بسم الله الرحمن الرحيم

SERUM MYOGLOBIN MEASURED BY LATEX AGGLUTINATION TEST AS AN EARLY INDICATOR OF ACUTE MYOCARDIAL INFARCTION

THESIS

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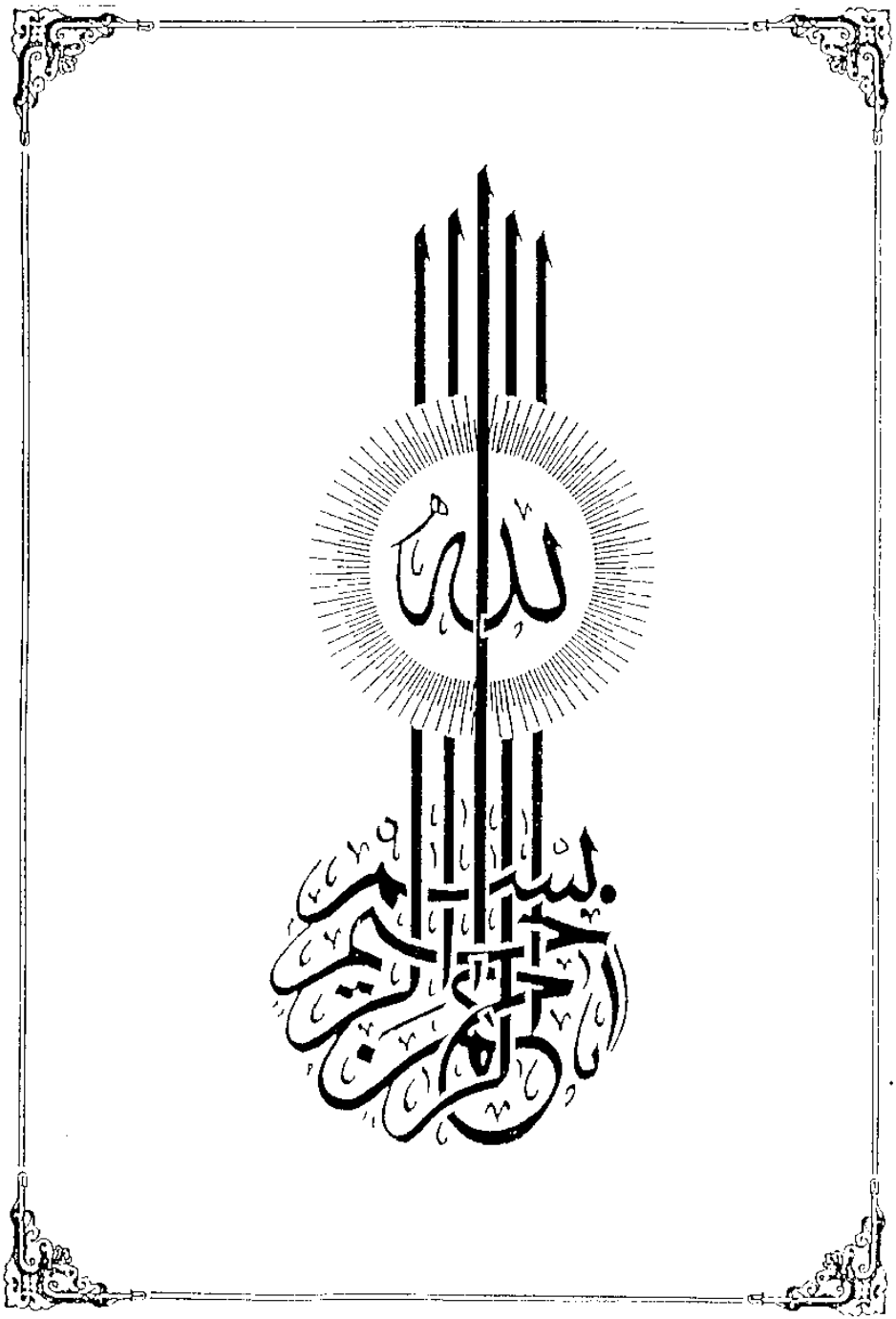

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To My Parents and Wife

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Thrombolytic therapy is now a standard initial treatment of patients with Acute Myocardial Infarction (AMI). Recent data have confirmed that early implementation of therapy is required for maximum reduction in mortality rates ***(Van Der Werf and Arnold, 1988).*** Consequently, delay of treatment to obtain confirmatory diagnostic information is precluded. However, accurate diagnosis of AMI in the early hours remains problematic. Chest discomfort and early electrocardiographic manifestations are nonspecific and do not distinguish transient myocardial ischaemia from necrosis; only 30% of patients hospitalized with suspected acute necrosis are subsequently confirmed to have AMI ***(Lee, et al., 1989).***

Recently, raised serum concentration of creatine kinase isoenzyme B and myoglobin help to identify patients during the early phase of myocardial infarction, but myoglobin, being a hemoprotein, is released rapidly due to its lower molecular weight and attains pathological values earlier than the specific enzyme creatine kinase isoenzyme B ***(Gibler, et al., 1987).***

Aim of The Work :

The aim of this work is to investigate the predictive value of the latex agglutination test "Rapi tex myoglobin Behring Institute" which is used to measure the serum myoglobin level as an early indicator of acute myocardial infarction.

