Approach to a convulsing neonate

Dr Surekha Rajadhyaksha,MD,DCH
Professor and Chief Pediatric Neurology,
Deenanath Mangeshkar Hospital.
& Bharati Vidyapeeth, Pune

Introduction

- Convulsions in the neonate are the most common manifestation of neurological dysfunction and seizures may be first and only sign of central nervous system disorder.
- Etiology is varied and neonates are at risk for the development of seizures because of metabolic, toxic, structural, genetic and infectious diseases which are more likely to be manifested during this time than during any other period of life.
- Such disturbances may have many causes contributing to their etiology, more so because of the immature nervous system of the new born, convulsions occur even to a minor insult. Newborn seizures are at risk for neonatal death, and survivors are at risk for neurological impairment, developmental delay and postnatal epilepsy.

Diagnosis

- The clinical diagnosis of neonatal seizures is difficult, particularly in the neonatal care units catering to critically ill infants as the new born exhibit multitude of epileptic and non-epileptic clinical manifestations.
- Previously seizures were diagnosed based only on clinical observation, but now EEG/video EEG plays a key role in diagnosis.
- Seizure classification previously proposed in 2017 for older children and adults cannot be appropriately used for the newborn, therefore a new classification is proposed.
- The proposed new neonatal classification framework emphasizes the role of EEG in the diagnosis of seizures in the neonate.
- Clinical seizures types can have a **motor** (automatisms, clonic movements, epileptic spasms, myoclonic, sequential, tonic) or **non-motor** (autonomic, behaviour arrest) as presenting manifestations.
- Detection of neonatal seizures is thus most reliable with continuous EEG monitoring, but requires expertise and is not always available.
- Amplitude integrated EEG is a simplified method and used for high-risk critically ill babies who require continuous monitoring of the brain and are at risk for brain injury.

Neonatal seizures:Salient points

1. **Electroclinical seizures**: When clinical seizures have a corresponding EEG correlate
2. Electrical seizure activity lasting more than 10 secs on the EEG, with no clinical correlate:also termed as **subclinical seizures or electrographic seizures.**
3. Episodes may occur with and without EEG correlate in the same neonate.
4. Many neonates have more than one type of clinical seizures.
5. **Neonatal status epilepticus** is defined as seizures that occupy more than 50% of an hour EEG epoch(e.g., a newborn with 30, 1-minute seizures in an hour would meet criteria for status epilepticus, as would an infant with a single seizure that lasts 30 minutes or greater).
6. **Recurrent tremor**:is non epileptic but may have a pathologic basis and should be differentiated from jitteriness

Etiologic consideration:

- 75-90% of neonatal seizures have etiology and Hypoxic-ischemic encephalopathy (HIE) contributesto 35-70% of cases.

Causes of Neonatal Seizures

- Hypoxic-ischemic encephalopathy
- Metabolic hypoglycemia, hypocalcemia, pyridoxine deficiency etc
- Intraventricular hemorrhage
- Stroke
- Bacterial meningitis
- Developmental malformations
- Benign familial neonatal convulsions
- Fifth-day fits
- Inborn error of metabolism

- Genetic origin such as observed in voltage gated Sodium /potassium channel (KCNQ2, KCNQ3, SCN1A, SCN2A SCN3A, SCN8A), ARX, CDKL5, SPTAN1, STXBP1 etc) disorders.
- **Syndromes**
    - Syndromes that present in the neonatal period include: the fifth day seizures and the self-limited (benign) familial neonatal epilepsy. The malignant syndromes with burst suppression pattern on EEG are the early myoclonic encephalopathy (EME), and early infantile epileptic encephalopathy ((Ohtahara syndrome)

Non epileptic events mimicking seizures

- Jitteriness
- Benign neonatal sleep myoclonus
- Motor automatisms
- Reflux/Sandifer syndrome
- Hyperekplexia

Early predictors of subsequent adverse Neurologic Outcome

1. Severe encephalopathy due to HIE / cerebral dysgenesis
2. Need for multiple antiepileptic drugs (AED)
3. Presence of moderately to severe abnormal background EEG patterns
4. Amount of EEG seizures
5. Mortality and morbidity increase significantly when recurrent neonatal seizures or with neonatal status epilepticus
6. Early onset seizures and drug resistance are poor prognostic signs

Investigations

1. Serum glucose and electrolytes - Transient neonatal hypocalcemia is a cause of neonatal seizures during the first 3 weeks of life; hypocalcemia associated with chromosome 22q11 deletion syndrome may also be a consideration.
2. Cerebrospinal fluid analysis: check for
    - Pleocytosis, Protein
    - Xanthochromia - Suggestive of blood breakdown products
    - Lactic acid and pyruvate - For evidence of mitochondrial cytopathies
    - Herpes virus - Using a polymerase chain reaction (PCR) assay

- Amino acids - To detect nonketotic hyperglycinemia
- Glucose concentration - Low values then rule out bacterial meningitis

In the absence of bacterial meningitis, persistently low CSF glucose concentrations may suggest a glucose transporter defect.

