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A STUDY OF ETIOLOGY, ONSET AND TYPE OF NEONATAL SEIZURES

Paediatrics

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ABSTRACT

Introduction: A seizure or convulsion is a paroxysmal, time-limited change in motor activity and/or behaviour that results from abnormal electrical activity in the brain. Neonatal seizures are abnormal electrical discharges in the central nervous System of neonates usually manifesting as a stereotyped muscular activity or autonomic changes.

Aims and Objectives: To Study Etiology, Onset and Type of Neonatal Seizures

Methodology: The present study included 107 neonates presenting with seizures admitted to the NICU of MGM Medical College & Hospital, Aurangabad, during the period of two years from 1st June 2013 to 31st May 2015. All participants in the study were subjected to all investigations mentioned in the proforma, except for neuroimaging which was an optional investigation. The data were analyzed using software like Epi-info, Microsoft Excel.

Result: Chi-squared for the onset of seizures on the first three days and more than three days with aetiology, $\chi 2 = 13.1312$ with a p-value of 0.0107. Seizures during the first three days of life have a statistically significant correlation with birth asphyxia with a P value of < 0.05. Out of 71 neonates with birth asphyxia, 36 (50.7%) had subtle seizures, followed by GTS in 26 neonates (36.62%) & MFC in 6 (8.45%) neonates. In neonates with hypoglycemic seizures, 7 out of 15 (46.67%) babies had subtle seizures followed by GTS in 6 (40%), neonates. In neonates with meningitis (10 neonates), 5 developed subtle seizures (50%) and 3 had MFC (30%). In our study, there was no correlation between the type of neonatal seizures with the aetiology ($p>0.05$).

Conclusion: The recognition of the aetiology of neonatal seizures is often helpful with respect to prognosis and treatment.

KEYWORDS

Neonatal Seizures, Etiology of Neonatal Seizures

INTRODUCTION

A seizure or convulsion is a paroxysmal, time-limited change in motor activity and/or behaviour that results from abnormal electrical activity in the brain.[1]Neonatal seizures are abnormal electrical discharges in the central nervous System of neonates usually manifesting as a stereotyped muscular activity or autonomic changes,[2]by definition though they occur within the first 4 weeks/ 28 days of life in a full-term infant and up to 44 weeks from conception for premature infants.[3]Neonatal seizures are the most frequent clinical manifestation of central nervous system dysfunction in the newborn. They are a strong predictor of later morbidity and mortality, frequently signalling significant brain pathologies such as hypoxic-ischemic injury, stroke, intracranial infection, and hypoglycemia, inborn errors of metabolism or brain malformations. Sometimes neonatal seizures may be of help in identifying a treatable disorder that, if not diagnosed, can cause permanent brain damage; hypoglycemia and bacterial meningitis, for example, can cause neonatal seizures, and prompt, timely, appropriate treatment may halt further progress of the disease and prevent additional damage to the brain.[4]Seizures represent the most distinctive signal of neurological disease in the newborn period. The convulsive phenomenon is the most frequent the overt manifestations of neonatal neurological disorders. Neonatal seizures are common and may be the first manifestations of neurological dysfunction after a variety of insults. Neonatal seizures are clinically significant because very few are idiopathic.It is critical to recognize neonatal seizures to determine their aetiology and to treat them for 3 major reasons: 1. First, seizures are usually related to significant illness, sometimes requiring specific therapy. 2. Second, neonatal seizures may interfere with important supportive measures, such as alimentation and assisted respiration for associated disorders. 3. Third, experimental data give a reason for concern that the seizures per se may be a cause of brain injury. Neonatal seizures present with varying manifestations like generalized tonic, multifocal clonic and subtle activity. Therefore it is important to recognize the seizures and treat it, as a delay in recognition and treatment may lead to brain damage. The time of onset of seizure has a relationship with the aetiology and prognosis. For example, birth asphyxia usually presents in the first three days of life whereas meningitis presents after the first week. If baby convulses within hours of delivery, it signifies poor prognosis and brain damage. Epidemiology: The incidence varies from 1.5-3.7/1000 live births in term babies and6-12% in babies weighing less than 1500gram.[11]Hughlings Jackson described seizure as "excessive discharge of nerve tissue on muscle". Jackson went on to say that this discharge occurs in all degrees, it occurs with all sorts of conditions of ill health, at all ages and under innumerable circumstances. These observations by Jackson remain as true today as they did 130 years ago.[5]Von Rosenstein in 1776 stated that "Lastly we may observe, to the great comfort and satisfaction of the parents of those young children subject to convulsion, that they need not be apprehensive for its changing into the true epilepsy, for it generally disappears by degree, as they grow older and acquire more strength".[6]The great Swedish Pediatrician Von Rosenstein in his rather optimistic prognosis for early convulsions, showed remarkable insight not only into the concerns of parents but also into the tendency toward spontaneous improvement. He clearly recognized the distinction made between those young children, who are subjected to seizures for a limited period and those who show a tendency to recurrent attacks somewhat late, justifying the use of the word epilepsy.[7]Taking above points into consideration, the study of aetiology, onset and clinical manifestations of neonatal seizures has a significant role. Following are the common causes of neonatal seizures and are Hypoxic-ischemic encephalopathy, Intracranial haemorrhage (ICH), Intraventricular haemorrhage (IVH) Subdural haemorrhage (SDH), Subarachnoid haemorrhage (SAH), Parenchymal haemorrhage. Central nervous system infections: Intrauterine, Postnatal. Congenital malformations: Induction anomalies, Migration anomalies. Cerebrovascular syndrome, Cerebral Infarction, Vascular infarction. Metabolic: Electrolyte and chemical abnormalities, Neurometabolic disorders. Drug withdrawal and toxins. Benign neonatal seizures. The most important etiologies and their usual time of onset are shown below: [8]First day: HIE, hypocalcemia, pyridoxine dependency, accidental injection of local anaesthetics.Between 1-3 days: ICH, hypoglycemia, inborn errors of metabolism. 4th – 7th day: Meningitis, TORCH infections, developmental malformations.> 7 days: Late-onset meningitis, hypocalcemia. Bacterial infections that produce neonatal seizures include group B Streptococcus, Listeria, E. Coli, etc. These infections usually occur towards the end of the first week or even later.[9]The epileptic syndrome BFNC is defined by the following: Onset of frequent brief seizures on the or after 2nd day of life, which disappear spontaneously within a few weeks; positive family history that features on Autosomal Dominant inheritance of neonatal seizures; exclusion of other causes of neonatal seizures; normal physical examination and subsequentneurodevelopment.[10]Leppert et al

