" Time of Peaking and rate of disappearance of CK - MB as an indicator of inhospital prognosis of patients with acute myocardial infarction ... "

Thesis

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M. S. degree in cardiology

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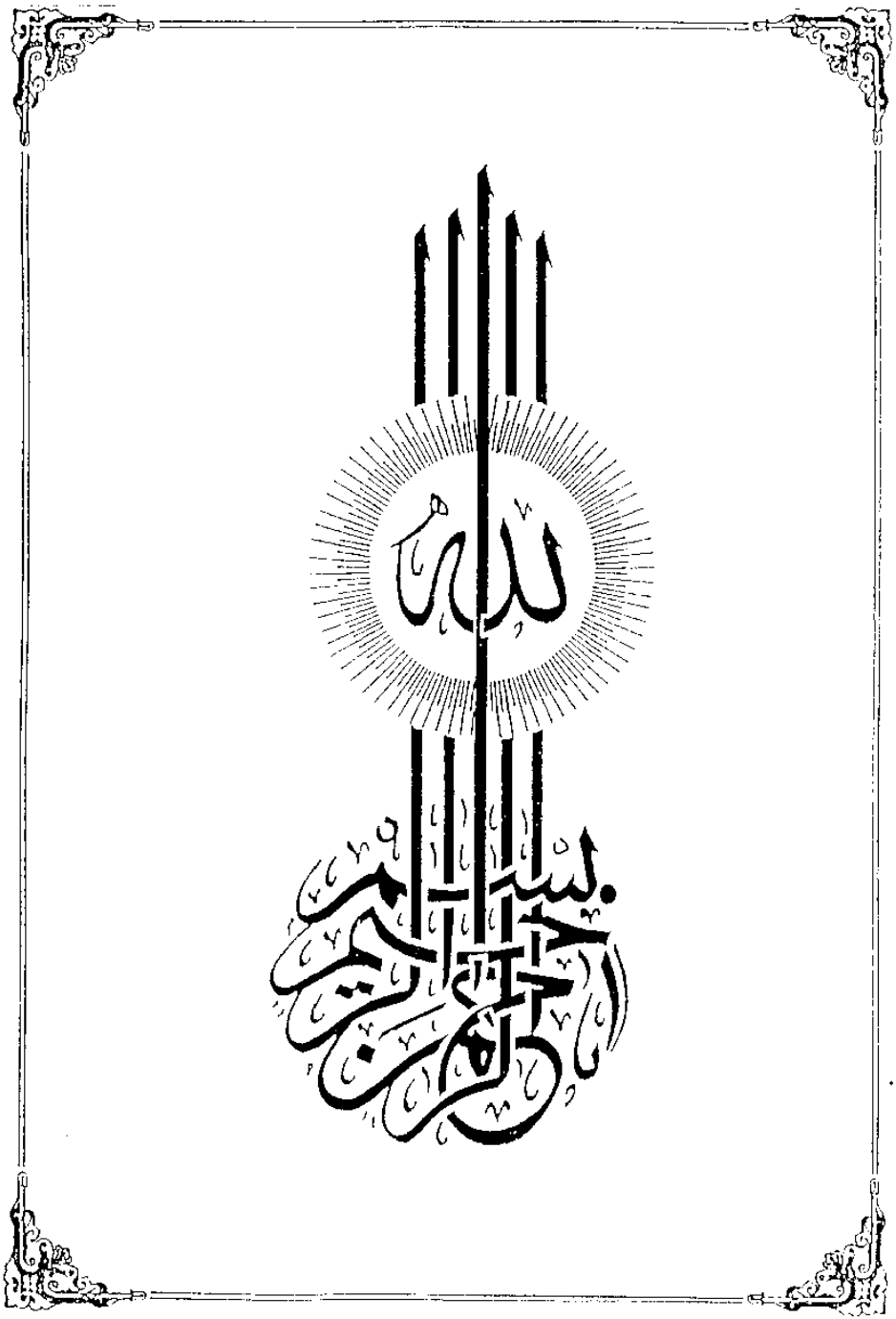
TO MY FAMILY



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CONTENTS

INTRODUCTION & AIM OF THE WORK

Introduction

In a recent review , *Lee and Goldman (1986)* stated that they do not recommend the use of a single cardiac enzyme assay to exclude the diagnosis of myocardial infarction in the emergency room .

They also stated that the sensitivity of the creatine kinase is poor because many patients arrive at the emergency room early in the course of myocardial infarction .

According to *Hackett and Cassem* experiences more than half of patients with acute myocardial infarction arrive at the emergency room more than 4 hours after the onset of symptoms .

- *Viskin and colleagues (1972)* had not presented convincing data to support their implication that a routine total creatine kinase was obtained in patients with chest pain in the emergency room or to dispute our explicit warning that a single level not to be used to exclude the diagnosis of myocardial infarction .

Lee et al . (1985) believed , however , that further research may help to identify subsets of patients who normaly would be discharged on the basis of their clinical characteristics and electrocardiograms , but for whom : doing a rapid CK- MBassay would be cost effective because a positive result would appropriatly convince the physician to continue to observe rather than to discharge the patient .

In 1975 Galen stated : the presence of CK - MB in sera indicates damage to the myocardium ; it is found during the 48 - hours period following acute myocardial infarction in all patients .

He also stated : After acute myocardial infarction CK - MB appears approximatly four to eight hours and reaches its peak level at 12 - 24 hours ; it may persist elevated throughout the initial 72 hours - period according to the infarct size . Creatine kinase - MB activity never exceeds 40 per cent of the total serum activity .

Aim of the work :

To find the relation between the value of CK - MB serum level and the time of its peaking in acute myocardial infarction as well as its extent and the short term prognosis of inhospital patients within the first week following acute myocardial infarction.