3.TORCH (toxoplasmosis, rubella, CMV, herpes) infection studies

4. Urine organic acids

5.Serum amino acid assay

6. Renal function tests –to rule out posthypoxic renal dysfunction

7.Chromosomal microarray - Chromosomal abnormalities

8.Epilepsy panel/genetic testing -

Electroencephalography:

- Electroencephalography plays a vital role in identifying and differentiating neonatal seizures from nonepileptic events.
- Video EEG monitoring and Continuous Amplitude integrated EEG or continuous video-EEG (cEEG) gives added information.
- It is likely that the combination of latest genetic testing and video-EEG monitoring willallow the identification of distinct etiology-specific electro-clinical phenotypes.

Treatment

There is great uncertainty about when to commence treatment for neonatal seizures.

A general consensus is to treat seizures that are:

- Prolonged – seizure lasting >3 minutes
- Frequent – 3 or more seizures per hour
- Associated with cardio respiratory compromise
- Subclinical - > 3 sub-clinical seizures within one hour
- If seizure activity (clinical or electrical) equates to more than 10 minutes in a 60 minutes period

Criteria for determination of adequacy of Treatment:

- Question arises that should AEDs be given to eliminate clinical seizuresonly or eliminate electrographic activity or the subclinical seizures also?

Electroclinical dissociation

- When evaluating the efficacy of medication, it is important to remember that electro-clinical dissociation may occur after administering AED, ie termination of clinical seizures but ongoing electrographic seizures may continue. There is a false feeling of effectiveness of medication unless monitored by EEG.
- The present opinion is that all seizure types including subclinical, electroclinical, subtle should be treated. But at the same time early termination of seizure medication as early as 7 days is recommended. Some may need longer treatment and reassessment at 3 months

