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Comparison of the effects of atorvastatin and rosuvastatin on the levels of inflammatory markers and lipid profile in the patients with acute coronary syndrome: Randomized controlled double - blind clinical trial

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Keywords: acute coronary syndrome; atorvastatin; rosuvastatin; inflammation; lipid profile.

Abstract

Background: The role of lipids and inflammation in the patients with cardiovascular complications has been reported. The primary aim of the current randomized controlled double-blind clinical trial was to compare the influence of Atorvastatin and Rosuvastatin on the lipid profile and inflammatory markers in the patients with Acute Coronary Syndrome (ACS).

Methods: This study included 84 cases with approved diagnosis of ACS. Patients were randomized into two groups (42 cases each) and received Atorvastatin (80 mg/day) or Rosuvastatin (40 mg/day) for two months. After this period, levels of tumor necrosis factor (TNF)-α, interleukin (IL)-6, C-reactive protein (CRP), and monocyte chemoattractant protein-1 (MCP-1) and lipid profile was determined in serum samples using enzyme-linked immunosorbent assay (ELISA).

Results: It was observed that there was a significant reduction in the TNF-α (P= 0.008) and MCP-1 (P= 0.001) levels in the Atorvastatin group. Moreover, there was a significant decrease in the TNF-α (P= 0.001) and MCP-1 (P= 0.003) levels in the Rosuvastatin group. Atorvastatin caused statistically significant decreased levels of LDL (P= 0.014), TG (P= 0.012), and total cholesterol (P= 0.011). As such, Rosuvastatin also caused statistically significant reduced levels of LDL (P= 0.028), TG (P= 0.010), and total cholesterol (P= 0.003). No differences were observed in the levels of inflammatory markers and lipid factors between patients receiving Atorvastatin comparted to Rosuvastatin.

Conclusions: Although both Atorvastatin and Rosuvastatin seem to beneficial in soothing inflammation and decreasing the levels of lipids in ACS patients, none of them privilege the other one within this context.

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Introduction

Acute Coronary Syndrome (ACS) is a coronary atherosclerotic disease that is characterized through diminished blood flow in the coronary arteries, leading to impaired function and necrosis of cardiomyocytes and finally Myocardial Infarction (MI) [1]. The most common clinical findings in ACS patients are chest pain and discomfort in one or both arms. Despite progresses in the diagnosis and treatment of myocardial infarction, death and heart failure after MI is still one of the biggest health problems [2].

Inflammation plays a critical role in the onset, perpetuation, and exacerbation of the coronary atherosclerotic diseases like ACS [3]. Inflammatory markers, including immune mediators like cytokines are involved in the etiopathogenesis of atherosclerosis and promote the atheroma progression from early leukocyte infiltration to final atherosclerotic plaque rupture [4]. During the initial stage of MI, destruction of the extracellular matrix by Matrix Metallopeptidases (MMPs) leads to expansion of the infarcted area, thinning of the ventricular wall, and dilation of the cavities [5-7]. This is followed by repair of the infarct tissue, during which the fibroblasts proliferate, and collagen deposition causes the formation of non-contractile and fibrotic scar tissue. These changes further dilate the ventricles and cause heart failure. Therefore, activation of MMPs along with extracellular matrix degradation and tissue remodeling by mediators like Transforming Growth Factor (TGF)-β plays an essential role in collagen synthesis and scar tissue formation in the infarcted area during repair [8]. These events finally lead to development of non-functional scares instead of cardiomyocytes. Modifications in the shape, size, and thickness of the left ventricle following MI in the infarcted and non-infarcted area can affect heart function and cause heart failure, resulting in increased mortality and morbidity in these patients [9]. As a consequence, researchers have been seeking for development of pharmacological strategies to prevent tissue damage and heart failure following MI.

Oxidized Low-Density Lipoprotein (ox-LDL) plays a key role in clinical pre-atherosclerosis and in the pathophysiology of ACS. Ox-LDL activates several inflammatory and atherogenic pathways and plays a key role in atherosclerosis [10]. The importance of lowering cholesterol levels in coronary heart diseases has been well-documented in European and American guidelines for such diseases [11,12]. These guidelines follow a therapeutic aim to decrease Ox-LDL levels in the ACS and other coronary heart diseases [13].

