Level of Resistin in Acute Myocardial Infarcti on Patients and its Relation to Lipid profile and Cardic Troponin I

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ABSTRACT:

BACKGROUND:

Inflammatory responses are involved in the initiation and progression of atherosclerotic plaques. Myocardial Infarction (MI) is most commonly due to occlusion of a coronary artery following the rupture of a vulnerable atherosclerotic plaque. It has been suggested that the adipose tissue may play an important role in mediating this chronic inflammatory process. Resistin is a cysteine-rich polypeptide that is expressed at relatively lower levels in human adipocytes but higher levels in macrophages. Troponin is found in cardiac muscle and used for diagnosis of AMI.

OBJECTIVE:

To investigate the level of resistin and its effect on lipid profile and Troponin I levels in acute myocardial infarction patients.

SUBJECT AND METHODS:

The study included 50 patients with AMI and forty healthy subjects as control group. In this study resistin , lipid profile and Troponin I were measured.

RESULTS:

The levels of resistin, cholesterol, LDL-C were significantly elevated with ($p<0.001$), while HDL-C was significantly lower with ($p<0.001$), there was positive correlation between resistin with cholesterol, LDL-C, triglyceride and VLDL, while there was negative correlation between resistin with HDL in acute myocardial infarction.

CONCLUSION:

There was a significant increase in resistin level, in acute myocardial infarction patients and this increase may be related to inflammation. Resistin negatively correlated with HDL and positively correlated with triglyceride and LDL this relationship makes us consider this hormone as possible atherosclerotic factor.

KEY WORD: resistin ,lipid profile , troponin I and acute myocardial infarction.

INTRODUCTION:

Inflammation contributes across the spectrum of cardiovascular disease, including the earliest steps in atherogenesis. This recognition has a profound impact on understanding the atherothrombosis as more than a disease of lipid accumulation, but rather as a disorder characterized by low-grade vascular inflammation. This concept can be used to predict future cardiovascular risk.[1]

Acute Myocardial Infarction (AMI) is the interruption of blood supply to part of the heart, causing some heart cells to die. This is most commonly due to occlusion of a coronary artery following the rupture of a vulnerable atherosclerotic plaque, which is an unstable collection of lipids and white blood cells (especially macrophages) in the wall of an artery. The result is restriction in blood supply and oxygen shortage. [2]

Adipose tissue is an important endocrine organ that secretes numerous protein hormones into circulation. These factors are generally referred to as adipocytokines or adipokines, however the strict definition of an adipokine is that it interacts with the immune system. In addition to secreting cytokines, adipose tissue secretes proteins that influence energy metabolism. [3] Very little is known about the potential function of resistin or its homologs. As fat cells (adipocytes) store more fat molecules and enlarge, they release several products that can modify body's sensitivity to insulin. Free fatty acids and TNF-α cause insulin resistance, and leptin, which regulates energy balance, probably causes insulin sensitivity.

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Thiazoladinedione drugs reduce insulin resistance and are used to treat type II diabetes. These drugs suppress the production of resistin by adipocytes, and their antidiabetes effects may, at least in part, be achieved through this mechanism. [4].

Troponin is attached to protein tropomyosin and lies within the groove between actin filaments in muscle tissue. In a relaxed muscle, tropomyosin blocks the attachment site for the myosin crossbridge, thus preventing contraction. When the muscle cell is stimulated to contract by an action potential, calcium channels open in the sarcoplasmic reticulum and release calcium into the sarcoplasm. Some of this calcium attaches to troponin, causing a conformational change that moves tropomyosin out of the way so that the cross bridges can attach to actin and produce muscle contraction. Troponin is found in both skeletal muscle and cardiac muscle, but the specific versions of troponin differ between types of muscle. The main difference is that the TnC subunit of troponin in skeletal muscle has four calcium ion binding sites, whereas cardiac muscle has only three. [5].

SUBJECTS:

This study was performed during the period from December 2009 to April 2010. This study included fifty patients with Acute Myocardial Infarction (AMI) who were admitted to Cardiac Care Unit (CCU) at Medical City Teaching Hospital and Ibn –AL-bitar hospital in Baghdad, with age range (20-78) years old. Blood samples were taken from patients after having thoroughly examined after exclusion of subjects with a history of AMI, diabetes mellitus or any chronic diseases. A group of forty (age, sex and BMI) matched and apparently healthy individuals, were included in this study as controlgroup.

