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EVALUATION OF NEONATAL SEIZUIRES WITH ETIOLOGICAL FACTORS AND IMMEDIATE OUTCOME

Paediatrics

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ABSTRACT

Introduction: The developing brain has an increased susceptibility to seizure activity and neonatal seizures can adversely affect neurodevelopment outcome.

In newborn infant, seizures are always due to an underlying, cerebral or biochemical abnormality. Seizures are associated with poor neurodevelopmental outcome if not diagnosed early and treated properly. So the purpose of the study was to evaluate the risk factors of seizures in low birth weight babies and evaluate the immediate clinical outcome.

Materials And Methods: A total of 100 low birth weight neonatal babies, admitted to Neonatal Unit from Feb 2015 to July 2016,Fifty low birth weight babies with neonatal seizures served as cases while, another 50 low birth weight babies matched for gestation and sex, not having seizures, served as controls.

Observations: Most common type of seizures observed were subtle (20) while myoclonic seizures (1) were least common.Neurological outcome was better with tonic generalized type (01.96%) and worst with clonic focal type (13.04%).Mortality was highest with tonic focal (48.57%) and lowest with subtle seizures.

Conclusion: Seizures are associated with poor neurodevelopmental outcome if not diagnosed early and treated properly

KEYWORDS

INTRODUCTION

The developing brain has an increased susceptibility to seizure activity and neonatal seizures can adversely affect neurodevelopment outcome.[1] In newborn infant, seizures are always due to an underlying, cerebral or biochemical abnormality.[2]

The seizure is defined as a paroxysmal, time limited change in motor activity and/or behavior that results from abnormal electrical activity in the brain. Thus neonatal seizures are paroxysmal alterations in neurological function. This can be behavioral, motor or autonomic.[3]

Subtle seizures are most common seizures. Due to incomplete development of axons, dendritic processes, arborization and poor myelination. The manifestation are more subtle and pleomorphic.[2]

The predominance of oral and buccal phenomena such as lip smacking, suckling and chewing as well as gaze abnormalities and apnea, may be related to the advanced development of limbic structures and their connections to the brain stem and diencephalons in comparison with other fore brain structure.[4]

Seizures are the most common neurological symptom in the neonatal period.[5]

Frequency of seizures is especially high in very low birth weight preterm babies. Seizures in the newborn period constitute a medical emergency. Subtle seizures are mild paroxysmal alterations in motor or autonomic activity and are unique to neonatal period. They are likely to be missed or confused with benign movements observed commonly in preterm and low birth weight neonates.[6] Seizures are associated with poor neurodevelopmental outcome if not diagnosed early and treated properly. Hence this study has been done to evaluate prenatal and perinatal risk factors for neonatal seizures.

MATERIALS AND METHODS

This was a case-control study conducted at Neonatal unit of , Niramay Hospital ,Satara. A total of 100 low birth weight neonatal babies, admitted to Neonatal Unit from Feb 2015 to July 2016,Fifty low birth weight babies with neonatal seizures served as cases while, another 50 low birth weight babies matched for gestation and sex, not having seizures, served as controls.

Low birth weight neonates with clinical seizures. Seizures occurring at any time from birth to 28 days of life in hospital , Inborn as well as outborn neonates fulfilling above criteria were included in study. Neonates with informers narrated history of seizures but no directly observed clinical seizures were excluded from the study.

Detailed antenatal, intranatal, postnatal history and if any investigations done were recorded with special emphasis on following risk factors like Consanguinity, Unregistered/ unbooked pregnancies, maternal height < 140 cm, maternal weight < 40 kg, antepartum hemorrhage, pre-eclampsia, anemia, premature rupture of membrane, maternal fever, mode of delivery, presentation, meconium stained liquor, magnesium sulphate to mother, general anaesthesia to mother, place of delivery, need for resuscitation, respiratory distress syndrome, jaundice, necrotizing enterocolitis, sepsis, polycythaemia and small for gestational age.

Clinical seizure types were noted.The treatment details were recorded with special emphasis on anticonvulsant drugs.Babies were followed up till the time of discharge.Thorough neonatal examination was carried out at the time of admission and discharge. Details of the cases and controls were recorded in a proforma attached herewith.

The sample size was determined by carrying out a pilot study of risk factors on 100 newborn babies. The sample size was calculated to achieve a confidence interval (CI) of 95% and power of 80%.[52]Calculated sample size was 50 cases and 50 controls.'*p*' value less than 0.05 was taken as statistically significant. Mean, averages, standard deviations and Odd's ratios were calculated for various parameters and risk factors.Calculations were done by using software *Epi Info 2002*.[52]

OBSERVATIONS

In this case controll study 100 cases of Neonatal Seizures treated in Niramay Hospital , Satara ,Maharashtra between the period of Feb 2015 to July 2016 were included.

Table – I : General characteristics

Characteristics	Cases	Controls
Gestational age (wks.) Mean ± S.D.	32.97 ± 2.49	34 ± 3.5
Sex Ratio : Male:Female	1.07:1	1.08:1
Birth weight (gms) Mean Range S.D.	 1684.76 840-2490 ± 406.6	 1646.70 800-2480 ± 402.59
Duration of Hospitalization (Days) Mean Range S.D.	 12.38 3-42 7.6	 8.62 1-32 5.6
Day of onset of seizure Mean Range	 5.5 1-17	 --

Cases and controls were comparable in terms of mean gestational age, mean birth weight and sex ratio. Mean duration of hospitalization was more in cases as compared to controls.

