STUDY OF CK-MB IN NEONATAL ASPHYXIA AND ITS CORRELATION WITH DIFFERENT STAGES OF HYPOXIC ISCHAEMIC ENCEPHALOPATHY

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ABSTRACT

BACKGROUND
Perinatal asphyxia is one of the leading causes of neonatal morbidity and mortality in the neonatal intensive care unit. Hypoxic ischaemic encephalopathy (HIE) refers to clinically observable CNS dysfunction associated with perinatal asphyxia.

The aim of the study is to determine the serum levels of cardiac marker (CK-MB) in newborns with perinatal asphyxia and its relationship with different stages of HIE.

MATERIALS AND METHODS
We have measured the serum concentration of CK-MB by Creatine Kinase method in 100 asphyxiated newborns (cases) and 100 healthy newborns (control group). Blood samples were collected on day 1 and day 3 of life in all newborns.

RESULTS
The mean serum values of CK-MB were found to be decreased on day 3 in asphyxiated neonates and a negative correlation was seen between day 1 and 3 for CK-MB. The mean values of CK-MB were decreased in different stages of HIE on day 3 as compared to day 1 and a negative correlation was observed between day 1 and day 3 for CK-MB in no HIE, HIE I, HIE II and HIE III stages.

CONCLUSION
We conclude that serum CK-MB concentrations were increased considerably after birth asphyxia, and the increase is associated with the severity of HIE with a poorer outcome.

KEYWORDS
Hypoxic-Ischemic Encephalopathy, Creatine Kinase.


BACKGROUND
Birth asphyxia refers to an impairment of the normal exchange of respiratory gases during parturition, and the ensuing adverse effects on the foetus. It is an important cause early neonatal death. It is probably better to use the term perinatal asphyxia since asphyxia may occur in utero, at birth or in the postnatal period. There is need for the identification of asphyxiated neonates who have a high risk for developing HIE and multi-organ dysfunction. When enough oxygen is not received by a baby before, during or after birth it leads to Birth asphyxia: It is a foetal or newborn insult due to hypoxia (lack of oxygen) and /or ischemia lack of perfusion (lack of perfusion) to various organs.1

During an asphyxic event, several physiological mechanisms occur to preserve the functions of vital organs such as the brain and heart. However other organs like the kidneys, GIT and skin are affected depending upon the duration of the episode.2,3

It may however progress to HIE which mainly involves the brain and the heart,4 inspite of all the compensatory mechanisms.

The Brain, Heart, Kidneys, GIT and Bone marrow are the main organs affected by perinatal asphyxia. The most frequent abnormalities involving kidneys (50%) followed by CNS (28%), cardiovascular (25%) and pulmonary system (23%)5 The degree of multi-organ dysfunction (MOD) predicts whether an asphyxiated neonate succumb due to
organ damage or recover completely. Generally, there are no long-term sequelae associated with these organ system derangements.

HIE (Hypoxic ischemic encephalopathy) refers to CNS dysfunction associated with neonatal asphyxia. In an asphyxiated neonate, HIE is of foremost concern because along with other system derangements it may lead to serious long-term neurological sequelae among survivors.

Nearly two-thirds of deaths of neonates occur each year within the first seven days of life due to asphyxia and thus the first few days of life are critical for the survival of a child and future health.

Cardiovascular instability, pulmonary dysfunction, hepatic impairment, gastrointestinal disorders and acute renal failure may be the cause of multiorgan dysfunction (MODS) and failure.\(^6\)\(^7\)\(^8\)

In most cases, multi organ dysfunction occurs as a result of systemic hypoxic-ischemia. Cardiac dysfunction is caused by transient myocardial ischemia and its incidence in perinatal asphyxia varies from 24–60%.\(^9\)

Myocardial damage may be determined by raised serum Creatine kinase MB fraction or cardiac troponin levels.

**MATERIALS AND METHODS**

The study was conducted in the department of Biochemistry S.A.I.M.S. Medical College & P.G. institute, Indore. The work included 100 asphyxiated newborns and 100 healthy newborns served as control group. The study was carried out in the following categories:

1. Control vs. Patients.
2. Day Wise as:
   - Within the group on day 1 and day 3.
   - Between cases and control on day 1 and day 3.
3. According to different stages of HIE: in cases:
   - Stage 0 (no HIE)
   - Stage I (mild)
   - Stage II (moderate)
   - Stage III (severe)

**Inclusion Criteria**

The newborns admitted in the Paediatrics Department and its neonatal intensive care unit were included in the study. A predesigned proforma for both the groups was taken to record the Gestational age, birth weight, relevant perinatal history, findings on physical examination and systemic signs.

**Exclusion Criteria**

Exclusion criteria for both the groups were congenital anomalies, tumours, maternal drug addiction, severe infections and congenital mental disorders.