Blood collection and laboratory analysis

From each patient 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 transferred to a plain tube for measured lipid profile. Lipid profile was measured by using standard methods with reagents from Bio-Maghreb Company – Tunisia, Resistin and troponin, were measured by using ELISA kits from United States Biological Company.

Statistical analysis

Statistical analysis was performed by statisticians with 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 error. *p* value of ≤ 0.05 was used as the level of significance. Correlation coefficient was used to find the correlation between studied markers by using Pearson correlation. Descriptive statistics for the clinical and laboratory results were formulated as mean and standard error.

RESULTS:

Resistin level with (lipid profile and troponin): Serum levels of lipid profile and troponin were compared between the patients groups and control group using analysis of variance t-test of significant as in table (1). The patients with AMI were found to have significantly higher serum cholesterol, LDL, LDL/HDL, and Troponin I ($p<0.001$) and significantly lower HDL ($p<0.001$) compared with control group.

Relation between resistin with (lipid profile and troponin I)

Results showed that there was strong positive correlation between resistin with triglyceride in male patients group (r=0.602), also between resistin and VLDL in male patients group(r=0.522), also between resistin with troponin in total patients group(r=0.534).

A positive correlation was found between resistin with cholesterol in female patients group (r=0.511), in female control group (r=0.401), in male patient group (r=0.410), in total patient group(r=0.411) and in total control(r=0.350). also found between resistin with triglycerides in female patients group (r=0.459), in female control group (r=0.424), in total patients (r=0.423) and total control(r=0.352), also between resistin with LDL in female patients (r=0.494), in female control (0.400), in male patient group (r=0.417), in male control group (0.408), in total patients group(r=0.450) and in total control group (r=0.414). Also between resistin with LDL/HDL in female patients group (r=0.441),in female control group (0.434), in male patients group(0.490), in male control group (r=0.353), in total control (r=0.385). the positive correlation was found also between resistin with VLDL in female patients group (r=0.459), in female control

group (0.421), in total patients (r=0.423) and in total control (r=0.418), also between resistin with troponin in female patients(r=0.480) and in male patients group (r=0.451). While there was strong negative correlation between resistin with HDL in female patients group (r=-0.532). A negative correlation was found between resistin with HDL in female control group (r=-0.442), in male patients group(r=-0.410) and in total patients (r=-0.408).

Table 1: Comparison between groups for (Resistin, lipid profile and troponin)

parameters	Female patients Mean±SR NO.=16	Female Control Mean±SR NO.=16	P-value	Male Patient Mean±SR NO.=24	Male Control Mean±SR NO=34	p -value	Total Patients Mean±SR N0.=50	Total Control Mean±SR N0.40	P- value
Resistin ng/ml	8.18 ±2.19	4.82 ±1.240	<0.001	9.53 ±2.30	4.515 ±1.109	<0.001	9.05 ±2.10	4.64 ±1.93	<0.001
Total cholesterol mg/dl	183.76 ±49.20	126.75 ±26.295	0.003	174.03 ±43.98	103.478 ±25.225	<0.001	177.40 ±25.59	104.17 22.68±	<0.001
Triglyceride mg/dl	142.937 ±14.576	138.05 ±16.62	0.484	152.96 ±11.71	133.478 19.153	0.051	141.26 ±12.93	137.35 ±18.87	0.744
HDL mg/dl	37.71 ±3.06	59.777 ±10.458	<0.001	29.36 ±8.82	69.737± 8.249	<0.001	39.26 ±2.50	67.26 ±11.08	<0.001
LDL mg/dl	154.36 ±6.64	100.937 ±10.959	<0.001	156.80 ±12.04	119.852 ±8.753	<0.001	149.42 ±25.50	106.26 ±2.50	<0.001
LDL/HDL	4.08	1.361	<0.001	5.340	1.718	<0.001	3.805	1.579	<0.001
VLDL mg/dl	35.387 ±6.746	27.57 ±2.32	0.508	39.58 ±6.33	26.521± 5.737	0.051	38.23 ±8.58	27.28 ±8.64	0.744
Troponin I ng/ml	34.63 ±6.51	---------	--	38.18 ±9.95	---------	--	30.21 ±8.36	0.0	-----