Researchers have indicated that statin decreases the relative risk of cardiovascular disease by 24-37% [14]. Cases receiving 10 mg/day atorvastatin in the Collaborative Atorvastatin Diabetes Study (CARDS) [15] and the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) [16] exhibited normal level of LDL-C and a one-third decrees in the main cardiovascular complications. A high dose of lipid-lowering medication by 80 mg/day atorvastatin in the Reversal of Atherosclerosis with Aggressive Lipid Lowering (REVERSAL) trial [17] caused reduced atherogenic lipoproteins and atheroma volume in cases with Coronary Heart Disease (CHD) in comparison to the moderate medication by a 40 mg/day dose of pravastatin.

Following the publication of the results of the Scandinavian Simvastatin Survival Study (4S) in 1994, Simvastatin at a dose of 20-40 mg became the most common treatment regimen to reduce lipid levels in coronary artery disease patients [18]. In more recent studies, patients with acute coronary syndrome have been shown to have greater benefits following lower serum LDL levels below 100 dl/mg [19]. However, the reduction in lipid under clinical conditions is not optimal, so that only one-second to one-third of patients treated with lipid-lowering drugs reach the target lipid level [20,21]. Such an inefficiency in the therapeutic targets imposes remarkable clinical and financial costs [22].

Given the importance of lowering LDL levels and suboptimal clinical conditions and the importance of reducing the level of inflammatory markers to prevent the process of improper tissue repair in patients with ACS, in this study we conducted a randomized controlled double-blind clinical trial to compare the effects of Atorvastatin and Rosuvastatin on the lipid profile and inflammatory markers in the ACS cases.

Study subjects and methods

Participants

In this randomized controlled double-blind clinical trial, 84 patients based on clinical findings with acute MI diagnosis were recruited from the 22 Bahman hospital, Neyshabur University of Medical Science, Iran. The protocol of this study was reviewed and approved by the local ethical committee from Neyshabur University of Medical Science (Ir.nums.rec.1394.22). All patients were explained about the study protocol and informed consent was obtained.

Diagnosis of acute MI was accomplished based on clinical symptoms, Electrocardiogram (ECG), and serum markers. Among the inclusion criteria with respect to age of cases were, an age over 18 years and a maximum age of 75 years. Among the exclusion criteria were those with renal failure (Urea>18 mg/dl, Cr>1.5 mg/dl), liver failure (liver enzymes AST, ALT, and CK≥1.5-times above normal, and a bilirubin Total<2, Direct>0.2), receiving medications like immunosuppressants, corticosteroids, or potent cytochrome P450 3A4 inhibitors (corticosteroids, azathioprine, mycophenolic acid, tacrolimus, etc.), pentoxifylline, and cilostazol, background diseases like inflammatory or infectious diseases, leukocytosis (WBC> 11 X 10^3), consumption of glucosamine (due to inhibitory effects on the inflammatory nuclear factor (NF)-κB pathway), consumption of berberine extract (due to inhibitory effects on the inflammatory NF-κB pathway), a history of diseases that cause malabsorption syndromes, a triglyceride (TG)>400, heart failure stage based on the New York Heart Association (NYHA) III or IV, uncontrolled Blood Pressure (BP) with a systolic BP>180 and a diastolic BP>100, and finally evidence of endocrine or metabolic disorders that affect the lipid profile.

Patient BP and 12-lead standard ECG were measured. All patients filled a questionnaire of medical history, along with individual characteristics, demographic findings, anthropometric parameters, and paraclinical tests. Clinical information, personal and family history of cardiovascular disease, diabetes, medication, as well as the angiographic results of patients were recorded according to standard criteria.

BP was measured with a standard mercury sphygmomanometer and cuff appropriate to the person's arm circumference after the patient was in the supine position for at least 15 min. The measurement was repeated 2 times with an interval of at least 5 min, and the average of the two pressures was considered as the person's BP. Phase I and IV of the korotkoff sounds were considered as systolic BP and diastolic BP, respectively.

Study design and sampling

The patients were randomized into two groups with equal numbers and received Atorvastatin dose of 80 mg/day or Rosuvastatin dose of 40 mg/day for two months, starting at the first 24 hours of the intervention, and then a single dose after dinner, along with the routine treatment regimen. At the beginning, 10 ml of peripheral blood samples and then fasting blood samples within 24-hours of hospitalization were obtained from all participants. The blood samples were tested for inflammatory markers, Fasting Blood Sugar (FBS), total cholesterol, TG, High Density Lipoprotein (HDL), creatinine, urea, and liver enzymes using ELISA technique. Friedewald Equation was used to calculate the LDL levels. Two months later, a blood sample was taken again from all patients to measure inflammatory markers, lipid profiles, and liver tests.

