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Serum Levels of Interleukin-1 Alpha and Interleukin-6 in Acute Coronary Syndrome Patients

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Abstract

Background Cytokines are responsible for the modulation of immunological and inflammatory processes and play a significant role in the pathogenesis of acute coronary syndrome patients (ACS).

Objective This study aims to investigate the serum levels of IL-1α and IL-6 in ACS patients.

Methods The study covered 140 subjects. It comprised a total of 101 patients with ACS patients [62 with acute myocardial infarction (AMI) and 39 with unstable angina (UA)], compared with 39 healthy individuals with no history of cardiac disease. Serum IL-1α and IL-6 analysis was performed by ELISA.

Results The present results revealed that there were significant elevation in mean serum levels of IL-1α and IL-6 in patients with ACS (AMI and UA) as compared to healthy control (P<0.001). Moreover, the levels of these cytokines were significantly higher in AMI patients when compared to UA patients (P<0.001).

Conclusion These finding suggest that IL-1α and IL-6 play an important role in pathogenesis of ACS.

Keywords Acute coronary syndrome, IL-1α and IL-6.

Introduction

Atherosclerosis is a complex multifactorial process resulting from an excessive inflammatory response to various forms of injurious stimuli to the arterial wall [(1)]. The transition of a stable coronary atherosclerotic lesion into a ruptured and/or eroded plaque results in the clinical manifestation of ACS [(2)]. The understanding of the factors that induce such events is essential for the prevention and treatment of atherosclerosis. Mechanistically, atherosclerotic plaque instability is the consequence of a complex inflammatory response of the vessel wall ignited by activated macrophages and T-cells leading to proteolytic degradation of connective tissue matrix, excessive pro-inflammatory cytokine production, and apoptosis of vascular wall cells [(3, 4)]. The well known locally generated markers of inflammation are TNF -α and IL-6 [(5)]. Together, TNF and IL-1 stimulate the production of IL-6 by smooth muscle cells [(6)]. IL-6 gene transcripts are expressed in human atheromatous lesions [(7)], and IL-6 is the main hepatic stimulus for C-reactive protein (CRP) production [(8)]. Patients with ACS demonstrate elevated serum levels of IL-1α and IL-6, indicative of a systemic inflammatory response [(9, 10)]. In contrast, serum levels of the potent anti-inflammatory cytokine IL-10 have recently been shown to be decreased in patients with ACS [(11)], thus it may favor plaque instability and the development of ACS. Whereas elevation of systemic markers of inflammation is firmly established to predict an unfavorable outcome in patients [(12)]. The present study was undertaken to assess the serum levels of IL-1α and IL-6 in patients with ACS.

Methods

Subjects

The patients group:

The current study comprised of 101 patients with ACS (37 females and 64 males; mean age 51.89 years, ranged between 21-85years

The patients group was classified into two groups: Group 1, includes 62(61.37%) patients with AMI and Group 2 includes 39 patients (38.63%) with UA.

The clinical examination and diagnosis were performed by physician specialized in in Ibn Al-Nafees Cardiac Specialty Teaching Hospital and AL-KindyTeaching Hospital.

The control group:

A control group included 39 subjects who had no history or clinical evidence of cardiac diseases or any chronic disease.

Estimation of serum of IL-1α and IL-6:

IL-1α and IL-6 were determined in serum using commercially available ELISA Kit. (BioSource, Europe S.A. Company, Belgium).

Statistical analysis:

Comparisons between groups were performed using ANOVA and student's *t* tests and P values less than 0.05 was considered statistically significant.

Results:

It is shown in Table 1, there were a significant elevation in the serum mean levels of IL-1α among AMI and UA patients (255.11 pg/ml and 64.58 pg/ml respectively) in comparison to that of healthy control (10.82 pg/ml) P<0.001. Significant differences were observed in the mean levels of IL-1α in patients with AMI as compared to those with UA (P<0.001).