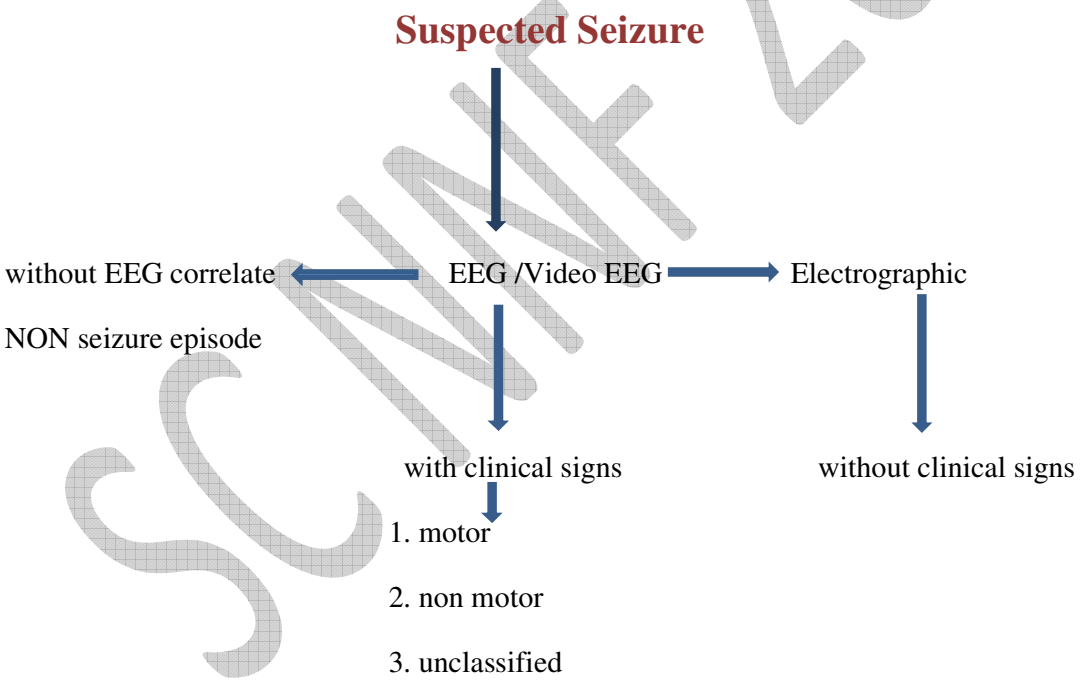

Fig. 1. Approach to a neonate with suspected seizures

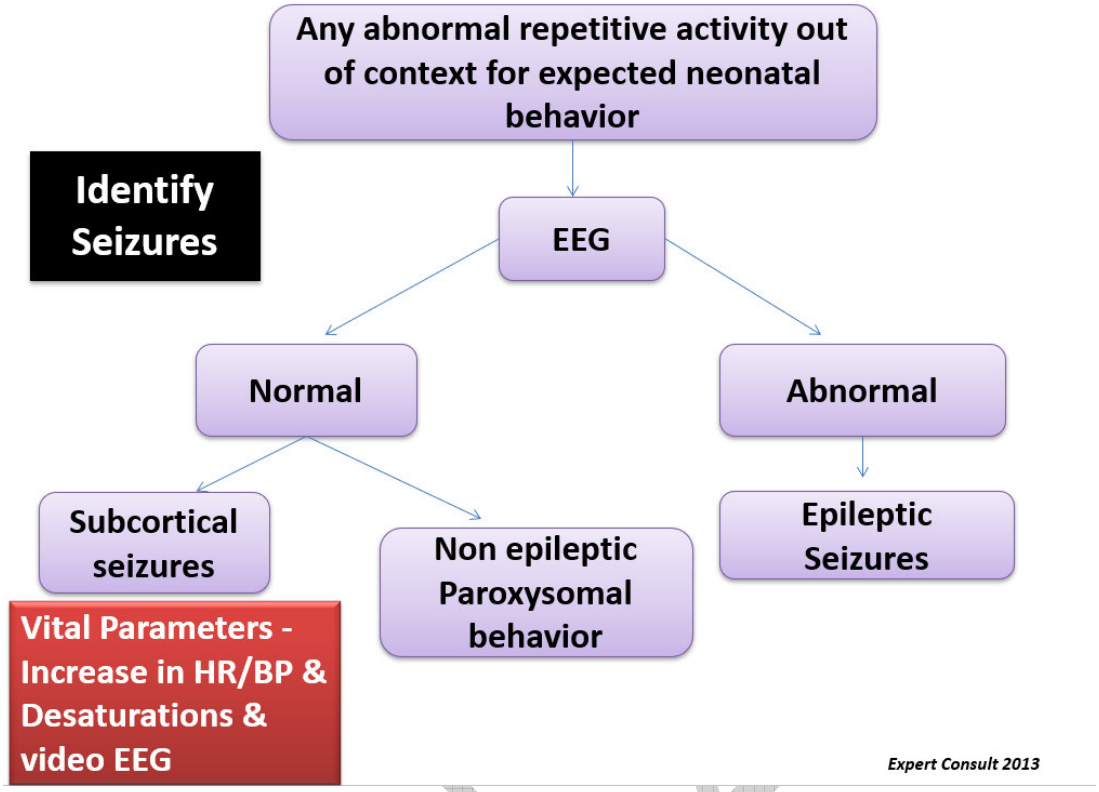

Fig. 2 Approach to a convulsing neonate part 1

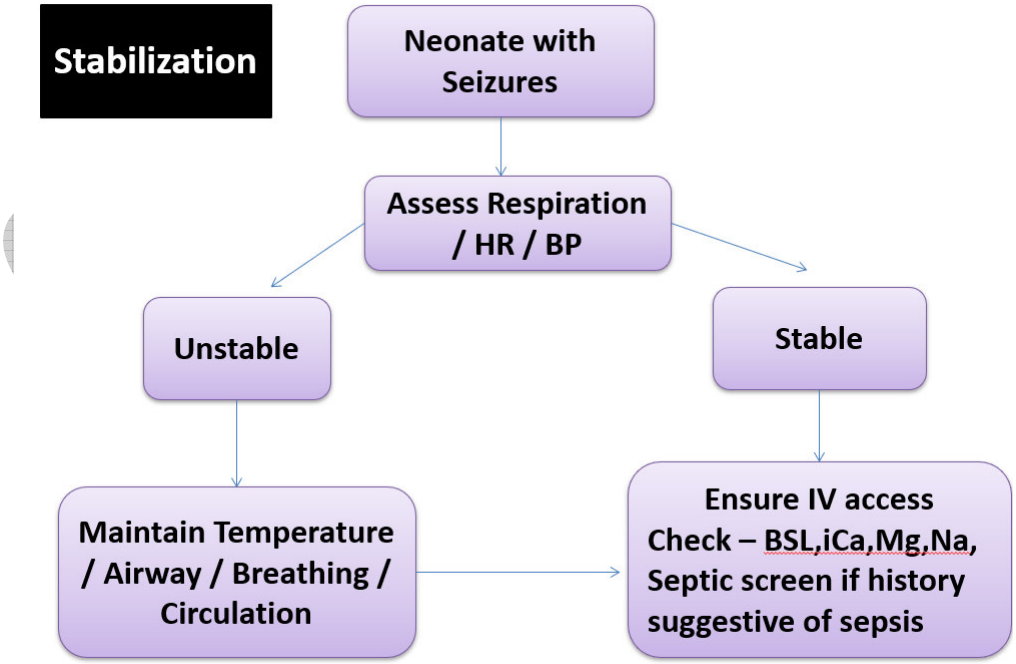

Fig. 3. Approach to a convulsing neonate part 2.