Randomization process

Individuals who were eligible for the study were randomly divided into two groups using 4 randomized blocking, including Atorvastatin and Rosuvastatin. In this study, we prepared 4 sheets that two sheets were typed on with the letter A (Atorvastatin) and on the other two sheets with the letter R (Rosuvastatin), and one card was assigned for each patient, without replacement of cards. As a consequence, here was an equal number of people at the end of each block who had received A treatment or R treatment. This process continued until the number of entered patients were as much as the total sample size. In order to prevent the predictability of randomization process, a person (secretary) performed the allocation process and both the patient and the physician were not aware of the size of the blocks and the type of treatment received (blinding). Sixty drugs were assigned in each Atorvastatin and Rosuvastatin groups with same packaging, and only the letter A or R was written on the packaging. Only the researcher himself was aware of the contents of the package and the type of medicine.

Statistical analysis

The statistical analysis of data was conducted via SPSS software v.24 (IBM SPSS Statistics). The normality of data distribution was assigned by the Kolmogorov-Smirnov (K-S) test. To determine the differences between groups, the independent *t*-test or non-parametric Mann–Whitney *U* test was used, according to the normality of data distribution as determined by the K-S test. Mean comparison within each group before and after treatment was accomplished by paired *t*-test or non-parametric Wilcoxon test, based on the K-S test. The data was represented as percentage or mean ± Standard Deviation (SD). The statistical significance level was determined through a *P* value less than 0.05.

Results

Baseline characteristics

The baseline characteristics and demographic data of the study participants are listed in the Table 1 with more details. These factors included sex, age, height, weight, systolic BP, diastolic BP, fasting blood sugar, LDL, HDL, TG, total cholesterol,

Table 1: Baseline characteristics and demographic presentations of the subjects included in the study.

Characteristic	Value (n=84)
Male/female (%)	42 (50%)/ 42 (50%)
Age (years, Mean ± SD)	54.5 ± 11.3
Height (cm, Mean ± SD)	168.54 ± 21.87
Weight (Kg, Mean ± SD)	79.23 ± 14.65
Systolic blood pressure (mmHg, Mean ± SD)	14.88 ± 1.23
Diastolic blood pressure (mmHg, Mean ± SD)	11.56 ± 1.40
Fasting blood sugar (mg/dl, Mean ± SD)	87.9 ± 4.7
Low density lipoprotein (mg/dl, Mean ± SD)	128.41 ± 20.11
High density lipoprotein (mg/dl, Mean ± SD)	35.14 ± 8.61
Total cholesterol (mg/dl, Mean ± SD)	242.25 ± 38.54
Triglyceride (mg/dl, Mean ± SD)	189.45 ± 24.89
Aspartate transaminase (mg/dl, Mean ± SD)	20.47 ± 8.51
Alanine aminotransferase (mg/dl, Mean ± SD)	32.88 ± 9.35
Alkaline Phosphatase (mg/dl, Mean ± SD)	114.24 ± 21.33
Totalbilirubin (mg/dl, Mean ± SD)	1.12 ± 0.43
Directbilirubin (mg/dl, Mean ± SD)	0.18 ± 0.04
White blood cells (count/ml, Mean ± SD)	9248 ± 248
Red blood cells (count/ml, Mean ± SD)	$5.2 \times 10^6 \pm 3.8 \times 10^4$
Sodium level (mEq/dl, Mean ± SD)	138.24 ± 4.88
Potassium level (mEq/dl, Mean ± SD)	4.1 ± 0.79
Urea (mg/dl, Mean ± SD)	16.24 ± 3.57
Creatinine (mg/dl, Mean ± SD)	0.8 ± 0.24
Vitamin D (ng/dl, Mean ± SD)	35.18 ± 3.68
Current smoking Yes/No (%)	23 (27.3%)/ 61 (72.8%)
Current addiction Yes/No (%)	3 (3.6%)/ 81 (96.4%)
Alcohol addiction Yes/No (%)	2 (2.4%)/ 82 (97.6%)
Familial history of diabetes Yes/No (%)	12 (14.3%)/ 72 (85.7%)
Familial history of cardiovascular diseases Yes/No (%)	18 (21.4%)/ 66 (88.6%)
Familial history of hypertension Yes/No (%)	21 (25%)/ 63 (75%)
Familial history of kidney disorders Yes/No (%)	51 (60.7%)/ 33 (39.3%)
History of hypertension Yes/No (%)	38 (45.3%)/ 46 (54.7%)
History of diabetes Yes/No (%)	41 (48.8%)/ 43 (51.2%)
History of hyperlipidemia Yes/No (%)	37 (44%)/ 47 (66%)
History of cancer Yes/No (%)	1 (1.2%)/ 83 (98.8%)
History of osteoporosis Yes/No (%)	2 (2.4%)/ 82 (97.6%)
History of bone fracture Yes/No (%)	5 (6%)/ 79 (96%)
History of weight loss Yes/No (%)	11 (13.1%)/ 73 (86.9%)
History of lactation Yes/No (%)	3 (3.6%)/ 81 (96.4%)
History of pregnancy Yes/No (%)	11 (13.1%)/ 73 (86.9%)

