

BIOCHEMICAL ABNORMALITIES IN NEONATAL SEIZURES

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ABSTRACT

Early diagnosis and appropriate treatment of biochemical abnormalities accompanying neonatal seizures is important for effective seizure control and to avoid further brain damage. The present study was carried out on 35 neonates to determine the frequency of various biochemical abnormalities in neonatal seizures. Diagnostic evaluation included estimation of levels of serum calcium, phosphorus, magnesium, sodium, potassium, zinc, and blood glucose. Two-thirds of the neonates with seizures had biochemical disturbances in their sera. A variety of abnormalities occurred in asphyxiated infants, including hyponatremia, hypoglycemia, hypocalcemia, and hypomagnesemia. Primary metabolic disorders accounted for one-fourth of the cases of neonatal seizures, the most common being hypoglycemia, hypoglycemia/hypocalcemia, and hypocalcemia/hyperphosphatemia. Inappropriate intrauterine growth, inadequate feeding, and feeding with cow's milk were the main risk factors for primary metabolic seizures. Hyponatremia was a frequent finding in seizures resulting from brain damage like birth asphyxia, meningitis, and intracranial hemorrhage. No infant had hypernatremia, hyperkalemia, hypokalemia, or low serum zinc.

Keywords: Neonate, Seizure, Biochemical disturbance.

Biochemical disturbances occur frequently in neonatal seizures either as an underlying cause or as an associated abnormality(1,2). In their presence it is difficult to control seizures and there is a risk of further brain damage. Early recognition and treatment of biochemical disturbances are essential for optimal management and satisfactory long-term outcome. There is a lack of information on this topic in the Indian literature. The aim of this study was to determine the biochemical abnormalities in neonatal seizures.

Material and Methods

Thirty five neonates with seizures were studied during June, 1990 to May, 1992. The gestational age of patients ranged from 34 to 41 weeks, 5 infants were born before 37 weeks, 6 infants were small for gestational age (SGA) (weight < 10th centile for gestation), and 3 large for gestational age (LGA) (weight > 90th centile for gestation). Neonates were categorized as appropriate or inappropriate for gestational age according to previously published data(3). Twelve neonates were referred from outside the hospital. Seizures were classified as focal clonic, multifocal clonic, tonic, myoclonic, and subtle as proposed by Volpe(4). Seizure activity was diagnosed by clinical observations

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*Received for publication: May 13, 1993;
Accepted: October 4, 1994*

made by one of the authors or resident doctors. Newborns with doubtful seizures were excluded. An electro-encephalogram was not required to make the diagnosis of a seizure disorder. Neonates with jitteriness were excluded by holding the limb to determine whether the movements could be stopped.

The serum levels of calcium, phosphorus, magnesium, sodium, potassium, zinc, and blood glucose were measured (on venous blood collected in deionized vials) as soon after a seizure as possible and before the institution of specific therapy. Calcium was determined by the precipitation method(5), phosphorus by the phosphomolybdate method(6), magnesium and zinc by the atomic absorption spectrophotometry(7), sodium and potassium by the flame photometry(8), and blood glucose by the glucose oxidase method(9). Serum zinc was determined in only 19 neonates. The criteria for diagnosing various biochemical disorders were as follows : hypocalcemia (Ca <7.0 mg/dl), hyperphosphatemia (P >8.0 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). Serum zinc levels of less than 65 ng/dl were considered low (10). Hypoglycemia was diagnosed if blood glucose levels were less than 30 mg/dl in term infants, and less than 20 mg/dl in preterm infants in the first 72 hours of life, and less than 40 mg/dl after the age of 72 hours.

Results

Twenty two (62.8%) neonates with seizures showed one or more metabolic

abnormalities (Table I). Six of the 9 newborns with birth asphyxia showed a combination of biochemical disturbance: hyponatremia and hypoglycemia occurred in three infants; hypocalcemia, hyperphosphatemia and hypomagnesemia in one; hypocalcemia and hypomagnesemia in one; and hyponatremia and hypermagnesemia in one newborn each. Two of the 4 newborns with meningitis had hyponatremia, one of whom also had hypoglycemia.

Primary metabolic disorders accounted for seizures in 9 neonates. Late onset hypocalcemia occurred in 2 cases who were fed with cow's milk, and early onset hypocalcemia in 1 term infant who was large for gestational age. Isolated hypoglycemia was seen in 3 newborns: 2 were term SGA and 1 was low birth weight preterm infant. All 3 neonates were born at home and had a history of being fed inadequately. Hypoglycemia with hypocalcemia was found in 2 cases, one was a term SGA infant, and the other, an appropriately grown term infant with infrequent feeding. The cause of hypomagnesemia and hyponatremia in one newborn who presented on 6th day of life could not be determined.

None of the infants had hypernatremia, hypokalemia, hyperkalemia, or low serum zinc. Two cases with seizures of unknown etiology presented after 2 weeks of age with multifocal clonic seizures. They failed therapeutic trial with pyridoxine and required phenobarbitone to control their seizures. Cranial CT was not obtained in these cases so the possibility of brain malformation could not be excluded.

TABLE I—Biochemical Abnormalities in Neonates with Seizures

Etiology (n=35)	Neonates showing metabolic abnormality	Hyponatremia	Hypocalcemia	Hyperphosphatemia	Hypomagnesemia	Hyper-magnese-mia	Hypoglycemia
Birth asphyxia (n=16)	9	6	2	1	2	1	4
Meningitis (n=4)	2	2	-	-	-	-	1
Septicemia (n=2)	1	-	-	-	-	-	1
Metabolic disorder (n=9)	9	1	5	2	1	-	5
Miscellaneous* (n=4)	1	1	-	-	-	-	-

* Includes 2 newborns with seizures of unknown etiology, 1 preterm neonate with kernicterus (Rh incompatibility), and 1 preterm neonate with intracranial hemorrhage who also showed hyponatremia.

