JPC

THE JOURNAL OF PEDIATRIC CLUB
Vol. 4, No. 1, January 2004

Published by:
Gharbia Pediatric Club Society, Tanta, Egypt.
Correspondence: AMR HAMAM, MD
Prof. of Pediatrics, Tanta Faculty of Medicine.
Tel.# 0403332566 - 0101471018. Fax. # 0403407734,
E mail: amrohamam @ Yahoo. Com

Troponin T as a useful marker for myocardial damage in neonates with perinatal asphyxia

Somaia Elwan, Mohamed El-Baz, Mohamed Zakaria, Adel Marzook* and Mohie El-Din El Helaily
Pediatrics and Clinical Pathology departments, Faculty of Medicine, Benha University*

Abstract
This study was designed to delineate the role of cardiac troponin T in neonates with perinatal asphyxia as a marker for myocardial damage. It included 25 neonates suffering from perinatal asphyxia. They were 15 males and 10 females and their gestational age ranged from 37 to 41 weeks (group I). Also 15 apparently healthy neonates of age and sex matched to group I were taken as control group (group II). All neonates in the study were subjected to laboratory investigations as CBC, C-reactive protein; arterial blood gases (ABGS), blood glucose level and serum level of cardiac troponin T (TNT). The mean serum level of (TNT) among asphyxiated neonates was 0.027 ± 0.017ng/ml and was 0.011 ± 0.002ng/ml in control and there was statistical significant difference between both groups. There were 7 cases (28%) with tachycardia, 3 cases of them (%12) had irregular rhythm and heart failure. The mean level of (TNT) in patients with HF was 0.062 ± 0.048ng/ml and the mean level in the rest of asphyxiated newborns was 0.020 ± 0.0033ng/ml. In this study there was high statistical significant negative correlation between TNT level and arterial PH, Po_2, HCo_3 and base excess (BE). There was also high significant positive correlation between the mean TNT level and PCo_2. This means that TNT mean level correlate with severity of perinatal asphyxia. In conclusion: It would be useful to measure cardiac troponin T in all asphyxiated neonates. Then these patients with high level of TNT can then submitted to electrocardiographic and echocardiographic examination for detection of cardiac affection and to offer apportune treatment when required.(JPC, Vol. 4, No. 1: 49-53, January 2004)

Introduction
Perinatal asphyxia (PA) exists when an antipartum event, labor or birth process diminishes the oxygen supply to the fetus, causing decreased fetal or newborn heart rate, the result is an impairment of oxygen and carbon dioxide exchange and inadequate perfusion of the tissues and organs[1]. The incidence of asphyxiated full term infant is still high in both high income and developing countries[2]. Perinatal asphyxia is one of the most common causes of neonatal deaths as reported in retrospective statistical Egyptian study carried out at Ain Shams Maternity Hospital by[3]. The fetal and neonatal myocardium able to sustain hypoxic insults with good recovery. However, the papillary muscles are more sensitive to hypoxia and may show early signs of infarction[4]. The incidence of perinatal asphyxia is about 1 to 1.5% in most centers. It is accounting for 20% of perinatal deathes[5]. Infants with PA may suffer transient myocardial ischemia. Many infants may have systolic murmurs at the lower sternal border due to tricuspid regurgitation. Sometimes those may show signs of congestive heart failure. The echocardiogram will show normal cardiac structures, but decreased left ventricular contractions especially of the posterior wall [6]. Troponin complex, a heterometric protein playing an important role in the regulation of skeletal and cardiac muscle contraction. Troponin complex consists of three different subunits: Troponin T (TNT), Troponin I (TNI) and Troponin C (TNC) [7]. The pronounced divergence of amino acids composition between cardiac and skeletal troponin T allows the differentiation of these molecules by immunological techniques and the development of a cardiac specific test system[8]. The diagnostic sensitivity of troponin T remains 100% until the fifth day after the onset of symptoms [9]. The measurement of troponin T will improve the diagnostic power for myocardial damage. It has high specificity and sensitivity [10]. So this study was carried out to determine the incidence of elevated cardiac troponin T in neonates with perinatal asphyxia and to detect any relation between elevated level and their cardiac affection.

