ORIGINAL RESEARCH PAPER

Paediatrics

CO-RELATION OF CREATINE KINASE–MYOCARDIAL BOUND (CK-MB) FRACTION LEVELS IN NEW BORNS WITH PERINATAL ASPHYXIA AND ITS ASSOCIATION WITH ITS MORBIDITY PROFILE

KEY WORDS: CK-MB level, HIE, perinatal asphyxia, respiratory distress ,shock

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ABSTRACT

Introduction- Perinatally asphyxiated newborns have no definitive diagnostic marker. In this study we have assayed the level of serum CK-MB level in such newborns and tried to correlate these levels with perinatal asphyxia and its morbidity profile such as HIE, respiratory distress and shock. **Objective-** To correlate Apgar score with the rise of CK-MB in perinatal asphyxia and to correlate the morbidity profile of a perinatally asphyxiated newborn with rise in serum CK-MB level. **Methodology-**Apgar scoring is done at 1minute of life in all perinatally asphyxiated newborn .Then 2 blood samples were collected for serum CK-MB level at 5-8 hours and at 24-33 hours of birth. Serum CK-MB levels were used to correlate with Apgar scoring at 1minute of life and the 3 major morbidities of perinatal asphyxia i.e hypoxic ischemic encephalopathy (HIE) ,shock and respiratory distress(RDS). **Results-**Serum CK-MB level was raised in all asphyxiated newborns. Those who had raised CK-MB values at 5-8 hours had poor Apgar score at 1 min of life(p value of 0.001) .Those who had raised CK-MB at 5-8 hours and 24-33 hours, most of them had and developed HIE and RDS . At 5-8 hours correlation of HIE with CK-MB values revealed sensitivity 92.15 %, positive predictive value(PPV) 74.60%. Correlation of shock with CK-MB revealed sensitivity of 100% %, PPV of 31.74% and negative predictive value(NPV) of 100%. Correlation of CKMB with RDS revealed the sensitivity of 89.09%, PPV of 77.78%. Correlation of HIE and raised CK-MB at 24-33 hours has sensitivity of 94.1%,PPV of 77.41%,NPV of 62.5%. Correlation of respiratory distress and raised CK-MB at 24-33 hours has sensitivity of 90.1%,PPV of 80.64. Correlation of shock and raised CK-MB had poor specificity, PPV and NPV. **Conclusion-** Raised CK-MB at 5-8 hours is associated with poor Apgar score at 1min of life. Raised CK-MB level at 5-8 hours and 24-33 hours is associated with HIE and respiratory distress in an asphyxiated newborn.

Introduction

The signs of perinatal asphyxia (PA) injury in a neonate are nonspecific and overlap with other illnesses. Newborns who have suffered perinatal stress develop CNS depression on 1st day of life along with respiratory distress or shock though their metabolic screen, sepsis parameters are normal .We can only get to know the cause of CNS depression by reviewing the antenatal records. No definite biochemical marker is available to diagnose a neonate who has suffered perinatal asphyxia. Perinatal asphyxia is associated with a significant myocardial injury which leads to raised Creatine Kinase-Myocardial Bound (CK-MB) fraction levels.1 We had conducted this study to know whether this altered serum CK-MB levels in the perinatally asphyxiated neonates is related to poor Apgar score and whether it is associated with the three major morbidites i.e hypoxic ischaemic encephalopathy (HIE), respiratory distress(RDS) and shock.

Method

Study setting: The present cross sectional study was conducted between for the period of one year in the Department of Pediatrics of a medical college in Tanda, Kangra Himachal Pradesh after due approval from Institutional Ethics committee of the institute.

Selection Criteria:

Inclusion Criteria: Inborn neonates(IB) with gestational age >37 weeks withApgar score of <7 at one minute of life, resuscitation with >1 minute of positive pressure ventilation before stable spontaneous respiration appropriate for gestational age and had intrapartum signs of fetal distress, as indicated by non-reassuring fetal heart rate, meconium staining of the amniotic fluid. Outborn (OB) asphyxiated neonates with a period of gestation >37 weeks and were referred from the periphery within 8 hours of birth with the history suggestive of perinatal asphyxia with or without resuscitation details available were also included in the study.

Exclusion criteria: were newborns <37 weeks gestation, congenital malformations, maternal drug addiction, chorioamnitis in mother, hypoglycaemic newborns, hypocalcemia in newborns, newborns born to mothers who would have received magnesium sulfate or opioids within 4 hours prior to delivery (pharmacological depression), and parents not willing to give consent.

