Biomedicine Hub

Biomed Hub 2017;2:481086 (DOI: 10.1159/000481086)

Received: June 12, 2017
Accepted: August 30, 2017
Published online: October 10, 2017

Research Article

The Evaluation of Cardiac Troponin T in Newborns

Agata Tarkowska Wanda Furmaga-Jabłońska

Department of Neonates' and Infants' Pathology, Medical University of Lublin, Lublin, Poland

What Is It about?

In this paper, we evaluated the physiologic ranges of cardiac troponin T serum concentrations in healthy newborns. This is significant because these ranges have not been determined yet, especially for newborns older than 7 days. Cardiac troponins are widely used as diagnostic markers in adults; however, they cannot be routinely used in infants due to lack of data concerning normal values in this age group.

Keywords

Cardiac biomarkers · Neonatology · Newborn · Troponins

Abstract

Introduction: In this paper, we evaluated the physiologic ranges of cardiac troponin T (cTnT) serum concentrations in healthy newborns. This is significant because these ranges have not been determined yet, especially for newborns older than 7 days. Cardiac troponins are widely used as diagnostic markers in adults; however, they cannot be routinely used in infants due to lack of data concerning normal values in this age group. ***Aim:*** To determine the physiologic ranges of cTnT concentrations in newborns and to evaluate the influence of factors such as age, sex, and blood saturation. ***Methods:*** The study involved 59 newborns up to 46 weeks of postmenstrual age (full-term and preterm). The exclusion criteria were severe perinatal asphyxia and presence of severe diseases. Troponin T concentrations were evaluated by the Roche CARDIAC T Quantitative Test. The obtained results were statistically analyzed by the use of the Statistica 9.0 computer program. ***Results:*** The study revealed that cTnT levels in newborns correlate with postmenstrual age, but not with chronologic or fetal age. Sex, delivery mode, and blood oxygenation did not influence cTnT concentrations in the studied patients. ***Conclusions:*** (1) Cardiac troponin T concentration depends on postmenstrual age in newborns. (2) Cardiac troponin T concentration in newborns does not depend on sex, mode of delivery, or blood saturation.

Dr. Agata Tarkowska
Department of Neonates' and Infants' Pathology
Medical University of Lublin, Raclawickie 1 Street
PL–20-059 Lublin (Poland)
E-Mail a_tar@poczta.onet.pl

Introduction

Cardiac troponins are protein components of the troponin-tropomyosin complex in the myocardium. The complex consists of three troponins: C, I, and T, and tropomyosin. In physiologic circumstances, troponins do not occur in extracellular space; therefore, their appearance in serum presents a sensitive and specific marker of myocardial damage [1]. In contrast to troponin C, myoglobin, creatinine kinase, and its isoenzyme B, both troponins cardiac troponin T (cTnT) and cardiac troponin I (cTnI) do not appear in any other tissues but the myocardium [2, 3]. Troponins appear in blood 2–4 h after insult, peak at about 12 h, and then remain elevated for 7–10 days [1, 2].

The significance of both cTnT and cTnI in the diagnosis of myocardial damage is clinically almost equal. They differ in intracellular compartments, biological half-life, and molecular weight [3]. There are also differences in the standardization and availability of commercial troponin kits. Absolute values of gained results are often incomparable; however, diagnostic features of particular methods are similar [3].

Cardiac troponins seem to have huge diagnostic value not only in adults, but also in pediatric patients with suspicion of myocardial injury. The following applications of cardiac troponin's diagnostic role in pediatrics are specified: acute myocarditis, heart arrhythmias, perinatal ischemia, perioperative myocardial damage, drug cardiotoxicity, and heart transplantation [2–5].

Cardiac troponins are biochemical markers of myocardial injury with unquestionable significance in diagnostic strategy in adults [1]. However, their role in diagnostics in neonates has not been fully explored yet. Cardiac troponins have not been used routinely in neonates mainly due to insufficient data concerning the normal ranges in this age group.

