ORIGINAL RESEARCH PAPER
Volume-8 | Issue-10 | October - 2019 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

CREATINE PHOPSHOKINASE (MUSCLE BRAIN - FRACTION) ISOENZYME MASS CONCENTRATIONS IN ASPYXIATED TERM NEONATES

Pediatrics

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ABSTRACT

INTRODUCTION- Perinatal asphyxia is a major factor contributing to perinatal and neonatal morbidity and mortality. Elevation of Creatine Phosphokinase Muscle brain Fraction (CPK –MB) isoenzymes in cord blood is a biochemical marker of perinatal asphyxia..

MATERIAL AND METHOD- This study was carried out on 120 term newborn babies in a neonatal unit of a tertiary care hospital in a rural setting of North Haryana ,out of 1352 total no ofdelieveriesfrom October 2016 to Jan 2018with equal number of cases and controls(60 each), control group being the newborns with APGAR score >7 at 1 & 5 minute of life and cases being the newborns who suffered from perinatal asphyxia with APGAR score <7 at 1& 5 minute of life.CPK -MB levels among cases and controls and among different grades of birth asphyxia of cordblood and at 6 hours of life were compared..

CONCLUSION- A strong correlation between the CPK MB levels of cases with increasing severity of birth asphyxia was documented.

KEYWORDS

Perinatal asphyxia ,creatine phosphokinase muscle brain fraction (CPK MB)

INTRODUCTION

Perinatal hypoxia is one of the leading causes of mortality and morbidity in developing countries like India, and even in developed countries. Asphyxia is an important cause of static developmental and neurologic handicaps both in Term and Preterm infants[1]

Perinatal asphyxia is defined as a condition in which impairment of exchange of the respiratory gases (oxygen and carbon dioxide) results in hypoxemia and hypercapnia,accompanied by metabolic acidosis.[2]

Perinatal asphyxia is a major factor contributing to perinatal and neonatal mortality, which is an indicator of the social and educational standards of a community.[3]Apgar score is a scoring system that is a fast and important method of assessing the clinical status of the newborn infant at 1st,5th,10th minute of age[4]

Creatinine kinase and its isoenzymes elevate because of ischemia induced leakage of enzymes from injured tissues due to hypoxic insult.Therefore, marked elevation of CK- MB maybe a sensitive indicator of myocardial damage.[1]

The MB isoenzyme of CK has the advantage over total CK as the concentrations are not found to be significant in extra cardiac tissues in comparison with its MB isoezyme and is therefore considered more specific. It has been found by various studies that there is elevation of creatinine kinase and its isoenzyme in asphyxiated infants as compared to the normal.[5,6,7]

CPK MB catalyzes the reversible transfer of the phosphoryl group from phosphocreatine to adenosine diphosphate, to regenerate adenosine triphosphate (ATP) [8]. Brain damage, low birth weight, term of delivery and skeletal injuries during delivery could be related to higher CK activity in cord blood [9]Persistent high activity may implicate some conditions such as rhabdomyolysis and significant brain injuries [10,11,12]. Measuring the CK activity in the cord blood and then analyzing them with various parameters will help to assess its correlation with different perinatal events.[13]

Asphyxial injury may involve virtually every organ system of the body but Hypoxic Ischaemic Enchepalopathy(H.I.E) is the most studied clinical condition and that exhibiting the most serious equivalent[14]

HIE is of concern in an asphyxiated neonate because it can lead serious long term neuromotor sequlae among survivors. Several studies have been conducted to evaluate better markers to differentiate various grades of asphyxia in neonates. CPK – MB is an easily available tool for the assessment of severity of asphyxia in a term neonate with reference to the Apgar scores at 1 minute of life. Therefore in this study we will evaluate the grades of asphyxia in relation to the CPK levels.

MATERIAL AND METHOD

This Prospective, Observational Case and Control study was conducted at a tertiary care centre of a teaching hospital during the period of October 2016 to January 2018. The protocol of the study was approved by the institute's ethics committee and written Informed consent was obtained from parentsof each neonate. APGAR score of newborns was evaluated at 1,5 and 10 min .[15] 60 term neonates who suffered from Perinatal asphyxia with Apgar score <7 at 1 minute of life were included and 60 term neonates who were born with Apgar score >7 at 1 minute of life were taken as controls.Preterm neonates (gestational age < 37 weeks), neonates with congenital malformation.- neonates of the parents who did not giving consent were excluded. Detailed maternal history, assessment of intrauterine fetal well being and other relevant information was recorded as per the Performa. They were managed in Neonatal Intensive Care Unit as per the managing consultant.

