Study of Serum Creatine Kinase Muscle-Brain Fraction (CK-MB), Cardiac-Troponin-T and Lactate Dehydrogenase (LDH) Levels Among Asphyxiated and Non-Asphyxiated Term Neonates

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Abstract

Objective: Perinatal asphyxia is a common neonatal problem and contributes significantly to neonatal morbidity and mortality. There is a need to identify neonates with asphyxia who will be at high risk for hypoxic ischemic encephalopathy and multi-organ dysfunction.

Hence, this study was conducted to compare the serum levels of creatine kinase muscle-brain fraction (CK-MB), c-troponin-t (c-TnT) and lactate dehydrogenase (LDH) among asphyxiated and non asphyxiated term neonates and to ascertain whether these enzymes can identify asphyxiated neonates.

Methods: A study was conducted on 30 neonates comprising the cases and 30 neonates comprising the controls born at AL GALAA teaching hospital from March 2012 to November 2012. Cases and Controls comprised of asphyxiated and non asphyxiated neonates, respectively. The blood samples for CK-MB, C-troponin-t were drawn at 8±2 hours and LDH at 72±2 hours of age and sent for analysis. A serum CK-MB value >92.6U/L, C-troponin value >0.1ng/m1 at 8 hours and LDH value >580U/L at 72 hours was taken as the cut-off level. The sensitivity, specificity, Positive predictive value (PPV), Negative predictive value (NPV) was calculated for CK-MB, C-troponin-t and LDH.

Results: CK-MB, C-troponin-t and LDH were significantly increased in babies with perinatal asphyxia. The mean CK-MB level among cases and control were (126.50±17.34U/L) and (33.63±18.14u/l) respectively with p<0.001, the mean C-troponin-T in cases and control were (0.22±0.01ng/m1) and (0.087±0.002ng/m1) respectively with p<0.001, while LDH levels in cases and control were (554.83±1.95U/1) and (402.57±1.85U/1) respectively with p<0.001.

The cut-off CK-MB value of >92.6U/L has 30% sensitivity with a specificity of 100%. With positive predictive value of 100% and a negative predictive value of 58.8%. The cut-off C-troponin value of >0.1ng/m1 has 26.7% sensitivity with a specificity of 96.7%. With a positive predictive value of 88.9% and a negative predictive value of 65.9%. The cut-off LDH value of >580 U/L has 96.3% sensitivity with a specificity of 87.9%. With a positive predictive value of 86.7% and a negative predictive value of 96.7%.

Conclusion: Estimation of CK-MB, C-troponin-t at 8 hours of life and LDH at 72 hours of life can help distinguish an asphyxiated from a non-asphyxiated term neonate in correlation with history and clinical features in the neonate.

Key Words: Neonatal Asphyxia — CK-MB — LDH — C.TT

Introduction

PERINATAL asphyxia is a common neonatal problem and contributes significantly to neonatal morbidity and mortality. Globally, hypoxia of the newborn (birth asphyxia) is estimated to account for 23% of the 4 million neonatal deaths and 26% of the 3.2 million stillbirths each year [ii. An estimated 1 million children who survive birth asphyxia live with chronic neuro developmental morbidities, including cerebral palsy, mental retardation, and learning disabilities. Every hour, 104 children die as a result of asphyxia [ii.

Although asphyxia is associated with multiple organ injuries, especially with adverse neurological outcomes, management still focuses on supportive care. A variety of markers have been examined to identify perinatal hypoxia including electronic fetal heart monitoring, low Apgar scores, cord PH, electroencephalograms (EEG), computed tomography (CT) and magnetic resonance imaging (MRI) scans and Doppler flow studies.

Perinatal asphyxia may result in adverse effects on all major body systems. Many of these complications are potentially fatal. In a term infant with perinatal asphyxia renal, neurologic, cardiac and hmg dysfunction occurs in 50%,28%,25% and 23% cases respectively [2].

Transient myocardial ischemia (TMI) with myocardial dysfunction may occur in any neonate
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with a history of perinatal asphyxia. An elevated serum creatine kinase muscle-brain fraction (CK-MB) fraction or cardiac troponin-T (cTnT) level may be helpful in determining the presence of myocardial damage. An elevation of serum CK-MB fraction of >5% to 10% may indicate myocardial injury [3].

Leakage of intracellular enzymes such as alanine aminotransferase (ALT), aspartate aminotransferase (AST) and lactate dehydrogenase (LDH) signaling multi organ dysfunction is seen together with HIE after perinatal asphyxia [4,5].

