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TO STUDY CLINICAL PRESENTATION AND TIME OF ONSET OF SEIZURE IN TERM AND PRETERM NEONATES AND THE BIOCHEMICAL ABNORMALITY IN SEIZURES IN TERM AND PRETERM NEONATES.

Pediatrics

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ABSTRACT

INTRODUCTION: Seizure is defined as paroxysmal involuntary disturbance of brain function. It may manifest as impairment or loss of consciousness, abnormal motor activity, behavioural abnormality, sensory disturbance or autonomic dysfunction. Any abnormal, repetitive and stereotypic behaviour in neonates should be evaluated as possible seizure. Neonatal seizures is a common neurological problem with a frequency range from 0.95 to 3.5/1000 live births.

AIMS & OBJECTIVES: To assess the importance of biochemical abnormalities in neonatal seizures and to evaluate clinical presentation & time of onset of seizures in term and preterm neonates.

MATERIAL & METHODS: A total of 90 neonates presenting with seizures admitted to NICU of National Institute of Medical Sciences & Research, Jaipur from conducted from 1st January 2019 till 30 th June 2020 were enrolled in the study. Detailed antenatal, natal, postnatal history along with detailed examination was done. Baseline characteristics of convulsing neonate including sex, gestational age, birth weight, head circumference & length were recorded at admission. Clinical details of each seizure episode reported by the mother and subsequently observed by the resident doctors on duty were recorded i.e. age at onset of seizures, duration of seizure, number and type of seizure. Relevant investigations including biochemical parameters were done immediately after baby had seizures and before instituting any specific treatment. Etiology of neonatal seizures and associated biochemical abnormalities were diagnosed.

RESULTS: In the present study, out of 90 neonates studied, 64 were full term of which 49(76.5%) were AGA and 15(23.5%) were SGA, whereas 26 cases were preterm. The male: female ratio is 1.3:1. Most neonatal seizures occur in first 3 days of life, i.e. 60 %. Most of them occurred on first day of life (34%). Birth asphyxia was the cause of neonatal seizures in 82 % neonates who developed seizures on day-1 of life. Birth asphyxia and septicemia are common cause of neonatal seizures in our study, followed by pure metabolic disturbances 20 %. In pure metabolic seizures, hypoglycemia (47.8%) is most common more in preterm babies (55%) followed by hypocalcemia. In cases of non- metabolic seizures, which showed associated biochemical abnormalities, hypoglycemia was most common abnormality 24 of 52 cases (46.15%). 12 cases (52.1%) are associated with birth asphyxia and 11 cases (47.9%) are associated with septicemia.

CONCLUSION: Biochemical abnormalities are common in neonatal seizures and often go unrecognized. These abnormalities may significantly contribute to seizure activity correction of these abnormalities may play a significant role in seizure control. Hence, a biochemical work up is necessary for all cases of neonatal seizures.

KEYWORDS

Neonatal Seizures, Hypoglycemia, Hypocalcemia, Birth Asphyxia.

INTRODUCTION:

Seizure is defined as paroxysmal involuntary disturbance of brain function. It may manifest as impairment or loss of consciousness, abnormal motor activity, behavioural abnormality, sensory disturbance or autonomic dysfunction[1]. Any abnormal, repetitive and stereotypic behaviour in neonates should be evaluated as possible seizure. Neonatal seizures by definition occur within the first 4 weeks of life in a full- term infant and up to 44 weeks from conception for premature infants[2] and are most frequent during the first 10 days of life[3]. Neonatal seizures is a common neurological problem with a frequency range from 0.95 to 3.5/1000 live births[4]. Seizure incidence is higher during this period than in any other period of life. Incidence is as high as 57.5 per 1000 in infants with birth weights lower than 1500 gms, and only 2.8 per 1000 in infants with birth weights of 2500 to 3999 gms[5-7]. Neonatal seizures represent the most distinctive signal of neurological disease in the newborn period. The convulsive phenomenon is clinically significant because very few are idiopathic. Neonatal seizures also differ considerably from seizures observed in older children, principally because the immature brain is less capable of propagating generalized or organized electrical discharges.[8] Seizure present with varying manifestations like generalized tonic, multifocal clonic and subtle activity. Therefore, it is important to recognize them and treat it, as delay in recognition and treatment may lead to brain damage.[10]

AIMS & OBJECTIVES:

1.To study clinical presentation and time of onset of seizures in term and preterm neonates.

