Original Article

Cardiac Enzyme Levels in Myocardial Dysfunction in Newborns with Perinatal Asphyxia

P.S. Rajakumar, B. Vishnu Bhat, M.G. Sridhar[1], J. Balachander[2], B.C. Konar[1], P. Narayanan and G. Chetan

Department of Paediatrics, [1]Biochemistry and [2]Cardiology, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India

ABSTRACT

Objective. To study the usefulness of cardiac enzymes in evaluating myocardial damage in perinatal asphyxia.

Methods. Thirty term babies with perinatal asphyxia and without any congenital malformations were selected as cases. They were compared with thirty healthy term babies without asphyxia. Myocardial dysfunction was evaluated using clinical, electrocardiography, echocardiography and cardiac enzymes i.e, troponin-T and CK-MB levels.

Results. Among the 30 cases 23 had evidence of myocardial involvement while one baby in the control group had ECG evidence compatible with cardiac involvement. Cardiac enzymes were significantly increased in babies with perinatal asphyxia. The mean level of C-troponin-T among cases and controls were 0.22±0.28 and 0.003±0.018 while CK-MB levels were 121±77.4 IU/L and 28.8 ± 20.2 IU/L respectively. C-troponin-T had higher sensitivity and specificity compared to CK-MB levels. Moreover, C troponin-T levels correlated well with severity and outcome in babies with perinatal asphyxia.

Conclusion. C-Tropopnin assay is useful in evaluating the severity of myocardial damage and outcome in perinatal asphyxia.
[Indian J Pediatr 2008; 75 (12) : 1223-1225] *E-mail: drvishnubhat@yahoo.com*

Key words : *Perinatal asphyxia; Myocardial damage; Cardia troponin-T; CK-MB enzyme; Outcome*

Perinatal asphyxia is a common problem with the incidence varying from 0.5 – 2% of live births.[1,2] The incidence of clinical cardiac dysfunction in perinatal asphyxia varies from 24–60%. The present study was to evaluate the role of cardiac enzymes especially cardiac Troponin-T in the diagnosis of myocardial dysfunction.

MATERIALS AND METHODS

This prospective case controlled study was conducted in the Neonatology unit of the hospital. The study was approved by the institute research council. The cases included 30 term babies delivered in the hospital with evidence of asphyxia indicated by any three of the following: (i) APGAR< 6/10 at 5 minutes. (ii) Changes in fetal heart rate (iii) Meconium stained amniotic fluid (iv) Cord blood pH less than 7.1.

Preterm babies, neonates with congenital malformation, congenital myopathy and who have received IM injection like vitamin K before collection of blood sample were excluded from the study. Thirty normal term newborns delivered immediately after the case without any evidence of asphyxia matched with cases for sex and birth weight were taken as controls. Informed consent was taken from the parents of all babies included in the study.

APGAR score of newborns was evaluated at 1, 5 and every 5 minutes there after till it is normal. Four ml of venous blood was collected within 6 hours of delivery by venipuncture in heparinized bottle. Cardiac Tropinin-T was assayed using 150 µL of heparinized whole venous blood in the quantitative cardiac reader kit (Roche Diagnostics, Germany). Creatine kinase-MB (CK-MB) was measured by Qualitest based on immunological principle of inhibition of CK-M monomer (Rashmi Diagnostics Pvt. Ltd., Bangalore). Clinical evaluation was done on the first day and repeated daily till discharge or death with particular reference to cardiac manifestation and neurological status. Twelve lead electrocardiography (ECG) and echocardiography (M-mode, Two-dimensional as well as Doppler study) were conducted within 24 hours of birth. The ECG and Echocardiography (ECHO) were repeated before discharge if initial ECG/ECHO was abnormal. The

Correspondence and Reprint requests : Dr. B. Vishnu Bhat, Director, Professor of Pediatrics, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry-605006, India. Phone : 0413-2251282
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cases who had cardiac involvement as evidenced by ECG, ECHO changes with or without clinical features were examined on follow up at 6 weeks for the presence of any murmur, respiratory distress or cardiac failure. A repeat ECG and ECHO were also done.

