Role of Interleukin-1α and Interleukin-8 in Myocardial Infarction

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Abstract

Objective: To study the effect of interleukin-1α and interleukin-8 in tissue injury during ischaemia and reperfusion in acute myocardial infarction patients.

Methods: Concentrations of (IL-1α) and (IL-8) for 25 patients with Acute Myocardial Infarction measured by enzyme linked immunosorbent assay (ELISA).

Results: All 25 patients with acute Myocardial Infarction had a significant rise in serum (IL-1α) and (IL-8) concentrations (33.62333±12.82255) (117.46±109.75) compared to normal subjects (14.032467±1.798464) (8.951± 5.7) respectively.

Conclusion: It is clear that (IL-1α) and (IL-8) results have a role in the development of tissue injury in acute myocardial infarction.

Key Words: Acute Myocardial Infarction (AML), Interleukin-1α (IL-1α) and Interleukin-8 (IL-8).

Introduction

Tissue injury after ischaemia and reperfusion in acute myocardial infarction is of a sequence of cellular interactions, and not a consequence of simple tissue anoxia. Several agents are involved including leucocytes [1,2], oxygen free radicals [3], and calcium ions[4]. Recent research shows that neutrophil cells are very important cause of myocardial tissue damage by forming reactive oxygen metabolites[5], proteolytic enzymes[3,6], and arachidonate derivatives[7].

So the mechanism of neutrophil recruitment from the blood stream to the myocardium during and after ischaemia and reperfusion should be explained[3,4]. Studies showed that risk of vascular disorders increase with raised levels of circulating C-reactive protein[8]. Advanced research studies showed that interleukin-8, interleukin-6 show high levels in AMI[9].

Interleukin-1α is a polypeptide hormone produced by activated macrophages that mediates a wide range of biological activities and interacts with surface receptors on numerous cell types[10]. (IL-1α) is an early proinflammatory cytokine, which cause a rapid up-regulation of other cytokines, chemokines and inflammatory factors as well as oxidative stress and inflammation[10,11].

Interleukin-8: it is well known that (IL-8) is a small basic protein (low molecular weight) consisting of a relatively short peptide chain, recent studies indicate that (IL-8) has a role in atherosclerosis[12,13]. (IL-8) is a cytokine which has regulatory and activating effects on neutrophils[14].

Aim of the study

To evaluate the serum concentrations of (IL-1α) and (IL-8) in patients with myocardial infarction to study the role of these cytokines during the process of tissue damage in AMI.

Materials and Methods:

Patient Selection

Patient's samples were collected from intensive care unit in Baghdad Teaching Hospital (The medical city) for the period from April 2011 to the end of June 2011. The study group comprised 25 patients (17 men, 8 women, mean age 58 yr, range 52 to 71) with AMI based on a history of prolonged ischemic chest pain and significant ST-segment elevations compared with 30 controls. Patients with interfering noncardiac diseases (D.M, Hypertensive, Uraemic) were excluded.

Blood sampling and measurement of (IL-1α) and (IL-8).

Fourty eight hours after infarction venous blood from patients was collected in to syringes by needle aspiration. Blood was kept at room temperature for 40 min. to clot and was centrifuged at 3,000 rpm for 15 min. Serum was stored at -70 ^{0} C until use. Concentrations of (IL-1α) and (IL-8) was measured by quantitative "sandwich" enzyme–linked immunosorbent assay (ELISA) technique. Briefly, standards and test samples were dispensed in duplicate into wells of 96-well microtiter plates, which had been pre-coated with monoclonal anti-human (IL-8) and (IL-1α) (Endogen, Woburn, MA, U.S.A.) antibodies, then, horse radish peroxidase (HRP)-conjugated detection antibodies were added into the wells followed by HPR-conjugated streptavidin (Endogen). For color reaction, 100ml of 3,3`,5,5`-tetramethylbenzidine substrate was added and wells were incubated for 15 to 30 min. The absorption at 450nm was determined using an automated ELISA microplate reader (Bio-tech, EL312e, Winooski, VT, USA).

Statistical analysis

All data are expressed as mean ± standard deviation (SD).

Difference between groups was analyzed by paired two-student t-test. Spearman s correlation test was used to assess relations between variables. P-values less than 0.05 was regarded as statically significant.

Results

Clinical Data:

The study group did not differ significantly from the control group with respect to age, sex distribution, risk factor profile, medication.

Serum Concentrations of (IL-1α) and (IL-8) in AMI:

Serum concentrations of (IL-1α) and (IL-8) were significantly increased in patients with AMI compared with the control Groups (*Table1 and Figure 1)* .