localized the gene causing BFNC to the long arm ofChr-20.[11]Neurocognitive development is normal in majority of the affected individuals. The risk for subsequent epilepsy is 16%. Most of the epilepsy that comes after BFNC is generalized tonic or tonic-clonic with the variable age at onset and duration.[12]Benign idiopathic neonatal convulsions or the fifth day fits describe multifocal clonic seizures, the peak time of onset of which is the fifth day, generally ceasing within 15 days. The cause is unknown, although low CSFzinc concentrations have been described in some cases. Very few cases have been reported recently. The term fifth day fits, probably represents a meaningless diagnosis and should be avoided.[13]

AIMS AND OBJECTIVES: To Study Etiology -Onset and Type of Neonatal Seizures.

METHODOLOGY: The present study included 107 neonates presenting with seizures admitted to the NICU of MGM Medical College & Hospital, Aurangabad, during the period of two years from 1st June 2013 to 31st May 2015. Neonates (first 28 days of life) presenting with at least one of the following clinical type of seizures : Generalized tonic seizures, Multifocal clonic seizuresFocal clonic seizures, Myoclonic seizures, With or without accompaniment of subtle motor movements, apneas or autonomic changes or the sole combination of subtle motor and autonomic manifestation were included in the study group. Neonates with the isolated subtle phenomenon, apnea or paroxysmal autonomic changes, i.e., only subtle motor moments or apnea without tachycardia or hypertension were excluded from the study. Jitteriness in neonatesTetanic spasms in neonates participants in the study was subjected to all investigations mentioned in the proforma, except for neuroimaging which was an optional investigation. The data was then analyzed using software like Epi-info, Microsoft Excel.

RESULT:

TABLE 1: Correlation of aetiology with a day of onset of neonatal seizures:

Aetiology of seizures	Day of Onset of Seizures		
	First 3 days	After 3 days	Total
Birth asphyxia	60	11	71
Row %	84.51%	15.49%	100.00%
Hypoglycemia	11	4	15
Row %	73.33%	26.67%	100.00%
Neonatal Meningitis	6	4	10
Row %	60.00%	40.00%	100.00%
Hypocalcemia	3	1	4
Row %	75.00%	25.00%	100.00%
Other	2	5	7
Row %	28.57%	71.43%	100.00%
Total	82	25	107
Row %	74.64%	23.36%	100.00%

$\chi 2 = 13.1312$;df=8 $p < 0.0107$.