The aim of the study was to evaluate physiologic ranges of cTnT in healthy newborns and the influence of factors like age, sex, blood saturation, or hemoglobin level on cTnT concentration.

Methods

Subjects

The study involved 59 healthy infants (both term and preterm) up to 46 weeks of postmenstrual age. Postmenstrual age was estimated according to current guidelines as the time elapsed between the first day of the last menstrual period and birth (gestational age) plus the time elapsed after birth (chronological age) [6]. The exclusion criteria were severe perinatal asphyxia (Apgar score ≤4 points in 1st and 5th min) and any significant disease. Heart disease was excluded according to comprehensive clinical evaluation; in case of any doubt ECHO and EKG examinations were additionally performed.

The studied group consisted of 59 infants (37 males and 22 females). The gestational age of studied newborns was 25–41 weeks (mean: 38). Chronological age (in days from the date of birth) was 6–109 days (mean: 33). Postmenstrual age was 34–46 weeks (mean: 42). The birth weights of the studied newborns were between 585 and 4,500 g (mean: 3,193). Apgar scores were between 5 and 10 points (mean: 9) in the 1st minute and 6–10 points (mean: 9) in the 5th minute.

Forty-three newborns were delivered the natural way and 16 were delivered by cesarean section. The mothers of the newborns were free of cardiac pathologies. However, in 14 cases mothers had a history of other diseases during pregnancy: respiratory tract infections (5 cases), genitourinary system infections (5 cases), and arterial hypertension (4 cases).

Table 1. Number of newborns with particular ranges of cardiac troponin T (cTnT) blood concentrations

cTnT, ng/mL	Patients, *n*	Percentage of the studied group
<0.03	12	20.34%
0.03–0.1	45	76.27%
>0.1	2	3.39%

Table 2. Mean cardiac troponin T (cTnT) concentrations according to patient age

	Mean cTnT concentration, ng/mL	3th percentile	97th percentile
Chronological age, days			
≤14	0.069	0.00	0.2
>14	0.053	0.00	0.07
Postmenstrual age, weeks			
<42	0.066	0.00	0.200
42–44	0.055	0.00	0.130
>44	0.027	0.00	0.070

Procedure

Troponin T levels were evaluated in 150 μL of venous blood immediately after collection by the use of the Roche CARDIAC T Quantitative Test (Third Generation; Roche Diagnostics). The test strip contains two monoclonal antibodies specific to cardiac troponin. The measuring range is 0.03–2 ng/mL. Hyperbilirubinemia (<20 mg/dL), hemolysis, or lipemia (triglycerides <440 mg/dL) do not interfere with the results.

The obtained results, after checking the normality of distribution, were statistically analyzed by the use of an appropriate test from the Statistica 9.0 packet. Right-handed asymmetry of certain distributions was eliminated by use of logarithmic transformation. Dependency analysis was performed based on the Pearson linear correlation coefficient (r) or Spearman (R) rank correlation test and t test significance of the correlation coefficient in the population. The results were considered statistically significant when $p < 0.05$.

The study protocol was approved by the Ethics Committee of Medical University of Lublin (Consent No. KE-0254/7/2007).

Results

The newborns from the studied group were divided into three categories according to the obtained results of cTnT concentration. The results are presented in Table 1.

CTnT Concentration and Patient Age

Mean cTnT concentrations according to age in healthy newborns are presented in Table 2. The Spearman rank correlation coefficient between cTnT concentration and chronological age was $R = -0.22$ and $p = 0.129$, which means that the results are not statistically significant. Similarly, correlation between gestational age and cTnT concentration was statistically insignificant (Spearman's rho was $R = -0.08$ and $p = 0.589$). However, the significant negative

correlation was found between postmenstrual age and cTnT concentration, as Spearman's rho was $R = -0.319$ and $p = 0.027$. Values of cTnT concentrations in different postmenstrual age groups are presented in Table 2.