Aims and objectives of the study:
1- To compare the serum levels of CK-MB, cardiac troponin-t and LDH among asphyxiated and non-asphyxiated term neonates.
2- To ascertain whether these enzymes can distinguish an asphyxiated from a non-asphyxiated term neonate.

Material and Methods

The study was a prospective study conducted on asphyxiated and non asphyxiated term neonates recruited from Neonatal Intensive Care Unit (NICU) at Al Galaa Teaching Hospital from March 2012 to November 2012. The blood samples from the 30 neonates comprising the cases (asphyxiated) and 30 neonates comprising the controls (non asphyxiated) constituted the material for the study.

Method of collection of data:
The study included two groups:
The case group: It included 30 neonates fulfilling the following criteria:

Inclusion criteria: Gestational age >37 weeks, Appropriate for gestational age. The neonates will be identified to have experienced perinatal asphyxia when at least 3 of the following are present:
A- Intrapartum signs of fetal distress, as indicated by continuous electronic fetal monitoring and/or by thick meconium staining of the amniotic fluid.
B- Apgar score of <7 at one minute of life.
C- Resuscitation with >1 minute of positive pressure ventilation before stable spontaneous respiration.
D- Profound metabolic or mixed acidemia (pH <7.00) in an umbilical artery blood sample.

Exclusion criteria:
- Congenital malformations.
- Maternal drug addiction.
- Neonates born to mothers who would have received magnesium sulphate within 4 hours prior to delivery or opioids (pharmacological depression).
- Hemolytic disease of the newborn.

The control group:
It included 30 term apparently healthy neonates appropriate for gestational age without signs of perinatal asphyxia as evidenced by normal fetal heart rate patterns, clear liquor and one minute Apgar score ≥7.

All neonates included in the study had the following done:
- Detailed maternal history, assessment of intraterine fetal well being by continuous electronic fetal monitoring, meconium staining of amniotic fluid, birth events, Apgar score, sex of the baby and weight of the baby were recorded. Gestational age was assessed by New Ballard scoring system.
- Arterial blood gas analysis (ABG) was done if umbilical arterial blood was obtained.
- Thorough clinical and neurological examination was done for all the neonates included in the study.
- Blood samples were collected from the neonates and sent for:
A- Creatine Kinase Muscle-Brain fraction (CK-MB) levels.
B- C-troponin level.
C- Lactate Dehydrogenase (LDH) levels.

Blood for CK-MB and C-troponin was drawn at 8±2 hours [6-8]. Blood for LDH was drawn at 72±2 hours of age [4-5,7]. The upper limit of the normal range of CK-MB at 5-8 hours of life is 7.9% of 1,175 U/L which is —92.6 U/L taken as the cut-off level [9].

We defined a positive test if cTnT blood levels were >0.1 ng/dL. The value of 0.1 ng/mL for a cut off was chosen according to the studies conducted in adults by Alpert et al., Ohman et al. and also by Costa et al., in newborns [10-12].

The normal reference value of LDH in neonates and infants <1 year is 170-580 U/L [9]. A value >580 U/L at 72 hours was taken as the cut-off level.
Sample collection:

Blood was collected each time from the peripheral venous site at 8±2 hours for CK-MB and Cardiac Tropinin-T was assayed using 150 u/L of heparinized whole venous blood in the quantitative cardiac reader kit (Roche Diagnostics, Germany) Serum LDH was analyzed by the liq-uidUV test on lmL clotted blood [14].

Statistical software:

The Statistical software namely, SPSS 15. And MedCalc 12.3.0, were used for the analysis of the data.

Results

Table (1) shows that cesarean section and meconium stained amniotic fluid were significantly higher in asphyxiated babies than control with p<0.001 with non significant difference regarding parity, birth weight and gender.

Table (2) shows that the mean CK-MB, C-TROPONIN-T and LDH were significantly higher in asphyxiated babies than non asphyxiated babies.

Discussion

Perinatal asphyxia is a common neonatal problem and contributes significantly to the neonatal morbidity and mortality. Birth asphyxia is a common and important cause of preventable cerebral injury occurring in the neonatal period.

In the present study an attempt has been made to ascertain whether CK-MB, C-troponin-T and LDH can distinguish an asphyxiated from a non-asphyxiated term neonate. These tests are routinely available in most centers.

Our study shows that cesarean section and meconium stained amniotic fluid were significantly higher in asphyxiated babies than control with p<0.001. This agrees with Reddy et al. [7] and Khreisat et al. mi.

