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Original Article

Evaluation of Serum Level of Interleukin-1 in Patients Suffering from Acute Coronary Syndrome, Admitted to the CCU Ward of Amir-Almomenin Hospital of Zahedan

Hossein Ali Khazaei[1], Ahmad Bolouri[2], Hony Harati[2], Mehdi Mohammadi[3], Sayed Mohammad Nasiraldin Tabatabei[1], Amin Khazaei[4], Masoud Pishjuo[1], Zahra Ayoubi Yazdi[1], Bahman Khazaei[1]*

[1] *Clinical Immunology Research Center and Dept. of Immunology and hematology, Zahedan University of Medical Sciences, Zahedan-Iran*
[2] *Department of Cardiovascular diseases of Zahedan University of Medical Sciences, Zahedan-Iran*
[3] *Department of Biostatistics of Zahedan University of Medical Sciences, Zahedan-Iran*
[4] *Dentists, Private Dentist, Zahedan-Iran*

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Abstract

Background: Atherosclerosis is a disease in which the particles of fat builds up in the blood vessel's walls. This build up leads to blood flow blockage or can cause the arteries to narrow, but until the stenosis of the vessel is not more than 70 percent, there won't be any obvious symptoms. Symptoms are dependent on the location of the stenosis that can bring about diseases such as, Unstable Angina (UA), Myocardial Infarction with Q Wave (MIQW) and Non Q Wave (NMIQW). The most common causes of death in most developed countries is Coronary Artery Disease (CAD), and since the inflammatory factors are one of the causes of these diseases, we decided to evaluate the level of the Interleukin-1 (IL-1) in patients with acute coronary syndrome.

Methods: 90 patients, suffering from the acute coronary syndrome were selected, which were previously diagnosed and referred to a cardiologist in the Imam Ali Ebneh hospital's cardiac ward, in 2011. Five ml of periphery blood was obtained from each patient, after 24 hours of hospitalization. Using the ELISA method, the level of interleukin-1 was measured in the three groups of patients, each with symptoms of UA, MIQW and MINQW.

Results: Our findings, showed the highest level of interleukin-1 in the MIQW patients, with the average of 46.55 pg/ml and, the lowest level in the MINQW patients, with the average of 28.17 pg/ml. Moreover, the average level of IL-1 in the patient's serum with UA, is determined equal to 31.28 pg/ml. Although, there was no significant correlations between the type of MI development and UA, there was a significant correlation between the level of IL-1 and the type of MI development.

Conclusion: Despite the fact, that the level of IL-1 was higher than normal in all the group types, and no significant correlation between the type of MI development and UA was found, there was statistically a significant correlation between the types of MI development and the level of IL-1.

Keywords: Atherosclerosis; Interleukin-1 ; Unstable Angina; Myocardial Infarction with Q Wave and Non Q Wave

***Corresponding Author:** Bahman Khazaei, MD
Zahedan University of Medical Sciences, Zahedan, Iran
E-mail: h_khazaei118@yahoo.com

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Introduction

Based the World Health Organization's (WHO) reports, cardiovascular diseases, kills around 12 million people around the world per year (1), and so, in the developing countries, half of the mortality in adults is related to such diseases. In spite of widespread advancement in diagnosis, still one third of the patients die from a heart attack and 5% of the survivors, die one year after the occurrence of the heart attack. In fact, the rate of mortality due to Myocardial infarction, are greater compared to the Unstable angina, and requires more accurate and proper care. Accordingly, quick differentiation and timely diagnosis and detection of the Myocardial infarction patients from patients with Unstable angina, has a substantial and significant impact on the efficient treatment and prevention of the MI's effects, as well as helping to improve the patients' recovery process (2).

Usually, Atherosclerosis does not show any symptoms, unless 70% of the internal artery wall's space is involved (3). In other words, symptoms associated with local scleroderma are heart attacks with strip variations and non-strip variations, and unstable angina (4). Unstable angina, refers to transient and temporary chest pains (5), a pain that can last for more than half an hour, and even resting and the nitroglycerin consumption dose not relieve the pain (6). Heart attacks can be accompanied by strip variation of Q wave and increased cardiac enzymes (7, 8) or without any strip variations of Q wave, along with the segment elevation of ST (indicator of the acute myocardial infarction) (9).

There are two major hypotheses about the formation of atherosclerosis. One is the high level of blood cholesterol that sticks to the artery walls and concentrates, and the other is, that throughout various mechanisms, because of the immune system's activities, the artery walls are led to changes, that forms the Atheromatosis (10-12).

There is another theory, that inflammatory processes, has an important role in the development of atherosclerosis (13, 14), since in these phenomenon, the white cell lymphocytes, monocytes and macrophages are presented, and Atherosclerosis begins when the white blood cells leave the blood flow and transform into foam cells that embraces cholesterol and other fats, and ultimately stick to the artery walls (15, 16).