REVIEW OF LITERATURE

Total creatine Kinase

Its role and its isoenzymes

The creatine kinase , also referred to as creatine phosphokinase (CPK.) , Catalyses the reversible phosphorylation of creatine by adenosine triphosphate (ATP.) into phosphocreatine (or creatine phosphate, cr. p.) and adenosine diphosphate (ADP .) in the presence of magnesium ions .

Creatine kinase activity is greatest in striated muscles , brain and heart tissue which contain some 2500 , 550 , and 470 u / g protein respectively . Other tissues , such as the kidney and the diaphragm contain significantly less activity (< 30 u / g protein) . The liver and erythrocytes are essentialy devoid of activity *(Hearse et ,al .)*

Creatine kinase is a dimer composed of two subunits which are : B or brain and M or muscle . They are the products of two distinct structural genes . So, since the active form of the enzyme is a dimer , only three different pairs of subunits can exist : BB (or CK - I) , MB. or (CK - II) , and MM or (CK - III) . The comission on biochemical nomenclature has recommended that isoenzymes should be numbered on the basis of their electrophoretic mobility with the most anodal form receiving the lowest number . Accordingly the CPK isoenzymes should be numbered CK. I , CK. II , CK. III . *(J . of biological chemistry . 1977 .)* .

The distribution of these isoenzymes in the various tissues of the human body are shown in table I . *(Des jarlais , Morin . 1980.)*

Creatine kinase BB predonimates in the brain , prostate , gut , lungs , urinary bladder , uterus , placenta and thyroid . While creatine kinase MM predominates in skeletal and cardiac muscles.

CREATINE KINASE ISOENZYME PATTERNS OF HUMAN TISSUES

Tissue	CK Activity (U/ g Wet Weight)	CK - III (%)	CK - II (%)	CK - I (%)
Skeletal muscle	2500	98.9	1.1	0. 06
Rectus abdominis		81	19	
Rectus abdominis		94	5	
Pectoralis major		100	0	
Gastrocnemius		70 - 82	18 - 30	
Brain	555	0	2.7	97.3
Heart	473	78.7	20.0	1.3
Left ventricle		54 ± 6	41 ± 7	
Papillary muscle		52 ± 4	46 ± 5	
Stomach	190	4.3		95.7
		10	0	90
Small intestine	112	1.2	0	98.8
		11 - 13	7 - 9	78-80
Colon	138	2.1	0	97.8
		3 - 4	0 - 1	96
Rectum	267	1.2	0	98.8
Kidney	32	2.8	0	97.2
		8-12	0	88-92
Bladder	145	6.6	0	93.4
		2	6	92
Prostate	114	6	0	94
Lung		34 - 39	2 - 6	59 - 60
		27 - 72	0 - 4	18 - 69
Liver	0.6	0	0	100
Uterus	115	2.3	0	97.4
		5 - 16	2-20	64 - 93
Placenta		0	0	100
Thyroid		4 - 26	0 - 1	73 - 96

Des Jarlais , F, Morin 1980 .

Creatine kinase MB is present to varying degrees in the cardiac muscle (25 - 46% of CK activity) and also to a minor degree in skeletal muscles (< 5 %) .

All three of these isoenzyme species are found in the cell in the cytosol or associated with myofibrillar structures . However , there exists a fourth form that differs from the others both immunologicaly and by electrophoretic mobility . This isoenzyme , CK - Mt is located between the inner and outer membranes of mitochondria and it constitutes , in the heart, for example, up to 15% of the total CK activity . Creatine kinase activity may also be found in macromolecular form, the so called macro CK. This exists in two forms, Types I and II . Type I is CK. I associated with IgG or sometimes CK. III with IgA . *(Lang, et al. 1981) , (Lang , and Wurzburg 1982) .*

Thus , in addition to the two subunits in CK III , there exist at least two other M Subunits , each of which is capable of hybridizing with other M or B subunits to form active enzyme species with electrophoretic mobilities slightly different from the original unmodified subunit. *(Elser et,al.1983 .)*

Creatine phosphate , the major phosphorylated compound in muscle , is present in about eight folds excess over ATP. When muscle contracts , ATP is consumed (to form ADP) and creatine kinase catalyses the rephosphorylation of ADP (to form ATP) using creatine phosphate as the phosphorylation reservoir .

The serum creatine kinase is subjected to a number of physiologic variations .

For example , the activity in serum appears to be a function of muscle mass of the individual .

This is persumably the basis for the finding that females have lower serum activity than males , and that slightly built individuals often have lower serum CK activities than more heavily built members of the same sex . It has also been found that race or origin is important , thus a black North American female has higher serum CK. activities than a white male *(Fast , Sampson ... 1983)* .

CLINICAL SIGNIFICANCE OF CK ISOENZYMES

DISEASES OF SKELETAL MUSCLES :

(Thompson, 1964)

Serum creatine kinase is greatly elevated in all types of muscular dystrophies, and especialy so in the Duchenne type in which level of CK rises up to 50 times the upper limit of normal . In progressive muscular dystrophy , enzyme activity in serum is highest in infancy and childhood (7 - 10 years of age) and may be elevated long before the disease is clinicaly apparent . Serum creatine kinase activity characteristicaly falls as the patient gets older and as the mass of functioning muscle diminishes with the progression of the disease . About 50 - 80 % of the asymptomatic female carriers of Duchenne dystrophy show three - to six folds elevation of CK activity , but values may be normal if specimens are obtained after patients have experienced a period of physical inactivity *(Foxall. 1975)* .

Quite high values of CK are seen in viral myositis , polymyositis , and similar muscle diseases . However , in neurogenic muscle diseases , such as myasthenia gravis , multiple sclerosis , poliomyelitis and parkinsonism , serum enzyme activity is normal .