Cardiac enzyme levels in cases and controls were compared using student t test and "P" value of less than 0.05 was considered as significant.

RESULTS

Respiratory distress was present in 20 (66.7%), cardiac failure in 11 (36.7%) cardiogenic shock in 5 (16.7%) while 8 babies were asymptomatic. Among the controls, respiratory distress was present in 1 (3.3%), while 29 were asymptomatic. None of the babies in the control group had cardiac failure or cardiogenic shock. ST segment depression was present in 7 (28.3%) cases, T wave inversion in 11 (36.7%) and T wave flattening in 10 (33.3%) cases. Significant Q wave indicating infarction was present in 3 (10%) cases. ECG was abnormal in 22 (73.3%) of cases. All the cases and controls had normal sinus rhythm. ECG changes were noted in 17(56.7%) of cases. Tricuspid regurgitation was present in 7 (23.3%), right ventricular hypokinesia in 6 (20%) and left ventricular hypokinesia in 4(13.3%) cases. The ventricular function was normal in all the controls.

The cardiac enzymes, C-troponin T and CK-MB were significantly elevated in cases when compared with controls. The cardiac Troponin-T level was elevated in 19 cases and the levels ranged from 0.1 to 1.2 ng/ml with a mean of 0.22±0.28 ng/ml. C-Troponin-T level was elevated only in one control (0.1 ng/ml). CK - MB levels were elevated in 13 cases and 9 controls. The mean CK-MB levels among cases and controls were 121±77.4 IU/L and 28.8±20.2 IU/L respectively (Table 1). Specificity and sensitivity of cardiac troponin-T were 82.6% and 97.3% respectively whereas specificity and sensitivity of CK- MB were 56.5% and 75.7% respectively.

Table 1. Cardiac Enzyme Changes in Cases and Controls

Enzymes	Cases (N=30)		Control (N=30)		
	Mean	SD	Mean	SD	P value
C–Troponin-T (ng/ml)	0.22	0.28	0.003	0.018	< 0.001
CK-MB (IU/L)	121	77.4	28.8	20.2	< 0.001

Evidence of cardiac dysfunction in one of the following – clinical, ECG, ECHO and biochemical changes were present in 23 of 30 cases. Nine (30%) cases expired and all of them had cardiac changes in one form or the other.

The incidence of cardiac changes and mortality increases with increasing levels of troponin-T. Mortality was found in 4 of 12 cases with levels < 0.2 and 5 of 7 with levels > 0.2ng/ml. There was no mortality in cases without elevation of troponin level. The mean troponin-T level in cases with cardiac dysfunction was 0.3ng/ml. But the mean level in cases without dysfunction was significantly lower (0.07ng/ml). (Table 2).

Out of 30 cases, 8 had HIE stage I, 18 stage II and 4 stage III, according to Sarnat's staging. The incidence of cardiac changes increases with increasing stage. Three out of 8 in stage I, 10 out of 18 in stage II and all 4 out of 4 in stage III had cardiac changes. All the survivors were normal on clinical examination with normal ECG and ECHO at discharge and follow up.

DISCUSSION

The various clinical features related to cardiac dysfunction documented were respiratory distress, congestive cardiac failure, cardiogenic shock and systolic murmur. The most common feature was respiratory distress.Congestive cardiac failure was present in 11 (33.3%) cases in the present study. This is comparable with the previous studies by Rowe, Flores *et al* and Mandal Ravi *et al,* who reported 21%, 20% and 36% respectively.[1,2,3] However Herdy *et al* have reported 9% congestive heart failure while none developed failure in the study by Martein *et al*.[4,5] The variation may be attributed to the type of cases selected. 8 out of 11 cases with cardiac failure in the study expired but the remaining 3 were normal without any cardiac dysfunction at discharge. Cardiogenic shock *i.e.* cardiac failure with hypotension or poor circulation requiring ionotropic support was documented in 5 (16.7%) cases. This is less than the incidence quoted by Mandal Ravi (44%). All the babies with cardiogenic shock succumbed either due to cardiac problem or due to the associated renal and neurological problems. These were the cases who had unequivocal changes in all parameters *i.e.* ECG, ECHO and biochemical. Pansystolic murmur along the left sternal border was found in 6 (20%) cases. This is

