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Article

Galectin-3: A novel prognostic marker for myocardial infarction

Rasha Hasan Jasim[1,], and Ahssan Ali Lefta[1]*
[1] Department of Chemistry, Faculty of Education for Girls, University of Kufa, Iraq
** Correspondence: Email: rasha.alfahham@uokufa.edu.iq*
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ABSTRACT

Background: Coronary heart disease (CHD), known as coronary artery disease (CAD) or ischemic heart disease (IHD), results from the hindrance of blood transit to the muscle of the lipid heart and cholesterol in the inner wall of the heart. Because of atherosclerosis, CAD contains many types of disease: stable angina, unstable angina, myocardial infarction(MI), and sudden cardiac death. Percutaneous Coronary Intervention (PCI), known as angioplasty, is a non-surgical operation performed using a catheter to cram either inflate a balloon in the narrowing place or stent (a very small and fin grid tube made of either plastic or metal of stainless steel). So, it is covered with medicine to prevent coronary artery blockage again), and to expand or open up the vessels in the heart's muscle that contains plaque buildup that causes stenosis. Galectin-3 (Gal-3) is a multi-functional protein that coordinates varied physiological and pathological processes in the body of humans. Gal–3 is located in many of the cells and types of tissue, and several functions can be described, such as macrophage migration promotion, proliferation of fibroblasts and synthesis of collagen. The best function of Gal–3 is its role as a preventer for acute and chronic inflammation. In the universe, it has been related to carcinoma and CVD. Gal–3 has been discovered in various types of cells, like stimulated macrophages, fibroblasts, dendritic cells, eosinophils, mast cells, chondrocytes and osteoblasts. Previous studies have shown that Gal–3 plays different functions in many tissues and plays its role in both intra and extracellular. Subjects: One hundred individuals were collected to contribute to the present study. These cases were divided into two groups. The first included 70 patients (their ages ranged between 30-66 years) with MI who underwent elective PCI and were divided into two subgroups: 30 patients with the first PCI and 40 patients who underwent more than one PCI. The second group involved 30 healthy individuals (aged 30-55 years) who were enrolled in the present study as a control group. Results: The results showed a significant increase ($p=0.001$) of serum Gal-3 levels in the patient's group compared to control individuals. Moreover, the result illustrated a statistically significant elevation in the Gal-3 levels ($p=0.000$) when comparing the two male subgroups (patients with one PCI and healthy). The same results were observed when the female subgroups were compared together. No significant differences were recorded when the two genders in the same group were compared ($p=0.093$ for one PCI patient and $p=0.563$ for healthy individuals).

Keywords: CVD, CHD, PCI, Lectins, Gal-3

INTRODUCTION

Coronary Heart Disease (CHD), known as coronary artery disease (CAD) or ischemic heart disease (IHD) [21], results from the hindrance of blood transit to the muscle of the lipid heart and cholesterol on the inner wall of the heart. Because of atherosclerosis, CAD contains many diseases: stable angina, unstable angina, myocardial infarction, and sudden cardiac death [4]. Coronary artery disease causes vary, including heredity factor, smoking, hyperglycemia, hypertension, obesity, elevated cholesterol and stress [22].

Percutaneous Coronary Intervention (PCI), known as angioplasty, is a non-surgical operation performed using a catheter (tube is flexible and thin) to cram either inflate a balloon in the narrowing place or stent (a very small and fin grid tube made of either plastic or metal of stainless steel). So it is covered with medicine to prevent the coronary artery blockage again), to expand or open up the vessels in the muscle of the heart that contains plaque buildup that causes stenosis [5, 14] The physician accesses the damaged arteries through a small incision in the thigh or arm, where the catheter is inserted through this opening, then delivered to the ascending aorta. Visualize the sites of damage in the arteries by using X-ray fluoroscopy after coronary arteries are injected by IV contrast (Radiopaque dye is a colorless liquid and is based on iodine) to determine the damage site [13].

Lectins are a special group of proteins free or bound by special sites on the outer cell surfaces; they are extensive and found in organisms with non-immune functions [15], where they distinguish and are reversibly linked to glycoconjugates and carbohydrates [2]. Lectins were first discovered in ricin and abrin of plants; they adhere and precipitate blood cells and are ribosome-inactivating proteins (RIPs), thus resembling the anti-bodies function. Generally, Lectins are proteins consisting of, at least, heterodimeric 2 chains of peptides linked by disulfide bounds [10, 15]. They participate in various biological processes such as signaling pathways, interactions of cells, development of cells, and immune responses [11].

