Serum calcium and magnesium levels in predicting short term outcome of term neonates with Hypoxic Ischemic Encephalopathy

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Abstract

Background: Hypoxic-ischemic encephalopathy (HIE) is defined as abnormal neurobehavioral state consisting of decreased level of consciousness and usually other signs of brain stem and/or motor dysfunction. Hypoxia decreases the blocking effect of magnesium ion channel thus causes a rapid influx of Ca+2 into the cell which has been reported to be the major cause of cell death.

Aim: To find out any correlation between levels of serum calcium and magnesium with short term outcome of Hypoxic ischemic encephalopathy (HIE).

Methods: This was a hospital based case series study. Ninety five term babies during period of 1st Jan 2016 to 31st Dec 2016 were selected based on inclusion and exclusion criteria and were studied. Estimation of Serum calcium and magnesium levels was done within 24hours of life. Short term outcome was noted at discharge as presence of seizures, hypotonia, poor sucking, lethargy and death.

Results: Of the 95 newborns with HIE, 52 had low levels of serum calcium and 43 had normal levels which showed significance in outcome of HIE with P value of 0.014; and. 20 had low serum magnesium levels and 75 had normal levels which was significant with P value 0.001.

Conclusion: Total serum calcium and total serum magnesium have prognostic values in neonates with HIE.

Key words: Hypoxic ischemic encephalopathy; serum calcium; serum magnesium.

Introduction

Perinatal asphyxia refers to a condition during the first and second stage of labor in which impaired gas exchange leads to fetal hypoxemia and hypercarbia.[1]

Asphyxia has been shown to be the third most common cause of neonatal death (23%) after preterm birth (28%) and severe infections (26%).

Hypoxic-ischemic encephalopathy (HIE) is defined as abnormal neurobehavioral state consisting of decreased level of consciousness and usually other signs of brain stem and/or motor dysfunction.[3]

Perinatal asphyxia is an end result of significant degree of global hypoxic ischemia during the time of birth. Lack of oxygen delivery from this episode often leads to multiorgan failure. A multisystem approach to management of perinatal asphyxia will help to minimize high mortality and morbidity associated with devastating condition which was said by Sexson in 1976.[4]

In same year Scott mentioned outcomes of severe birth asphyxia.[5]

Robertson et al define HIE as “an acute non-static encephalopathy caused by intrapartum or late antepartum brain hypoxia and ischemia.[6]

American Academy of Pediatrics (AAP) and American College of Obstetrics and Gynecology (ACOG)[7] proposed the criteria for birth asphyxia as:

- profound metabolic or mixed acidemia,
- persistence of Apgar scores 0-3 for longer than 5 minutes,
- neonatal neurologic HIE (e.g., seizures, coma, hypotonia) and multiple organs (of kidney, lungs, liver, heart, intestine) involvement.

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In India, 8.4% of inborn babies have a one minute Apgar score less than 7 and 1.4% suffer from hypoxic ischemic encephalopathy.[8]

Data from National Neonatal Perinatal database (NNPD) suggests that the incidence in India is 14 per 1000 live births with birth asphyxia causing 30% of neonatal and 50% of perinatal deaths.[8]

Among the neonates with HIE, 10-15% will die, 10-15% will develop cerebral palsy and upto 40% will develop other disabilities, severe and permanent neuropsychological sequele, including mental retardation, visual motor or visual perceptive dysfunction, increased hyperactivity, cerebral palsy and epilepsy.[9]

A variety of markers have been examined to identify perinatal hypoxia but studies for early determination of tissue damages due to birth asphyxia are still lacking.

N-Methyl-D-aspartic (NMDA) acid channel is normally closed by magnesium ions in a voltage dependent manner.

Hypoxia decreases the blocking effect of magnesium ion channel thus causes a rapid influx of Ca+2 into the cell which has been reported to be the major cause of cell death[10].

Objectives

- To study the serum calcium and magnesium levels in asphyxiated newborns at time of admission.
- To find out any correlation between levels of serum calcium and magnesium with short term outcome of Hypoxic ischemic encephalopathy (HIE).

Materials and methods

This study was a hospital based case series study conducted in NICU of HSK Hospital, Bagalkot.

95 term babies during the period of 1st Jan 2016 to 31st Dec 2016 were selected based on inclusion and exclusion criteria and were studied.