Subjects and Methods
This study was carried out in neonatal intensive care unite of Benha University Hospital and Benha Teaching Hospital from April to November 2002. It included 25 neonates suffering from perinatal asphyxia. They were 15 males and 10 females and their gestational ages ranged from 37 weeks to 41 weeks, taken as group I. The diagnosis of asphyxia was based on the presence of: 1-History of difficult labor and depressed fetal heart rate. 2-An Apgar score 0-3 at one minute or below 6 at 5 minute. 3- Arterial umbilical blood PH taken shortly after delivery below 7.20. 4- CNS irritability and other organs affection [11, 12]. Exclusion criteria: the only exclusion criterion is babies under toclolytic drugs. Also 15 apparently healthy neonates of age and sex matched to group I were taken as control group (group II). All neonates

included in the study were subjected to the following: 1- Detailed history taking. 2- Thorough clinical examination including Apgar score at one and five minute. 3- Laboratory investigations as: 1-Complete blood picture. 2- C-reactive protein. 3- Arterial blood gases (ABGS). 4- Blood glucose level. 5- Determination of serum level of troponin T (TNT) of cord blood by the electrochemiluminessence immunoassay (ECLIA) using Roche Elecsys 1010 immunoassay analyzer using commercial kit (Roch diagnostic Gm bH, Mannheim, Germany). Elecsys 1010 automatically calculate the troponin T concentration of each sample either in (ng/ml or ul/L). The upper reference limit (99th percentile) for troponin T was found to be < 0.01ng/ml.

Statistical methods

SPSS software package, echo soft corp., USA, 1998 was used to analyze these data. All values were expressed as mean ± SD. The student's t test for comparison between the mean of the different groups. Qualitative variables were compared in different groups using Chi square or Z test. Correlation were done by regression analysis (r).

Results

The results of the present study are presented in tables (1-7).

Table (1): Different maternal problems among group I.

Maternal problems	Number	%
Meconium staining	12	48
Multiple gestation	1	4
Pre-eclampsia	1	4
Premature rupture of membrane	11	44
Hypertension	5	20
Ante-partum hemorrhage	—	—
Diabetes mellitus	3	12

Table (2): Statistical comparison between group I and group II as regard birth weight.

	Group I n= 25	Group II n= 15	t	P value
Birth weight in kg	3.04 ± 0.29	3.32 ± 0.33	- 2.823	< 0.01

Table (3): Statistical comparison between group I and group II as regard Apgar score at one and five minutes.

	Group I n= 25	Group II n= 15	t	P value
At one minute	3.0 ± 0.95	6.53 ± 0.51	13.14	< 0.001
At five minute	5.32 ± 1.02	8.26 ± 0.45	10.44	< 0.001

Table (4): Statistical comparison between group I and group II as regard blood glucose level.

	Group I n= 25	Group II n= 15	t	P value
Blood glucose mg/dL	74.64 ± 19.53	89.20 ± 18.08	- 2.344	< 0.05

Table (5): Statistical comparison between group I and group II as regard arterial blood gases.

	Group I n= 25	Group II n= 15	T	P value
PH	7.098 ± 0.086	7.36 ± 0.028	11.635	< 0.001
Pco_2 (mmHg)	44.52 ± 5.60	37.53 ± 1.92	4.645	< 0.001
Po_2 (mmHg)	67.16 ± 8.69	86.73 ± 3.26	- 4.502	< 0.001
Hco_3 meq/L	21.60 ± 2.73	25.06 ± 1.33	- 4.570	< 0.001
BE* meq/L	- 1.90 ± 0.71	- 4.04 ± 1.83	5.254	< 0.001

BE: Base excess.*

Table (6): Statistical distribution of the mean troponin (TNT) levels among the studied groups.