BIRTH ASPHYXIA

Grades of asphyxia at time of admission were categorized as per the Apgar score at 1 minute of life of neonates as per NNPD guidelines:Moderate perinatal asphyxia: slow/gasping breathing or an apgar score of 4 to 6 at 1 minute.Severe perinatal asphyxia: no breathing or an APGAR score of 0-3 at 1 minute of life.

- Upon delievery , a specimen of cordblood (2ml)was collected from eligible neonates categorized as cases and controls for measurement of CPK –MB and cord blood pH. After admission to NICU, all asphyxiated neonates(cases) were managed as per the managing consultant and (2 ml)venous blood at 6 hours of life in plain vial was collected.

Creatine phosphokinase - muscle brain fraction (CPK-MB) was measured by quantitative determination based on immunoassay using auto analyzer that is Siemens Dimension Clinical Chemistry System using MBI Flex reagent cartridge, Cat . No Df32.

STATISTICAL ANALYSIS

The qualitative variables have been expressed as percentages and quantitative variables have been expressed as mean and standard deviation. Association among qualitative data has been established using Mann Whitney U test and spearman's correlation. The correlation between quantitative data was established using t – test . P <0.05 was taken as significant at 95% confidence interval . All the analysis was carried out using SPSS version 20.

RESULTS

During the study period 60 neonates admitted admitted to NICU were diagnosed to have perinatal asphyxia. These neonates were matched against 60 healthy neonates taken as controls. TABLE 1 compares the baseline characteristics of asphyxiated and control neonates . both were matched for gender, cord blood ph and CPK MB of cord blood. The male: female ratio in cases was 1.4:1, whereas it was 1.77 :1 in control group which was not significant. Cord blood pH of asphyxiated neonates was significantly lower than controls (p<0.001).

The serum CPK MB mass concentrations of asphyxiated infants were significantly higher than those of controls (p <0.001)(TABLE 1)

TABLE 1

Variables	Perinatal asphyxia (n =60)	Controls (n = 60)	p values
Males	35	32	NS
Females	25	28	NS
Cord blood ph Mean (SD)	6.182(0.408)	7.6(0.2623)	<0.001
CPK MB CBMean(SD)	649.13(528.429)	120.40(63.280)	<0.001

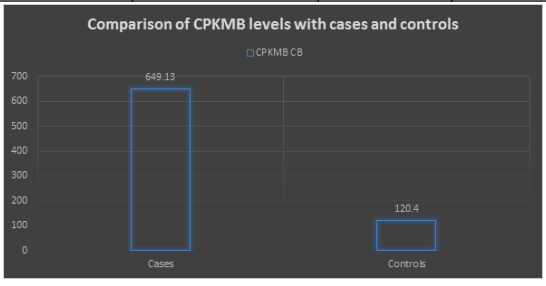

Figure 1

Above bar diagram compared CPK MB of cord blood at birth of cases and controls and concluded it to be statistically significant (p<0.001).(figure 1)

CPK MB OF CORD BLOOD AND AT 6 HOURS WITH SEVERITY OF ASPHYXIA

The serum CPK MB concentrations of asphyxiated neonates were significantly higher in cases of severe asphyxia in comparison to moderate asphyxia at birth than those at 6 hours of life (p<0.001) as depicted in the Table 2.The enzyme levels were considered abnormal when it were above our refrence laboratory values (CPK MB >25U/L).

TABLE 2		Severity of Asphyxia	NO	Mean	Mean difference	P-value#
Cases	CPKMB (CB)	Mod PA	45	628.711	486.819	0.005
		Sev PA	15	1115.53		
	CPKMB 6HRS	Mod PA	45	282.244	51.826	0.116
		Sev PA	15	334.07		

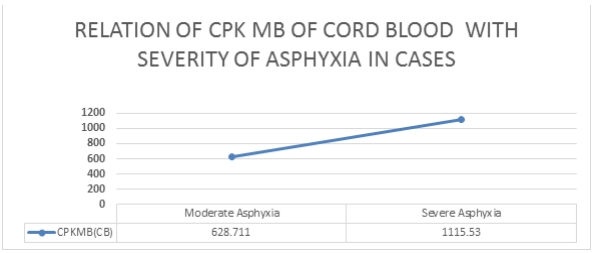

Figure 2 :Comparison of CPK MB isoenzyme between neonates with moderate and severe asphyxia.

