ESTIMATION OF C-REACTIVE PROTEIN LEVEL IN PATIENTS WITH UNSTABLE ANGINA PECTORIS

رسالة

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By

Nady Kamal Michel
M.B.B.ch.

616.122
N.K

Supervisors

Prof. Dr. Ramez Raouf Guindy
Prof. of Cardiology
Faculty of Medicine - Ain Shams University

مكتبة

Dr. Maiy Hamdy ElSayed
Lecturer of Cardiology
Faculty of Medicine - Ain Shams University

Faculty of Medicine
Ain Shams University
1993

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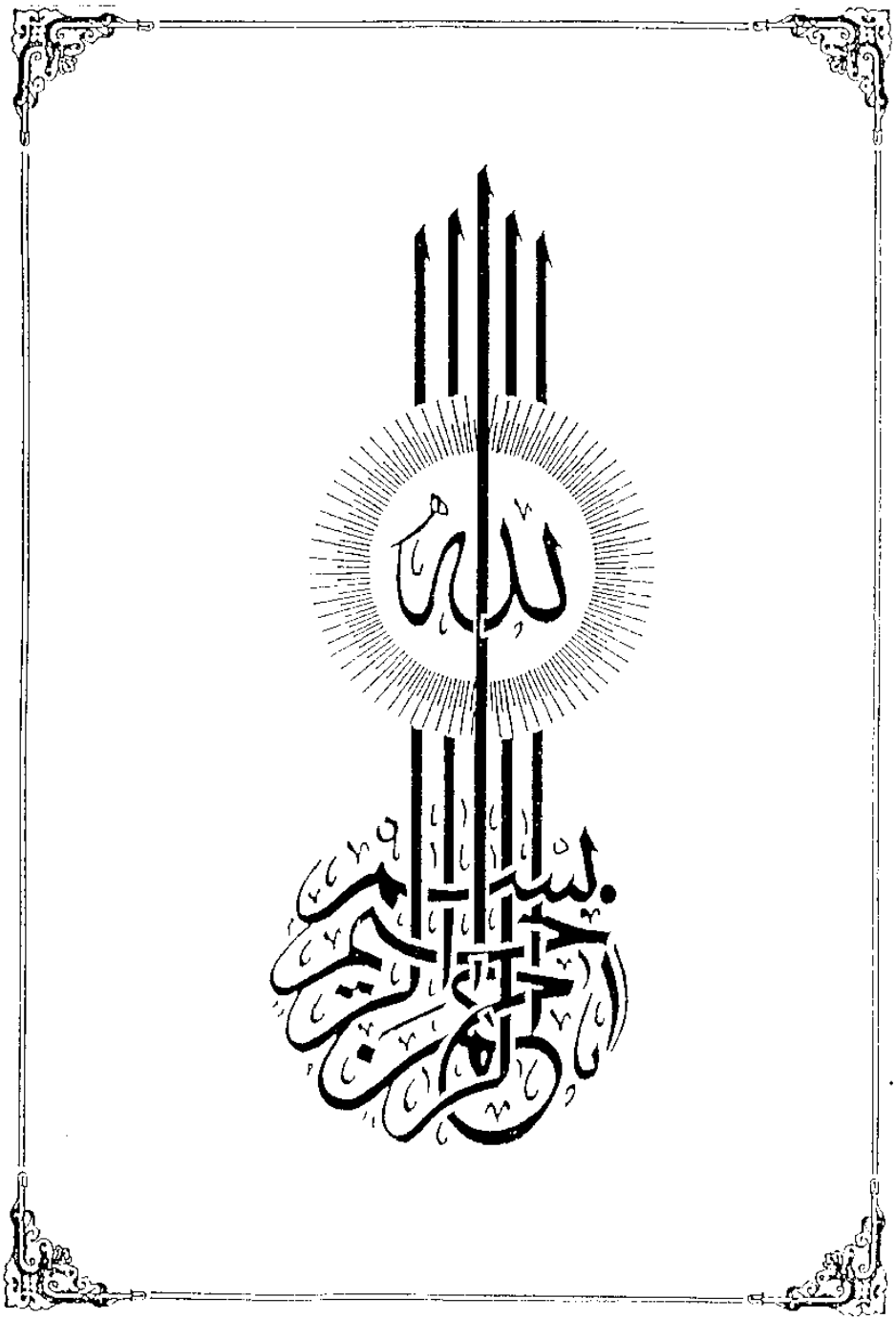

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TO MY FAMILY

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INTRODUCTION
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INTRODUCTION

Unstable angina is a clinical syndrome interposed in severity between myocardial infarction and chronic stable angina, it is important to be diagnosed as early as possible because of its frightening, disabling nature and the possibility that it heralds acute myocardial infarction.

