Original Research Article

Study and correlation of the severity of birth asphyxia with serum levels of glucose, uric acid and electrolytes in the cord blood of asphyxiated neonates

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ABSTRACT

Background: Perinatal asphyxia one of the most common primary cause of mortality and morbidity among neonates in India and is the commonest cause of stillbirths.

Methods: This prospective study was conducted for a period of 18 months which included cases (124) and controls (124) comprised of asphyxiated and non-asphyxiated neonates respectively. The umbilical cord arterial blood was collected by double clamp technique and sent for analysis of electrolytes, uric acid and glucose.

Results: Umbilical arterial sodium, calcium and glucose concentration was significantly lower in cases as compared to controls and potassium, uric acid and creatinine concentration was found to be on the higher in the cases as compared to the controls, and the difference was statistically significant with p<0.001.

Conclusions: Metabolic abnormalities like hyponatremia, hypocalcaemia and hyperuricemia are significant risk factors for perinatal brain injury. Identification and treatment of such abnormalities results in improved outcome in affected neonates.

Keywords: Calcium, Glucose, Hypoxic ischemic encephalopathy (HIE), Perinatal asphyxia, sodium, Uric acid

INTRODUCTION

Birth asphyxia is one of the leading cause of perinatal death and a recognizable cause of brain damage in newborn. Hypoxic-ischemic encephalopathy (HIE) prevalence ranges from 0.1% to 0.5% of total live births and is the cause of around 23% neonatal death worldwide. The common complications of asphyxia are cerebral palsy, irreversible renal cortical necrosis, persistent pulmonary hypertension of the newborn, hypotension, cardiogenic shock or heart failure. The biochemical abnormalities which are associated with poor outcome in birth asphyxia are, fluctuating level of sugar, hyperuricemia, hyperkalemia, hypocalcemia, hyponatremia and increased creatinine level. This research points out the different spectrum of clinical presentation of birth asphyxia and its biochemical derangements leading to increased morbidity and mortality.

Due to cellular damage the levels of serum potassium increase, consequently the levels of sodium reduce due to increased secretion of ADH, water retention and hypoxic injury to the renal tubules. Serum levels of calcium also tend to drop due to hypoxic ischemic damage to the parathyroid glands. Serum levels of glucose tend to fall due to increased anaerobic degradation and increased cellular extraction. When hypoglycemia and hypoxia are present together the extent of brain injury noticed is significantly higher. Lack of ATP and increased...
excitotoxic cellular damage leads to an accumulation of adenosine diphosphate (ADP) and adenosine monophosphate (AMP), which is then catabolized to adenosine, inosine and hypoxanthine.²⁻¹¹

METHODS

This was a prospective study conducted on asphyxiated and non-asphyxiated term neonates recruited from Neonatal Intensive Care Unit (NICU) Cheluvamba hospital attached to MMC and RI, Mysore from January 2017 to June 2018. 124 Cases and 124 Controls comprised of asphyxiated and non-asphyxiated neonates, respectively.

The inclusion criteria for case group was defined as full term neonates with gestation age ≥37 weeks and weighing ≥2.5kg, Apgar score of <7 at one minute of life, resuscitation with >1 minute of positive pressure ventilation before stable spontaneous respiration. Mild, moderate or severe hypoxic ischemic encephalopathy (HIE), as defined by Sarnat and Sarnat.¹²

Neonates with congenital malformations, neonates with Suspected inborn error of metabolism and neonates born to mothers having received diuretics, pethidine, phenobarbitone, magnesium sulphate, general anaesthesia and any other drugs likely to cause CNS or respiratory depression in baby were excluded from the study.

The control group included 124 term apparently healthy neonates appropriate for gestational age without signs of perinatal asphyxia as evidenced by normal foetal heart rate patterns, clear liquor and one minute Apgar score ≥7.

Detailed clinical and neurological examination was done for all the neonates included in the study. Cases were classified into mild, moderate or severe hypoxic ischemic encephalopathy (HIE), as defined by Sarnat and Sarnat.¹² The asphyxiated neonates (case group) were monitored for seizures, hypotonia and HIE in the immediate neonatal period in the NICU. Cord blood sample was drawn in the labour room and sent for analysis of serum electrolytes, serum calcium, serum glucose, serum uric acid levels and serum creatinine levels. Calcium, uric acid and glucose was estimated by A25 autoanalyzer of biosystems by Arsenazo, uricase peroxidase and glucose oxidase method respectively. Serum electrolytes were analysed by ST-100 autoanalyzer.

Statistical methods

Descriptive and inferential statistical analysis has been carried out in the present study. Significance is assessed at 5% level of significance. Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Leven’s test for homogeneity of variance has been performed to assess the homogeneity of variance.

RESULTS

Among the cases, 73 (58.9%) neonates were delivered normally, 37 (29.8%) were delivered by caesarean section and 14(11.3%) had instrumental delivery. Among the controls 104 (83.9%) were delivered normally, 20 (16.1%) neonates by caesarean section and none had instrumental delivery. The mean weight in cases was 2.93±0.35 kg and 2.95±0.33 kg among control group.