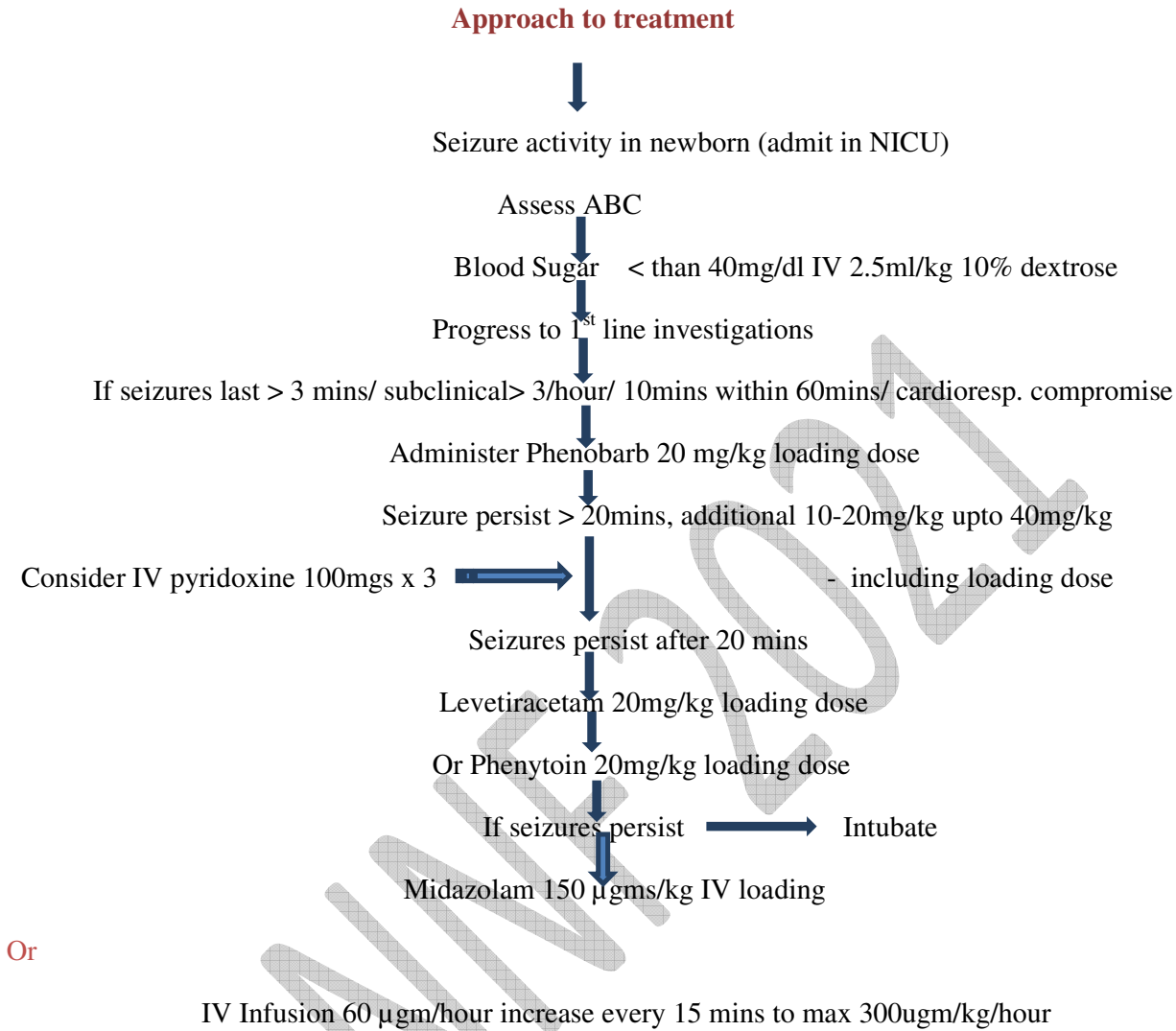

Fig. 4. Approach to treatment of neonatal seizures