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Concomitant measurements of serum annexin A5 levels and hematological indices as markers in recent and old myocardial infarction with low ejection fraction: A preliminary study

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ABSTRACT

Background: Serum annexin A5 (anxA5) level is significantly increased in patients with acute coronary syndrome. Hematological indices are significantly increased in patients with ischemic heart disease. This study aimed to demonstrate the changes in the distribution of blood cells and the levels of anxA5 in patients presented with significant low ejection fraction ST-elevation acute myocardial infarction (STEMI) in comparison with corresponding patients with ischemic heart disease.
Methods: Patients with low ejection fraction presenting at Hospital of Diyala University of Iraq were enrolled. Electrocardiograph (ECG), echocardiograph, hematological indices, serum annexin V (anxV) levels and the determinants of the cardio-metabolic risk factors were performed. Based on clinical examination, ECG findings and laboratory tests, patients were divided into healthy subjects (n = 20); patients with acute MI (n = 40) and with chronic MI (n = 12).
Results: Acute MI has significant high levels of serum triglyceride, uric acid and high mean value of red cell distribution width (RDW) compared with healthy subjects and chronic MI. Platelet distribution width (PDW) is significantly reduced in patients of acute MI and chronic MI compared with healthy subjects, whereas the plateletcrit (PCT) is significantly higher in acute MI compared with healthy subjects. There is an insignificant difference between the means of serum anxA5 levels of acute MI (35.6 ± 7.2 ng/ml) and chronic MI (32.4 ± 8.9 ng/ml), but significantly higher than the cutoff level of the healthy subjects (5 ng/ml).
Conclusions: Measurement of serum annexin level is a useful diagnostic marker of acute or chronic MI with low ejection fraction.

1. Introduction

Annexin A5 (anxA5) is among the annexins family of calcium-dependent phospholipid binding proteins. AnxA5 has both extracellular and intracellular presence, particularly in endothelial cells and blood platelets [9]. Patients with heart failure, the serum anxA5 levels are increased compared with healthy subjects and considered as a prognostic marker to predict the mortality in those patients [14]. The counts of small-size annexin V binding microparticle (sAMP) and small-size endothelial microparticle (sEMP) are reduced in patients with ST-elevation acute myocardial infarction (MI) after percutaneous coronary intervention (PCI) [12]. The levels of sAMP and sEMP were significantly higher in patients with acute MI at the time of admission compared with patients presented with stable angina and tended to decline thereafter [4]. Regarding the cardio-metabolic risk factors, the levels of circulating anxA5 do not serve as a good diagnostic or prognostic marker. In familial hypercholesterolemia, a risk factor of cardiovascular events and atherosclerosis, the circulating levels of anxA5 do not associate with the extension of atherosclerosis that demonstrated with thickness of intima-media (IMT) of carotid artery and it does not predict the cardiovascular events [10]. Seok et al. found that specific anxA5

Abbreviation: AnxA5, annexin A5; MI, myocardial infarction; BMI, body mass index; ECG, electrocardiograph; RDW, red cell distribution width; PDW, platelet distribution width; MPV, mean platelet volume; PCT, plateletcrit; ESR, erythrocytes sedimentation rate; sAMP, small-size annexin V binding microparticle; sEMP, small-size endothelial microparticle; PCI, percutaneous coronary intervention; IMT, intima-media thickness; NLR, neutrophil-to-lymphocyte ratio; CCU, coronary care unit; IHD, ischemic heart disease; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; EF%, ejection fraction percent; ES, end systole; ED, end diastolic; BP, blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; ELISA, Enzyme Linked ImmunoSorbent Assay; SD, standard deviation.

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polymorphisms may be associated with the development of obesity [15]. Recent studies investigate certain hematological indices as a marker of ischemic heart disease. Dehghani et al. found that significant high values of mean platelet volume (MPV) and platelet distribution width (PDW) observed in patients with chest pain of acute MI on admission compared with non-cardiac chest pain [6]. Moreover, these platelet indices are useful markers to predict the mortality as a higher mortality rate associated with a higher MPV and PDW in the survivals [13]. In patients with non-ST elevation acute MI (NSTEMI), the baseline red cell distribution width is high and significantly correlated with troponin levels [18]. Recently neutrophil-to-lymphocyte ratio (NLR) is significantly higher in patients with NSTEMI and significantly correlated with the clinical and angiographic findings [17]. The rationale of this study is to criticize the association of the circulating blood cells as a marker of acute cardiac events and the circulation of anxA5. Therefore, this study aimed to demonstrate the changes in the distribution of blood cells and the levels of anxA5 in patients presented with significant low ejection fraction ST-elevation acute MI (STEMI) in comparison with corresponding patients with ischemic heart disease.

2. Methods

2.1. Patients

Patients who are admitted into the coronary care unit (CCU) for management at the Hospital of Diyala University of Iraq from February 1st to June 30th 2015 were enrolled. Based on clinical examination, electrocardiographic (ECG) findings and laboratory tests, patients were grouped into twenty healthy subjects; forty patients with acute MI and twelve patients with chronic MI. The eligible patients were both genders of whatever age. Inclusion and exclusion criteria are listed in Table 1. Due to exclusion criteria the final study population consisted of 72 patients.

