Assessment of Plasma Troponin I, Total Creatine Kinase and Creatine Kinase -MB as Biomarkers for Acute Coronary Syndrome in El-Obied City

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Abstract

Acute coronary syndrome is one of the world's major killers and has a high morbidity and mortality rates. The aim of this study to assess the role of different markers used in the diagnosis of acute coronary syndrome. Descriptive case - control study conducted during the period from October 2015 to August 2016 to determine the plasma levels of total creatine kinase (CK), creatine kinase – MB (CK-MB) and troponin I as diagnostic markers for acute coronary syndrome. Statistical package for social science (SPSS version 17) computer software was used for data analysis. The result of this study showed significant high level of CK and CK-MB of the test group when compared with control group and significant elevated means of plasma levels of total CK and CK-MB of myocardial infarction patients when compared with unstable angina within test group. The result of this study also revealed that; the plasma troponin I is positive in myocardial infarction when compared with unstable angina in test group. Conclusion: Qualitative assessment of plasma level of cardiac troponin and measuring of the plasma activity of total CK and CK-MB are helpful markers for diagnosis of patients with acute coronary syndrome.

Key words: mycardial infarction, unstable angina, North Kordofan.

مستلخص

يعتبر مرض متلازمة الشريان التاجي الحادة واحدا من الأمراض الرئيسية القاتلة على مستوى العالم و ذو معدل عالي من الإمراضية و الوفيات. الهدف من هذه الدراسة هو تقييم دور الدلائل المختلفة المستخدمة في تشخيص مرض متلازمة الشريان التاجي الحادة. أجريت هذه الدراسة الوصفية في الفترة من أكتوبر 2015 و حتي أغسطس 2016 لتحديد النشاط الكمي لإنزيمي الكرياتين ناقل الفوسفات والكرياتين ناقل الفوسفات العضلي الدماغي و تحديدا كيفيا لبروتين التروبونين في مصل الدم لدى المرضي السودانيين المصابين بمرض متلازمة الشريان التاجي الحادة. أستخدم برنامج الحزمة الإحصائية للعلوم الإجتماعية لتحليل النتائج النسخة 17. أظهرت نتائج هذه الدراسة ارتفاع ذو دلالة إحصائية في متوسطي إنزيمي الكرياتين ناقل الفوسفات والكرياتين ناقل الفوسفات العضلي الدماغي في مجموعة الإختبار عند مقارنتها مع المجموعة الضابطة. وأيضا أظهرت نتائج هذه الدراسة زيادة ذات دلالة إحصائية في متوسطات إنزيمي الكرياتين ناقل الفوسفات والكرياتين ناقل الفوسفات العضلي الدماغي فى المرضى المصابين بالذبحة القلبية عند مقارنتها مع المرضى المصابين بالنوبة القلبية غير المستقرة في مجموعة الإختبار. وأشارت هذه الدراسة الي وجود نتيجة كيفية إيجابية في بروتين التروبونين آي لدى المرضى المصابين بالذبحة القلبية عند مقارنتها مع المرضى المصابين بالنوبة القلبية غير المستقرة في مجموعة الإختبار. ونستخلص من هذه الدراسة الي أن تحديد نشاط إنزيمي الكرياتين ناقل الفوسفات و الكرياتين ناقل الفوسفات العضلي الدماغي مؤشر مساعد لتشخيص مرض متلازمة الشريان التاجي الحادة.

Introduction

Ischemic heart disease (IHD) is a major health problem worldwide and is the most common cause of death in most western countries, Nearly 500,000 Americans die of IHD annually, IHD has been increasing in Japan and is now the second leading cause of death there, IHD had become the leading cause of death by 2004 accounting for 1.46 million deaths and deaths due to IHD were expected to double in 2015, Its predicted that by 2030; 23 million people will die from IHD [1]. Acute coronary syndrome (ACS) constitutes a major cause of morbidity and mortality worldwide [2]. The incidence of ACS varies greatly among different European countries, partly due to disparities in dietary habits and the prevalence of cardiovascular risk factor, although timely and appropriate treatment reduces the risk of an immediate or subsequent poor outcome, the high prevalence of risk factor for coronary artery disease ensures that the development of future ACS will also be high, and is associated with lower mortality if diagnosed early, the diagnosis is based on clinical symptoms, electrocardiogram (ECG) and circulating biomarker level changes [3]. Cardiac biomarkers have a major impact on the management of this disease and are now the cornerstone in its diagnosis and prognosis and have role in highlighting not only myocardial necrosis but also different facets of the Pathophysiology of acute coronary syndrome. The use of multiple biomarker testing lead to better characterization of each individual case and thus aid to singularize the stratagem of management of each case in the short and long term [3]. Cardiac necrosis markers are routinely assessed in ST segment elevation myocardial infarction, but the results are mainly used for confirmation of infarct diagnosis, rather than the estimation of infarct size. Usually, a larger release of cardiac necrosis markers is correlated with a larger extent of myocardial injury, and a faster release (wash-