Correlation between cTnT Concentration and Apgar Scoring

No significant correlation was found between cTnT concentration and Apgar scoring in newborns born in good or moderate condition. Patients born severely depressed were excluded from the study.

Correlation between cTnT and Blood Hemoglobin Concentrations

The relationship between cTnT and blood hemoglobin concentrations was evaluated as well, and no significant correlation was found.

Relationship between cTnT Concentration and Sex

No differences were found in cTnT concentrations depending on the sex of studied newborns.

CTnT Concentration and Mode of Delivery

No significant difference in cTnT concentration was found between newborns delivered by cesarean section and those delivered the natural way.

Relationship between cTnT Concentration and Blood Oxygenation

No significant correlation was found between blood oxygenation and cTnT concentration in healthy newborns ($R = 0.148$, $p = 0.310$).

Discussion

Heart diseases are a significant cause of morbidity and mortality in newborns. The diagnostic methods indicating cardiac disease in newborn are often not sufficient or, in many cases, cannot be used due to high technical requirements or their invasive nature. Medical knowledge concerning biomarkers in diagnosis of the circulatory system in adult patients has experienced great advancements. Among them, cardiac troponins play the main role. In the current literature, there is still not enough data about their physiologic features in the newborn period, as well as concerning variability of these markers in newborns with heart diseases. Due to the lack of this knowledge, cardiac troponins are not routinely used in cardiac diagnostic procedures in newborns.

The aim of the study was to evaluate physiologic variability of cTnT in healthy newborns, including determination of percentile normal ranges depending on chronological and postmenstrual age.

Despite the obvious usefulness of troponins in cardiac diseases in adult patients, even in this group there are still some problems with cT analysis and interpretation, especially concerning boundary values [7]. There are no unequivocal guidelines concerning interpretation of cardiac troponins concentrations in neonatology. A few research groups tried to determine cTnT referential ranges in preterm and full-term newborns. An aggregate statement of cTnT values achieved by particular research teams is presented in Table 3.

In one of the largest studies, published by Baum et al. [8], distribution of cTnT in cord blood was evaluated in 869 healthy newborns. The authors revealed statistically significant differences in cTnT concentrations between male and female patients – higher values were observed in females. The study did not take Apgar scoring into account. The authors stated

Table 3. Cardiac troponin T (cTnT) in newborns on the basis of selected publications

Author	Patients, *n*	Age		Result, ng/mL	
Baum et al. [8]	869	Cord blood		Mean Range 97.5th percentile	0.014 0–1.26 0.074
Fortunato et al. [9]	87	Cord blood		Mean Range	0.005 0–0.062
Clark et al. [10]	215	Cord blood		Median IQR 95th percentile	0.010 0.010–0.014 0.05
Clark et al. [11]	14	1 day		Median IQR	0.010 0.010–0.011
Clark et al. [12]	113	68 h		Median IQR	0.025 0.010–0.062
Clark et al. [11]	14	3 days		Median IQR	0.034 0.022–0.046
Boo et al. [13]	50	0–48 h		median IQR 90th percentile	0.02 0.01–0.011 <0.03
Awada et al. [14]	116	Median of age IQR	23 h 12–34	Median IQR	0.044 0.01–0.279 0.06±0.05
Güneś et al. [15]	15	0–15 days			0.04±0.02

IQR, interquartile range.

that healthy full-term newborns presented higher cTnT concentrations in comparison to adults. This fact must be considered when construing elevated cTnT concentration in newborns [8].

The difference in cTnT concentration between males and females was not confirmed in studies conducted by Clark et al. [10]. The aim of their research was to evaluate troponin T reference ranges in cord blood of healthy newborns. The study included 215 healthy neonates born at 37–41 weeks' gestational age. Data concerning gestational age, birth weight, sex, mode of delivery, and Apgar scoring was taken into consideration in the studied group. There was no significant correlation stated between cardiac troponin T concentration and gestational age, birth weight, or Apgar scoring in the 1st minute. Similarly, there was no significant difference in cTnT concentrations in boys and girls or between newborns delivered by cesarean section and the natural way [10]. Consecutive study, conducted by the same authors, confirmed a lack of correlation between mode of delivery, gestational age, sex, and Agar scoring at the 5th minute in healthy full-term newborns [12].

