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Original Article

Significance of Total Creatine Kinase and Creatine kinase-MB Levels In Patients With Acute Myocardial Infarction

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ABSTRACT

The aim of this study was to determine the significace of measuring total creatine kinase and creatine kinase-MB levels in the diagnosis of acute myocardial infarction.A strategy for diagnosing acute myocardial infarction was evaluated by studying 500 suspected patients aged 30-65 years. The control group,which included 200 subjects,was randomly selected from the casualty department. Investigations were carried out at Prince Rashid Bin Al-Hassan Military Hospital in the north region of jordan over one year period in 2009-2010. Total creatine kinase and creatin kinase-MB were measured in serum applying the creatine kinase,creatine kinase-MB NAC activated methods (Boehringer Mannheim's) using the Hitashi -912 autoanalyzer. In acute myocardial infarction patients,the mean value of total creatine kinase was greater than that of normal range. Results of 25-900U/L for creatin kinase((for both sexes) were obtained at admission. Also the mean value of creatine kinase-MB(8-40U/L)and % cratine kinase-MB were geater than that of the normal range in both sexes. The maximum peak was found after 8-12 hours from the time of admission of myocardial infarction patients,both males and females. This study demonstrated that measurement of total creatine kinase and creatine kinase-MB is currently the test of choice to confirm the diagnosis of an acute myocardial infarction.Measurement of total creatine kinase and creatine kinase-MB every 8-12 hours is an adequate and costeffective method for the diagnosis of acute myocardial infarction. It was found that measurements of total creatin kinase and creatine kinase-MB are useful parameters for identifying people at high risk for acute myocardial infarction.

1. Introduction

Diagnosis of acute myocardial infarction is based on clinical features,presence of risk factors,electrocardiographic changes,and levels of cardic biomarkers.Some patients with myocardial infarction have atypical signs and symptoms.Thirty percent have little or no chest discomfort,and the electrocardiographic changes may not indicate the diagnosis.Therefor,ancillary testing is necessary.Cardic biomarkers are a useful diagnostic tool,especilly 4 to 6 hour after the onset of signs and symptoms. In patients with possible acute myocardial infarction who have atypical signs and symptoms and inconclusive electrocardiographic findings,measurements of levels of biomarkers are used to assist in the diagnosis and appropriate triage.

Clinically,measurement of the level(s) of one or more specific cardic biomarkers is used to determine the extent of myocardial damage and to assess a patient's prognosis.Historically,creatin kinase (CK),CK-MB,CK mass,and lactate dehydrogenase have been used for routine clinical management [1].

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The determination of creatine kinase (CK) and creatine kinase MB (CK-MB) plays a major role in the differential diagnosis and in monitoring of myocardial infarction patients.

Although the methods for determination of these parameters are easy to apply, they are not specific for cardic muscle damage [2].Indeed,an increased CK-MB level in patients with normal total CK has been reported [3].

The kinetic assay with immuno-inhibition of CK-MB is a convenient procedure for cardic care unit patients,and is charecterized by simplicity of the procedure and the availability of results that make a significant contribution to clinical diagnosis [4]. .Measurement of total creatine kinase,and immunoassay of creatine kinase-MB play a major role in the differential diagnosis and monitoring of myocardial infarction. It has been reported that elevated CK activety appears within 6 hours of the acute cpisode. At the time of maximum activity,approximately 10-20 hours after the onset of the infarct,the CK activity attains levels between 160 and 2000U/L.(Using Wurzburg U.et al methods).Creatin kinase returns to normal after3-4 days [5].

An incrase in CK may be caused by myocardial disease or a skeletal muscle lesion. Creatine activites are greatest in skletal muscles,followed by the heart,brain and smooth muscles [5,6].
Early emergency determination of CK and CK-MB enzymes carry a considerable risk of fasely negative results,and in fact,may instill a false feeling of security to the clinician,leading to erroneous decisions. Because acute myocardial infarction (AMI) can be definitely excluded by means of these enzymatic tests only in the 10-20 hour interval after the onest of symptoms,it is rational to obtain samples only within this time limit [7].

CK and CK-MB may be increased in some patients earlier than 10 hours after the onset of symptoms. However, it would appear irresponsible to deny a patient adequate care until a laboratory verification of an AMI has been obtained,especialy because the risk of dangerous arrhythmias is greater during initial phase of an AMI [7-10].

Creatin kinase is abundant in most tissues. Activites as high as 12000IU/g and as low as 225IU/g have been reported in striated muscles. There are approximately 1600 IU of CK activity per gram in myocardium.15% to 30% of which is CK-MB .Results with sensetive mass assays have shown that most skeletal muscles contain small amounts (1-3%) of CK-MB. Whene a skeletal muscle is injured, it produces increased amounts of the B subunit, just as it dose during fetal development. Transient increase in the percentage of CK-MB in the skeletal muscle and elevations in circulating levels occur after acute muscle injury, including extremly rigorous exrcise [8-10].