Sample size calculation was done using open EPI software version 2.3.1 At 95% confidence levels. According to study conducted by Vamne A et al[11], abnormal serum calcium levels in stage 3 HIE was found in 57% of patients. At 10% absolute precision, sample size calculated is 95.

Newborns diagnosed as having HIE under inclusion criteria were subjected to thorough history, full clinical examination.

Patients were grouped according to Sarnat & Sarnats[12] staging into 3 groups:

- Group 1 (Mild HIE)
- Group 2 (Moderate HIE)
- Group 3 (Severe HIE)

Estimation of Serum calcium and magnesium levels was done within 24hours of life.

Short term outcome was estimated at the time of discharge as -

- improved without neurological deficit,
- improved with neurological deficit
- discharged against medical advice
- death

Inclusion Criteria

- All babies with 37 completed weeks of gestation with history of birth asphyxia and evidence of HIE
- Five minute APGAR score less than 5
- Delayed first breath beyond 5min after birth.

Exclusion criteria

- Small for date babies(IUGR)
- Newborns with congenital malformations
- Newborns with Intracranial Hemorrhage

Neonates were grouped according to Sarnat and Sarnat's staging into Mild, Moderate and Severe HIE.

Short term outcome was noted at discharge as presence of seizures, hypotonia, poor sucking, lethargy and death.

Results

Total 95 number of babies were included in the study, out of which 61(64.2%) were males and 34(35.8%) were females; 62 (65.3%) were born vaginally and 33 (34.7%) were born by LSCS. 65 (68.4%) babies were born in HSK Hospital whereas 30 (31.6%) were born in other outside hospitals.

In the present study, out of a total 95 newborns, 59 (62.5%) improved without neurological deficit, 14 (14.5%) improved with neurological deficit i.e., poor sucking hypotonia, absent moros reflex, lethargic whereas 13 (13.5%) went against medical advice and 9 (10%) death.

Outcome of HIE based on serum calcium

Of the 95 newborns with HIE, 52 had low levels of serum calcium and 43 had normal levels which showed significance in outcome of HIE with P value of 0.014 using Kruskal wallis test (Table 1).

Table 1: Outcome of HIE based on levels of serum calcium

Outcome	Serum calcium	
	low	normal
Improved without neurological deficit	29	30
Improved with neurological deficit	10	4
Against medical advice	8	5
Death	5	4
Total	52	43

Table 2: Outcome of HIE based on levels of serum magnesium

Outcome	Serum magnesium	
	Low	Normal
Improved without neurological deficit	6	55
Improved with neurological deficit	4	8
Against medical advice	5	8
Death	5	4
Total	20	75

Outcome of HIE based on serum magnesium

Out of 95 newborns with HIE, 20 had low serum magnesium levels and 75 had normal levels, which was significant with P value 0.001 using Kruskal wallis test (Table 2).

There was decrease in mean serum calcium levels in severe disease i.e., with poor outcome (Table 3)

Table 3. Comparison of mean serum calcium levels with outcome of HIE

Outcome	Serum Calcium in mg/dl Mean (SD)
Improved without neurological deficit	9.43 (1.19)
Improved with neurological deficit	8.71 (0.85)
Against medical advice	8.77 (1.01)
Death	8.40 (0.86)

There was decrease in mean serum calcium levels in severe disease i.e., with poor outcome (Table 4).

Table 4. Comparison of mean serum magnesium levels with outcome of HIE

Outcome	Serum Magnesium in mg/dl Mean (SD)
Improved without neurological deficit	2.36 (0.66)
Improved with neurological deficit	1.61 (0.40)
Against medical advice	1.80 (0.65)
Death	1.34 (0.15)

Discussion

In the present study, there was lower serum calcium levels in term newborns with HIE similar to a study by Jajoo et al[13] and hypomagnesemia as similar to a study by Gwen et al[14].

In the present study, there was hypomagnesemia with mean serum magnesium levels correlating with outcome of HIE, similar to a study conducted by Ilves et al.[15]

There was significant correlation between decreased levels of serum magnesium and decreased survival rate, as in a study conducted by Lila et al[16].

Conclusion

Decreased total serum calcium and magnesium levels in neonates with HIE was observed on 1st day of life with significant correlation between decreased serum calcium and magnesium levels to HIE disease outcome. Hence, serum calcium and magnesium levels can be of value as prognostic indicators in HIE.

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