Galectins are a class of animal lectins with an affinity for beta-galactosides [1]. They are varieties that dissolve in water, globular proteins non-glycosylated that can react with carbohydrates in a cation II-separate manner [16]. Galectins are differentiated in the cytoplasm and both nuclear and compartments of cytoplasmic function. They excrete a matrix of extracellular outer membranes of cells and, in circulation, are existent. There are 15 various human galectins. They are classified into proto-, chimera-, and tandem–repeat depending on their temple [20]. During this behavior, galectins can react with the cell surface and glycoproteins in the extracellular matrix within a reaction of lectin–carbohydrate. Galectins foster the growth of the cells, impact the survival of the cells, modify adhesion and prompt migration of cell [1].

Galectin-3 (Gal-3) is the chimera category in the family of galectin, contains 251 amino acid residues with a molecular weight of 32–35 kDa, an extremely preserved atypical N end domain (ND) and carbohydrate-recognition domain (CRD) [26]. The CRD maintains the lectin activity, involves 130 amino acid residues and can be digested proteolytically via trypsin. The ND contains about 120 amino acids and involves a re-duplicate of 9 amino acid residues rich in glycine, tyrosine, and proline, which are necessary for Gal-3 biological activity [6]. The ND can be cleaved by proteases, such as collagenase and matrix metalloproteinase (MMPs) [8]. Gal-3 is a multifunctional protein that coordinates the body's varied physiological and pathological processes [17]. Gal–3 contributes to several processes, such as macrophage migration promotion, fibroblast proliferation, and the synthesis of collagen [25]. The main function of Gal–3 is its role in the acute and chronic inflammation [24]. The universe has been related to

cancers and cardiovascular disease when discovered in various types of cells like stimulated macrophages, fibroblasts, dendritic cells, eosinophils, mast cells, chondrocytes and osteoblasts [18]. Previous studies have shown that Gal–3 plays different functions in many tissues and plays its role in all intra and extracellular [19]. Gal–3 intracellular involvement in nuclear, mRNA-linked and safeguarding cells from apoptotic prompted by Fas signaling, chemotherapy agents or radiation [3]. In the genome of humans, the gene LGALS3 is single Gal-3; this gene contains five introns and six exons on chromosome 14, covering nearly 17-kilo bases and a locus in the q-arm in spots between q21-q22 [9, 12].

MATERIALS AND METHODS

A hundred individuals in the present work were divided into two main groups. The first included 70 patients aged between 30 and 66 years with MI who underwent elective PCI (30 underwent it for the first time, and the remaining number underwent it more than once). The second group involved 30 healthy individuals aged 30-55 years who were enrolled in the present study as a control group. Exclusion criteria included individuals with the Covid-19 virus, cancer, thyroid diseases, liver diseases, and diabetes complications added to cardiopathy. In addition, patients who underwent surgical intervention during 5 years of MI occurring whether or not the surgery involved heart disease, patients who are on the keto diet during the onset of symptoms of heart attack and alcohol drinkers. The members of the control group were selected from the work environment; the selection was based on several criteria: they should have no medical history of heart disorders, be non-smokers and not alcohol drinkers, they should not take any medication during at least one year before study carrying out as well as they haven't undergone surgical intervention or any illness requiring hospitalization.

After subjecting to the PCI procedure, sera samples of patients were collected from The Heart Center in Al-Diwaniyah Teaching Hospital, Al-Diwaniyah Governorate, Iraq. The initial diagnosis was performed by specialist doctors and through several clinical and laboratory evaluation specialists for patients. Information about the current study individuals was provided through oral meetings with patients and in support of the supervising physicians. The questionnaire, prepared in advance based on the opinion of CVD specialists, included age, gender, place of residence, profession, period of onset of symptoms, medical history, investigation of diabetes and hypertension, type of treatments used by patients, and number of PCI times. The participants (patients and controls) subjects were fasting for 8-12 hours before blood collection. Sandwich-ELISA technique was applied to measure Gal–3 concentration in the sera samples. The statistical analysis of results was done using the Statistical Package for the Social Science (SPSS) software for Windows, version 23.0; p-values less than 5% ($p<0.05$) were considered statistically significant.

RESULTS AND DISCUSSION

Levels of Gal-3 in the sera samples of the study groups were measured, and results showed a significant ($p=0.000$) increase in the Gal-3 level in the patient's group compared to controls Table 1.