Another study, in which serial measurements of cTnT concentrations in full-term newborns were performed, revealed cTnT increased with peak levels on the 3rd day of life. Healthy preterm newborns presented higher troponin levels than full-terms, but the difference was not statistically significant [11]. Clark et al. [16] also stated that troponin concentrations in both full-term and preterm newborns were higher than reference ranges for adults. The above results, especially in preterm newborns, are probably caused by changes occurring in circu-

latory and respiratory systems, and not by prematurity itself. Rapid exposure to high-pressure system and loss of low-pressure placental circulation might be a troponin-releasing factor [17]. Additionally, cross reaction with fetal muscular troponin T cannot be excluded. The theory seems to be confirmed by studies conducted by Fortunato et al. [9] in which cTnT concentrations in 22 healthy fetuses at 22–25 weeks of gestational age were comparable to concentrations found in preterm newborns born at 30 weeks of gestational age [9]. However, the studies performed by Clark et al. [16] revealed that postnatal cTnT concentrations were usually higher than evaluated in cord blood. The results of the above studies indicate the necessity of considering chronological or postmenstrual age while interpreting cTnT concentrations in newborns.

On the basis of the present study, the significant negative correlation between postmenstrual age and cTnT concentration was confirmed. Postmenstrual age is now recommended as the most proper tool to evaluate development of premature infants, especially when comparing infants born in different gestational ages.

The physiologic levels of serum troponin T in newborns have not been established yet, inter alia because results achieved by scientific groups varied from each other. However, none of the research groups had taken postmenstrual age into considerations, although there were studies conducted on both term and preterm newborns.

Data from our study indicates that cTnT concentrations in newborns correlate with postmenstrual age, which can be the first step towards establishing referential values in this age group. These results can be inspiring to conduct other studies, on bigger groups, to confirm this theory.

No significant correlation was found between cTnT concentrations and gestational age, which is consistent with most literature data [10–12, 16]. On the other hand, research by Awada et al. [14], including 116 healthy newborns on the 1st day of life, revealed a significant correlation between these parameters – the highest cTnT was found in preterm newborns.

The results of the present study did not confirm significant differences in cTnT concentrations according to chronological age. Previously performed studies revealed an increase of troponin level right after birth and maintenance of elevated concentration (comparing to adults) to the 7th or (according to other authors) 15th day of life [11, 15]. In the current literature there were no studies found evaluating cTnT in infants over 2 weeks of age. In the present research, no correlation between cTnT and chronological age in newborns ≥7th day of life was stated. Furthermore, no correlation between cTnT and sex, mode of delivery, or saturation was found in the studied group. The results of the study are accordant with most of the literature data [10–12, 14]. Only Baum et al. [8] found a significant difference in cTnT concentrations in males and females (higher in boys). Although it is the only study with such results, it includes the largest number of patients.

Güneś et al. [15], Boo et al. [13], and Costa et al. [18] revealed that newborns born with severe perinatal anoxia had significantly higher cTnT concentrations during the first hours of life, compared with newborns born in good or moderate condition. Cardiac troponin T concentrations remained high also on the 3rd and 7th day of life [13, 15, 18]. In the present study no correlation between cTnT concentrations and Agar scoring in the 1st or 5th minute of life was found. While interpreting the results, it must be considered that there were no newborns with severe perinatal asphyxia in the studied group (Apgar scoring <4 points was one of the exclusion criteria) and that the studied patients were over 1 week of age. Other studies which included healthy newborns (without asphyxia in perinatal period) also did not reveal any relation between cTnT concentrations and Apgar scoring [10, 12].

This is the first study that includes newborns older than 2 weeks of age. Most of the cited studies focused on very young neonates during their first 3 days of life. There was only one study cited that included patients up to 15 days of age, but it evaluated only several newborns. Moreover, the results of most of the cited studies differed from each other.