	Group I n= 25	Group II n= 15	t	P value
Troponin ng/ml	0.027 ± 0.01	0.011 ± 0.002	3.227	< 0.01

Table (7): Statistical correlation of TNT levels with parameters of blood gases among group I.

Troponin T	Group I			
		R	P value	Significance
ABGs	PH	- 0.646	< 0.001	HS
	Pco_2	0.457	< 0.001	HS
	Po_2	0.602	< 0.001	HS
	Hco_3	- 0.604	< 0.001	HS
	BE	- 0.156	< 0.001	HS

ABG's: arterial blood gases HS: highly significant

Discussion

This study included 40 full term neonates, 22 males and 18 females. Their gestational age ranged from 37-41 weeks. They were divided into two groups, (group I) comprised 25 neonates with perinatal asphyxia and (group II) included 15 healthy neonates as control. Maternal problems which more common among asphyxiated group were meconium staining (48%), premature rupture of membrane (44%), hypertension (20%), diabetes mellitus (12%), preeclampsia (4%) and multiple gestation (4%) (Table 1). Snyder and Colherty [6] stated that the incidence of hypoxia is higher in full term infants of diabetic and toxemic mothers. In cases of meconium aspiration, there is failure of adaptation of the newborn to the neonatal cardiopulmonary circulation. Also Kliegman and Stoll [13] showed that impaired placental perfusion as in maternal hypertension, preeclampsia and premature placental separation were associated with perinatal asphyxia. In our study the mean birth weight among group I was 3.04 ± 0.29kg and was 3.32 ± 0.33kgm in group II and there was high statistical significant difference between both groups (table 2). This agreed with Jazsyri et al [14] who stated that growth restricted newborns have significantly lower PH, Po_2 and Apgar score at one and five minutes than appropriately grown newborns. Growth restricted babies often have decreased physiologic reserve and are at higher risk of asphyxia[15]. This study showed that the mean Apgar score at one minute and five minute respectively were (3.0 ± 0.95), (5.32 ± 1.02) in group I and were (6.53 ± 0.51), (8.26 ± 0.45) in group II. There were high statistical significant differences between both groups (table 3). Ellis et al [16] agreed with our results as they found that an Apgar score of 3 or less at one minute is a useful screening test for clinically significant birth asphyxia. While Tapia et al [17] found that no significant difference in Apgar score between asphyxiated and normal neonates. In this study the mean value of blood glucose level among group I was 74.64 ± 19.53gm/dL and was 89.20 ± 18.08gm/dL in group II. There was significant statistical difference between both groups (table 4). This agreed with Snyder and Cloherty [6] & Kliegman and Stoll [13] who stated that hypoglycemia in asphyxiated neonates is due to glycogen depletion secondary to catecholamine release. This occurs after an initial phase of hyperglycemia and hypoinsulinemia. Gunn et al [18] mentioned that during asphyxia glucose is released into circulation to supply the vital organs. This difference may be due to difference in time used for sampling blood glucose between their cases and ours. In our study the mean values of arterial blood gases parameters among asphyxiated group were PH (7.098 ± 0.086), PCo_2 (44.520 ± 5.605mmHg), Po_2 (76.160 ± 8.697mmHg), H Co_3 (21.60 ± 2.73meq/L) and BE (-1.90 ± 0.71meq/L) compared with control group parameters, which were PH (7.366 ± 0.028), PCo_2 (37.533 ± 1.922mmHg), Po_2 (86.733 ± 3.261mmHg), HCo_3 (25.06 ± 1.33meq/L) and BE (-4.04 ± 1.83meq/L). There were high statistical significant differences in all arterial blood gases parameters between both groups (table 5). The most accurate and satisfactory way of assessing neonates with asphyxia is to measure the umbilical artery blood gases and PH immediately after delivery, which is useful in guiding subsequent management[19]. Hiran and Dominc [20] said that arterial blood gases in the newborn have special consideration and play an important role in