The world health organization critria for the diagnosis of AMI generated in 1994, suggest that an atypical rising and falling pattern of CK-MB alone in the proper clinical setting should suffice for confirmation of AMI [10].However, recent puplications suggest that the CK-MB isoform type 2 may detect earlier stages of AMI [11,12]. Earlier publications [13], indicated that controversial findings of CK and CK-MB were seen in percataneous transluminal coronary angioplasty(PTCA) patients.

2.Method and Subjects

A total of 500 patients (300males and 200 females) aged,between,30-65 years; suspected to have AMI admited to the coronary care unit(CCU) at Rashid Bin Al-Hassan Military Hospital were included in the study. All of them had symptoms of AMI within the previous 24 hours. For a control group,200 non-AMI patients were entrolled in the study. They were chosen from the casualty deparetment with various discomfort complaints.Seven specimens were collected from each patient within 48 hours,after admission suffering from the acute symptoms. Samples were taken at time 0, 4, 8, 12,16, 24, and 48 hours.

The samples were centerifuged and analysis was done within one hour after collection.Serum total CKand CK-MB were done by CK,CK-MB NAC-activated immunoassay with sample start using the kit manufactured by (Boehringer Mannheim)and using the Hitashi -917 autoanalyzer. Testing was carried out on the system that uses prepared reagent analytic measurement based on Wurzburg's method ,where a specific antibody inhibits the CK-M moiety without affecting the CK-B moiety. The system can safely handle high-risk specimens by washing the instrument with 1% Sodium hypochlorite then with distilled water [11,14]. The kit's chemical details are as follows: CK NAC-activated creatine kinase EC.2.7.3.2 Cat No.144384 (CK-MB NAC-activated-Wurzburg.U.et al(1976).Klin.Wschr,54:357) intervals of 1 and 2.

3.Results

Both seum total CK and seum CK-MB approached their respective peak activaties within 4 to 8 hours after the admission with the acute symptoms.

Table I shows the results of total serum CK,serum CK-MB and percentage of CK-MB in both sexes. As can be seen,the mean value of total serum CK in males at admission time (T0) was greater than the normal range (80 U/L) and control group but in females was approximately equal to the normal range. Also ,the mean value of CK-MB and % CK-MB in males or females was higher than that of the normal value and control groups.

The mean value of total serum CK,CK-MB and %CK-MB in males and females reached maximum levels at T8 and T12.

Table I shows that the mean value of total CK,CK-MB at T12 start to decrase in both sexes while the percentage of CK-MB is approximately similar to the upper range of the normal value.

Table II shows the results ot total CK, CK-MB in males and females as a control group.

4.Discussion

The literature cited indicates that it is desirable for enzyme activities to be determined as soon as possible after the acute episode,with further tests performed after 6,12,24 and 48 hours and then at days [14]. In contrast,this study was performed at admission time,4,8,12,16,24 and 48 hours. Early determination of enzyme ctivities permits the detection of any pre-exisiting abnormal levels, as they may occur,for example in patients with liver or muscle diseases. CK-MB is mainly found in the heart muscle,where more than 20%of the total CK activity is present as

Table I.Distribution of CK,CK-MB and %CK-MB among the study group according to time.

	CK(U/L)		CK-MB(U/L)		%CK-MB	
	Meles	Females	Meles	Females	%Meles	%Females
T0	130	80	21	15.2	6.5	6.2
T4	(25-825)710	(25-270)353	(8.1-40)36.6	(9.2-17.5)33	(3.5-10.9)7.6	(3.6-9)9.6
T8	(65-2902)1285.2	(55-1350)1025	(5.1-16.8)96.3	(13.5-68.2)73.3	(4.4-14.1)10.4	(5.1-14)10.3
T12	(251-2935)1255.4	(620-1560)1015	(21-265)85.2	(35-138)70.3	(5.1-15.4)8.7	(5.4-15.1)7.8
T16	(240-2980)1122	(270-2270)754	(43-272.4)68.7	(32.2-121.3)45	(4.3-12.5)6.1	(5.2-10.8)6.2
T24	(225-1630)804.1	(215-1440)510	(8.8-133)41.5	(15.3-69)22.9	(3.6-9.7)5.2	(4.9-7.7)5.8
T48	(110-2155)220.5	(190-910)325	(5.5-79.4)8.5	(7-37.5)15.7	(2.3-7.5)4.8	(3.8-7)4.7
	(70-560)	(115-420)	(3.1-16.2)	(4.8-30)	(2.0-6.29	(3-5.8)