Test	Cases	N	Mean ± S.D.	Min.	Mix.	Range	p
Gal-3 (ng/mL)	Patient	70	9.863 ± 2.208	2.77	13.86	11.09	0.000
	Healthy	18	3.282 ± 1.809	1.02	7.80	6.78	

Table 1: Levels (Mean ± S.D.) of Galectin-3 (ng/mL) in the sera of the study subjects

Based on gender, groups of the present study were also divided into 4 subgroups. When the ANOVA test was applied, the results in Table 2 showed significant increases (p=0.000) when comparing males in the two subgroups (patients with one PCI and controls), as well as for females (p=0.00). There are no significant differences when comparing the genders in the same group. Moreover, it was also noted that the highest Gal-3 concentration (13.86 ng/mL) in the female patient.

Test & samples		N	Mean ± S.D.	Min.	Mix.	Range	p-value
Galectin-3 (ng/mL)	Female with one PCI	13	10.290 ± 2.230	6.21	13.86	7.65	0.093 1 vs 2
	Male with one PCI	17	8.977± 2.253	4.34	13.79	9.45	0.000 1 vs 3
	Healthy Female	10	3.025 ± 1.790	1.02	5.55	4.53	0.563 3 vs 4
	Healthy Male	8	3.603 ± 1.901	1.32	7.80	6.4	0.000 2 vs 4

Table 2. Levels (Mean ± S.D.) of Galectin-3 (ng/mL) in the sera of one PCI patients and control subjects

Table 3 revealed statistical comparisons among the subgroups of MI patients who underwent to 2 or more PCI procedures and controls. The results showed an increase (p=0.000) in the levels of Gal-3 in the sera of samples of patients of both sexes when compared with their peers of the same sex in the control group. No statistical differences were recorded when the two genders in the same group were compared together.

Test & samples		N	Mean ± S.D.	Min.	Mix.	Range	p-value
Galectin-3 (ng/mL)	Females with more PCI	13	10.905 ± 1.697	8.62	13.45	4.83	0.096 1 vs 2
	Males with more PCI	27	9.713 ± 2.240	2.77	13.68	10.91	0.000 1 vs 3
	Female healthy	10	3.025 ± 1.790	1.02	5.55	4.53	0.563 3 vs 4
	Male healthy	8	3.603 ± 1.901	1.32	7.80	6.4	0.000 2 vs 4

Table 3. Levels (Mean ± S.D.) of Galectin-3 (ng/mL) in The Sera of More PCI Patients and Control Subjects

The comparison among PCI patients who underwent one and those who were subjected to PCI equally or more than twice illustrates no significant differences between the genders in the same groups and between patients with the same gender in the two subgroups, as shown in Table 4.

Test & samples		N	Mean ± S.D.	Min.	Mix.	Range	p-value
Galectin-3 (ng/mL)	Female with one PCI	13	10.290 ± 2.230	6.21	13.86	7.65	0.093
	Male with one PCI	17	8.977 ± 2.253	4.34	13.79	9.45	1 vs 2 0.457
	Females with more PCI	13	10.905 ± 1.697	8.62	13.45	4.83	1 vs 3 0.260
	Males with more PCI	27	9.713 ± 2.240	2.77	13.68	10.91	2 vs 4 0.096
							3 vs 4

Table 4. Levels (Mean ± S.D.) of Galectin-3 (ng/mL) in The Sera of One PCI Patients and More PCI Patients

DISCUSSION

One of the most complex inflammatory processes is happening during atherosclerosis, which is associated with different markers of inflammation. Gal-3 levels showed a significant increase in human plaque (atherosclerosis). Elevation of Gal-3 levels can affect endothelial cells, which are among the cells that cause atherosclerosis and blockages in case of loss of their functions. Chronic inflammation and the continued activity of the endothelial cells under this inflammation causes them to lose their function and transform them into endothelial cell dysfunction, and this is the first step for the onset of arteriosclerosis and cardiovascular disease. Previous studies have shown that oxidized low-density lipoprotein (ox-LDL) causes endothelial cell injury by altering proinflammatory gene expression and that Gal-3 accumulates ox-LDL-mediated endothelial injury by persuading inflammation [27,23]. The results of the current study agree with several previous studies [7,26,27].

CONCLUSION

It was also noted that the highest level of Gal-3 (13.86 ng/mL) in the sample of female patients. Despite the observed increase in the levels of Gal-3 in elderly patients with MI who underwent PCI more than once, the study did not find significant differences in the Gal-3 levels of their samples compared to younger patients or those who underwent elective PCI for the first time.

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