Baseline data collection and management:

Enrolled newborns were divided into 2 groups. For the inborn newborns complete maternal history, birth events, birth resuscitation details, and Apgar score was noted at 1 minute of life2.For the neonates who were born outside our hospital and reported within 8 hours of life, only maternal details and birth details were noted. 2 serum samples of 1 ml volume of each was collected and sent to the hospital laboratory for CK-MB level measurement. The first sample was taken at 5-8 hours of life and second sample at 24-33 hours of life. A serum CK-MB value at 5-8 hours>92.8 U/L and at 24-33 hours >60 U/L was taken as cut-off values for perinatal asphyxia.3 of CK-MB was assayed by immune-inhibition method by Beckman Coulter, Inc. 250S, Kraemer Blvd Brea, CA 92821, USA whose principle is based on International Federation of Clinical Chemistry method (IFCC).4A detailed clinical and neurological examination was done and treated as per protocol for the management of perinatal asphyxia. The asphyxiated neonates were monitored for signs of Hypoxic ischaemic encephalopathy (HIE),respiratory distress and shock in day 1st day of life. Clinical grading system by Sarnat and Sarnat was used to grade the severity of HIE.5All the details recorded in the patients proforma was put on Microsoft excel sheet for statistical analysis(Table-1). Statistical analysis had been done with the help of EPI info software.

Results:

Of the 49 inborn newborns, 43 (87.75%) newborns required positive pressure ventilation ,seven (14.28%) newborns

required chest compression , two (4.08%) required injection adrenaline. We found that out of 49 inborn newborn,36 (51.4%) newborns had score between 4 to 7 Apgar score at 1 minute of life,13 (18.5%) newborns had Apgar score at 1 minute of life between 0 to 3.We were unable to collect the Apgar score and resusitation details of outborn newborns.In all of the 49 inborrn and 21 outborn newborns CK-MB level was collected at 5-8 hours and 24-33 hours.The CK-MB level at 5-8 hours and poor Apgar score had p-value of 0.001. At 5-8 hours, 63(90%) newborns had CK-MB more than cut off range i.e 92.8 U/L. At 24-33 hours, 62(88.57%) newborns had a CK-MB level more than cut off range i.e 60 U/L. The range of CK-MB levels at 5- 8 hours was 50 U/L to 2056 U/L and mean was 376.13 U/L. At 24-33 hours, the range of CK-MB levels was from 46 U/L to 1919 U/L and mean was 227.19 U/L. We found that in most of the cases CK-MB levels remained above the respective cut-off points although it showed a decreasing trend from 5 to 33 hours.

At 5-8 hours most of them had features of respiratory distress, HIE, shock which were overlapping. Out of 70 newborns,7(10%) newborns had a CK-MB value less than 92.8U/L. Of them 4(5.71%) newborns developed HIE,6(8.57%) developed respiratory distress.63(90%) newborns had a CK-MB level more than 92.8 U/L. Of them 47(67.14%) developed HIE, 20(28.57%) developed shock,49(70%) had respiratory distress. Correlation of HIE with CK-MB revealed sensitivity was 92.15 %, specificity was 15.78%, PPV was 74.60% and NPV was 42.85%. Correlation of shock with CK-MB revealed sensitivity is 100% %, specificity is 14%, PPV is 31.74% and NPV is 100%. Correlation of CKMB with respiratory distress revealed the sensitivity of 89.09%, specificity 6.67%, PPV 77.78% and NPV 14.29%.

At 24-33hours of life out of 70 newborns, 8(11.42%) newborns had a CK-MB level less than cutoff i.e60 U/L. Of them 3 newborns(4.28%) had features of HIE,5(7.1%) had persistent respiratory distress.62(88.51%) newborns had a CK-MB level more than 60 U/L. Of them 48(68.57%) had HIE,20(28.57%) had shock requiring inotropes , 50(71.42%) had persistent respiratory distress. Correlation of CK-MB with HIE revealed the sensitivity of 94.11%, specificity 26.31%, positive predictive value 77.14% and negative predictive value 62.5%.Correlation of CK-MB with shock revealed the sensitivity of 100%, specificity 14%, positive predictive value 31.74% and negative predictive value 100%. Correlation of CK-MB with respiratory distress revealed the sensitivity of 90.91%, specificity 20%, positive predictive value 80.65% and negative predictive value 37.50%.

Discussion

Our study showed that those newborns who had suffered perinatal asphyxia had raised CK-MB level in most of them. Poor Apgar score at 1minute of life and raised CKMB level had a good correlation. Studies done by Fronseca etal6 showed that antepartum fetal distress is associated with release of CK-MB, which indicate brain and myocardial damage. Similar results were also seen in related studies. But Moller etal7 showed the cardiac enzyme, cardiac troponin T is more sensitive in identifying newborns with asphyxia and circulatory failure but CK-MB has no diagnostic value. Szymankiewicz etal8 showed both cardiac troponin T and CK-MB level are strong indicators of myocardial injury due to perinatal asphyxia.

Jedeiken described that the normal levels of all iso-enzymes of CK in newborns peaked at 5-33 hours postnatally.12 Reddy etal also documented that CK-MB levels raised in other sick infants, but the magnitude of elevation is higher in asphyxiated neonates .1If a newborn suffered perinatal asphyxia and born outside proper hospital set up and we don't know the birth history, we can do serum CK-MB level to rule out perinatal asphyxia.

Our study also documented increased level of CK MB from 5-8 hours and fall by 24-33 hours.