Our study included patients over 6 days of age, and according to data from literature this is the first attempt to evaluate physiological ranges of serum troponin T in such newborns. This is most likely the reason why some of our findings differed from other cited studies.

Conclusions

We draw two conclusions from our research: (1) cTnT concentration depends on post-menstrual age in newborns and (2) cTnT concentration in newborns does not depend on sex, mode of delivery, or blood saturation.

Disclosure Statement

The authors declare no conflicts of interest.

References

1 Solnica B: Troponiny sercowe. Medycyna Praktyczna 2004;10:133–136.
2 Braunwald E, Fauci AS, Kasper DL. Harrison's Principles of Internal Medicine, ed 15. McGraw-Hill, New York, 2001.
3 Adamcova M: Troponins in children and neonates. Acta Paediatr 2003;92:1373.
4 Horwich TB, Patel J, MacLean WR, Fonarow GC: Cardiac troponin I is associated with impaired hemodynamics, progressive left ventricular dysfunction and increased mortality rate in advanced heart failure. Circulation 2003;108:833–838.
5 Kaplan S: Biochemical markers of myocardial injury in children. Circulation 1997;96:2496.
6 American Academy of Pediatrics: Policy statement: age terminology during perinatal period. Pediatrics 2004; 114:1362–1364.
7 Agzew Y: Elevated serum cardiac troponin in non-acute coronary syndrome. Clin Cardiol 2009;32:15–20.
8 Baum H, Hinze A, Bartels P, Neumeier D: Reference values for cardiac troponins T and I in healthy neonates. Clin Biochem 2004;37:1079.
9 Fortunato G, Carandente GP, Martinelli P, Sglavo G, Vasallo M, Tomeo L, Rea M, Paladini D: Cardiac troponin T and amino-terminal pro-brain natriuretic peptide concentrations in fetuses in the second trimester and in healthy neonates. Clin Chem Lab Med 2006;44:834–836.
10 Clark SJ, Newland P, Yoxall CW, Subhedar NV: Cardiac troponin T in cord blood. Arch Dis Child Fetal Neonatal Ed 2001;84:F34–F37.
11 Clark SJ, Newland P, Yoxall CW, Subhedar NV: Sequential cardiac troponin T following delivery and its relationship with myocardial performance in neonates with respiratory distress syndrome. Eur J Pediatr 2006; 165:87–93.
12 Clark SJ, Newland P, Yoxall CW, Subhedar NV: Concentration of cardiac troponin T in neonates with and without respiratory distress. Arch Dis Child Fetal Neonatal Ed 2004;89:F348–F352.
13 Boo NY, Hafid H, Nawawi HM, Cheah FC, Fadzil YJ, Abdul-Aziz BB, Ismail Z: Comparison of serum cardiac troponin T and creatine kinase MB isoenzyme mass concentrations in asphyxiated term infants during the first 48 h of life. J Paediatr Child Health 2005;41:331.
14 Awada H, Al-Tannir M, Ziade MF, Alameh J, El Rajab M: Cardiac troponin T a useful early marker for cardiac and respiratory dysfunction in neonates. Neonatology 2007;92:105–110.
15 Güneś T, Oztürk MA, Köklü SM, Narin N, Köklü E: Troponin-T levels in perinatally asphyxiated infants during the first 15 days of life. Acta Paediatr 2005;94:1638.
16 Clark SJ, Newland P, Yoxall CW, Subhedar NV: Cardiac troponin T in neonates. Acta Paediatr 2001;90:957–959.
17 Noori S, Seri I: Pathophysiology of newborn hypotension outside the transitional period. Early Hum Dev 2005; 81:399–404.
18 Costa S, Zecca E, De Rosa G, De Luca D, Barbato G, Pardeo M, Romagnoli C: Is serum troponin T a useful marker of myocardial damage in newborn infants with perinatal asphyxia? Acta Paediatr 2007;96:181.