Table 2: The correlation between resistin with (lipid profile and troponin) for studied groups.

parameters	Female Patients No.=16	Female Control No.=16	Male Patients No.=34	Male Control No.=24	Total Patients No.=50	Total Control No.=40
Cholesterol mg/dl	0.511	0.401	0.410	0.318	0. 411	0.350
Triglyceride mg/dl	0.459	0.424	0.602	0.269	0. 423	0.352
HDL mg/dl	-0.532	-0.442	-0. 41	-0.357	-0.408	-0.397
LDL mg/dl	0.494	0.400	0. 417	0.408	0. 400	0.414
LDL/HDL mg/dl	0.441	0.434	0.490	0.353	0. 512	0.385
VLDL mg/dl	0.459	0.421	0.522	0.266	0. 423	0.418
Troponin I ng/ml	0.480	---	0.451	--	0.534	-----

DISCUSSION :

The results revealed that there was significantly higher level of resistin among AMI patient in male and female as shown in table (1) This study agrees with a study done by Islamabad and Gujranwala 2010 [6] who found a strong association between the elevated resistin levels and CAD in a Chinese population. Resistin directly activates the endothelium through up regulation of adhesion molecules. Resistin also induces production of the proinflammatory cytokines endothelin-1, monocyte chemoattractant protein (MCP)-1, and pentraxin by endothelial cells. It also promotes migratory activity of vascular smooth muscle cells. In macrophages resistin facilitates lipid accumulation, thereby promoting formation of foam cells; this effect is also antagonized by adiponectin. Furthermore, resistin induces production of the proinflammatory cytokines tumor necrosis factor-α and interleukin (IL)-12 by macrophages through activation of nuclear factor κB. [7]

Sabir Hussain, et al., in 2010[7] found that resistin could increases the cell surface area of cardiomyocytes and could also be involved in activation of hypertrophic signal transduction processes (eg, MAPKs). Hyper-resistinemia may contribute to the development of pathologic cardiac hypertrophy; resistin- transduced ventricular cardiomyocytes lead to the impairment of myocytes relaxation. A negative effect of resistin on the cardiac function is also supported by the association of the cytokine with high risk in patients with congestive heart failure. [7]. From our results we noticed that patients with higher levels of resistin have the longest time to stay in CCU. Which could be explained by the relation of resistin with nitric oxide that was mentioned by Noboru Toda et al., 2010[8]

Resistin with Lipid profile

As shown in table (2) it was found that cholesterol and LDL-C were significantly higher in patients group than control groups. It is believed that classical cardiovascular risk factors including LDL cholesterol, hypertension, smoking, and diabetes can instigate vascular release of pro-inflammatory cytokines and subsequent promotion of low-grade inflammation. These pro-inflammatory cytokines increase serum levels of CRP, supporting the concept that CRP acts as an integrator for many inflammatory stimuli, which is in association with plasma LDL-cholesterol levels and can predict cardiovascular risk. Thus lipid and inflammatory parameters appear to be assessing different biological pathways that carry separate prognostic value. In support of this hypothesis, study by Antoni Paul et al.,[9] established that the risk of recurrent myocardial infarction (MI) or death from coronary causes among patients with

acute myocardial syndromes (ACS) is best predicted by the combination of LDL cholesterol and CRP levels.[9]

As shown in table (2) there was significantly positive correlation between resistin and LDL-C in all study groups.

LDL accumulation and modification in the sub-endothelium trigger monocyte and lymphocyte recruitment. Thereafter, activated macrophages and lymphocytes secrete abundant amounts of cytokines that in turn can activate endothelial cell (EC), SMC, and macrophages/lymphocytes to foster cytokine production, leading to a self-perpetuating inflammatory process that becomes less dependent on the presence of oxLDL. [10]

In this study HDL had significantly negative correlation with resistin in all study groups as shown in table (2). The association between adiponectin and CHD was abrogated by including HDL in the model adjusted for conventional risk factors. The most important anti-atherogenic function of HDL is considered a participation in the reverse cholesterol transport which delivers excess cholesterol from systemic vasculature to the liver for disposal as bile salt. In addition, HDL also has antioxidant and anti-inflammatory properties.[11]

Resistin with Troponin I:

As shown in table (2) there was significantly positive correlation between resistin and troponin. Troponin in this study was used to measure the infarction size and as resistin is positively correlated with troponin that means that patients with higher levels of resistin will have higher levels of troponin and bigger infarction size so this patient will have bad or slow progress to cure.

