Comparison study of Interleukin-1 alpha between Unstable Angina and Acute Myocardial Infarction patients

Ammal E. Ibrahim* ***Zeina I. Ibrahem****
Hamsa thamer*

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Abstract

Multiple studies support a role for inflammation in the pathogenesis of coronary atherosclerosis and unstable cardiac syndromes. However, of the known pro-inflammatory cytokines, only elevated plasma levels of interleukin-6(IL-6) have been linked to Unstable Angina. We sought to examine the plasma levels of other major proinflammatory cytokines in similar clinical settings patients with unstable angina and acute myocardial infarction and the relationship extent between them. This study aimed to investigate and compare the level of IL-1 in Unstable Angina and Acute Myocardial Infarction patients. Thirty patients with unstable angina and thirty patients with Acute Myocardial Infarction, also thirty healthy individual as control were included in this study to measure the levels of IL-1alpha, lipid profile and Body Mass Index. There was a significant increase in the level of IL-1 α in patients with acute myocardial infarction or with unstable angina compared with control group. IL-1 α positively correlated with total cholesterol, triglycerides, Low Density Lipoprotein and Very Low Density Lipoprotein, while there was a negative correlation with High Density Lipoprotein. In conclusionInterleukin-1 α significantly increases in patients with acute myocardial infarction or with unstable angina. There was no significant difference in level of IL-1α between AMI and unstable angina patients.

Key word: Unstable angina, Acute Myocardial Infarction, and IL-1α

Introduction

Interleukin-1 (IL1) is known to be an important mediator of the immune system, produced primarily by mononuclear phagocytes in response to injury and infection[1].Interleukin-1 alpha and interleukin-1 beta (IL-1 alpha) are cytokines that participate in the regulation of immune responses, inflammatory reactions, and hematopoiesis [2]. The importance of IL-1 in the initiation and maintenance of adequate response to invasion has been established quite clearly and reported in detail in several excellent review articles[3], [4].

Over the past two decades, many experimental and human studies have examined the role of cytokines, chemoattractants, and adhesives molecules in the initiation, progression, and clinical emergency of the atherosclerotic plaque[5].

IL-1 is likely to be involved in the inflammatory process associated with the acute coronary syndromes because it is known to induce IL-6, which increases gene expression for clotting factors and inhibitors of fibrinolysis,

*College of science Al-nahrain unv.

and contribute to transendothelial passage of neutrophils by increasing the surface expression of endothelial adhesion molecules and the production of IL-8.[6]. Increased concentrations of interleukin 6 have been detected in patients with severe unstable angina and have been shown to be potent predictors of a poor short term outcome [7]. Unstable angina is characterized by increased levels of the acute-phase reactants fibrinogen, C-reactive protein (CRP), and serum amyloid A protein and of the cytokine interleukin IL-6, the major inducer of CRP production in the liver, and their elevation is associated with a worse short- and long-term prognosis [8].

Unstable angina is angina pectoris caused by disruption of an atherosclerotic plaque with partial thrombosis and possibly embolization or vasospasm. It is characterized by at least one of the following: (1) occurs at rest or minimal exertion and usually lasts for >20 minutes (if nitroglycerin is not administered); (2) being severed and described as frank pain, and of new onset (i.e., within 1 month); (3) occurs with a crescendo pattern (more severe, prolonged, or increased frequency than previously). 50% of people with unstable angina will have evidence of myocardial necrosis based on elevated cardiac serum markers such as creatine kinase isoenzyme (CK)-MB and troponin T or I[9].

Acute myocardial infarction (AMI), commonly known as a heart attack, results from the interruption of blood supply to a part of the heart, causing heart cells to die. This is most commonly due to occlusion (blockage) of a coronary artery following the rupture of a vulnerable atherosclerotic plaque, which is an unstable collection of lipids (cholesterol and fatty acids) and white blood cells (especially macrophages) in the wall of an artery. The resulting ischemia (restriction in blood supply) and ensuing oxygen shortage, if left untreated for a sufficient period of time, can cause damage or death (*infarction*) of heart muscle tissue.[10]

Aim: to investigate and compare the level of IL-1 in Unstable Angina and Acute Myocardial Infarction patients.