the assessment of neonates with respiratory distress. Da-Silva et al [21] confirmed the value of base deficit in the neonates exposed to perinatal asphyxia. In this study troponin T (TNT) mean level among asphyxiated neonates was 0.027 ± 0.017ng/ml and was 0.011 ± 0.002ng/ml in control and there was statistical significant difference between both groups (table 6). We also found by clinical examination 7 cases (28%) with tachycardia, 3 cases (12%) of them have irregular rhythm and heart failure. The mean level of (TNT) in patients with HF was 0.062 ± 0.048ng/m and the level of (TNT) in rest of asphyxiated newborn was 0.020 ± 0.0033ng/ml Sanad et al [4] demonstrated cardiac abnormalities in 28-50% of their cases. Transient myocardial ischemia are often underdiagnosed and require a high index of suspicion Ranjit [22] & Meinerts and Hamm [22] agreed with our study, they stated that troponin have became a new gold standard for biochemical detection of cardiac injury. In addition, the so called minor myocardial injury can be detected, which usually escapes routine measurement of creatinine kinase, MB. High level of cardiac TNT in full term neonates of mild preeclamptic mothers presumably associated with myocardial damage in them[24]. In asphyxiated infants with heart failure, troponin T was significantly higher than in the other asphyxiated infants [7]. Transitory myocardial ischemia is seen as a complication of severe asphyxia. Its presentation is variable, ranging from tachypnea to cardiogenic shock. It is often masked by the predominant disease17. In this study there were high statistical significant negative correlation between TNT level and arterial PH, Po_2, HCo_3 and BE and there was high significant positive correlation between TNT level and PCo_2 (table 7). This means that TNT mean level correlate with the severity of perinatal asphyxia. Clark et al [25] stated that cardiac troponin levels in cord blood are unaffected by gestational age, birth weight, sex or mode of delivery. It is an ideal marker for myocardial necrosis. Elevated its levels in cord blood may be associated with intrauterine hypoxia and increased perinatal morbidity. We concluded that: transient myocardial ischemia secondary to perinatal asphyxia is more frequent, thus it would be useful in all asphyxiated newborn to measure cardiac troponin T. Patients can then submitted to electrocardiogram and echocardiographic examination for detection of cardiac affection and to offer opportune treatment when required.