Table II. Distribution of CK and CK-MB among the control group according to time

	Total CK(U/L)			CK-MB(U/L)	
	Mean	Males	Females	Males	Females
T0	58	22-63	45(21-71)	2.5(2.1-3.4)	2.0(1.3-2.6)
T4	63	37-76	61(49-86)	3.0(2.6-3.8)	2.3(1.5-3.0)
T8	92	85-100	83(57-100)	4.0 (3.2-5.5)	3.4(3.2-4.5)
T12	87	75-97	92(84-101)	3.6(3.2-5.0)	4.1(3.5-5.4)
T16	78	69-89	85(72-92)	3.3(3.0-4.7)	3.7(3.2-4.8)
T24	65	52-74	64(56-76)	2.6(2.1-3.5)	2.6(2.1-3.8)
T36	55	49-66	60(52-63)	2.3(2.0-3.1)	2.2(1.6-3.1)
T48	48	33-56	51(49-56)	2.1(1.5-2.5)	2.1(1.2-2.6)

CK-MB, and nearly 80%as CK-MM.The MB isoenzyme is not considered to be myocardium- specific.Skletal muscles contain predominantly CK-MM.The CK-MB content in skeletal muscles is less than 3%. Ck-MB is demonstrable in the brain,but is also found in the stomach,intestine,and uterus.In healthy individuals,the total CK activity in the serum consists almost exclusively of CK-MM [15].

An increase in CK-MB is virtually always detectable in patients with recent infarcts.The diagnosis of MI is determined by the fraction of total CK contributed by the MB isoenzyme.CK activities greater than 100U/L and a CK-MB fraction exceeding 6% of the total CK activity raise the suspicion of myocardial infarction [4].

The same serum secimen that is used for the determination of the total CK activity shoud be taken for the assay of CK-MB.CK-MB rises,as dose the total CK,during the first hours after the infarction episode.Maximum CK-MB activites may appear shortly befor the peak of the total CK.CK-MB usually reverts to normal on the second or third day [6,15].

Increases in CK-MB in plasma are usually attributable to the release from the myocardium in the conditions known to increase CK-MB in muscles.

Patients withe a rising and falling pattern of CK-MB and a peak value that exceeds the upper limit of the refernce range should be considered to have an AMI until shown otherwise [16].

Measurement of CK-MB is currently the test of choice to confirm the diagnosis of an AMI [17].

Ellis et al [17].reported that increases in plasma levels usually occure between 6 to 10 hours after the onest of infarction (in the absence of thrombolysis),peak at 24 hours,and return to normal by 36 to 72 hours.

In contrast,in this study,increases in plasma levels occured between 4 to 8 hours after the onset of infarction,peaked at (8-12) hours,and returend to normal by 72 hours. Given these kinetics.measurement of CK-MB every12 hours is adequate and a costeffective method for diagnosis of AMI.Obtaining values more frequently will increase the diagnostic sensitivity. Levels of CK-MB peak slightly earlier,and the MB farction disappers slightly more rapidly than total CK [18].

The time for enzyme concentration to peak is earlier for small infarctions,leading some to hypothesize that non-Q was infarctions which also tend to be smaller,result from occlusion and reperfusion [19].

5.Conclusion

Increased CK-MB activity may also be found in conditions such as progressive muscular dystrophy,toxic myopathy,sever poisoning,polymyositis,and sever scleroderma,so the CK-MB alone is not a good practical way for the diagnosis of AMI. Patents with a rising and falling patteren of CK-MB and a peak value that exceds the upper limit of the reference range should be considered to have an AMI until shown otherwise.

Measurement of CK-MB and CK is currently the test of choice to confirm the diagnosis of an AMI. Increases in plasma level usually occure between 4 to 8 hours after the onset of infarction (in the absence of thrombolysis) peak at 8-12 hours,and return to normal by 48 hour. Given these kinetic ,measurement of total CK,CK-MB every 8-12 hours for admitted patients is an adequate,cost-effective method for diagnosis of AMI.In general, small amounts of damage to healthy skeletal muscle do not release enough CK-MB into plasma to cause diagnostic confusion, for example, intramuscular injections. Approximately 20% of myocardial infacts are silent,occuring particularly in diabetics, the eldrly, and hypertensitive subjects. Increased serum CK activity is liable to occure, if there is damage to skeletal or cardic muscles.

In this study most patients(males and females) had a peak CK,CK-MB,%CK-MB at 8-12 hours after the onset of MI.

It was found that measurement of total CK &CK-MB is an effective way to identify patients at high risk of AMI.

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