While atherosclerosis, platelet aggregation, thrombosis and vasospasm have been clearly implicated in the pathogenesis of unstable angina, there is little information concerning the mechanisms responsible for the transition from the clinically stable to unstable state.

The episodic nature of unstable angina and the frequent lack of correlation between the extent of coronary stenosis and the clinical instability raise the possibility that cyclic changes in the activity of the atherosclerotic process itself may be involved.

AIM OF THE WORK

The aim of this work is to investigate whether an inflammatory component in unstable angina may contribute to the instability of atherosclerotic plaque and the susceptibility of these patients to coronary vasospasm and thrombosis.

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REVIEW OF LITERATURE

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ISCHEMIC HEART DISEASE

Myocardial ischemia is the result of a deficiency of arterial blood supply to the heart muscle. This deficiency must be evaluated in terms of the requirements of the heart muscle for oxygen and nutrients. The clinical spectrum of myocardial ischemia is heterogenous, one extreme of this spectrum is represented by the patients with asymptomatic coronary artery disease, whereas the other extreme includes the patients who suffers sudden cardiac death as the first clinical expression of coronary artery disease. In between these two extrems lie the clinical syndromes of stable angine, unstable angina and acute myocardial infarction. (Bulkely, 1990).

Myocardial infarction is defined as a process in which a segment of the myocardium is progressing from ischemia to actual necrosis. Creatine phosphokinase (CPK), lactate dehydrogenase (LDH), and serum glutamic - oxaloacetic transaminase (SGOT) are all released by memberan disruption. C-reactive protein which is known to be markedly elevated in tissue injury and inflammation has been also found to increase after myocardial infarction (Kroop et al., 1957; Kushner et al., 1978; De Beer et al., 1982).

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UNSTABLE ANGINA

The syndrome of unstable angina is a dramatic presentation of ischemic heart disease. Early in this century both myocardial infarction and stable angina had already been well described, but it has taken much longer to define a syndrome that is intermediate in severity between these two conditions; unstable angina (Braunwald, 1989).

In 1923, Wearn described in a group of 19 patients with acute myocardial infarction confirmed at necropsy, attacks of angina pectoris that may precede myocardial infarction and serve as warnings of the presence of coronary artery disease. In 1937, Sampson and Eliaser and Feil separately described a syndrome consisting of severe, prolonged anginal pain that often led to acute myocardial infarction and they termed it "impending acute myocardial infarction". Other terms that have been used for this condition include "acute coronary insufficiency" (Wood, 1961), "intermediate coronary

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syndrome" (Vakil, 1961), "preinfarction angina" (Vakil, 1964), "crescendo angina" and "acclerated angina" (Scanlon et al., 1973), but the term most frequently used now "unstable angina" was first used by Folwer and Conti et al. in 1971.

Definition:

Unstable angina is defined - in addition to absence of clear cut electrocardiographic or enzyme changes diagnostic of myocardial infarction - by one or more of the following features. (Rutherford, 1992).

- angina pectoris of new onset that appears in a patient who has been assymptomatic for the last 2 months.
- angina pectoris at rest as well as with minimal exertion.
- development of crescendo angina (more sever, prolonged or frequent) superimposed on a preexisting pattern of relatively stable, exertion - related angina pectoris.

The International Commitee of Standard Nomenclature for ischemic heart disease has proposed the use of the specific terms: do novo effort angina, spontaneous angina, worsening effort angina; in place of the generic term "unstable angina" to comprise its three subsets.

Pathophysiology:

Myocardial ischemia in coronary artery disease results from imbalance in myocardial oxygen consumption and

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myocardial oxygen delivery. In the stable phase of coronary artery disease, in which angina occurs mostly during physical effort or emotional arousal, increases in heart rate, wall tension, or the contractile state of myocardium frequently trigger ischemia by increasing, myocardial oxygen demand. Because of a flow - limiting coronary stenosis, the coronary flow reserve is inadequate and therefore increase in myocardial oxygen demand is not associated with a commensurate increase in coronary blood flow, leading to a supply/ demand inbalance and ischemia. (Sanders et al., 1977; Mirvis et al., 1986) Changes in coronary vascular tone also may trigger myocardial ischemia in the stable phase of coronary artery disease by inducing primary reduction in flow with or without antecedent increases in myocardial oxygen demand. (Hillis and Braunwald, 1978; Epestein and Talbot, 1981).