In addition vaginal delivery was significantly associated with non asphyxiated babies, with non significant difference regarding parity, birth weight and gender.

In the present study the mean level of CK-MB is significantly higher in cases (126.50±17.34 U/L) when compared to controls (33.63±18.14 U/L) with p<0.001, the mean C-troponin-t level was significantly higher in cases (0.220±.01 ng/ml) than control (0.087±0.002 ng/ml) with p<0.001 and the mean LDH levels in cases (554.83±1.95

Table (3): Comparative study of CK-MB level cut-off of 92.6 U/L, C-troponin-T level cut-off of 0.1 ng/ml and LDH level cut-off of 580 U/L in cases and controls.

Table (4): Sensitivity, specificity and predictive values of CK-MB, C-Troponin and LDH.
U/L) were significantly higher compared to controls (402.57±1.85 U/L) with p<0.001.

In a study by Primhak, et al. [16], the CK-MB levels were higher in asphyxiated babies than non asphyxiated babies.

Sanchez-Nava, et al. [17] showed that SGOT, SGPT and LDH were raised among asphyxiated babies.

Barberi, et al. [18] reported that CK, CK-MB, CK-MB/CK ratio and LDH were all increased in asphyxiated babies.

Lackmann, et al. [19] found that newborn infants with asphyxia have significantly higher values of SGOT, LDH and hydroxybutyrate.

It has been well established that troponin-T is elevated in myocardial ischemia in perinatal asphyxia [20,21].

Adamcov’a et al. [20] studying the cTnT in the blood cord of newborns suggested that its increase would indicate fetal distress and myocardial compromise.

In 2005, Boo NY et al. [21] showed that at birth, asphyxiated infants had significantly higher concentrations of cTnT and CK-MB than controls. Unlike CK-MB, serum cTnT concentrations were significantly higher in asphyxiated infants who died or developed cardiac dysfunction.

Costa et al., and Rajakumar et al., in two separate studies found a correlation between increased cTnT and signs of myocardial damage in infants with perinatal asphyxia [12,22].

Gunes T et al. [23], demonstrated that infants with severe asphyxia had significantly higher cardiac troponin-T levels than grade I and II asphyxiated and healthy neonates.

Szymankiewicz et al., studied 39 asphyxiated newborn versus 44 nonasphyxiated newborns. The cTnT was measured within 12 hours of life. The asphyxiated infants had higher levels of cTnT (0.141 versus 0.087 ng/mL) than the nonasphyxiated infants (p<0.01) [24].

Our findings are similar to many other studies that suggested a positive association of cTnT and asphyxia in the neonatal period [25,26,12-22].

The cut-off CK-MB value of >92.6 U/L has 30% sensitivity with a specificity of 100%. With positive predictive value of 100% and a negative predictive value of 58.8%. The cut-off LDH value of >580 U/L has 96.3% sensitivity with a specificity of 87.9%. With a positive predictive value of 86.7% and a negative predictive value of 96.7%. This agree with Reddy, et al. [7]. The cut-off C-troponin value of >0.1 ng/ml has 26.7% sensitivity with a specificity of 96.7%. With a positive predictive value of 88.9% and a negative predictive value of 65.9%.

Rajakumar et al., found that c-troponin-t in asphyxiated babies has sensitivity of 97.3% and Specificity of 82.6% respectively but they studied asphyxiated babied with myocardial dysfunction [22].

LDH has sensitivity of 96.3%, CK-MB has specificity of 100% and c-troponin-t has specificity of 96%.

We conclude that LDH at 72 hr of life is most accurate at differentiating asphyxiated from non-asphyxiated babies [7].

An elevated serum creatine kinase muscle-brain fraction (CK-MB) fraction or cardiac troponin-T (cTnT) level may be helpful in determining the presence of myocardial damage in asphyxiated babies.

Conculsion:

Estimation of CK-MB, C-troponin-t at 8 hours of life and LDH at 72 hours of life can help distinguish an asphyxiated from a non-asphyxiated term neonate in correlation with history and clinical features in the neonate.

LDH at 72 hours of life was the most accurate test for discriminating asphyxia from other illnesses among neonates who presented with non-specific signs of illness [7].

An elevated serum creatine kinase muscle-brain fraction (CK-MB) fraction or cardiac troponin-T (cTnT) level may be helpful in determining the presence of myocardial damage in asphyxiated babies [3].

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