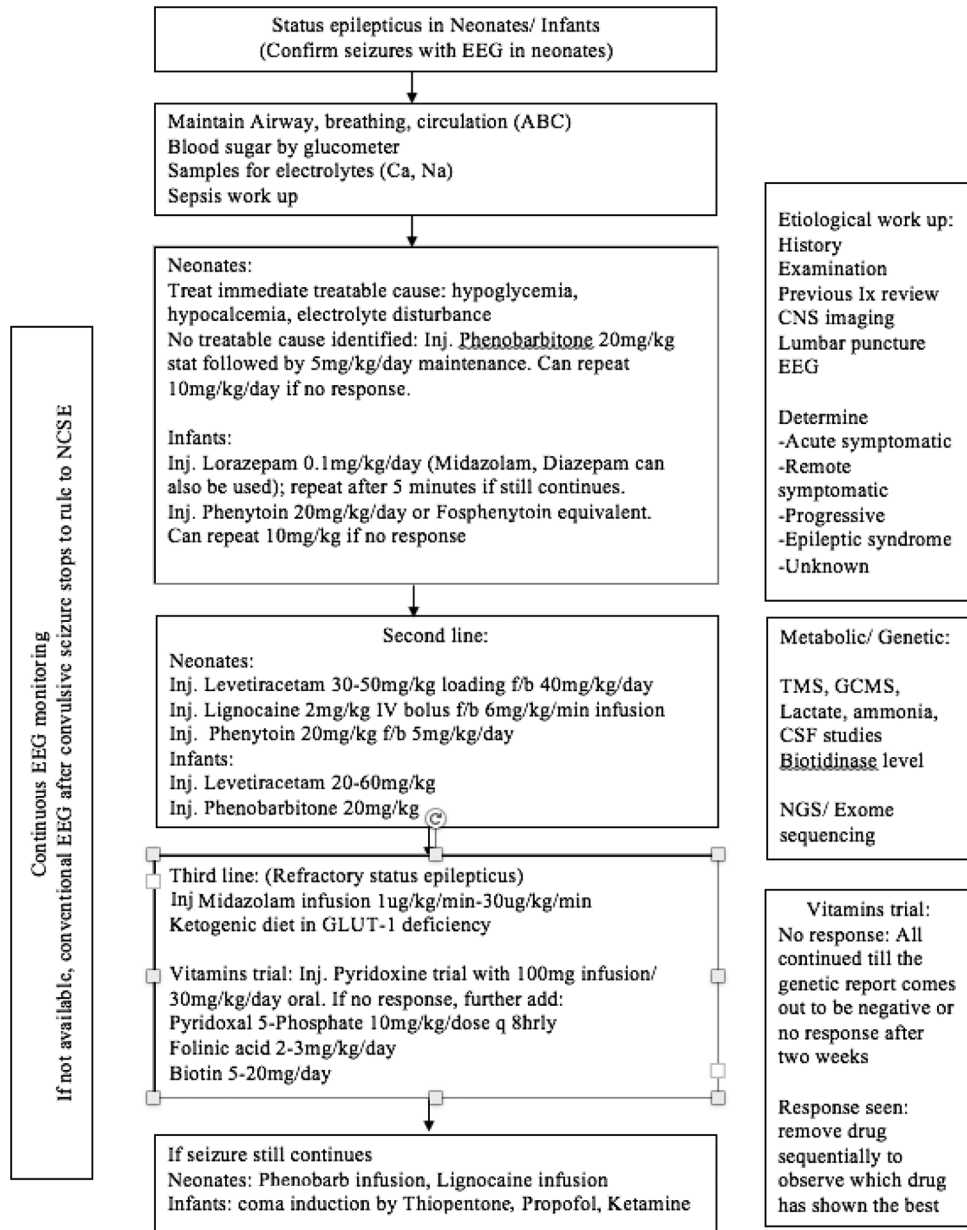
Figure 1: Management algorithm for status epilepticus in neonates and infants*.

case of a critically ill child with SE, all vitamins may be added simultaneously and later, may be sequentially withdrawn to assess individual vitamin response. However, in children who have recurrent seizures but not qualifying as SE, sequential trial of vitamins is suggested to assess individual response. Pyridoxine at a dose of 100 mg intravenously followed by 30 mg/kg/day for three days should be initiated to treat possible pyridoxine dependent epilepsy. Oral biotin up to 10 mg per day for biotinidase deficiency and folinic acid 5 mg/kg/day orally or 2.5 mg intravenously may be started for folinic-acid responsive SE. If SE persists, pyridoxal-5′-phospate should also be added.