Table 2. Outcome in Relation to Levels of Cadiac Troponin-T

CARDIAC TROPONIN-T (n)	Asymptomatic	Cardiac changes	Mortality		P value
			Number	Percentage	
Negative (11)	6	2	0	0	
< 0.2 (12)	4	11	4	26.7	0.04
0.2 – 1 (6)	1	5	4	66.7	0.05
> 1 (1)	0	1	1	100	—

higher than that quoted previously by Martein *et al* and Ravi *et al*, which were 2% and 12% respectively [3, 5]. But Herdy *et al* have reported a very high incidence of 50% systolic murmur in their study.[4] The Pansystolic murmur was only transient and none of the survivors had persisting murmur on discharge or follow up.

ECG changes were present in 22 (73.3%) of cases. The most common finding in the study was 'T' wave inversion in 11 (36.7%) followed by 'T' wave flattening in 10 (33.3%). 'T' wave flattening and inversion were graded by Rowe as Grade I in their initial description of Transient Myocardial Ischemia (TMI) of newborn.[1] Two patients in the study developed tall 'T' waves and widening of QRS complex. Both had documented hyperkalemia and one patient required peritoneal dialysis due to renal failure.

The incidence of Tricuspid regurgitation was 23.3%. This is more than that reported in the previous studies by Rowe *et al*. Flores *et al* and Martein *et al* who documented 12%, 7% and 21% respectively.[1, 4, 6] However Herdy *et al* have observed these changes in 7% cases.[7] Though Mitral regurgitation has been documented in previous studies[1], none of the babies in the present study had MR. Ventricular dysfunction due to ischemia was documented in 9 (30%) cases. This is consistent with the observation of Perlman et al who reported LV dysfunction in 10% and RV dysfunction in 30% of cases.[8] Bennhagen *et al* and Mandal Ravi *et al* have reported higher incidence of ventricular dysfunction, i.e. 50% and 56% respectively.[7, 8]

Mean CK-MB level among cases and controls were 121±77.4 IU/L and 28.8±20.2 IU/L respectively. This is lower than the value reported by Warburton *et al* and Mandal Ravi *et al* who reported CK-MB values as high as 328 IU/L and 823.5 IU/L in cases respectively.[3, 7] Tapia-Rombo *et al* have reported the usefulness of CK-MB in detecting TMI in newborns with asphyxia.[9] CK-MB is also found in skeletal muscle in newborn period. Hence the elevation of the enzyme in these babies could be explained by their non-specific nature. But C-troponin-T level was elevated in all but 11 cases. Troponin-T could not be detected in controls except in one who had 0.1ng/ml.

It has been well established that troponin-T is elevated in myocardial ischemia in perinatal asphyxia[10-13]. Cardiac troponin-T is more specific and sensitive than CK- MB in diagnosis of cardiac dysfunction in perinatal asphyxia. The mean troponin-T level in cases with cardiac dysfunction was significantly higher than that seen in cases without cardiac dysfunction. All cases who expired had cardiac involvement and elevation of troponin-T. There is a linear relationship between increasing levels of cardiac troponin-T and cardiac dysfunction and mortality. However, no similar relationship could be established between CK-MB level and cardiac dysfunction. Hence troponin-T level may be useful in predicting the mortality and outcome in perinatal asphyxia. Boo *et al* also concluded that unlike CK-MB, serum cardiac troponoin- T concentrations are significantly higher in asphyxiated infants who die or develop cardiac dysfunction.[13]

CONCLUSION

The follow up study on surviving babies with initial abnormal findings showed that all had normal clinical, ECG and ECHO features without any cardiac dysfunction. This proves the contention that cardiac dysfunction in perinatal asphyxia does not leave any sequelae in the surviving babies.

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