SD: Standard Deviation

Aspartate Transaminase (AST), Alanine Aminotransferase (ALT), alkaline phosphatase, total bilirubin, direct bilirubin, white blood cells, red blood cells, blood sodium level, blood potassium level, urea, creatinine, vitamin D, current smoking status, current addiction status, alcohol addiction, familial history of diabetes, familial history of cardiovascular diseases, familial history of hypertension, familial history of kidney disorders, history of hypertension, history of diabetes, history of hyperlipidemia, history of cancer, history of osteoporosis, history of bone fracture, history of weight loss, history of lactation, and history of pregnancy.

Inflammatory markers and lipid levels in the Atorvastatin group

It was observed that there was a significant reduction in the TNF-α (*P*= 0.008) and MCP-1 (*P*= 0.001) levels after treatment of the patients with Atorvastatin. Nonetheless, levels of CRP and IL-6 did not change significantly. With respect to lipid factors, the treatment of the patients with Atorvastatin caused statistically significant decreased levels of LDL (*P*= 0.014), TG (*P*= 0.012), and total cholesterol (*P*= 0.011). However, no significant changes in the levels of HDL was detected (Table 2).

Table 2: Comparison of the inflammatory markers and lipid levels before and after treatment of the patients with Atorvastatin.

Factor	Before treatment	After treatment	*P* value
CRP	0.55 ± 0.14	0.57 ± 0.11	0.647
TNF-α	34.14 ± 5.48	14.25 ± 2.14	0.008
IL-6	385.4 ± 54.3	344.17 ± 53.74	0.598
MCP-1	106.28 ± 36.32	82.19 ± 29.45	0.001
LDL	127.25 ± 19.89	99.24 ± 16.78	0.014
HDL	35.28± 8.74	36.24 ± 9.25	0.715
TG	188.25 ± 24.17	139 ± 18.35	0.012
Total cholesterol	242.78 ± 38.41	168.25 ± 27.63	0.001

CRP: C-Reactive Protein; TNF: Tumor Necrosis Factor; IL-6: Interleukin-6; MCP-1: Monocyte Chemoattractant Protein-1; LDL: Low Density Lipoprotein; HDL: High Density Lipoprotein; TG: Triglyceride.

Inflammatory markers and lipid levels in the rosuvastatin group

There was a significant decrease in the TNF-α (*P*= 0.001) and MCP-1 (*P*= 0.003) levels after treatment of the patients with Rosuvastatin. However, levels of CRP and IL-6 did not show changes significantly after treatment with Rosuvastatin. Considering the lipid factors, the treatment of the patients with Rosuvastatin caused statistically significant reduced levels of LDL (*P*= 0.028), TG (*P*= 0.010), and total cholesterol (*P*= 0.003). Nonetheless, no significant changes in the levels of HDL was detected (Table 3).

Comparison of the effects of atorvastatin and rosuvastatin

The comparison of the inflammatory factors after treatment indicated that there was no significant differences in the levels of CRP (*P*= 0.954), TNF-α (*P*= 0.097), IL-6 (*P*= 0.329), and MCP-1 (*P*= 0.087) between cases treated with Atorvastatin in comparison to Rosuvastatin. Similarly, no significant alterations were detected in the levels of LDL (*P*= 0.514), HDL (*P*= 0.456), TG (*P*= 0.418), and total cholesterol (*P*= 0.792) between patients received Atorvastatin in comparison to Rosuvastatin (Table 4).

