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BIOCHEMICAL ABNORMALITIES IN NEONATAL SEIZURES IN A TERTIARY CARE RURAL TEACHING HOSPITAL OF SOUTH INDIA

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ABSTRACT

Context : Seizures during neonatal period is a common problem. Biochemical abnormalities may be the underlying cause or they may be associated with other causes of seizures. Early recognition and management of biochemical disturbances in neonatal seizures is important to prevent further brain damage.

Aims : To analyse the serum biochemical abnormalities in neonatal seizures.

Settings and Design : Prospective study in a tertiary care rural teaching hospital of South India.

Material and Methods : 100 neonates with history of seizures were included in the study. Inclusion criteria consisted of all neonates (<28 days of life) admitted to NICU with history of seizures and those who developed seizures after admission. Apart from completed blood count (CBC), septic screening, blood for culture and sensitivity, serum levels of calcium (Ca), Phosphate (P), magnesium (Mg), sodium (Na), potassium (K) and blood glucose were measured as soon as possible after seizure and before institution of specific therapy.

Results : Out of 100 neonates with seizures, 69 were out born (referred to our hospital from outside) and 31 were in born. Seizures occurred more frequently among term infants (78%). One or more biochemical abnormalities were observed in 82% of neonates with seizures. Hypoglycemia (44/82=53.65 %) was the most common abnormality followed by hypocalcemia (26/82=31.7%).

Conclusion : Hypoglycemia and hypocalcemia were the most common disturbances present not only as primary disorders but also associated with specific etiology. Early recognition and treatment is of utmost importance in order to decrease morbidity and mortality.

Key words : Neonatal seizures, Biochemical abnormalities, Hypoglycemia, Hypocalcemia.

INTRODUCTION

Seizures during neonatal period is a common problem. Although the most common cause of neonatal seizures is hypoxic ischemic encephalopathy (HIE), many additional disorders are likely to cause seizures including metabolic, infections, structural, traumatic, hemorrhagic and maternal disturbances [1]. Biochemical abnormalities are frequent occurrences in neonatal seizures. They may be the underlying cause or they may be associated with other causes of seizures[2,3]. Early recognition and management of biochemical disturbances in neonatal seizures is important to prevent further brain damage. Medline search on biochemical abnormalities in neonatal seizures in India yielded a few studies from North India[4-6] and only one from South India[7]. So, the present study was undertaken to analyse the serum biochemical abnormalities in neonatal seizures in a tertiary care rural teaching hospital of South India.

MATERIALS AND METHODS

This prospective study was conducted in the neonatology unit of Department of Pediatrics, R. L. Jalappa Hospital and Research Centre (RLJH&RC), Kolar, attached to Sri Devraj Urs Medical College (SDUMC) from January 2007 to December 2007 after obtaining consent from the ethical committee.

During the study period, a total of 1100 neonates were admitted to the Neonatal Intensive Care Unit (NICU) of which 100 neonates with history of seizures were included in the study. Inclusion criteria consisted of all neonates (<28 days of life) admitted to NICU with history of seizures and those who developed seizures after admission. Exclusion criteria consisted of neonates born with obvious central nervous system anomalies.

A detailed history was recorded including type of seizures, age of onset of initial seizure, maternal

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diabetes, perinatal asphyxia, type of delivery, birth weight and feeding pattern of neonates. Classification of seizures as focal clonic, multifocal clonic, tonic, myoclonic and subtle as proposed by Volpe[8] was recorded. New Ballard Scoring parameter was employed to estimate the gestational age[9].

Apart from complete blood count (CBC), septic screening, blood for culture and sensitivity, serum levels of calcium (Ca), phosphate(P), magnesium(Mg), sodium(Na), potassium (K) and blood glucose were measured as soon as possible, after seizure and before institution of specific therapy.

Criteria for diagnosing biochemical disorders were as follows: hypoglycemia (blood glucose levels < 40 mg/dl), hypocalcemia (Ca < 7.0 mg/dl), hypomagnesemia (Mg < 1.5 mg/dl), hypermagnesemia (Mg > 2.5 mg/dl), hyponatremia (Na <130 mEq/L), hypernatremia (Na > 150 mEq/L), hypokalemia (K < 3.5 mEq/L) and hyperkalemia (K > 5.5 mEq/L). Various methods employed for biochemical estimation were as follows: serum Ca by Arsenazo colorimetric end point method[10], serum P by UV end point method[10], serum Mg by Xylidyl blue colorimetric end point method[11], serum Na and K by ISE method[12] and blood glucose by glucose oxidase method[13]. Cerebrospinal fluid analysis, cranial ultrasonography and CT scan of brain was done as and when indicated. History, findings on examination and investigations were recorded on a pretested proforma.

RESULTS

Out of 100 neonates with seizures, 69 were outborn (referred to our hospital from outside) and 31 were inborn. There was a male preponderance (58%) with a male to female ratio of 1.39:1. Seizures occurred more frequently among term infants (78%) as compared to preterms in both outborn and inborn groups (Table 1). Subtle seizures were the commonest (38%) while tonic, clonic, myoclonic and combined seizures constituted 30%, 19%, 2% and 11% respectively. One or more biochemical abnormalities were observed in 82% of neonates with seizures. Primary biochemical abnormalities were present in 16 out of 82 cases, while in the remaining 66 cases, they were associated with other co-morbid conditions (Table- 2).