In most patients with unstable angina, ischemic episodes are frequent and generally occur at rest without antecedent increases in determinant of myocardial oxygen demand, although secondary changes in heart rate and blood pressure, induced by ischemia, may help perpetuate or accentuate myocardial ischemia (Figueras et al., 1979; Maseri et al., 1980). Chierchia et al., 1980 found in patients with unstable angina who are continuosly monitored a characteristic sequence of events. First, there is usually a reduction of coronary sinus oxygen saturation (which, in

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the presence of constant oxygen needs, signifies a reduction of coronary blood flow). This is followed by characteristic ECG changes, and then chest discomfort appears. Secondary to the latter, blood pressure and/or heart rate may rise (Fig.1). Thus in most patient with unstable angina, episodic reduction in coronary blood flow appears to be the main trigger for ischemic episodes, rather than an increase in oxygen demand. It is possible that in some instances an increase in myocardial oxygen demand and a reduction in supply occur simultaneously (Specchia et al., 1979), but the increased oxygen demand is unlikely to be the sole mechanism involved in unstable angina (Berndt et al., 1977; Neill et al., 1980).

The reduction of oxygen supply contributing to precipitation of ischemic episodes in patients with unstable angina results from an interplay between multiple factors including progression of atherosclerosis, platelet aggregation, thrombosis and coronary spasm (Epestin & Palmeri, 1984). (Table 1).

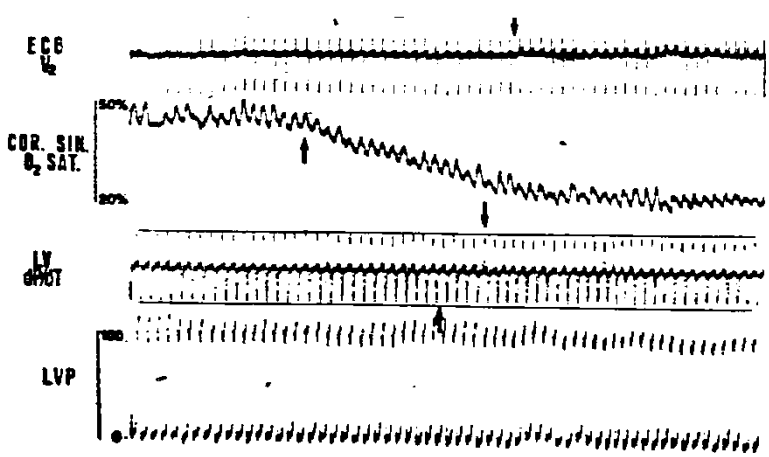

Figure (1): Continuous recording of electrocardiogram, coronary sinus oxygen saturation, left ventricular dP/dT, and blood pressure in a patient with rest angina. (Adapted from Chrerchia S. et al; Circulation 61: 759. 1980.

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Table 1

Pathophysiology of unstable angina

Interaction occurs
between:
Fixed coronary stenosis
Atherosclerotic plaque
and :
Dynamic coronary obstruction
Platelet aggregation
Thrombosis
Coronary spasm.

(Adapted from shah P.K.: pathophysiology of unstable angina In Crawferd M.H. (ed.): Cardiology Clinics, unstable angina. W.B. Saunders company, Philadelphia. vol.9 No.1: 11, 1991)

I. Progression of atherosclerosis:

Angiographic studies have shown that patients with stable and unstable angina do not differ from each other when traditional indices of the severity of coronary artery disease (the number of vessels with significant stenosis, the percentage diameter of stenosis, the minimal diameter of stenosis, the length of stenosis and the presence or absence of collaterals) are examined. (Alison et al., 1975; Wilson et al., 1986). A closer and more detailed examination of the morphology of coronary stenosis in the culprit coronary arteries, using antemortem as well as postmortem angiography, showed, however, that, in at least 70% of patients with unstable angina, the coronary stenosis tends

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to be eccentric with overhanging or irregular margins and intraluminal haziness or radiolucent filling defects, features that are infrequent (<20% of patients) in the coronary arteries of patients with stable angina (Levin and Fallon 1982; Ambrose et al., 1985). (Fig.2).

Detailed postmortem examination has shown that the atherosclerotic plaques in the culprit coronary arteries of patients with unstable angina has undergone marked recent progression with fissures or cracks in the fibrous cap of the plaque (Falk, 1983; Davies and Thomas, 1984). Most fissures averaged arround 300 to 400 µg in length and varied in width from narrow slits to large gaps or ulcerations of the plaque surface. (Fig.3).

Sherman et al., 1988 used the recently developed fiberoptic coronary angioscopy in examination of 17 arteries in 10 patients with stable angina and 15 arteries in another 10 patients with unstable angina undergoing coronary artery bypass surgery. They found that non of the 17 arteries of the patients with stable coronary disease had either a complex plaque or thrombus. In the "offending" arteries of the patients with unstable angina, three patients were found to have complex plaque and seven patients had thrombi in the culprit arteries (Fig.4).

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