Seizures appeared within 2 days of life in all 16 cases of birth asphyxia, in 3 cases of isolated hypoglycemia, and in one case each of hypoglycemia/hypocalcemia, and intracranial hemorrhage. Of the twelve newborns who had onset of seizures beyond 4 days of life, 4 had bacterial meningitis, 3 had hypocalcemia, 2 had seizures of unknown origin, and one each had hypoglycemia /hypocalcemia, septicemia, and kernicterus.

Discussion

Two-thirds of neonates with seizures demonstrated one or more biochemical abnormalities in their sera. A variety of metabolic problems were present in

asphyxiated infants, including hyponatremia, hypoglycemia, hypocalcemia, and hypomagnesemia. Some of these biochemical disturbances may trigger seizures or potentiate further brain damage in asphyxiated infants. Therefore, close biochemical monitoring of infants with asphyxia is suggested for appropriate management. Neonates with birth asphyxia may have hyponatremia due to fluid overload as a result of renal compromise, or due to inappropriate secretion of antidiuretic hormone(11). We also found hyponatremia in infants with intracranial hemorrhage, meningitis, and septicemia which can be explained again on the basis of inappropriate secretion of antidiuretic hormone seen in these conditions(12).

In this series, one-fourth of infants with birth asphyxia developed hypoglycemia. This finding is in close agreement with others(13). Similar to earlier observations(13), we found hypocalcemia with or without hyperphosphatemia in 12.5% cases of birth asphyxia. Hypocalcemia in these cases is attributed to transient, functional hypoparathyroidism, increased phosphate loads, and bicarbonate therapy(14).

Primary metabolic disorders accounted for a significant number (25.7%) of cases in this series. This is in contrast to report from western countries where improvements in infant feeding practices have made this category an uncommon cause of seizures(15). This study highlights the role of delayed and infrequent feeding in the causation of neonatal seizures, especially in SGA neonates. Late onset hypocalcemia due to cow's milk feeding is still common in our set up. This can be eliminated by promoting exclusive breastfeeding.

Infants with septicemia/septic meningitis may have hypoglycemia. It is attributed to inadequate intake, increased metabolic rate, increased glucose utilization, and impaired ability to mobilize glucose(16). The time of onset of seizures is an important clue to etiology. All cases of birth asphyxia had onset of seizures within two days of life. In fact, this etiology was responsible for nearly 80% of cases with onset of seizures during this period. Neonates with seizures secondary to metabolic disorders and infection developed seizures in accordance with the timing of these events.

Acute zinc deficiency has been pos-

tulated to cause "fifth day fits"(17). None of our infants would fit into this category and no infant had low zinc levels. Similarly, we did not find hypernatremia, hypokalemia, or hyperkalemia in any of the infants with seizures.

REFERENCES

1. Cockburn F, Brown JK, Belton NR, Forfar JO. Neonatal convulsions associated with primary disturbance of calcium, phosphorus, and magnesium metabolism. *Arch Dis Child* 1973, 48: 99-108.
2. Brown JK, Cockburn F, Forfar JO. Clinical and chemical correlates in convulsions of the newborn. *Lancet* 1972,1:135-139.
3. Bhatia BD, Bhargava V, Chatterjee M, Kota VL, Singh LI, Jain NP. Studies on fetal growth patterns. Intrauterine growth percentiles for singleton live born babies. *Indian Pediatr* 1981, 18: 647-653.
4. Volpe J. Neonatal seizures. *N Engl J Med* 1973, 289: 413-416.
5. Trinder P. Calcium estimation by precipitation. *Analyst* 1960, 85: 889.
6. Fiske CH, Subbarow Y. The colorimetric determination of phosphorus. *J Biol Chem* 1925,66: 375-400.
7. Perkin-Elmer Corporation. Analytical methods for atomic absorption spectrophotometry. Norwalk, Connecticut, USA 1976.
8. Wootton IDP. Electrolytes. *In: Microanalysis in Medical Biochemistry*, 5th edn. Ed. Wootton IDP. Edinburgh, Churchill Livingstone, 1974, pp 44-72.
9. Raabo E, Terkildson TC. On the enzymatic determination of blood glucose. *Scand J Clin Invest* 1960,12: 402.
10. Kumar SP, Anday EK. Edema,

- hypoproteinemia and zinc deficiency in low birth weight infants. *Pediatrics* 1984, 73: 327-329.
11. Feldman W, Drummond KN, Klein M. Hyponatremia following asphyxia neonatorum. *Acta Paediatr Scand* 1970, 59: 52-57.
 12. Scher M, Painter MJ. Controversies concerning neonatal seizures. *Pediatr Clin North Am* 1989, 36: 281-310.
 13. Eriksson M, Zetterstrom R. Neonatal convulsions. Incidence and causes in the Stockholm area. *Acta Paediatr Scand* 1979, 68: 807-811.
 14. Tsang RC, Chen I, Hayes W, Atkinson W, Atherton H, Edwards N. Neonatal hypocalcemia in infants with birth asphyxia. *J Pediatr* 1974, 84: 428-433.
 15. Calciolari G, Perlman JM, Volpe JJ. Seizures in the intensive care unit of the 1980s. Types, etiologies, timing. *Clin Pediatr* 1988, 27:119-123.
 16. Leake RD, Fisher RH, Oh W. Rapid glucose disappearance in infants with infection. *Clin Pediatr* 1981, 20: 397-401.
 17. Goldberg HJ, Sheehy EM. Fifth day fits: an acute zinc deficiency syndrome ? *Arch Dis Child* 1982, 57: 633-635.
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