Materials and Methods:

This study was performed during the period from April 2010 to December 2011. This study included fifty patients with Acute Myocardial Infarction (AMI) and thirty patients with unstable angina were admitted to Cardiac Care Unit (CCU) at Medical City Teaching Hospital and Ibn – ALbetar Hospital in Baghdad patients, with rang (20-78) years old. Blood samples were taken from patients after examined thoroughly and after exclusion of subjects with a history of MI or diabetes mellitus or any chronic diseases. Control group contains fifty age, sex and BMI matched, apparently healthy individuals that were included in this study as control group.

Blood collection and laboratory analysis:

From each patients and control, five ml venous blood were aspirated from a suitable vein. Samples were collected between (8-9 A.M.) after 10 hours fast. Blood samples were divided into two parts, three ml transferred to a plain tube for lipid profile. The remaining of blood transferred to another sterile plain tubes for storage to measure the IL-1 alpha. The non heparinized blood in the plain tubes were left to clot and then centrifuged at 4000 rpm for 5 minutes to separate the serum and dispensed into tightly closed Eppendorf tubes in 1.0 ml and stored at -20 C° until used. Each serum sample

was analyzed for urea and creatinin to excluded kidney diseases. The parameters included in this study are Lipid profile which were measured by using kit reagents from BioMaghreb Company – Tunisia, IL-1 alpha was measured by using ELISA kits from United States Biological Company.

Statistical analysis:

Statistical analysis was performed by statisticians using the SPSS 15.01 Statistical Package for Social Sciences and also Excel 2003. Data analysis was done using chi- square test for tables with frequencies, while we used independent sample t-test for tables with means and standard deviations. Value with $p \leq 0.05$ was considered significant. Correlation coefficient was used to find the correlation between studied parameters by using Pearson correlation. Descriptive statistics for the clinical and laboratory results were formulated as mean and standard error.

Results

Table (1) comparison between groups for (Age, BMI, IL-1 α and lipid profile)

Parameters	Acute myocardial infarction patients	Unstable angina patients	Control group
Age (years)	65±10.12	60±12.46	63.71±12.02
BMI (kg/m^2)	30.03±5.11	28.51±7.01	27.09±5.66
IL-1 α (pg/ml)	593.45±52.9	568.22±98.7	310.23±131.67
Total cholesterol (mg/dl)	184.64±13.8	177.88±23.56	155.81±19.03
LDL(mg/dl)	173.7±20.44	172.97±13.09	152.93±22.08
Triglyceride (mg/dl)	171.98±21.23	169.96±33.7	158.06±19.83
VLDL (mg/dl)	57.07±7.34	56.28±10.02	52.06±6.33
HDL (mg/dl)	25.14±5.39	28.08±9.11	41.90±5.09

Table (2) The p-value between the studied groups for IL-1α.

	AMI group	Unstable angina group	Control group
AMI group	----------	0.07	≤0.01
Unstable angina group	0.07	---------	≤0.01
Control group	≤0.01	≤0.01	--------

Table (3) The correlation between IL-α with(lipid profile) between AMI and unstable angina.

Parameters	AMI (r)	Unstable angina (r)
Total cholesterol	0.451	0.312
LDL	0.378	0.392
Triglyceride	0.321	0.202
VLDL	0.332	0.202
HDL	-0.321	-0.472