Organ dysfunction in asphyxiated neonates depends on the duration of asphyxia and the early management. Our study found that those newborns who had raised CK-MB levels at 5-8 hours and 24-33 hours approximately 73% developed HIE though we could not correlate the severity of HIE with raised CK-MB levels. Agrawal etal9 had revealed increased CK-MB with the severity of HIE. Sanjay etal10 had showed that raised CK-MB cut off donot correlate with the severity of HIE.

Out of 63 newborns who had raised CK-MB at 5-8 hours, 20 (32.25%) developed shock. At 24-33 hours those 20 required persistent inotropic support. No patient developed shock who had low CK-MB level. On statistical correlation of CK-MB level with shock revealed good sensitivity but had poor specificity, negative predictive value and positive predictive value. Similar result is shown by Primhaketal11, Jedeikinetal12 which revealed though myocardial injury is associated with raised CK-MB level but it lacks cardiac specificity. Kang etal had13 compared CK-MB with Troponin T and showed Trop-t to be more cardiac specific diagnostic marker.

Fifty five(78.57%) neonates developed respiratory distress .Correlation of CK-MB level with respiratory distress revealed good sensitivity and positive predictive value but lacks specificity. Agrawal et al9 found that out of 60 neonates respiratory distress was present in 32 (53.33%) neonates. Rajakumar et al studied in 30 neonates and reported respiratory distress in 20 (66.7%) neonates.[14]

Limitations of this study is that we could not collect the reliable resuscitation details and Apgar scoring of the outborn newborns.To assess myocardial injury we had included shock as the parameter but we had not included ECG and echocardiography .We could not correlate the severity of HIE ,myocardial injury and respiratory distress with the levels of CK-MB.

Conclusion: High CK-MB level at 5-8 hours of life is associated with poor Apgar score at 1 minute of life. If a baby born outside hospital setup had high CK-MB level at 5-8 hours then the baby must have poor Apgar score at 1min of life. Raised CK-MB levels at 5-8 hours and 24-33 hours is associated with HIE and respiratory distress but it is not myocardial injury specific isoenzyme.

Recommendation-CK-MB levels to be done at 5-8 and 24-33 hours of life.

Table I- Patient charecteristics.
Table II- Correlation of raised CK-MB level with morbidity profile.
Table III- Statistical Correlation of raised CK-MB level with morbidity profile.
Figure I-Study design.

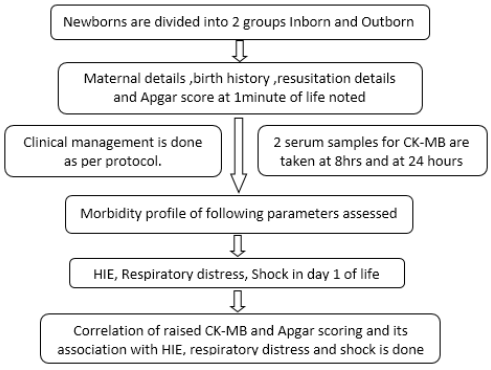

Figure 1 : Study Design

Table-I Patient characteristics

Patient characteristi	Newborns With PA (n=70)			
	Inborn-49(70%)		Outborn-21(30%)	
Gender	Male-31(63.26%)	Female-18(36.73%)	Male-14 (66.66 %)	Female-7 (33.33%)
Antenatal morbidity of Mother	14		7	
Parity of mother	Primigravida-30	Multigravida-19	Primi Gravida-14	Multi Gravida-7
Abnormality in fetal heart Rate	43			Data not known
Meconium stained liquor	30			17
Mode of delivery	NVD -21	LSCS -21	Instrumental delivery-7	Normal vaginal delivery

Table II- Correlation of raised CK-MB level with morbidity profile

Cut-off value		HIE				Respiratory distress		Shock	
		No HIE	I	II	III	present	Absent	present	Absent
CK-MB at 5-8 hours (U/L) (n=70)	<92.8	3 (4.2 %)	4 (5.71 %)	0	0	6 (8.57 %)	1 (1.4 %)	7(10 %)	0
	>92.8	16 (22.85%)	19 (27.14 %)	16 (22.85%)	12 (17.14%)	49 (70%)	14 (20 %)	43(61.42%)	20(28.7 %)
CK-MB at 24-33 hours (U/L) (n=70)	<60	5(7.1 %)	2 (2.8%)	1 (1.4 %)	0	(7.1 %)	(4.28%)	8(13.33%)	0
	>60	14 (20 %)	21 (30%)	15 (21.42%)	12(17.14%)	50 (71.42%)	12 (17.14%)	42(60 %)	20(28.57 %)

Table III- Statistical Correlation of raised CK-MB level with morbidity profile

CK-MB	HIE				Shock				Respiratory distress			
	Sensitivity	specificity	PPV	NPV	Sensitivity	specificity	PPV	NPV	sensitivity	specificity	PPV	NPV
5-8 hours	92.15%	15.78 %	74.60 %	42.85 %	100%	14%	31.74%	100 %	89.90%	6.67 %	77.78%	14.29%
24-33 hours	94.11%	26.31 %	77.41 %	62.5 %	100%	16%	32.26%	100 %	90.91%		80.64%	37.50%

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