Several reports have been published in association with increasing levels of inflammatory cytokines such as IL-1 in relation to Atherosclerosis. The IL-1 gene, codifies 3 peptides, that are associated to structure and performance (17). The IL-1 family gene in the cluster form, is located over the chromosome 2q14. IL-1 includes two isoforms, as IL-1α and IL-1β that are produced by monocytes, macrophages and epithelial cells and participate in aggressive microbes, inflammations and ammine modifications. Certain locus in this gene cluster, is associated with the increase in protein production of IL-1, which leads to tissue destruction (18). The IL-1α plays a significant role in the regulation of the immune system's activities as well, and is one of the activating agents of TNF α. This IL causes inflammation and increases the fever (19).

As a result, since one of the causes of the acute coronary syndrome is the inflammatory factors, we attempted to study the relationship between the inflammatory factors, such as IL-1 in the patients, with symptoms of acute coronary syndrome such as, heart attack with Q wave or without Q wave and unstable angina. In case there is some relationship between these factors, proper prevention and treatments needs to be done.

Material and methods

In the present study, IL-1 value in 90 patients with acute coronary syndrome symptoms, that were admitted to the CCU ward of Amir-Almomenin Hospital of Zahedan city in 1390, was evaluated in three simulated groups including, 30 patients with unstable angina, 30 with Q wave heart attack and 30 without Q wave. The criteria for patients, was based on the published acute coronary syndrome criteria in 2008 (20), including the self-reported patients bearing symptoms. The risk signs include the following: At the time of the study they were suffering from the acute coronary syndrome symptoms (unstable angina, previous heart attack with Q wave and non Q wave) and were in the range age of 40-60 years old.

Exclusion criteria included the patients without atherosclerosis symptoms and the risk factors included are as followed: At the time of the study, they should not suffer from the acute

coronary syndrome's symptoms (unstable angina, previous infarction with Q wave and non Q wave), autoimmune diseases, collagen vascular, chronic renal failure, acute infections in the last 3 months, pregnancy, and no history of inflammatory medicine consumption in the last six months.

The Information gathered from these three groups of patients, was obtained by talking and using a questionnaire form containing epidemiological data, and the mentioned tests were done. Then a 5ml peripheral blood sample was taken, 24 hours after the hospital's admission. After the blood samples were collected, the serum was separated and kept below 80 centigrade. Measurement of the IL-1's concentration, was done using the ELISA method, and then evaluated by the statistical Mann-Whitney test, in order to compare the amount of mean IL-1, between the three groups using the SPSS.17 software. In addition, the *P*-value was determined significantly less than 0.05.

Results

The mean age of the individuals under study, was 52. 70 patients were suffering from hypertension, 52 from diabetes mellitus, 40 were smokers and 38 had increasing CRP. In those who were suffering from the Unstable Angina (UA), the mean value of IL-1 was reported 31/28±33/51 pg/ml, in the Myocardial Infarction with No Q Wave (NQWMI) group, the value was 28/17±27/84 pg/ml and in the Myocardial Infarction with Q Wave (QWMI), it was 46/55±31/90 pg/ml (**Table 1** and **Figure 1**).

In this section, based on the statistical Mann-Whiney test, we examined the amount of IL-1 in various groups, to determine any correlations to the type of the disease. According to this parameter, values of P, which is an indication of the relationship of, the three groups of patients with the level of IL-1, were calculated in each case. The results revealed that, between the increased amount of IL-1 and MIQW and UA, there was no significant correlation ((P>0.05). Between the increased amount of IL-1 and MINQW and UA, there was no significant correlation too ((P>0.05) and finally between the increased amount of IL-1 and MIQW and MINQW, there was a significant correlation (P<0.05) (**Table 2**).

In other words, it has been noted that in comparison between the tree groups of the disease, there was no correlation between the

Table 1. The comparison of mean IL-1 levels between different patient groups

Level / Type of disease	Mean	Standard deviation	The lowest	The highest
NQWMI	28.17	27.84	0	45.67
QWMI	46.55	31.90	0	116.20
UA	31.28	33.51	0	116

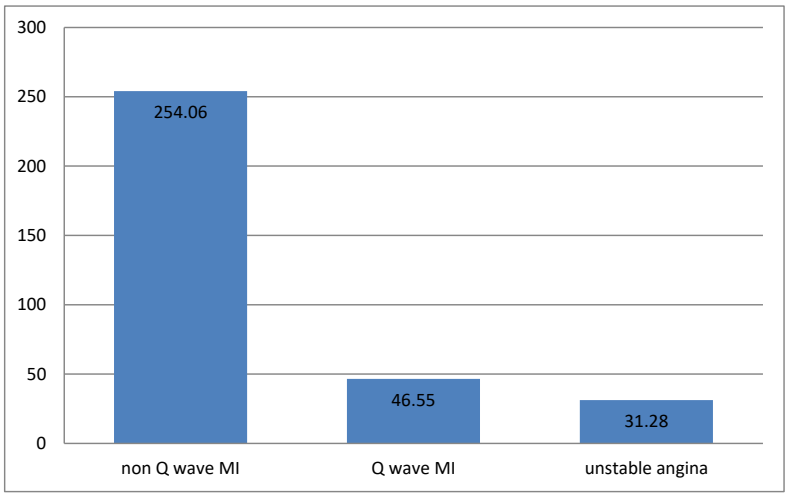

Figure 1. The level of IL-1 in different patient groups

Table 2. The comparison between the correlation of increased amount of IL-1 and different patient groups based on Mann-Whitney test

Group	*P*-value
MIQW and UA	0.087
MINQW and UA	0.683
MIQW and MINQW	0.035

increased amount of IL-1 and UA, and the type of MI, whereas there was a correlation between the increased amount of IL-1 and the type of MI.