Table 3: Comparison of the inflammatory markers and lipid levels before and after treatment of the patients with Rosuvastatin.

Factor	Before treatment	After treatment	*P* value
CRP	0.65 ± 0.30	0.57 ± 0.19	0.096
TNF-α	34.14 ± 5.48	13.26 ± 2.14	0.001
IL-6	388.37 ± 54.65	358.24 ± 50.64	0.407
MCP-1	107.50 ± 35.44	91.16 ± 29.45	0.003
LDL	128.38 ± 19.25	98.15 ± 16.11	0.028
HDL	35.81± 8.65	35.11 ± 9.48	0.851
TG	187.41 ± 23.45	137 ± 17.25	0.010
Total cholesterol	242.11 ± 38.12	165.14 ± 28.18	0.003

CRP: C-Reactive Protein; TNF: Tumor Necrosis Factor; IL-6; Interleukin-6; MCP-1; Monocyte Chemoattractant Protein-1; LDL: Low Density Lipoprotein; HDL: High Density Lipoprotein; TG: Triglyceride.

Table 4: Comparison of the inflammatory markers and lipid levels between patients treated Atorvastatin and Rosuvastatin.

Factor	Atorvastatin	Rosuvastatin	P value
CRP	0.57 ± 0.11	0.57 ± 0.19	0.954
TNF-α	18.25 ± 2.14	14.26 ± 2.14	0.097
IL-6	344.17 ± 53.74	358.24 ± 50.64	0.329
MCP-1	82.19 ± 29.45	91.16 ± 29.45	0.087
LDL	99.24 ± 16.78	98.15 ± 16.11	0.514
HDL	36.24 ± 9.25	35.11 ± 9.48	0.456

CRP: C-Reactive Protein; TNF: Tumor Necrosis Factor; IL-6; Interleukin-6; MCP-1; Monocyte Chemoattractant Protein-1; LDL: Low Density Lipoprotein; HDL: High Density Lipoprotein; TG: Triglyceride.

Discussion

The importance of ox-LDL in atherosclerosis and the pathophysiology of ACS has been established. LDL oxidation activates many inflammatory and atherogenic pathways. Here in the current study, we carried out a randomized controlled double-blind clinical trial to compare the influence of Atorvastatin and Rosuvastatin on the lipid profile and inflammatory markers in the patients with ACS. Our analysis indicated that both treatments were able to decrease inflammatory markers (including TNF-α and MCP-1) as well as lipid factors (including LDL, TG, and total cholesterol) after medication of the patients. Nonetheless, no differences were observed in the levels of inflammatory markers and lipid factors between patients receiving Atorvastatin comparted to Rosuvastatin. Hence, none of these drugs privileged the other one with respect to efficacy in decreasing inflammation and lipids.

In the pathogenesis of cardiovascular disorders, inflammatory cytokines like IL-6 and TNF-α cause exacerbation of the atherosclerotic lesions. MCP-1 has been reported to play a significant role in the infiltration of monocytes to the atherosclerotic lesions and has been implicated as a contributing factor to the initiation and progression of atherosclerosis. The important cell types involved in the etiopathogenesis of atherosclerosis,

including vessel wall endothelial cells, smooth muscle cells, and macrophages are involved in the production of MCP-1 in the atherosclerotic lesions [23]. As a consequence, the primary target of treatments in the patients with cardiovascular involvement is to decrease the inflammation level in the patients, above an beyond lowering the lipid levels.

In a 2015 study by Aydin *et al*. [10] on 120 patients with acute MI, patients received Atorvastatin (80 mg per day) or Rosuvastatin (20 mg per day). Levels of total cholesterol, LDL, ox-LDL, HDL, apolipoprotein (Apo) B, ApoA, TNF-α, IL-6, and high-sensitivity CRP (hs-CRP) were measured between the two groups at baseline and 4 weeks after treatment. After treatment in both groups, the levels of LDL, ox-LDL, TNF-α, IL-6 and hs-CRP were decreased in both groups. The only difference was the level of HDL, which had a slight non-significant increase in the Atorvastatin group, while the increase was significant in cases receiving Rosuvastatin. Based on the results, the researchers concluded that both statin regimens had acceptable and comparable results on the LDL and ox-LDL levels as well as inflammatory markers. Moreover, Rosuvastatin was considered to be more useful due to its ability to increase HDL levels. Accordingly, a dose of 20 mg per day of Rosuvastatin may be an alternative to 80 mg of Atorvastatin in patients with ACS [10]. Additionally, in a study, Fox and his colleagues [24] compared the effects of Atorvastatin, Rosuvastatin, and Simvastatin on the LDL levels in patients with hyperlipidemia. Patients treated with any type of statin showed an LDL level decrease after conversion of treatment to Rosuvastatin compared to Atorvastatin. In a subgroup of patients treated with Atorvastatin, the reduction in LDL was significantly greater after treatment change to Rosuvastatin compared to Simvastatin. Therefore, in order to achieve well-decreased LDL levels, it is important to choose the best type of statin.