CPK MB AND RELATION WITH HIE AND IT'S GRADES IN CASES

TABLE 3	NO OF BABIES	MEAN CPK MB CB	MEAN CPK MB 6HRS
HIE 1	5	556.80	380.40
HIE 2	9	925.22	287.89
HIE 3	13	1181.00	366.54

In our study out of 60 cases suffering from birth asphyxia , 27 (45%) suffered from Hypoxic ischemic encephalopathy . Further they were subdivided into HIE 1 , 2 ,3 on the basis of Levene staging .Out of 27 ,5 (18%)suffered from HIE -1, 9(33%) cases as HIE -2, and 13(48%) graded as HIE- 3. The table 3 compares CPK MB levels at birth and at 6 hours with HIE . The correlations between these levels at various grades was found to be significant (p< 0.001)

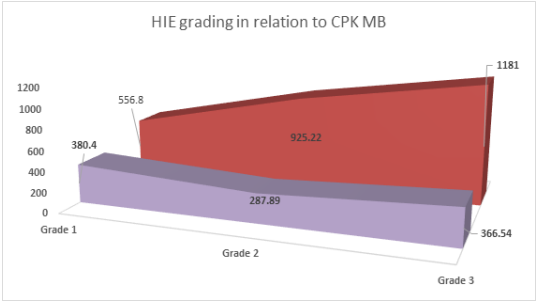

Figure 3:HIE grading in relation to CPK MB .

Out of the total 60 cases ,11(18%) did not survive and their mean enzyme values are mentioned in the table with statistical significance(p value -0.003) for cord blood CPK MB level.(Table 4)

TABLE 4		Survival Status	N0	Mean	Mean difference	P-value
Cases	CPK- MB (CB)	SURVIVED	49	645.98	572.599	0.003
		NOT SURVIVED	11	1218.9		

DISCUSSION

Perinatal asphyxia remains one of the most important fields of research for pediatrician , and innumerable studies have been conducted on the various aspects of perinatal asphyxia.. Increased CPK activity is due to ischemia induced leakage of enzymes therefore marked elevation may be a sensitive indicator of myocardial damage.

Birth asphyxia

The CPK MB cord blood levels were recorded both in cases(term asphyxiated neonates) and controls(term healthy neonates) .In our study , all the cases that is term neonates with birth asphyxia had significant high concentration CPK MB levels , the p value being <0.001 which is highly significant. A Agrawal et al[16] in their study in 2012; concluded that abnormal cardiac enzyme levels are found in neonates with high birth asphyxia and can lead to poor outcome due to myocardial damage which supports the results in our study.

Yun boo N et al[17] in 2005 did a study and showed that at birth,asphyxiated neonates had significantly higher concentrations of CPK MB than the normal neonates , p value being highly significant (p value <0.001) ; supporting the conclusion of our story.

The CPK MB levels of cases having severe birth asphyxia at birth were significantly elevated than moderate perinatal asphyxia and statistically significant (p value 0.005). The mean CPK MB levels of cases at birth having moderate birth asphyxia was 628.71IU/L while those having severe birth asphyxia at birth was 1115.53 IU/L clearly depicting that there is a significant change amongst these two groups and favouring the severity of HIE grade.

HIE

In our study, we grouped the term neonates having birth asphyxia in three grades according tolevene staging. The following table depicts the grade of HIE in various studies.

TABLE 5

HIE GRADE	Agrawal J et al(16)	Senthil et al(1)	Present study
1	13(21.7%)	13(21.6%)	5(8.3%)
2	27(45%)	9(15%)	9(15%)
3	20(33.3%)	10(33.3%)	13(21.6%)

In our study there is a dramatic increase in theMean CPK MB levels with increasing severity of birth asphyxia.

Agrawal J. et.al[16], studied in 2012 about the enzymatic correlation with outcome in neonates with hypoxic ischemic encephalopathy and concluded that the CPK MB levels showed an exponential increase with increasing severity of birth asphyxia. The mean CPK MB levels in their study was 75 , 100 and 260 IU/L in grade 1,2,and 3 birth asphyxia respectively which is in favour of results of our study. The CPK MB levels are quite higher with increasing severity of birth asphyxia in our study , further concluding that high CPK MB levels and severity of birth asphyxia go hand in hand.

CONCLUSION

This study suggests CPK MB levels rise with increasing severity of birth asphyxia .CPK MB levels were not affected by gender in our study.

What is already known on this topic -Cord blood Ph is significantly low in asphyxiated neonates

What this study adds - CPK MB levels correlate with severity of asphyxia.

ACKNOWLEDGEMENTS

Authors would like to thank Department of Obstetrics and Gynecology, Department of Biochemistry, M.M.I.M.S.R, MMU, Mullana, India for their support in conducting this study.

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