out) has been considered as an indicator of successful reperfusion [4]. Therefore these biomarkers are tools used to identify high risk individuals, quickly and accurately, and determine treatment plans and prognosis [5]. The General objective of this study was to assess the plasma levels of troponin I, total CK and CK-MB among acute coronary syndrome patients in El-Obied city. The specific objectives were to assess the plasma levels of troponin I, total CK and CK-MB among myocardial infarction –unstable angina patients in El-Obied city compared to control subject and to assess the relationship between the plasma levels of total CK, CK-MB and troponin I in myocardial infarction – unstable angina patients with the duration of chest pain.

Materials and methods

This is quantitative, case-control, descriptive study carried in El-Obied city in north kordofan state. The data obtained from El-Obied teaching hospital (Cardiac Care Unit) during the period from October 2015 to August 2016. A thirty patients with acute coronary syndromes were selected after taking their consents as (test group). Each volunteer in this study was asked to come to El-Obied teaching hospital for medical assessment and sample collection. A thirty apparently healthy subjects were selected as a control group who were age and sex matched to the acute coronary syndrome group (test group). Clinical data was obtained from the history and recorded on a questionnaire. Clinical assessment of the study group was done by a medical doctor according to the questionnaire. Clinical history and diagnosis of the test group and the control group were done by a physician. After informed consent, and use of antiseptic alcohol swab for the skin (70% ethanol), 5 ml of venous blood was collected from each volunteer included in this study. Plasma was separated by centrifugation at 3000 rpm for 5 minutes at room temperature.

The supernatant plasma was collected by means of micropipette

in tightly sealed container and kept at -20° C till used later. The plasma then allowed to thaw at room temperature and investigated for troponin qualitatively and total CK and CK-MB activity quantitatively by using spectrophotometer. In this study all chemical and reagents used were obtained from Biosystem Company. A kinetic method for quantitative in vitro determination of CK and CK-MB in human plasma with spectrophotometer was used in this study [6,7]. while a chromatographic immunoassay for the qualitative determination of troponin in human was used. The precision and accuracy of all methods used in this study were checked by including commercially prepared control sera. The data collected in this study were analyzed by using SPSS computer program package version 17. The mean and standard deviation of plasma total CK and CK-MB activity was used to compare between the test group and the control group. The *p* value was obtained using the (t) test. Correlation between the plasma total CK, CK-MB and the duration of chest pain was tested using person correlation. *p* values < 0.05 was considered to be statistically significant.

Results

Table (1) showed a significant difference between the means of the plasma total CK activity in the test group and control group. (Mean ± STD) (347.83± 395.458) U/L versus (102.77± 39.037) U/L respectively; (*P* value = 0.000), as well revealed a significant difference between the means of the plasma CK-MB activity in the test group and control group. (Mean ± STD) (50.60± 64.583) U/L versus (16.80±6.071) U/L respectively; (*p* value 0.000).

Table (2) Showed significant difference between the means of plasma total CK activity among patients with acute coronary syndrome (myocardial infarction (MI) and unstable angina). (Mean ± STD) (572.19 ± 431.907) U/L versus (91.43 ± 29.485) U/L (*p* value 0.000) respectively, furthermore showed a significant difference between the

means of the plasma evels of CK-MB activity among patients with acute coronary syndrome (MI and unstable angina). (Mean ± STD) (82.56 ± 75.490) U/L versus (14.07 ± 4.665) U/L respectively (*p* value 0.000) the mean of MI group is significantly raised.

Table (1). Comparison of the means of plasma total CK and CK-MB activities of the test group and control group.

Variables	Test group (n=30)	Control group (n=30)	*p* value
Plasma total CK (U/L) Range	347.83± 395.458 (53 – 1300)	102.77± 39.037 (44 – 186)	0.000
Plasma CKMB (U/L) Range	50.60± 64.538 (6 – 246)	16.80 ± 6.071 (5 – 25)	0.000

- The table shows the mean ± STD, range in brackets and probability (*p* value).
- *t* test was used for comparison.
- *p* value ≤ 0.05 is considered significant.

Table (2). Comparison of the mean of the plasma total CK and CK-MB activities among patients with acute coronary syndrome.

Variable	MI group (n = 16)	Unstable angina (n = 14)	*p* value
Plasma total CK (U/L) Range	572.19±431.907 (53 – 1300)	91.43±29.485 (60 – 127)	0.000
Plasma CKMB (U/L) Range	82.56±75.490 (6 – 246)	14.07±4.665 (8 – 24)	0.000

- The table shows the mean ± STD, range in brackets and probability (*p* value).
- *t* test was used for comparison.
- *p* value ≤ 0.05 is considered significant.

