



NEONATAL SEIZURES

INTRODUCTION

- Different from seizures in adults
- Due to incomplete myelination and arborization of axons and dendritic processes in neonatal brain—propagation of seizure discharge does not occur.
- Generalized seizures or partial seizures with secondary generalization are very uncommon in first month of life

DEFINITION

- A seizure is defined clinically as a paroxysmal alteration in neurologic function (behavioral, autonomic or motor function)*

INCIDENCE

- Ranges from 1.5 to 14 per 1000 live births

*Volpe, 2001

PATHOPHYSIOLOGY

Abnormal synchronous electrical discharge (depolarization) of a group of neurons within the Central Nervous System. Features that make the immature brain more vulnerable to seizures are : relative excess of excitatory circuits (eg. NMDA) and relative deficiency with delayed maturation of inhibitory systems (eg. GABA, Adenosine, 5 HT), shorter refractory period /hyper polarization during postictal phase.

ETIOLOGY

- Perinatal asphyxia
- Intracranial hemorrhage- subarachnoid, periventricular or intraventricular, subdural
- Metabolic abnormalities-
 - Hypoglycemia-infant of diabetic mother
 - Hypocalcaemia-LBW, IDM, asphyxiated infants, DiGeorge syndrome, Infants born to mothers with hyperparathyroidism

Hyponatremia -due to improper fluid management, sodium losses or SIADH

Hypernatremia - dehydration, incorrect dilution of concentrated formula

Hypomagnesaemia -seen associated with hypocalcaemia

- Amino Acid Disorders-urea cycle, mitochondrial defects, glucose transporter deficiency etc
- Congenital malformations

- Infections- Meningitis, Encephalitis, Syphilis, CMV, Toxoplasmosis, Herpes Simplex, Coxsackie B, Cerebral Abscess
(organisms commonly associated with neonatal bacterial infections are Group B Streptococcus, Listeria monocytogenes and Escherichia coli)
- Drug withdrawal-Heroin, Methadone, Alcohol, Secobarbital
- Toxin exposure-particularly local anesthetics

- Inherited seizure disorders-Benign familial epilepsy, Tuberosus sclerosis, Zelleweger syndrome
- Pyridoxine dependency-seizures resistant to anticonvulsants

CLINICAL FEATURES

Difficult to identify and classify. In the neonatal brain glial proliferation, neuronal migration, establishment of axonal and dendritic contacts and myelin deposition are incomplete. As a result, some of the neonatal seizures may be brainstem or sub cortically mediated, with little or no surface representation on conventional Video EEG monitoring

SEIZURE TYPES :

SUBTLE SEIZURES-Bicycling movements, lip smacking, roving eye movements, staring spells, chewing, autonomic phenomena.

Apnea as a manifestation of seizures is usually accompanied or preceded by other subtle manifestations and with EEG changes

CLONIC SEIZURES-More common in term babies. Associated with EEG changes. Two types:

Focal Seizures-well localized, rhythmic, slow jerking

movements involving face, trunk or extremities on one side

Multifocal Seizures-several body parts seize in a sequential, nonjacksonian pattern

TONIC SEIZURES-Occur primarily in preterm infants

Focal seizures-sustained posturing of a limb, asymmetric posturing of trunk or neck-usually associated with EEG changes

- Generalized seizures-tonic extension of both upper and lower extremities(as in decerebrate posturing) or tonic flexion of the upper extremities with extension of the lower extremities(as in decorticate posturing). Usually not associated with EEG changes
- MYOCLONIC SEIZURES-seen in both term and preterm babies. May or may not be associated with EEG changes. Types:
- Focal Seizures-involves flexor muscles of upper extremity

- Multifocal Seizures-asynchronous twitching of several parts of the body
- Generalized Seizures-Bilateral jerks of flexion of upper and sometimes lower extremities

JITTERINESS Vs SEIZURES:

In jitteriness, movements are stimulus sensitive and not jerky. It is not accompanied by abnormal eye movements and movements cease with application of passive flexion