The bulk of cardiac Troponin T forms an important component of the myocardial sarcomere the remainder is free in the cytoplasm. When myocardial damage occurs, the cytoplasmic pool is released, followed by the protracted release of myofilament tropoinin. Troponin is a much more sensitive measure of cardiac damage than the conventional MB isoenzyme fraction of myocardial creatine kinase. Cardiac troponin levels in the blood predict short-term prognosis in acute coronary syndromes particularly in microinfarction. Troponin I has also been shown to inhibit angiogenesis in vivo and in vitro.[12]

CONCLUSION:

- There was significant increase in levels of resistin, in acute myocardial infarction.
- Resistin negatively correlate with HDL and positively correlated with triglyceride and LDL this relation allows this hormone to act as a possible atherosclerotic factor.

REFERENCES:

1. Dennis Schade, Jürke Kotthaus, Bernd Clement."Modulating the NO generating system from a medicinal chemistry perspective: Current trends and therapeutic options in cardiovascular disease Review Article". Pharmacology & Therapeutics; 2010;126:289-300.
2. Kosuge, M; Kimura K, Ishikawa T et al. "Differences between men and women in terms of clinical features of ST-segment elevation acute myocardial infarction". Circulation Journal. March 2006;70:222–26.
3. Rondinone CM. Adipocyte-derived hormones, cytokines, and mediators.. Department Endocrine Metabolic Diseases, Hoffmann-La Roche, Nutley, New Jersey 07110, USA. 2006;29:81-90.
4. Hotamisligil G. The irresistible biology of resistin. J Clin Invest 2003;111:173-74.
5. Ammann P, Pfisterer M, Fehr T, Rickli H. "Raised cardiac troponins." BMJ. 2004;328:1028-29.
6. Islamabad and Gujranwala."Resistin gene promoter region polymorphism and the risk of hypertrophic cardiomyopathy in patients". Translational Research 2010;155:142–47.
7. Sabir Hussain, Muhammad Asghar, Qamar Javed."Resistin gene promoter region polymorphism and the risk of hypertrophic cardiomyopathy in patients." Translational Research; 2010:155:142-47.
8. Noboru Toda, Takeshi Imamura, Tomio Okamura." Alteration of nitric oxide-mediated blood flow regulation in diabetes mellitus". Pharmacology&Therapeutics;2010 :127:189-209.
9. Antoni Paul, Kerry W.S. Ko, Lan Li, MD; Vijay Yechoor, Mark A. McCrory, Alexander J. Szalai, Lawrence Chan."C-Reactive Protein Accelerates the Progression of Atherosclerosis in Apolipoprotein E–Deficient Mice. "American Heart Association :2009;114 :43-51.

10. P. R. J. Ames, I. Antinolfi, A. Ciampa, J. Batuca, G. Scenna, L. R. Lopez, J. Delgado Alves L. Iannaccone and E. Matsuura."Primary antiphospholipid syndrome: a low-grade auto-inflammatory disease?". Rheumatology 2008;47:1832–37.

11. Kobayashi, Naoki Terasaka, Toshimori Inaba, Tohru Funahashi and Yuji Matsuzawa Masahiro Kumada, Koji Ohashi, Naohiko Sakai, Iichiro Shimomura, Hideki Yoshihisa Okamoto, Shinji Kihara, Noriyuki Ouchi, Makoto Nishida, Yukio Arita."Adiponectin Reduces Atherosclerosis in Apolipoprotein E-Deficient Mice." American Heart Association. Circulation 2009;106:2767-70.

12. Moses, Marsha A.; Wiederschain D.; Wu I.; Fernandez, C.; Ghazizadeh V.; Lane W.; Flynn E.; Sytkowski A.; Tao T.; Langer R. "Troponin I is present in human cartilage and inhibits angiogenesis". Proceedings of the National Academy of Sciences of the United States of America; 2009;96:2645–50.