The study was conducted in accordance with the Declaration of Helsinki and was prospectively reviewed by the Scientific Committee at the Department of Medicine and approved by the Council of College of Medicine in the Diyala University.

2.2. Study procedures and data collection

At the time of entry, information related to the disease was recorded. Each potentially eligible patient examined clinically, and then subjected to the electrocardiography, echocardiography, blood pressure, blood analysis and Anthropometric measurements.

Table 1
Inclusion and exclusion criteria.

No.	Inclusion and exclusion criteria	Healthy subjects	Acute MI	Chronic MI
1.	Clinically presented with (chest pain of cardiac origin)	+	+	+
2.	Low ejection fraction	−	+	+
3.	ECG (significant elevation of ST segment)	−	+	−
4.	ECG (pathological Q waves)	−	−	+
5.	Laboratory test (positive cardiac troponin test of >4 ng/ml)	−	+	−
6.	Laboratory test (negative cardiac troponin test of <4 ng/ml)	−	−	+
7.	Complications (cardiac arrhythmias, cardiac shock)	−	−	−
8.	Evidence of acute renal failure	−	−	−
9.	Serum creatinine level above 1 mg/dl	−	−	−
10.	Debilitating patients	−	−	−
11.	Previous history of ischemic heart disease (IHD)	−	−	−
12.	Suboptimal echocardiographic imaging quality	−	−	−
13.	Structural heart valve pathology (including previous valvular surgery)	−	−	−
14.	More than mild aortic valve insufficiency	−	−	−
15.	known Ischemic mitral regurgitation (MR)	−	−	−

(+) referred to inclusion and (−) referred to exclusion criteria. mg/dl (milligrams per deciliter of blood). ng/ml (nanogram/milliliter).

2.2.1. Echocardiography

At rest in the left lateral supine position, experienced cardiologists examined all the patients using an ultrasound of the heart and a 1.5–4.5 MHz probe. Left ventricular ejection fraction (LVEF) is the fraction of outbound blood ejected by the left ventricle with each heartbeat. In the range of normal values, ejection fraction percent (EF%) is 55–75%. The Simpson method was recruited to calculate the EF% by dividing the volume of blood ejected by the heart at end systole (ES) by the total end-diastolic (ED) volume. $EF\% = [ED_{VOL} - ES_{VOL} / ED_{VOL}] \times 100$. In this study only patients with below normal ejection fraction of <55% were included.

2.2.2. Electrocardiography

The diagnosis of acute MI was confirmed based on patient's history, clinically (chest pain of cardiac origin), electrocardiography findings (more than 1 mm ST-segment elevation on two concordant ECG leads) and laboratory tests (positive cardiac troponin test of >0.04 ng/ml). The diagnosis of old or chronic MI was confirmed based on the electrocardiography changes (pathological Q waves of ≥0.02 s or QS complex in leads V2,V3, and ≥0.03 s and 0.1 mV deep or QS complex in leads I, aVL, V6, V4 to V6, II, III, aVF) and laboratory tests (negative cardiac troponin test of <0.04 ng/ml).

2.2.3. Blood pressure measurement

Arterial blood pressure (BP) was measured during in-hospital stay at the sitting position by using the manual mercury sphygmomanometer. Arterial hypertension was defined as presence of increased blood pressure (BP) > 140/90 mm Hg. The mean of the three readings at sitting position was taken. The pulse pressure is equal to the difference between systolic and diastolic blood pressure and the calculated mean arterial pressure is equal to the diastolic pressure plus 1/3 pulse pressure.

2.2.4. Blood analyses

Venous blood samples have been collected after an overnight fast and subdivided into two portions. The first one is used for the measurements of hematological indices: hemoglobin (Hb), red cell distribution width [RDW], neutrophil to lymphocyte ratio [NLR], platelet count, plateletcrit [PCT], mean platelet volume [MPV], platelet distribution width [PDW], and erythrocytes sedimentation rate [ESR] using the Coulter machine.

The second portion was centrifuged at 3000 rpm (revolutions per minute) for 10 min. The sera were separated for the following measurements: serum triglycerides, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), glucose, troponin, creatinine, uric acid, lipid profile and Serum anxA5 levels.

Patients considered at risk of dyslipidemia when the total cholesterol elevated more than 200 mg/dl or LDL-C levels increased over 130 mg/dl, or levels of HDL-C being less than 50 mg/dl and the triglyceride being of more than 150 mg/dl. Serum anxA5 level was measured by applying the Enzyme Linked ImmunoSorbent Assay (ELISA) technology taking the cutoff level of healthy subjects is <5 ng/ml.

Diabetes mellitus was confirmed based on established medical history or by detecting elevated fasting plasma glucose ≥ 7.0 mmol/l (millimoles/liter) on serial in-hospital measurements. Patient was considered as a smoker if he/she was currently smoking or was a smoker in the past.

2.2.5. Anthropometric measurements

Height (cm) and weight (kg) were measured using a stadiometer (Seca model) and a scale (Sensitive Computer). Body mass index (BMI) was calculated by using Quetelet's equation and expressed in units of kg/m^2, resulting from body mass in kilograms (kg) over the height squared meters (m^2).