Table 1: Statistical analysis of IL-8 and IL-1α in AMI and Control subjects.

Parameters	AMI (Mean±SD)	Control (Mean±SD)	P-Value
IL-8 (ng/ml)	117.46 ± 10.975	8.951± 5.7	0.0001
IL-α (ng/ml)	33.62333± 12.823	14.32467 ± 1.798	0.00001

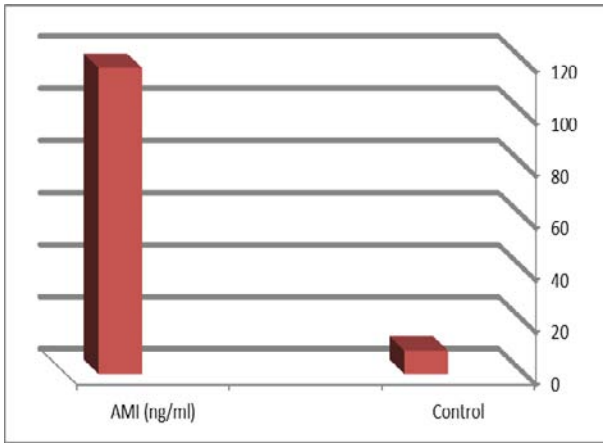

Figure 2: IL-1α level in AMI and control subjects

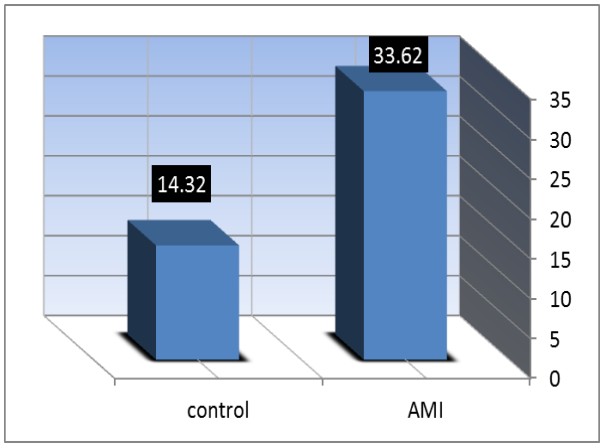

Figure 1: IL-8 level in AMI and control subjects

Discussion:

Interleukin-1 (IL-1) is a multifunctional cytokine, primarily involved in the regulation of inflammatory processes; it mediates most of the acute phase response to infection including induction of fever.[15] Recent evidence indicates that (IL-1) produced within tissues contributes to local inflammatory reactions.[16]

Other biological activities of interleukin-1 include induction of fibroblast growth, ICAM-1 expression and growth and differentiation of B and T cells[17]. Two genes are expressed for (IL-1):(IL-1α) and (IL-1β). Although, these genes show only 20-30% amino acid homology they were shown to bind the same high-affinity receptor.[18] (IL-1) does not posses a typical hydrophobic signal sequence secretion and may be processed extracellulary by limited proteolysis from a high molecular mass intracellular precursor of 33 kDa to an active 17 kD.[19,20] (IL-1) is produced mainly by macrophages/monocytes,T cells, B cells, fibroblasts, keratinocytes, astrocytes and endothelial cells.[17]

A variety of cytokines including (IL-1), (IL-6) and (IL-8) as well as TNF-α have been proposed as important mediators of myocardial ischemia reperfusion injury.

For example, (IL-1) was found in the circulating monocytes within hours of cardiopulmonary bypass.[21] Maximal amounts of (IL-1) were observed 24h after extracorporeal circulation.

Kalfin RE et al,(1993) have demonstrated the induction of (IL-8) in circulating leukocytes of human patients with peak levels at 24h post bypass.[22]

(IL-1α) and (IL-8) are proinflammatory cytokines and chemokines secreted by vascular endothelial cells and responsible for the development of inflammatory responses[23].

Recent research indicates that (IL-8) concentration increased remarkably during and after myocardial injury[24]. The observations of this study are also consistent with previous studies, which showed increased serum levels of (IL-1α) and (IL-8) in AMI patients. These findings suggest that serum levels of (IL-1α) and (IL-8) might be related with vascular disorders[25].

Conclusion:

Serum (IL-1α) and (IL-8) concentrations showed significant rise during AMI.

In comparison with recent research studies indicating the importance of activities of neutrophils as a cause of tissue damage in acute myocardial infarction and the stimulation of neutrophils by (IL-1α) and (IL-8). The above results suggest that (IL-1α) is more significant than (IL-8) in the development of myocardial injury in acute myocardial infarction**.**

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