2. To study the biochemical abnormalities in seizures in term and preterm neonates

Selection Criteria Of Patients:

A total of 90 neonates presenting with seizures admitted to NICU of National Institute of Medical Sciences & Research, Jaipur conducted from 1st January 2019 till 30 th June 2020 were enrolled in the study.

Inclusion Criteria:

1.Age less than 28 days.

2.Neonates with seizures irrespective of gesta tional age & birth weight with at least one of the following clinical type of seizures are included in the study.

- Subtle seizures.
- Multifocal clonic seizures.
- Focal clonic seizures.
- Myoclonic seizures.
- Generalized tonic seizures.

Exclusion Criteria:

1. Neonates with doubtful seizures, jitteriness and tetanic spasms.
2. Neonates with major congenital malformations.

- Detailed antenatal, natal and postnatal history was taken as per the proforma enclosed.
- Feeding History:
- History of lethargy, poor feeding, drowsiness, excessive cry, fever, vomiting and seizures were taken.
- Family History
- History of consanguinity and early fetal or neonatal deaths were enquired.

History of seizures in parents or sibs were taken

Examination:

Vital signs: Heart Rate, Respiratory Rate, Blood pressure, Peripheral Pulses, Capillary filling time & Temperature were recorded.

General physical examination to rule out any evidence of birth trauma,

dysmorphic features & neurocutaneous markers.

Anthropometry of neonate was recorded & gestational age assessed according to New Ballard's scoring.

CNS examination was done as per the proforma.

A detailed systemic examination of other systems was done as per proforma.

Investigations:
Relevant investigations will be carried out depending upon clinical presentation

Complete blood count

Sepsis screening (TLC, ANC, immature to total neutrophil ratio, CRP)

Blood glucose: Hypoglycemia is defined as RBS < 40 mg/dl.

Serum Electrolytes
Hyponatremia - Serum sodium <120 mEq/L and Hypernatremia - serum sodium >150 mEq/L.

b. Hypokalemia - serum potassium <3.5 mEq/L and Hyperkalemia - serum potassium > 5.5 mEq/L.

Total and ionized serum calcium levels(colorimetric method):-
a. Hypocalcemia - Total serum calcium <7mg/dl (preterm) & < 8mg/dl (term) or ionized calcium <4 mg/dl or 1 mmol/L (preterm) & < 4.4mg/dl or 1.1 mmol/L (term).
b. Hypercalcemia - Total serum calcium > 11mg/dl or ionized calcium >1.45mmol/L.

Serum phosphorus:-
a. Hyphosphatemia - serum phosphorus <3.5 mg/dl.
b. Hyperphosphatemia- serum phosphorus > 8mg/dl.

Serum magnesium:
a. Hypomagnesemia - serum magnesium < 1.5 mg/dl.
b. Hypermagnesemia - serum magnesium > 3mg/dl
Other metabolic screening includes serum ammonia, serum lactate, urine ketones and urine for reducing substance if metabolic disorders were suspected.

CSF analysis

Neurosonogram

EEG - EEG was done in all neonates requiring anti-convulsant therapy
CT scan and MRI Brain – CT scan or MRI Brain was done as and when necessary.

Statistical Methods:
Descriptive statistics such as mean and standard deviation (SD) for continuous variables, frequencies and percentages were calculated for categorical Variables were determined. Bar charts and Pie charts were used for visual representation of the analyzed data. Level of significance was set at 0.05. Data was entered into Microsoft Excel (Windows 7; Version 2007) and analyses were done using the Statistical Package for Social Sciences (SPSS) for Windows software (version 20.0; SPSS Inc, Chicago).

RESULTS:
Analysis of Cases and Result: : A total of 90 neonates presenting with seizures admitted to NICU of National Institute of Medical Sciences & Research, Jaipur during the period of one and half year were analyzed according to different characteristics.