Along with the studies mentioned above, several other studies implied to the beneficial effects of Atorvastatin and Rosuvastatin in decreasing the lipid profile as well as the inflammatory markers in the patients with impaired cholesterol metabolisms as well as CVD [25-29]. For example, a study revealed greater hypercholesterolemic effects of Atorvastatin than Pravastatin in patients with familial hyperlipidemia [30]. In addition, Sadeghi*et al*. reported that Non-ST-elevation myocardial infarction (NSTEMI) patients experienced decreased LDL and CRP levels in patients treated with both Atorvastatin and Rosuvastatin; however, higher doses of Atorvastatin were much more efficient in decreasing CRP levels, regardless of indifferent LDL levels between the Atorvastatin and Rosuvastatin groups [31]. Nonetheless, our study revealed that there were no differences in the inflammatory markers and lipid profile of the ACS cases receiving Atorvastatin (80 mg/day) and Rosuvastatin (40 mg/day) for two months. However, each drug alone was able to decrease the inflammatory markers in the patients with ACS. Our analysis indicated that both treatments were able to decrease inflammatory markers (including TNF-α and MCP-1) as well as lipid factors (including LDL, TG, and total cholesterol) after medication of the patients.

Conclusion

Considering all the facts, the randomized controlled double-blind clinical trial to compare the influence of Atorvastatin and Rosuvastatin on the lipid profile and inflammatory markers in the patients with ACS revealed that both treatments were able to decrease inflammatory markers (TNF-α and MCP-1) as well as lipid factors (LDL, TG, and total cholesterol. However, these treatments did not impress the levels of CRP and IL-6 as well as HDL. In addition, no differences were observed in the levels of inflammatory markers and lipid factors between patients receiving Atorvastatin comparted to Rosuvastatin. Hence, none of these drugs privileged the other one with respect to efficacy in decreasing inflammation and lipids. Further studies in large trials is still needed to divulge the precise beneficial perspectives of Atorvastatin and Rosuvastatin in patients with cardiovascular complications.

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References

1. Sanchis Gomar F, Perez Quilis C, Leischik R, Lucia A. Epidemiology of coronary heart disease and acute coronary syndrome. Annals of translational medicine. 2016; 4.
2. Kayani WT, Khan MR, Deshotels MR, Jneid H. Challenges and Controversies in the Management of ACS in Elderly Patients. Current Cardiology Reports. 2020; 22: 51.
3. Poole L, Dickens C, Steptoe A. The puzzle of depression and acute coronary syndrome: Reviewing the role of acute inflammation. Journal of psychosomatic research. 2011; 71: 61-68.
4. Sager HB, Nahrendorf M. Inflammation: a trigger for acute coronary syndrome. The quarterly journal of nuclear medicine and molecular imaging: Official publication of the Italian Association of Nuclear Medicine (AIMN)[and] the International Association of Radiopharmacology (IAR), [and] Section of the Society of. 2016; 60: 185-193.
5. Awad MM, Shweash M, Alaaraji SF. The relationship between matrix metallopeptidase 9 with interleukins 6, 12, 13, 18 and 20 among male atherosclerosis Iraqi patients. Eurasian Journal of Biosciences. 2020; 14: 1105-1112.
6. He Z, Wang Y, He Q, Chen M. microRNA-491-5p protects against atherosclerosis by targeting matrix metallopeptidase-9. Open Medicine. 2020; 15: 492-500.
7. Zhi H, Wang H, Ren L, Shi Z, Peng H, Cui L, et al. Functional polymorphisms of matrix metallopeptidase-9 and risk of coronary artery disease in a Chinese population. Molecular biology reports. 2010; 37: 13-20.
8. Spinale FG, Gunasinghe H, Sprunger PD, Baskin JM, Bradham WC. Extracellular degradative pathways in myocardial remodeling and progression to heart failure. Journal of cardiac failure. 2002; 8: S332-S338.
9. Prabhu SD, Frangogiannis NG. The biological basis for cardiac repair after myocardial infarction: From inflammation to fibrosis. Circulation research. 2016; 119: 91-112.
10. Aydin MU, Aygul N, Altunkeser BB, Unlu A, Taner A. Comparative effects of high-dose atorvastatin versus moderate-dose rosuvastatin on lipid parameters, oxidized-LDL and inflammatory markers in ST elevation myocardial infarction. Atherosclerosis. 2015; 239: 439-443.
11. Detection NCEPEPo, Adults ToHBCi. Third report of the National Cholesterol Education Program (NCEP) Expert Panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III): National Cholesterol Education Program, National Heart, Lung, and Blood. 2002.
12. Graham I, Atar D, Borch-Johnsen K, Boysen G, Burell G, Cifkova R, et al. European guidelines on cardiovascular disease prevention in clinical practice: executive summary: Fourth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (Con-