Table – 2 : Frequency of various types of seizures (n=50)

Type of seizure	Total Numbers (%)
Subtle	20 (40%)
Tonic focal	8(16%)
Tonic generalized	6(12%)
Clonic focal	9 (18%)
Clonic Muitifocal	6 (12%)
Myoclonic	1(2%)

- Most common type of seizures observed were subtle (20) while myoclonic seizures (1) were least common.

Table – 3: Neurological outcome based on clinical seizure type

Seizure type	Total No. of seizures	Neurological abnormalities n (%)	Mortality n (%)
Subtle	188	10(05.31)	44(23.40)
Tonic focal	70	08(11.42)	34(48.57)
Tonic generalized	51	01(01.96)	21(41.17)
Clonic Multifocal	42	03(07.14)	11(26.19)
Clonic focal	23	03(13.04)	06(26.08)

Neurological outcome was better with tonic generalized type (01.96%) and worst with clonic focal type (13.04%).

Mortality was highest with tonic focal (48.57%) and lowest with subtle seizures.

Table – 4: Neurological outcome based on anticonvulsant used

Anticonvulsant	No. of cases n (%)	Neurological abnormalities n (%)	Mortality n (%)
Phenobarbitone	45(90)	25(08.06)	116(37.41)
Phenobarbitone plus Phenytoin	3(6)	04(19.04)	13(61.90)
Phenobarbitone plus Phenytoin plus Benzodiazepine	2(4)	02(22.22)	05(55.55)

Maximum numbers of cases received only phenobarbitone (90%) and only (4%) cases required more than two drugs.Neurological outcome was better with only phenobarbitone group (8.06%) and poor with patients requiring more than two drugs (22.22%). Mortality was highest (61.9%) amongst the patients requiring phenytoin in addition to phenobarbitone.

DISCUSSION :

In our study Cases and controls were comparable in terms of mean gestational age, mean birth weight and sex ratio. Mean duration of hospitalization was more in cases as compared to controls.

Neonatal Risk Factors in our study , gender difference was not significantly associated with neonatal seizures [Male OR =0.1,p>0.05 and Female OR =1.01p>0.05]. Aprino et al [7] and Kohelet et al [1] had similar observations. However, Saliba et al [8] reported male infants were 1.8 times likely to have seizures. However in this study gender was no longer a significant factor for tem babies.

Need for resuscitation in our study was observed as a significant risk factor for neonatal seizures [OR = 1.97,p<0.05].Similar observation was noted by Kohelet et al [1].Babies who were resuscitated usually had hypoxia and ischemia. Hypoxia and ischemia can cause disturbance in energy production in the nervous system and associated convulsive phenomenon by mechanisms including the excessive release and extracellular accumulation of excitatory neurotransmitter (glutamate)in the cortex, relative deficiency of inhibitory neurotransmitter (GABA) and Na+ - K+ pump failure1.

Respiratory Distress Syndrome was significantly associated with neonatal seizures [OR =1.60,p<0.05].Similar observation was noted by kohelet et al [1].The exact relationship between RDS and brain damage remains unclear.Severe respiratory distress can be directly associated in pathogenesis of intraventricular haemorhage and periventricular leukomalacia by causing fluctuations in PaO2 or PaCO2 or by changes in intrathoracic pressure leading to unstable blood flow.In addition hypoxia ,ischemia and reperfusion ,reoxygenation occurring during pulmonary air leak can result in cerebral circulatory changes.[9,10]

Jaundice was significantly associated with neonatal seizures [OR = 52,p<0.05].Similar observation was noted by Aprino et al[7].Hyperbilirubinaemia has a potential to cause cerebral damage and increased risk of neonatal seizures owing to its possible neurotoxicity cannot be ruled out.[11,12]

Necrotizing Enterocolitis was observed as a significant risk factor for neonatal seizures [OR=2.08,p<0.05]. Similar observation was noted Kohelet et al 1.Two potential mechanisms might account for NEC with brain damage in preterm infants. Asphyxial insult which causes redistribution of blood flow away from gut to maintain vital organ function ,compromises gut integrity and preterm infants with NEC can show increased plasma levels of cytokines which are implicated in damage to the developing white matter of neonate. [13,14]

Polycythaemia was observed as a significant risk factor for neonatal seizures [OR=2.085,p<0.05].To the best of our knowledge no other study has reported this association. Probable reason for association for polycythaemia and seizures can be explained as polycythaemia is associated with CNS manifestations like apathy ,lethargy, hypotonia and poor feeding,these features of CNS depression are often followed by irritability ,tremulousness and seizures over next few hours. Along with it hypoglycemia ,hypocalcemia and hypomagnesemia are common metabolic complications especially in small for date babies .These metabolic alterations may account for some of the CNS manifestations.[15,16,17]

Sepsis had no significant association with neonatal seizures [OR=2.25,p>0.05].However ,infants with septicaemia /septic meningitis may have convulsions because of direct brain damage due to CNS infection and associated increased chances of hypoglycemia ,circulatory abnormalities,electrolyte imbalance,predisposing baby for seizures.[18]

Small for gestational age:(SGA) Though the incidence of SGA was higher in cases as compared to controls it was not statistically significant .However Saliba et al [8],observed that term SGA infants were about two times as likely to have seizures as infants who were appropriate for gestational age.SGA babies have decreased tissue glycogen stores ,decreased gluconeogenesis, hyperinsulinism, increased glucose need for hypoxia ,hypothermia,all factors making them prone for hypoglycemia and seizures. [8]

Seizures are likely to be missed or confused with benign movements observed commonly in preterm and low birth weight neonates. Seizures are associated with poor neurodevelopmental outcome if not diagnosed early and treated properly.

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