REVIEW OF LITERATURE

PATHOPHYSIOLOGY OF ACUTE MYOCARDIAL INFARCTION

Acute Myocardial Infarction may be defined as a sudden irreversible damage of myocardium resulting from a critical imbalance between the oxygen supply and demand ***(Dewood, et al., 1980).***

In the majority of cases, myocardial infarction is a result of severe atherosclerosis of coronary arteries with or without acute thrombosis. Recently, however, a spasm of one or more of the diseased vessels has been implicated as a factor in its pathogenesis ***(Maseri,et al.,1978).*** Alteration of lumen dimensions and contour resulting from changes in medial coat tonus or spasm can give rise to shearing stresses in the diseased arterial wall and lead to intimal damage and haemorrhage ***(Pepine, 1989).*** In the presence of damage to the endothelium, the endothelium is unable to make or release endothlial derived relaxation factors and the important protective vasodilatory and antiplatelet aggregating actions are lost. In addition, during acute endothelial damage monocellular infilteration of the coronary arteries has the potential to release factors (such as thromboxane, leukotrines and sertonin) that may cause platelet aggregation, enhance blood coagulation, attract other white blood cells and exert further vasoconstricting effects on the coronary tree ***(Pepine,1989).***

To place those pathophysiological findings into clinical perspective, it is useful to separate the causes of myocardial infarction into two phases, the evolving and convalescent phase ***(Pepine, 1989).***

A. Evolving phase:

The evolving phase comprises of the first 6 hours after the onset of symptoms suggestive of myocardial infarction. Intervention during these 6 hours has the greatest likelihood of altering the course. During the evolving phase, hydrogen ion rapidly accumulates in the myocardium. Calcium ion is displaced from contractile proteins in the endoplasmic reticulum. Probably as a result of acidosis and the displaced calcium ion, distensibility is altered. Contraction ceases first, followed by migration of potassium ion outside the cell. This sets the stage for potentially lethal arrythmias. Sodium migrates into the cell, setting the stage for swelling and edema. Alteration of the membrane potential, again interacting with the efflux of potassium, poses the risk of arrythmias. Proteolytic enzymes leak out, cells swell and calcium migrates to the mitochondria, usually with toxic effects ***(Pepine,1989).***

There are also important vascular changes in this evolving phase. The blood vessels in the region of the infarct undergo profound changes. Embolization of atheromatous material and platelet fibrin masses has been demonstrated ***(Davis, et al., 1986)*** and the endothelial cell swelling has been observed. Platelets, leukocytes and fibrin block the small vessels and compress capillaries. Collateral vessels are compromised, capillaries leak, creating the risk of heamorrhage ***(Pepine,1989).***

B. Convalescent phase:

The convalescent phase encompasses myocardial changes occurring after the first 6 hours. During this phase, the myocardium undergoes

extensive geometric remodeling characterized by a thinning of the infarct wall and expansion of infarct zone ***(Pepine,1989).***

There are three types of irreversible cell injury which can be identified pathologically.

1) Coagulative necrosis :

This usually occurs with permanent interruption of the blood flow after thrombotic occlusion. The coagulation infarct is pale, being devoid of blood, and within 12 hours, a thin wavy fiber pattern can be seen microscopically in which the injured cells become thin and stretched out ***(Bulkley, 1986).***

2) Contraction band necrosis :

This occurs when myocardial ischaemia is followed by reperfusion, occurring in patients with coronary spasm and on the margins of coagulation necrosis. Grossly, the infarct appears red with a frank haemorrhage into the extracellular spaces. ***(Bulkley, 1986).***

3) Myocytolysis :

This type of necrosis affects focal nests of cells on the border of the infarcted area or in the subendocardium. There is subcellular damage, with loss of organelles and myofibroils. The cells survive for a time. Later some of them degenerate or die and become replaced by scar tissue ***(Bulkley, 1986).***

DETERMINANTS OF THE OUTCOME OF ISCHAEMIC INJURY

It has become apparent in recent years that the determinants of the end result are most important in pathophysiology of acute myocardial infarction.

Important factors are:

1) The duration of obstruction and its recurrence :

Experimental models provide an opportunity to study the evolution of infarction by removing the arterial clip at varying times and re-establishing the flow. Such work reveals that infarction is not an instantaneous process in which all the myocardial cells at risk undergo death at the same moment. Infarcts reperfused after an interval longer than 6 hours are not different morphologically from those which have not been reperfused. The infarct is transmural, extending from endocardium to pericardium. Comparison of nonperfused and reperfused infarcts at a time interval up to 6 hours after occlusion shows that re-establishing the blood flow reduces the infarct size by factors related to time. This reduction in size is in the depth to which the infarction extends through the wall from the subendocardial zone and not in the centrifugal extent of the infarct ***(Reimer, et al., 1977).***

Limitation of infarction by reperfusion within the period from 40 minutes to 4-6 hours is therefore due to sparing of the subepicardial zone; this has given rise to the concept that infarction spreads as a wave front through the ventricular wall from endocardium to epicardium over a time