Refractory SE (RSE) is defined as SE that fails to respond to first- and second-line agents. Super Refractory SE (SRSE) is

defined as SE occurring for greater than 24 h on an anaesthetic agent or recurring on withdrawal of the anaesthetic agent. These are critical neurological emergencies the management of which is variable and with limited evidence beyond anaesthetic agents. SRSE may occur in up to 7% of children with SE. For RSE, an anaesthetic agent must be initiated promptly. The goals of therapy include cessation of seizures and achievement of burst-suppression pattern on EEG which should be maintained for 2448 h before withdrawal of the anaesthetic. Additional options with extremely limited evidence include immunomodulation, ketogenic diet, vagus nerve stimulation, hypothermia and even electroconvulsive therapy.[39]

PROGNOSIS

SE in neonates and infants is potentially devastating with high risk of mortality (9-15%) and poor long- term outcome in terms of development of epilepsy and neuro-cognitive sequelae.[4] SE is reported to be a risk for poor neurological outcomes as well as epilepsy. Neonatal SE has also been reported to be associated with later development of unilateral hippocampal sclerosis and temporal lobe epilepsy.[40] Risk factors for adverse outcome include low birth weight (below 2.5 kg), Apgar score at 1 min (<8), neurologic examination at seizure onset (moderately/severely abnormal), cerebral ultrasound abnormalities, efficacy of anticonvulsant therapy (partial/no response and presence of neonatal status epilepticus.[41] In infants, mortality up to 1016% has been reported, with neurocognitive delay in 36-54% cases.[10] Aetiology, neuroimaging abnormality, poor response to antiepileptic therapy, EEG background abnormality and age of onset of seizure predicts outcome in infants.[10,42] Permanent neurological injury in SE in immature brain has been attributed to neuronal cell loss causing structural and functional changes.[43]

DIFFERENCES FROM DEVELOPED COUNTRIES

Incidence of neonatal seizures from developed countries suggests a low incidence of 2.6 per 1000.[44] In India, the incidence among neonates admitted to neonatal ICUs is 12% consistent with the fact that in developing countries such as India, babies are usually born in smaller medical establishments and nursing homes.[45]Aetiology plays an important role in determining prognosis. Poor outcomes are associated with cortical malformations, hypoxic ischemic encephalopathy and infections of the CNS. In India, acute metabolic abnormalities such as hypoglycaemia are more common in neonatal status and may be associated with unfavourable prognosis.[46] Video EEG should ideally be used in the management of neonatal and infantile SE. However, in developing countries, video EEG may not be available or affordable and may also be technically challenging to interpret. Hence, clinical detection of seizures may be acceptable, with the corollary that some nonepileptic events may be overinterpreted as seizures.

CONCLUSION

Status epilepticus in infants and neonates is a common neurologic emergency. It may have a great toll in the affected child's life in terms of high mortality and overall morbidity in terms of neurodevelopmental delay and persistent epilepsy. Extensive investigations are often needed to establish aetiology. Despite aggressive management, outcomes continue to be poor. There is lack of evidence to support treatments in this age group, and most treatments continue to be experience-based. Phenobarbitone continues to be the first-line agent in these age groups. Newer antiseizure drugs such as levetiracetam and topiramate have limited evidence but appear to be effective and with favourable adverse effect profile. More research is needed in this area to find newer therapies more tailored to the developmental neurochemistry of the neonatal brain.

Conflicts of interest

There are no conflicts of interest.

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