Hypoglycemia (44/82=53.65%) was the most common abnormality followed by hypocalcemia (26/82=31.7%), while hypermagnesemia was observed in 2.43% (2/82) – (Table- 2). Relationship of biochemical abnormalities with etiology of seizures is depicted in Table- 2. Out of 16 neonates with primary biochemical disturbances, hypoglycemia was most frequently encountered. However 2 neonates showed more than one biochemical abnormality- (Table-2). Late onset hypocalcemia occurred in 4 term neonates fed on cow's milk while early onset hypocalcemia was present in 2 preterm neonates.

Table1: Distribution of cases in relation to sex, gestation and place of birth

Sex	Outborn (n= 69)		Inborn (n= 31)		Total
	Term	Preterm	Term	Preterm	
Male	36	6	12	4	58 (58%)
Female	17	10	13	2	42 (42%)
Total	53	16	25	6	100 (100%)

DISCUSSION

Neonatal seizures have always been a topic of interest because of their universal occurrence. The presence of a seizure does not constitute a diagnosis but is a symptom of underlying CNS disorder due to systemic or biochemical disturbances[14].

The results of the present study showed biochemical abnormalities in 82% of neonates with seizures which is higher compared to studies conducted by Kumar et al (22/35= 62.8%)[4], Sood et al (29/59= 49.15%)[5] and Taskande et al (25/110= 22.7%)[6]. The present study and those conducted by Kumar et al[4] and Sood et al[5] showed primary biochemical abnormalities and also in association with birth asphyxia (BA), HIE, intra cranial bleed, meningitis and infections. Irrespective of the etiology of seizures more than one biochemical abnormality was present in our series which is in agreement with other studies[4,5].

Table 2: Distribution of cases in relation to etiology and biochemical abnormalities

Etiology (No of cases)	No. of cases with biochemical abnormalities	Hypo - glycemia	Hypo - calcemia	Hypo - natremia	Hypo - magnesemia	Hyper - magnesemia
Birth asphyxia (44)	33(75%)	14(42.4%)	8(24.2%)	12(36.3%)	1(3.03%)	1(3.03%)
Intra cranial Hemorrhage (10)	6(60%)	2(33.3%)	3(50%)	3(50%)	-	-
Meningitis (8)	5(62.5%)	3(60%)	1(20%)	3(60%)	-	-
Primary disorder (16)	16(100%)	10(62.5%)	6(37.5%)	-	1(6.25%)	1(6.25%)
Sepsis (22)	22(100%)	15(68.18%)	8(36.36%)	6(27.27%)	1(4.54%)	-
Total 100	82(82%)	44(53.65%)	26(31.7%)	24(29.26%)	3(3.65%)	2(2.43%)

Hypoglycemia was the principal cause for seizures in 53.65% of neonates which corroborated with the findigs published by Kumar et al[4] and Sood et al[5]. Hypocalcemia affected 31.7% of neonates with seizures which is similar to that of a study reported by Kumar et al (31.8%)[4] . However Sood et al[5] reported a higher incidence (48.27%). Similar to hypoglycemia, hypocalcemia was also observed both as a primary disorder as well as secondary to other causes which is comparable to that of Kumar et al[4], Sood et al[5] and Prasad et al[7]. Hypoglycemia and hypocalcemia are known to occur in neonates with perinatal asphyxia[14]. In our study almost all neonates with hypoglycemia and hypocalcemia as primary metabolic disorders had history of delayed feeding and/ or feeding with diluted cow's or buffalo's milk Similar observations have been made by Kumar et al[4] and Sood et al[5]. Surprisingly none of the neonates in our study had hyperphosphatemia whereas it was present in other studies[4,5].

Hyponatremia (29.26%) was the third most common abnormality in the present study. BA accounted for 50% (12/24) of cases with hyponatremia while meningitis, ICH and sepsis accounted for the remaining cases. The most probable explanation for occurrence of hyponatremia might be due to fluid overload as a result of renal compromise or due to syndrome of inappropriate secretion of anti diuretic hormone[15]. Kumar et al[4] reported hyponatremia in 10 out of 22 (45.45%) cases which is higher compared to our study, while Sood et al[5] have reported a lower incidence (17.24%). Contrary to other studies[4,5] , we observed hypomagnesemia only in 3.65% of cases which can be explained by the larger number of cases in our study. Hypermagnesemia was the least encountered biochemical abnormality (2/82=2.43%). History in these cases revealed maternal administration of magnesium sulphate ($MgSO_4$) for eclampsia in both cases. Hypermagnesemia in neonates is usually due to an exogenous magnesium load as part of treatment for hypomagnesemia or $MgSO_4$ therapy for maternal pre eclampsia[16].

Surprisingly all neonates with sepsis had one or more biochemical abnormality of which hypoglycemia was

once again the commonest. Most of the neonates with sepsis and meningitis were outborn and referred to our hospital from outside with history of poor feeding, bottle feeding with diluted cow's or buffalo's milk and branding of skin. The possible attributions to hypoglycemia are poor intake, increased metabolic rate coupled with increased glucose utilisation and impaired ability to mobilise glucose[17].

CONCLUSION

Serum biochemical abnormalities are a common occurrence in neonatal seizures. Irrespective of the etiology more than one biochemical abnormality was present. Hypoglycemia and hypocalcemia were the most common disturbances present not only as primary disorders but also associated with specific etiology. Early recognition and treatment is of utmost importance in order to decrease morbidity and mortality. Health education of pregnant women particularly with respect to good breast feeding practices might go a long way in alleviating primary metabolic disturbances like hypoglycemia and hypocalcemia.

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