References

1. *Jack Welch: Perinatal asphyxia. Neonataology on internet, Net Scut Home perinatol, 20(4): 256-259, 2002.*
2. *Gcuyener K and Ergenekon E: Why hypothermia in neonatal hypoxic ischemic encephalopath? Turk. J. Pediatr., 43(1): 19-23, 2001.*
3. *Muhammad SE: Perinatal mortality. MD thesis, Faculty of Medicine, Ain Shams University, 1995.*
4. *Sanad R, El-Shalzy A, and Felifel M: Evaluation of cardiac ischemia in the newborn with perinatal asphyxia. Egypt. J. Ped. Vol. 14, No. 3:307-315, 1997.*
5. *El-Ghadban H., Waheed H. and Saber K.: Response of plasma erythropoietin to acute and chronic perinatal hypoxia. The Egyptian Journal of Neonatology. Vol. 2, No. 3 Sept, 2001.*
6. *Snyder E and Cloherty J: Perinatal asphyxia. In: Manual of Neonatal Care. Cloherty J. and Stark, AP (eds) 4th edition. Little brown and lippincott-Raven Co., Boston, P.393 and 515, 1998.*
7. *Moller JC, Thielsen B and Schaible TF: Value of myocardial hypoxia marker (creatiene kinase and its MB-fraction, troponin-T, QT-intervals) and serum creatinin for the retrospective diagnosis of perinatal asphyxia. Bio. Neonate 73(6): 367-374, 1998.*
8. *Hallermayer K, Katus A, Looser S, Remppis A, Scheffold T and Borgya A: Development and in vitro characterization of a new immunoassay of cardiac troponin T. Clin. Chem. Vol. 38, No. 3:386-393, 1992.*
9. *Apple FS: Serum cardiac markers for the 1990s. acute myocardial infarction and coronary reperfusion. Clin. Chem. Vol. 2: 15-18, 1992.*
10. *Katus HA, Remppis A, and Neumann EJ: Diagnostic efficiency of troponin T measurement in acute myocardial infarction. Circulation, 83:902-912, 1992.*
11. *Nagel HTC, Vandenbussche FP, Oepkes D, Jenekens-Schinkel A, and Kaon LA: Follow-up of children with an umbilical arterial PH < 7. Am. J. Obest. Gynecol., 173: 1758-1764, 1995.*
12. *American Academy of pediatrics (AAP) and American College of obestetricians and gynecologists (ACOG): "Relationship between perinatal factors and neurologic outcome". In guidelines for perinatal care. Eds. Poland RL and Freeman RK (3rd ed) Elk Grove village illions, American Academy of pediatrics, P. 221, 1996.*
13. *Kliegman KM and Stoll BJ: The fetus and neonatal infant in: Nelson Textbook of pediatrics. Behraman, RE, Kliegman, KM and Jenson, HB (eds), 16th edition, WB Saunders Co., Philadelphia, P. 451, 2000.*
14. *Jazayeri A, Tsibris JC and Spellacy WN: Fetal erythropoietin levels in growth restricted and appropriately grown neonates with and without abnormal fetal heart rate tracings: a comparison with cord blood gases and Apgar score. J. Perinatol., 19(4): 255-259, 1999.*

15. Gabbe SG, Niebyl JR, and Simpson JL: Normal and problem pregnancies. Obestetrics. 3rd ed., churchill Livingstone, New York, P. 864, 1996.
16. Ellis M, Manandhar N, Manandhar DS and Del-Castello AM: Apgar score of three or less at one minute is not diagnostic of birth asphyxia. Indian Pediatr., 35(5): 415-421, 1998.
17. Tapia Rombo CA, Caprio-Hernandez JC, Salazer Acuma AH, and Alvarez-Vazquez E: Detection of transitory myocardial ischaemia secondary to perinatal asphyxia Arch. Med. Res., 31(4): 377-383, 2000.
18. Gunn AJ, Parer JT and Mallard E: Cerebral histological and electrophysiological changes after asphyxia in fetal sheep. Ped. Res., 31: 486-491, 1992.
19. Roberton NR: Resuscitation of the newborn in: Manual of neonatal intensive care, third ed., Edward Arnold, London, Melbourne, Auckland, P. 49-67 and 73-76, 1993.
20. Hiran C and Dominc A: Monitoring oxygen in the blood. Recent Advances in pediatrics 18(4): 47-59, 2000.
21. Da-Silva S, Hennebert N, Denis R and Wayenberg JL: Clinical value of a single postnatal lactate measurement after intrapartum asphyxia. Acta. Pediatr. 89(3): 320-323, 2000.
22. Ranjit MS: Cardiac abnormalities in birth asphyxia. Indian J. Pediatr. 67(3 Suppl.): 526-529, 2000.
23. Meinerts T and Haman CW: Rapid testing for cardiac troponins in patients with acute chest pain in the emergency room. European heart Journal 19: 973-974, 1998.
24. Narin N, Narin F, Tutus A and Tayyar M: Increased endothelin in infants of pre-eclamptic mothers. Pediatr. Int. 44(2): 131-133, 2002.
25. Clark SJ, Newland P, Yoxall CW and Subhedar NV: Cardiac troponin T in cord blood. Arch. Dis. Child Fetal Neonatal 84(1): 34-37, 2001.