- Consent from the Institutional Ethical Committee was also taken to carry out the above research.
- Venous blood sample was drawn from all subjects in plain tube on day 1 and day 3 of life. The serum was separated by centrifugation.

Serum CK-MB - was analysed on Vitros 950, dry chemistry auto analyser by recommended method for estimation of Creatine Kinase.\(^1\)\(^0\)

**Statistical Analysis**

The present study was a case control study, and the method of sampling used was non-random-purposive. We used SPSS Software version 16 (IBM Corp) for statistical analysis. To compare between control and cases group, we used statistical tools-descriptive statistics, diagrammatic representation, unpaired t-test and paired t-test. Pearson’s correlation coefficient (two-tailed) was used to calculate Correlation. Software STATA (Stata Corp. LP) was used to calculate Confidence.

**RESULTS**

In our study total 100 asphyxiated neonates and 100 healthy neonates were included. The mean gestational age of cases is 38.02 ± 2.53 and of controls is 38.44 ± 2.22. The mean birth weight in cases and controls were 2.68 ± 0.69 and 2.77 ± 0.54 respectively. Number of male/female in the cases and controls were 67/33 and 54/46 respectively. The number of babies delivered by vaginal/caesarean lower segment caesarean section in cases and controls were 58/60 and 42/40 respectively (Table 1). Of the 100 cases, 2 asphyxiated neonates expired on day 3. Out 100 asphyxiated neonates, 18 had no HIE, 20 developed HIE Grade I, 41 Grade II, and 21 Grade III.

The concentrations of serum CK-MB on day 1 and day 3 were found to be statistically highly significant in the asphyxiated group as compared to the control group (P < 0.001). Serum CK-MB concentrations in asphyxiated neonates on day 1 was 133.18 ± 265.24 U/L while on day 3 was, 73.91 ± 80.67 U/L (Table 2).

Among the infants having HIE, the mean serum value of CK-MB in Stage 0 (No HIE), HIE I, HIE II and HIE III were found to be 46.78±19.61 U/L, 59.89±16.54 U/L, 124.27±133.72 U/L and 293.48±522.31 U/L respectively on day 1.

On day 3, the mean serum value of CK-MB in Stage 0 (No HIE), HIE I, HIE II and HIE III were found to be 29.39±15.24 U/L, 32.70±14.35 U/L, 73.30±69.32 U/L and 156.40±110.09 U/L respectively (Table 3).

The mean values of CK-MB were found to be decreased in different stages of HIE on day 3 as compared to day 1 in asphyxiated neonates.

<table>
<thead>
<tr>
<th>Demographic Variables</th>
<th>CASES</th>
<th>CONTROLS</th>
</tr>
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<tbody>
<tr>
<td>Number of newborns</td>
<td>100</td>
<td>100</td>
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<tr>
<td>Gestational age(weeks)</td>
<td>38.02±2.53</td>
<td>38.44±2.22</td>
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<tr>
<td>Birth Weight (Kg)</td>
<td>2.68±0.69</td>
<td>2.77±0.54</td>
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<tr>
<td>Male/Female</td>
<td>67/33</td>
<td>54/46</td>
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<tr>
<td>No. of vaginal deliveries</td>
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<td>60</td>
</tr>
<tr>
<td>No. of LSCS deliveries</td>
<td>42</td>
<td>40</td>
</tr>
</tbody>
</table>

**Table 1. Demographic Profile of Study Group (Cases) and Controls**

LSCS: Lower Segment Caesarean Section
The concentration of serum CK-MB is an important biochemical marker of neonatal myocardial damage. The major disadvantage of CK-MB is lack of its cardiac specificity in children below four years of age, it lacks cardiac specificity. In the neonatal period CK-MB is also present in skeletal muscle. After myocardial injury, abnormal CK-MB activity can be detected within 3-6 hours, reaches peak in about 12–24 hours and returns to normal by 3rd day. This could explain the decrease in CK-MB on day 3.

A high concentration of CK-MB protein is present in serum of healthy infants as compared to adult reference limits. Thus, the adult upper reference limit for CK-MB should not be used for infants. Furthermore, the relation between enzyme concentrations and gestational age should also be considered while interpreting concentration of this marker after birth. The reason is probably increased synthesis of the B subunit in skeletal muscle of foetus. Therefore, cardiac Troponin T is more specific and reliable marker of cardiac damage.

CONCLUSION
On day 3, decreased mean serum values of CK-MB were found in asphyxiated neonates and a negative correlation was seen between day 1 and 3. The mean values of CK-MB were decreased in different stages of HIE on day 3 as compared to day 1 and a negative correlation was observed between day 1 and day 3 for CK-MB in no HIE, HIE I, HIE II & HIE III stages.

This shows a greater myocardial involvement in severely asphyxiated infants.

REFERENCES