Discussion

Several studies have shown the effects of the serum IL-1 levels in patients with acute Myocardial Infarction (MI). This proinflammatory cytokine, acts as an integrator for many inflammatory stimuli, supporting the concept in association with the plasma cholesterol levels, so this protein may predict the cardiovascular risk in the MI patients The aim of this study, was to evaluate quantitative value of IL-1 in the acute coronary syndrome patients, to better understand the role of this cytokine in inducing the disease in the three groups of Unstable Angina (UA), Myocardial Infarction (MI) with Q Wave (MIQW) and Non Q Wave (NMIQW).

Keep in mind that the natural and normal range of IL-1 is about 1.5 to 2.5 IU/ml in healthy people. But as mentioned, the IL-1 value in all the studied groups, was significantly higher than normal, therefore, we conclude that in the UA, MIQW and MINQW patients, the IL-1 value is rather higher than the normal value. In this study, in order to identify the relationship between the increased level of IL-1 and the type of heart disease, the statistical Mann-Whitney and SPSS tests were used. In the comparison between the groups, no significant statistical relationship was found between the type of the disease and UA, while a significant statistical relationship was found between the type of the disease and the IL-1 values ($P<0.05$).

Many investigations were carried out regarding the relationship between the IL-1 value and the myocardial arteries. However, some in vitro studies have shown the inflammatory effects of IL-1 on vascular cells, as an etiological factor in inflammation and atherosclerosis. They conclude that the IL-1, contributes to atherosclerosis in mice. Hansson and colleagues identified the activation of Th1 and Th2 cytokines in the advanced human atherosclerotic plaques. A number of growth factors and cytokines such as IL-1, TNF-α, IFN-γ, M-CSF and some chemokines such as MCP-1, have been produced by these types of cells and have been used in identification of the human atherosclerotic plaques, mainly from carotid endarterectomy specimens (21).

On the other hand, among different researches, several studies have investigated the association of the IL-1 value and unstable angina, but none of them explicitly deal with the comparison of the IL-1 and unstable angina with the MI Q wave of non Q wave. As well, none of the studies dealt with the association of the IL-1 value and existence of Q wave explicitly.

The study of Yan HB eta in 2011, showed that the IL-1 value in the patients suffering from unstable angina vs control group, was explicitly higher from the statistical point of view. In our study the mean of the IL-1 value in the group of unstable angina was 31.28 pg/ml which is rather higher than the normal range (22).

Another study by Biasucci LM et al, showed that the IL-1 value in unstable angina was significantly higher than the normal group, which is consistent with the findings of our study (10). Interestingly, it has been shown that the IL-1 value and other inflammatory cytokine in unstable angina and acute MI, increases and this finding is statically of higher significance compared to the healthy control group (11).

Another study done by Simon AD et.al in New York in 2000, showed that the IL-1 value in unstable angina patients compared with stable angina, was reported to be considerably higher. In this study IL-1 was recognized as a pathogenesis agent of unstable angina (12). Barbarash OL et al in 2011 in Russia, reported that the IL-1 value in STEMI, significantly increases (13). Adlbrecht C et al in a study in Austria, on 39 people suffering

from acute MI, showed that the IL-1 value in patients of acute MI, considerably rises, and this value, statistically in people suffering from unstable angina is of higher significance (14). Balbay y et al in a study in Ankara, indicated that the IL-1 value in 15 people with acute MI, is significantly higher than the control group (15). Another investigation carried out by Pudil R et al in 1999 in the Czech Republic, indicated that the IL-1 value and other inflammatory factors increases in the first 96 hours, after the acute MI was investigated.

Results showed that the IL-1value, continuously increases in the first 96 hours after acute MI and the peak value in average is 22 (16).

Accordingly, we concluded that IL-1 in acute MI and unstable angina, significantly increases, and the results achieved in our study are compatible with what has been achieved in other studies. In the studies, slight comparison is done between IL-1 in acute MI and unstable angina patients. But in the study by Ablbrecht C, it was stated that the IL-1 value in acute MI patients was significantly higher than the unstable angina patients and these finding are contradictory to ours.

Conclusion

In our study, we examined the relationship between the IL-1 value and MI type, based on existence or non-existence of Q wave in the cardiac graph of patients and this can be the forte of our study, since so far in none of the studies this topic was considered, while according to the analyses, there was significant differences between the existence and non-existence of Q wave and the IL-1 values.

Conflict of interest

The authors declare that there is no conflict of interest.

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