Discussion

IL-1 is expressed by many cells and has multiple functions including local inflammation. Cells known to express IL-1a include fibroblasts, hepatocytes,keratinocytes, brown fat adipocytes, thymic myoid cells,T cells, macrophages, monocytes and oligodendrocytes.[11] Following bacterial or immunoglobulin ligation of monocyte/macrophage CD14 (the LPS receptor) or CD64 (the IgG receptor), IL-1 can be released into a local environment. Within this environment, IL-1 impacts a number of cells[12]. First, capillary endothelial cells are induced to do two things; one, secrete chemokines such as MCP-1and two, upregulate the expression of vascular adhesion molecules such as E-Selectin, ICAM-1 and VCAM-1[13]. MCP-1 provides a stimulus for chemotaxis and activates mononuclear cell integrins, thus facilitating mononuclear infiltration into an area of early inflammation. IL-1 also induces expression of itself in newly arriving monocytes, thus reinforcing the overall process. In terms of other pro-inflammatory molecules, IL-1 apparently is needed for the efficient production of IFN-gamma. On resident NK cells, IL-1 apparently works in conjunction with macrophage-derived IL-12 to induce IFN-gamma induced activation of macrophages.[14] Finally, IL-1 also induces the expression of MMPs from resident fibroblasts. This can have at least two effects: first, extracellular matrix degradation can facilitate monocyte migration, and second, MMPs are known to degrade IL-1, thus down-modulating the local inflammatory response initiated by IL-1.[15]

The development of atherosclerotic lesions in the arterial walls of apolipoprotein E (ApoE) or low-density lipoprotein (LDL) receptor-
deficient mice is markedly reduced in mice deficient in the IL-1 receptor or in the IL-1α or IL-1β themselves. The lesions are increased, however, in mice deficient in the naturally occurring IL-1 receptor antagonist (16).
The culprit in the formation of atherosclerotic lesions is IL-1 produced by the myeloid cells rather than the endothelium or mesenchymal cells (17).

Recent insights have suggested an important role of IL-1 in atherosclerosis by inducing formation of the foam cell, which enters the arterial wall and orchestrates the inflammatory plaque. Indeed, foam cells are full of IL-1α.. On the other hand, one should not forget that the cytokine- induced cholesterol release has been most likely evolved as a protective mechanism during infections. Proinflammatory cytokines both activate host defense mechanisms and induce the release of lipoproteins that bind and neutralize lipopolysaccharide and other toxic bacterial products (17).

Conclusions

- Interleukin-1 α significantly increases in patients with acute myocardial infarction or with unstable angina.
- There was no significant difference in the level of IL-1α between AMI and unstable angina patients.

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مقارنة مستوى IL-1 α بين مرضى الذبحة الصدرية و مرضى الاحتشاء القلبي

آمال إسماعيل إبراهيم *** ***زينة إسماعيل إبراهيم *** ***همسة ثامر*

*كلية العلوم/ جامعة النهرين /قسم الكيمياء

الخلاصة:

دعمت بعض الدراسات دور الالتهابات في تطور مرض نصلب الشرايين و أمراض القلب الوعائية لكن هذه الدراسات أخذت IL-6 فقط بنظر الاعتبار وربطته مع الذبحة الصدرية. في هذا البحث تمت دراسة معاملات التهاب أخرى في مرضى الذبحة الصدرية ومرضى الاحتشاء القلبي و دراسة العلاقة بينهم. هدف الدراسة لتحري ومقارنة مستوى IL-1 α في مرضى الذبحة الصدرية و مرضى الاحتشاء القلبي. تضمنت الدراسة ثلاثون مريضا بالذبحة الصدرية و ثلاثون مريضا بالاحتساء القلبي و ثلاثون من الأصحاء كمجوعة قياسية تم قياس IL-1 α و مستويات الدهون في الدم إضافة إلى معامل كتلة الجسم. أظهرت الدراسة ارتفاعا ملحوظا في مستويات IL-1 α في مرضى الاحتشاء القلبي و مرضى الذبحة الصدرية مقارنة بالمجوعة القياسية وأيضا ارتباطا ايجابيا بين IL-1 α مع الدهون الثلاثية و الكولسترول و ومستوى البروتين ألدهني قليل الكثافة و ارتباط سلبي بينIL-1 α و مستويات البروتين ألدهني عالي الكثافة ولم يكن هنالك اختلاف معنوي في IL-1 α بين مرضى الاحتشاء القلبي ومرضى الذبحة الصدرية.