APPROACH TO DIAGNOSIS

- *History*
- Positive family history-inborn errors of metabolism and benign familial neonatal seizures
- Maternal Drug history-narcotic withdrawal syndrome
- Delivery-maternal infection during pregnancy, maternal analgesia, mode and nature of delivery, chorioamnionitis, fetal intrapartum status and resuscitative measures used.
- Physical Examination :Thorough physical exam to look for skin lesions, Hepatosplenomegaly, Gestational age, Blood Pressure etc

- *Neurologic evaluation*- detailed evaluation to assess the anterior fontanelle and sutural diastasis, retinal hemorrhages, chorioretinitis, pupillary size and reaction to light, extra ocular movements, changes in muscle tone and status of primary reflexes.
- *Seizure type*: should be evaluated in detail (preferably by a witness) including site of onset, spread, nature, duration and level of consciousness.
- *Subtle Seizure*- important to recognize early

LABORATORY STUDIES

- *Serum Chemistry*: estimation of serum glucose, calcium, sodium, BUN, magnesium, blood gas levels.
- *Spinal fluid examination*: CSF analysis is essential to diagnosis and promptly treat bacterial meningitis
- *Metabolic disorders*: important clues-positive family history of neonatal convulsions, peculiar odor of the infant, milk intolerance, acidosis, alkalosis, seizures resistant to anticonvulsants.
 - a. Serum ammonia levels
 - b. Amino acids in urine and plasma

- 2,4-dinitrophenylhydrazine (2,4-DNPH) testing of urine for Maple Syrup urine disease

RADIOLOGIC STUDIES:

- Head Ultrasound to r/o IVH or periventricular hemorrhage
- CT Scan or MRI to look for evidence of infarction, hemorrhage, calcification and cerebral malformations.
- EEG- valuable to confirm presence of seizures in subtle seizures or when neuromuscular paralyzing agents have been given. Diagnostic value is greater when obtained in the first few days.

MANAGEMENT

- Provide 100% oxygen to every baby initially
- Hypoglycemia- D10W bolus 2ml/kg followed by continuous infusion at 6-8 mg/kg/min
- Hypocalcaemia- 10% calcium gluconate 0.5-1 ml/kg iv bolus slowly-watch for bradycardia
- Hypomagnesaemia - Magnesium sulfate 10%-0.25 ml/kg bolus slowly
- Hyponatremia - sodium deficit is calculated as:
 $0.7 \times \text{weight} \times (\text{desired Na} - \text{actual Na})$. Replace half the deficit over 12 hours

Anticonvulsant Therapy:

- Phenobarbital-load at 20 mg/kg. Can repeat 10 mg/kg twice. If seizures are not controlled at Phenobarbital dose of 40 mg/kg a second agent is added
- Phenytoin (Dilantin)-load at 20 mg/kg at a maximum rate of 1mg/kg/min followed by maintenance of 5-8 mg/kg/day divided q12-24 hours. Fosphenytoin has the advantage of being soluble in aqueous solutions and can be given iv rapidly-also has less side effects than phenytoin
- Lorazepam (Ativan) 0.05-0.1 mg/kg/dose IV q4-8 hours prn

4. Other agents used are Midazolam, Carbamazepine, Paraldehyde, lamotrigine, felbamate, levetiracetam
5. Pyridoxine-given to babies with pyridoxine dependent seizures or empirically in refractory seizures- 100mg/kg iv

OUTCOME OF NEONATAL SEIZURES

- In general, babies with electrographic evidence of seizures had more mortality and worse outcomes-eg .severe encephalopathy, cerebral palsy, epilepsy etc
- Late-onset hypocalcaemia or subarachnoid hemorrhage-recover without sequelae
- Seizures secondary to congenital malformations have poor prognosis
- Symptomatic hypoglycemia-50% risk of death or complications
- CNS infections-70% risk of death or complications
- Asphyxiated infants with seizures have 50% chance of poor outcome

- 
- 17% of patients with neonatal seizures have recurrent seizures later in life