Table (3) revealed distribution of qualitative troponin I results among patients with acute myocardial infarction and unstable angina

Table (3). Distribution of qualitative troponin I among Patients with acute myocardial infarction and unstable angina.

Count		ACS		Total
		MI	UA	
Troponin I	Positive	16	0	16
	Negative	0	14	14
Total		16	14	30

Figure (1) showed significant positive correlation between onset of chest pain in (hours) and the plasma total CK activity (U/L) among patients with acute coronary syndrome (R= 0.2 , $p = 0.020$).

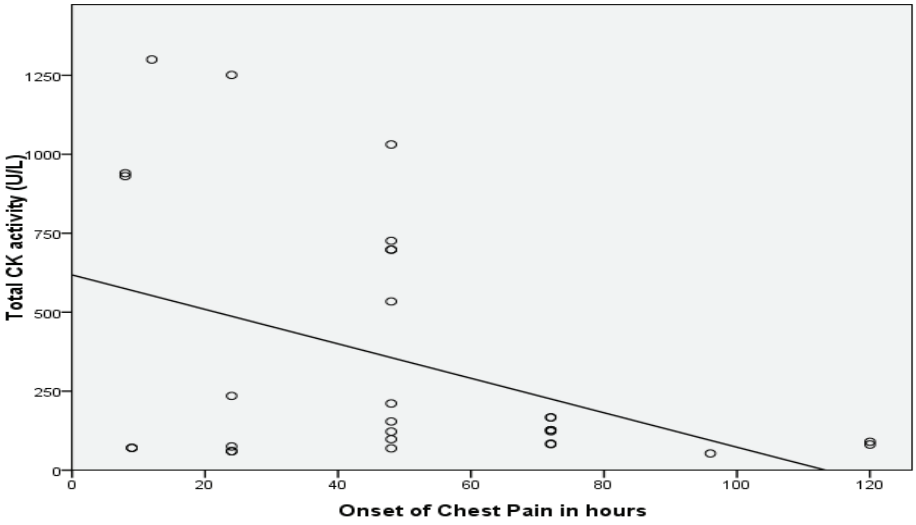

Fig. (1). The relationship between the onset of chest pain in (hours) and the plasma total CK activity among patients with acute coronary syndrome (r =0.2, $p = 0.020$). (weak positive correlation)

Figure (2) showed a significant positive correlation between the onset of chest pain in (hours) and the plasma CK-MB activity (U/L) among patients with acute coronary syndrome. (R= 0.126, $p = 0.054$).

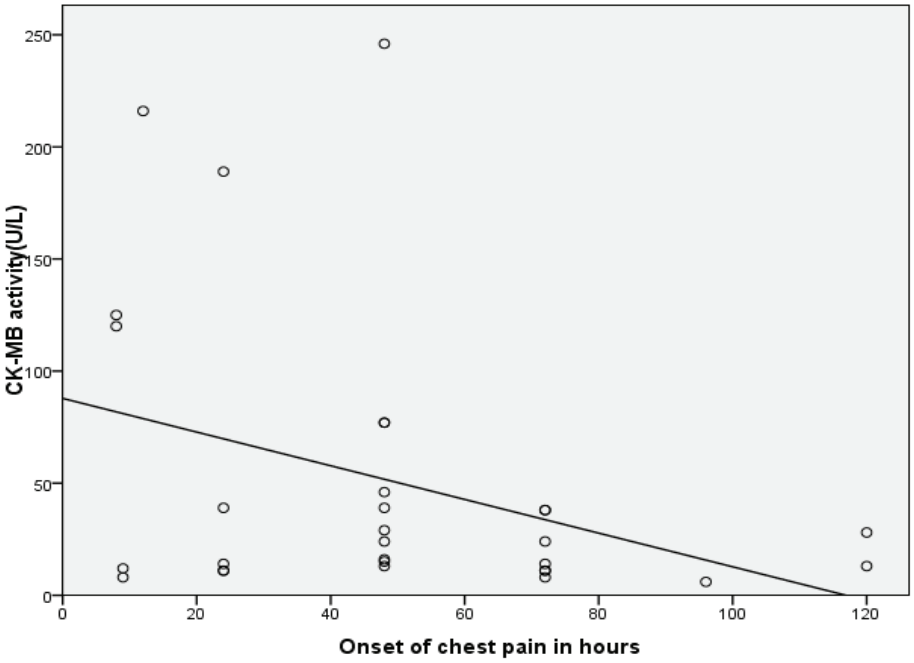

Fig. (2). The relationship between the onset of chest pain in (hours) and the plasma CK-MB activity among patients with acute coronary syndrome (r = 0.126, p =0 .054). (weak positive correlation).