Regarding the concentration of serum IL-6, Table 2 revealed significant increase in AMI and UA patients (266.11 pg/ml &91.77 pg/ml respectively) in comparison to that of healthy control (5.71 pg/ml) (P<0.01). Moreover, significant increase was noticed in serum levels of IL-6 in AMI when compared to UA patients (P<0.05).

Table 1: IL-1α level in patients with myocardial infarction and unstable angina compared to the healthy controls

Serum IL-1α	Acute Myocardial infarction	unstable angina	healthy controls	P (ANOVA-TEST)
Minimum	110.61	46.77	3.06	
Maximum	131	166.55	28.83	
Mean±SEM	255.11±7.40	64.58±3.70	10.82±0.70	<0.001
Number	62	39	39	
P (T-TEST)				
AMI versus UA: p<0.001				
ACS versus HC: p<0.001				

Table 2: IL-6 level in patients with myocardial infarction and unstable angina compared to the healthy controls

Serum IL-6	myocardial infarction	unstable angina	healthy controls	P (ANOVA-TEST
Minimum	98.65	57.83	3.06	
Maximum	389.98	185.65	10.89	
Mean±SEM	266.11±7.16	91.77±4.97	5.711±0.37	<0.001
No.	62	39	39	
P (T-TEST)				
AMI versus UA p<0.001				
ACS versus HC p<0.001				

Discussion

Thrombus formation over vulnerable disrupted atherosclerotic plaques has been implicated as an important mechanism in the development of the acute ischemic syndromes of unstable angina, AMI and sudden death [13]. Inflammatory and immunologic mediators may play crucial roles in plaque rupture. Macrophages and T-cells are known to be important components of atherosclerotic lesions, which can generate and release cytokines that play important roles in ACS. Various inflammatory markers and cytokines are associated with atherosclerosis and its progression to clinical syndromes. A number of pro-inflammatory cytokines, including IL-1, IL-6, IL-12 and interferon- are expressed in human atherosclerotic plaques. These cytokines alone or in combination contribute to the local inflammatory response, and may have great impact on plaque formation and progression [14].

High level of IL-1α and IL-6 in ACS patients observed in this study was comparable with other studies [15-17] who reported similar increase of these cytokines. IL-1α has wide range of target cells including cardiomyocytes and vascular smooth muscle cells. IL-1α induces postanoid dependent hypotension in rabbits *in vivo* and stimulates human smooth muscle cells to secrete IL-6. In chronically ischemic myocardium where focal necrosis was documented, enhanced levels of IL-1 mRNAs were found indicating a role of this cytokine in myocardial inflammation [18]. In contrast with present results Heinisch et al, did not find elevation in IL-1α levels, but they noticed elevation in IL-β in AMI patients [19].

Human vascular smooth muscle cells express and secrete IL-6 after IL-1 stimulation or during proliferation. Furthermore, hypoxic cardiomyocytes have been shown to produce IL-6 which could contribute to ventricular dysfunction as observed after myocardial ischemia and reperfusion [18]. Hirano *et al*. reported that IL-6 was expressed in cardiac myxoma cells at much higher levels than inactivated lymphocytes. There is now evidence that in patients suffering from acute myocardial infarction, IL-6 may affect the progression and the healing process of this illness, because IL-6 serum levels seem to be elevated in these patients [20].

In agreement with current results, Luo and associates reported that serum levels of IL-6 was significantly higher in ACS patients (including AMI and UA) than in healthy control and stable angina patients [21]. Similarly Sen and Sharman studied 100 patients with ACS and they found that serum IL-6 was elevated in ACs patients as compared to healthy control, furthermore, they observed that levels of IL-6 was significantly higher in AMI patients than in UA patients . So they concluded that IL-6 with other pro-inflammatory cytokines may be used for the identification patients with AMI /UA [22].

In conclusion the findings suggest that IL-1α and IL-6 play an important role in pathogenesis of ACS. Serum levels of IL-1α and IL-6 may have some diagnostic value for ACS, and can be useful marker reflecting disease stability.

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