Table 1: Gender distribution of neonates studied.

| Gender | Cases (n=124) | Controls (n=124) | P value |
|--------|--------------|-----------------|---------|
| Male   | 73 58.9%     | 75 60.5%        |         |
| Female | 51 41.1%     | 49 39.5%        |         |
| Total  | 124 100%     | 124 100%        |         |

Table 2: Distribution of Apgar score in two groups of neonates studied.

| Apgar score | Cases (n=124) | Controls (n=124) | P value |
|-------------|---------------|-----------------|---------|
|             | No. | %  | No. | %   |       |
| At 1 minute |     |    |     |     | <0.001** |
| 0-3         | 15  | 12.1 | 0   | 0.0 |       |
| 4-6         | 109 | 87.9 | 0   | 0.0 |       |
| 7 and above | 0   | 0   | 124 | 100.0 |       |

Table 3: Distribution of HIE stage in case group.

| HIE stage | Number of neonates (n=124) | % |
|-----------|----------------------------|---|
| Stage 0   | 0                          | 0 |
| Stage 1   | 80                         | 64.5 |
| Stage 2   | 32                         | 25.8 |
| Stage 3   | 12                         | 9.7 |
| Total     | 124                        | 100.0 |

Figure 1: Comparison of serum calcium values in the three stages of HIE of neonates studied.

Among the asphyxiated neonates serum sodium, calcium and glucose levels in arterial cord blood was significantly lower and has a linear correlation with the severity of birth asphyxia and different stages of HIE. The serum potassium and serum creatinine levels were higher in asphyxiated neonates and were correlating with the severity of asphyxia.
Table 4: Comparison of biochemical parameters in three stages of HIE of neonates studied.

| Biochemical parameters | HIE Stage 0 (controls) | Stage 1 | Stage 2 | Stage 3 | p value |
|------------------------|------------------------|---------|---------|---------|---------|
| Sodium (Na) meq/l      | 137.38±3.23            | 135.4±3.38 | 132.13±3.21 | 126.25±2.95 | <0.001** |
| Potassium (k) meq/l    | 4.43±0.80              | 4.75±0.82  | 4.77±0.93  | 5.30±0.54  | 0.001   |
| Chloride meq/l         | 100.91±5.22            | 100.32±4.46 | 100.82±4.81 | 99.71±4.86  | 0.483   |
| Calcium mg/dl          | 9.81±0.60              | 9.47±0.73  | 8.73±0.54  | 8.14±0.18  | 0.001*  |
| Uric acid mg/dl        | 4.50±0.59              | 5.06±1.11  | 5.23±0.95  | 5.70±0.92  | 0.001   |
| Glucose mg/dl          | 77.75±19.97            | 86.35±40.40 | 64.03±28.26 | 52.75±15.78 | 0.001*  |
| Creatinine mg/dl       | 0.55±0.12              | 0.76±0.13  | 0.95±0.21  | 1.09±0.215 | 0.001   |

DISCUSSION

Perinatal asphyxia is a devastating clinical condition because of its potential for causing permanent damage, even death of the fetus or newborn infant. The Apgar score has a limited role in predicting the immediate outcome, such as that of HIE and the long-term sequelae.

The results of the present study were in concordance with those of Basu et al, reported that serum sodium (122.1±6.0 meq/l) and calcium (6.85±0.95 mg/dl) levels were significantly lower in asphyxiated neonates, compared to non-asphyxiated neonates serum sodium (138.8±2.7 meq/l; p<0.001) and calcium (9.50±0.51 mg/dl; p<0.001) levels. They also found a significant positive correlation between serum levels of sodium and calcium with the Apgar score. Basu et al also came to a conclusion that serum calcium levels (8.7mg/dl) were significantly lower in asphyxiated neonates, compared to non-asphyxiated neonates serum calcium (9.50±0.51 mg/dl; p<0.001). They also found a significant positive correlation between serum levels of sodium and calcium with the Apgar score. Basu et al also found a significant positive correlation between serum calcium and the Apgar score and a significant negative correlation between them and stages of HIE. Gupta et al found that serum creatinine values (1.08±0.49mg/dl) were higher in asphyxiated infants compared to non-asphyxiated infants.

Our results are in concordance with Alphonsus et al and Najaf et al which concluded that asphyxiated neonates had lower serum calcium levels compared to controls. While numerous indicators for asphyxia are recognized, no single indicator has been found to be predictive of subsequent morbidity. However, we found the umbilical cord arterial sodium, calcium and glucose estimation to be a good, simple screening test for the early assessment of perinatal asphyxia. Furthermore, there is a correlation between the degree of hyponatremia, hypocalcaemia and hypoglycaemia and the severity of the encephalopathy, indicating the degree of injury at an early stage when other quantitative methods frequently cannot be carried out.

Limitations

Cord Blood pH was not taken into consideration which can affect serum potassium level. Our classification of HIE was according to Sarnath and Sarnath stage which is simple but it doesn’t take various parameters into consideration like EEG and pH. Intravenous fluid and oxytocin used in pregnant women might affect the electrolyte status in mother and hence in the newborn. This was also not taken into consideration.

CONCLUSION

There is a need to identify neonates who will be at high risk for HIE and early neonatal death as a consequence of perinatal hypoxia. So estimation of umbilical cord arterial serum sodium, serum calcium and glucose concentration...
is an easy and affordable test and at the same time early biochemical marker of birth asphyxia which biochemically supports the clinical diagnosis and severity grading of asphyxia by Apgar score and correlates well with the severity of HIE. Knowledge of these abnormalities among asphyxiated new-borns is very valuable to the paediatricians as it is an important variable affecting perinatal mortality.

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