Discussion

Measurement of total CK; CK-MB and troponin I are currently the tests of choice to confirm the diagnosis of acute coronary syndrome; in addition to ECG and, increase in the plasma level usually occur between approximately 4 to 8 hours after the onset of infarction peak at 8-24 hours and return to normal after 72 hours [8]. In the current study there is significant difference between the mean of the plasma activity of total CK and CK-MB in the test

group when compared with that of the control group, the mean of the test group is significantly raised as shown in Table (1) (p value = 0.000) and this may be due to the release of the enzyme from the myocardium of the patients with acute coronary syndrome. This agrees with previous study [8] who reported that; the mean value of total CK and CK-MB was greater than the normal range in both sexes. And it's found that the measurement of total CK and CK-MB are useful parameters for identifying people at high risk for acute myocardial infarction. This study showed a significant positive correlation between the plasma activities of total CK and CK-MB with the onset of chest pain and this reflected that the CK and CK-MB approximately start to elevate in about 4 hours; peaks in 8 to 24 hours; then after return to normal in about 72 hours from the onset of the chest pain reflecting the suitable time for CK and CK-MB activity determination which should be in between 4 to 8 hours and not less than 4 hours in order to produce a sensitive CK and CK-MB results for patients diagnosis; this agrees with previous study [9].

Conclusion: This study concluded that; these biomarkers are tools used to identify high risk individuals, quickly and accurately, and determine treatment plans and prognosis. The elevation of total CK and CK-MB activities and positive qualitative results of troponin I may be attributable to the release of intracellular proteins from damaged cells resulted from acute coronary syndrome.

Recommendation:

1. Plasma total CK, CK-MB and troponin I are usually the measurements of choice in patient with acute coronary syndrome since its increase and positive in the greatest number of cases.
2. Measurement of other novel cardiac biomarkers to assess the diagnosis of acute coronary syndrome.
3. Take care by controlling the factor that results in the disease (smocking, hyperlipidemia, and hypertension).
4. Quantitative measurement of troponin is

more reliable for the diagnosis of patients with acute coronary syndrome.

5. Determination of CK-MB isoenzymes; CK-MB1 and CK-MB is recommended.

References:

[1]. Thom T, Haase N, Rosamond W, Howard VJ, Rumsfeld J, Manolio T, Zheng ZJ, Flegal K, O'Donnell C, Kittner S, Lloyd-Jones D, Goff DC Jr, Hong Y, Adams R, Friday G, Furie K, Gorelick P, Kissela B, Marler J, Meigs J, Roger V, Sidney S, Sorlie P, Steinberger J, Wasserthiel-Smoller S, Wilson M, Wolf P. 2006. Heart disease and stroke statistics. A report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation. 113 (6): 85-151.

[2]. Andrikopoulos G, Tzeis S, Mantas I, Olympios C, Kitsiou A, Kartalis A, Kranidis A, Tsaknakis T, Richter D, Pras A, Pipilis A, Lampropoulos S, Oikonomou K, Gotsis A, Anastasiou-Nana M, Triposkiadis F, Goudevenos J, Theodorakis G, Vardas P. 2012. Epidemiological characteristics and in-hospital management of acute coronary syndrome patients in Greece: results from the TARGET study. Hellenic J Cardiol. 53 (1): 33-40.

[3]. Rognonia A, Cavallino C, Lupi A, Seccog G, Veia A, Bacchini S, Rosso R, Rametta F, Bango A. 2014. The role of biomarkers in diagnosis of acute coronary syndrome. 12: 1119-24.

[4]. Tomasz R, Artur D, Jacek L , Pawel K, Agata Brzozowska C, Zbigniew S, Andrzej U, Jacek S, Dariusz D. 2014. Creatine Kinase-MB Assessed in Patients with Acute Myocardial Infarction Correlates with Cardiac Magnetic Resonance Infarct Size at 6-Month Follow Up. Hellenic J Cardiol. 55: 4-8.

[5]. Scott M, Wells D, Meg S. 2008. Cardiac troponin. Journal of Veterinary Emergency and Critical Care. 18: 235-245.

[6]. IFCC. 2010. Reference Procedures for Measurement of Catalytic Concentrations of Enzymes: Corrigendum, Notes and Useful Advice. Clin Chem Lab Med. 48: 615-21.

[7]. Burtis C, Ashwood E, Burns D, Tietz. 2005. Textbook of Clinical Chemistry and

Molecular Diagnostics. Saunders . 4th edition.

[8]. Fathi A. Bin Alhassan R. 2011. Military Laboratory Department. Royal Medical Services. Jordan. Int J Bio Med Res. 2: 762-65.

[9]. Moe KT, Wong P. 2010. Current trends in diagnostic biomarkers of acute coronary syndrome. Ann Acad Med Singapore. 39 (3): 210-5.