Gestational Age And Sex Wise Distribution:

Table 1: Association Between Gestational Age And Gender

Gender	Group			Total
	Preterm (n=26) n (%)	Term AGA (n=49) n (%)	Term SGA (n=15) n (%)	
Female	15 (58)	21 (42.9)	8 (53.3)	44
Male	11 (42)	28 (57.1)	7 (46.7)	46
Chi-Square Test, P Value = 0.728, Not Significant				

In our study, out of 90 babies, 46(51%) were males and 44(49%) were female babies with a male to female ratio of 1.28:1.

Table 2 : Association Between Gestational Age And Place Of Delivery

Place of Delivery	Group			Total
	Preterm (n=26) n (%)	Term AGA (n=49) n (%)	Term SGA (n=15) n (%)	
Home	3 (11.5)	4 (8.2)	3 (20.0)	10
Hospital	23 (88.5)	45 (91.8)	12 (80.0)	80-
Chi-Square Test, P Value = 0.424, Not Significant				

Inborn/Outborn:

Table 3 : Association Between Gestational Age And Inborn/ outborn

Inborn/ Outborn	Group			Total
	Preterm (n=26) n (%)	Term AGA (n=49) n (%)	Term SGA (n=15) n (%)	
Inborn	16 (61.9)	19 (38.8)	6 (40.0)	41
Outborn	10 (38.9)	30 (61.2)	9(60.0)	49

Type of Seizures:
In our study, most common type of seizures was subtle (32 cases), followed by focal clonic (19 cases), multifocal clonic (18 cases), generalized tonic (14 cases), subtle with GTC (4 cases) and subtle with clonic (3 cases).

Most common type of seizures in term is subtle (32 of 64 cases) followed by multifocal clonic seizures (18 of 64 cases). Whereas in preterm most common type is subtle (18 of 26 cases) followed by focal clonic seizures (8 of 26 cases).

Etiology Of Seizures:

Table 4: Association Between Gestational Age And Etiology

Etiology	Group			Total
	Preterm (n=26) n(%)	Term AGA (n=49) n(%)	Term SGA (n=15) n(%)	
Birth asphyxia	4(15)	29(59.1)	5(33.3)	38
Septicemia	12(46)	14(28.5)	6(40.0)	32
Metabolic	8(31)	3(6.1)	4(26.7)	15
IC Bleed	2(8)	1(2.0)	0(0.0)	3
Unknown	0(0.0)	2(4.0)	0(0.0)	2

Birth asphyxia (38 cases) and septicaemia(32cases) were common causes of neonatal seizures in our study followed by pure metabolic disturbances were seen in 15 cases, intracranial bleed in 3 cases and unknown etiology in 2 cases.

Most common causes of neonatal seizures in term was birth asphyxia (38 of 64 cases) followed by septicemia (32 of 64 cases). Whereas in preterm most common cause was septicemia (12 of 26 cases) followed by pure metabolic disturbance (8 of 26 cases).

CONCLUSION:
Neonatal seizures are major manifestation of central nervous system. They are rarely idiopathic and are considered as non-specific responses of the immature central nervous system to different insults. The seizures in neonates are different compared to adults because of the immaturity of nervous system.

The recognition of the etiology for the neonatal seizures is often helpful with respect to prognosis and treatment. The most common etiology for neonatal seizures is hypoxic-ischemic encephalopathy.

HIE is frequently associated with perinatal complications, which can be prevented by proper antenatal and perinatal care.The time of onset of neonatal seizures is significantly associated with the etiology (e.g. onset of seizures within first three days is significantly associated with birth asphyxia). Subtle seizures are most common type of seizures, which are clinically difficult to identify, therefore careful observation of at risk newborns is necessary for diagnosis.

The most common biochemical abnormality in neonatal seizures is hypoglycemia 45.3% (34 of 75 cases) followed by hypocalcemia 22.7% (17 of 75 cases).

Among pure metabolic abnormalities hypoglycemia 47.8% (11 of 23 cases) followed by hypocalcemia (21.7%), hypophosphatemia (17.4%) and hypomagnesemia (13%).

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