Chi-squared for the onset of seizures on the first three days and more than three days with aetiology, $\chi 2 = 13.1312$ with a p-value of 0.0107. Seizures during the first three days of life have a statistically significant correlation with birth asphyxia with a P value of < 0.05

In neonates with hypoglycemic seizures, 7 out of 15 (46.67%) babies had subtle seizures followed by GTS in 6 (40%), neonates. In neonates with meningitis (10 neonates), 5 developed subtle seizures (50%) and 3 had MFC (30%). In our study, there was no correlation between the type of neonatal seizures with the aetiology ($p>0.05$).

TABLE 2: Correlation of Etiology with the type of neonatal seizures

Aetiology of seizures	Type of Seizure					
	Subtle	Generalized Tonic	Multifocal Clonic	Focal Clonic	Mixed	Total
Birth asphyxia	36	26	6	1	2	71
Row %	50.70%	36.62%	8.45%	1.41%	2.82%	100%
Hypoglycemia	7	6	1	1	0	15
Row %	46.70%	40.00%	6.67%	6.67%	0.00%	100.00 %
Neonatal Meningitis	5	0	3	1	1	10
Row %	50.00%	0.00%	30.00%	10.00 %	10.00%	100.0 0%
Hypocalcaemia	3	1	0	0	0	4
Row %	45.00%	25.00%	0.00%	0.00%	0.00%	100.0 0%
Other	3	1	0	1	0	7
Row %	42.86%	42.86%	0.00%	14.29 %	0.00%	100.0 0%
Total	54	36	10	4	3	107
Row %	54.47%	33.64%	9.35%	3.74%	2.80%	100%

$X2 = 17.5995$; d. f. =16 $p < 0.3479$.

In the present study, out of 71 neonates with birth asphyxia, 36 (50.7%) had subtle seizures, followed by GTS in 26 neonates (36.62%) & MFC in 6 (8.45%), neonates.

Discussion: In the present study 107 neonates with seizures were studied over a 2 years period. Both inborn and outborn babies were included in the study. In our study neonatal seizures during the first two days were mostly due to birth asphyxia (74.32%) and the onset of seizures due to birth asphyxia during first three days of life was seen in 60 out of 82 cases (73.17%) with a significant p-value of <.0.05. Seizures due to hypoglycemia manifested from the first day itself, with incidence more in the first 3 days and decreases as the days go on. In our study, out of 15 cases of hypoglycemia 11 (73.33%) had convulsions by the third day of life. At the end of the first week, seizures are mostly due to neonatal meningitis, which also extends to early second week and later. After the first week, the onset of seizures are less likely and are mostly due to meningitis and late-onset hypocalcemia in our study. In a study of neonatal seizures by Rose Arthur L et al[14], majority of babies with perinatal anoxia convulsed on the first day of life (5/10 – 50%), hypoglycemic neonates convulsed on second and third day (5/7 – 71%), majority of neonates with CNS infection convulsed at the end of first week and early second week (9/13 – 69%) and babies with hypocalcemia present with convulsions during first and second day of life (6/28) and again during late first week and second week (19/28). Birth asphyxia usually presents with seizures within the first three days of life, preferably within first 48 hours. Hypoglycemia presents on the second and third day, as there is depletion of glycogen stores. Hypocalcemia presents on the first and second day if it is early onset hypocalcemia and later i.e., late first week and second week, if it is late onset hypocalcemia. Neonatal meningitis presents with seizures during late first week and second week.

In the present study, 50.7% of neonatal seizures with birth asphyxia had a subtle type of seizures, followed by GTS in 36.2% & MFC in 8.45%. In neonates with hypoglycemic seizures, 46.67% had subtle seizures & 40% had GTS. In neonates with meningitis, 50% had subtle seizures and 30% had MFC. There was no correlation between the type of neonatal seizures with aetiology in our study with $p>0.05$. In a study of neonatal seizures compared with EEG studies by Mizrahi M et al[13]GTS & subtle seizures were likely to be caused by diffuse pathologic processes such as HIE. Clonic seizures were more likely to be associated with focal or regional lesions such as infarction or ICH with $p=0.0047$.

CONCLUSIONS

Hypoglycemia &Hypocalcemia which are one of the commonest causes, should be suspected & detected as early as possible & treatment started before it can cause any additional brain damage. Hypoglycemic seizures are usually more common in LBW babies. Treatable causes should be evaluated before standard anticonvulsants are administered to the neonate. The time of onset of neonatal seizures is significantly associated with the aetiology (e.g. onset of seizures within the first three days is significantly associated with birth asphyxia).

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