stituted by representatives of nine societies and by invited experts). European heart journal. 2007; 28: 2375-2414.

13. Hayashida K, Kume N, Murase T, Minami M, Nakagawa D, Inada T, et al. Serum soluble lectin-like oxidized low-density lipoprotein receptor-1 levels are elevated in acute coronary syndrome: A novel marker for early diagnosis. Circulation. 2005; 112: 812-818.

14. Stroes E. Statins and LDL-cholesterol lowering: An overview. Current medical research and opinion. 2005; 21(sup6): S9-S16.

15. Colhoun HM, Betteridge DJ, Durrington PN, Hitman GA, Neil HAW, Livingstone SJ, et al. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. The Lancet. 2004; 364: 685-696.

16. Sever PS, Dahlöf B, Poulter NR, Wedel H, Beevers G, Caulfield M, et al. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial—Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial. The Lancet. 2003; 361: 1149-1158.

17. Nissen SE. Effect of intensive lipid lowering on progression of coronary atherosclerosis: evidence for an early benefit from the Reversal of Atherosclerosis with Aggressive Lipid Lowering (REVERSAL) trial. The American journal of cardiology. 2005; 96: 61-68.

18. Group SSSS. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). The Lancet. 1994; 344: 1383-1389.

19. Cannon CP, Braunwald E, McCabe CH, Rader DJ, Rouleau JL, Belder R, et al. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. New England journal of medicine. 2004; 350: 1495-1504.

20. Straka RJ, Taheri R, Cooper SL, Tan AW, Smith JC. Assessment of hypercholesterolemia control in a managed care organization. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. 2001; 21: 818-827.

21. Latts LM. Assessing the results: phase 1 hyperlipidemia outcomes in 27 health plans. The American journal of medicine. 2001; 110: 17-23.

22. Durrington P. The human and economic costs of undertreatment with statins. International journal of clinical practice. 2002; 56: 357.

23. Aiello RJ, Bourassa P-AK, Lindsey S, Weng W, Natoli E, Rollins BJ, et al. Monocyte chemoattractant protein-1 accelerates atherosclerosis in apolipoprotein E-deficient mice. Arteriosclerosis, thrombosis, and vascular biology. 1999; 19: 1518-1525.

24. Fox KM, Gandhi SK, Ohsfeldt RL, Davidson MH. Comparison of low-density lipoprotein cholesterol reduction after switching patients on other statins to rosuvastatin or simvastatin in a real-world clinical practice setting. American Journal of Managed Care. 2007; 13: S270.

25. Cho Y-K, Hur S-H, Han C-D, Park H-S, Yoon H-J, Kim H, et al. Comparison of ezetimibe/simvastatin 10/20 mg versus atorvastatin 20 mg in achieving a target low density lipoprotein-cholesterol goal for patients with very high risk. Korean Circulation Journal. 2011; 41: 149-153.

26. Marketou ME, Zacharis EA, Nikitovic D, Ganotakis ES, Parthenakis FI, Maliaraki N, et al. Early effects of simvastatin versus atorvastatin on oxidative stress and proinflammatory cytokines in hyperlipidemic subjects. Angiology. 2006; 57: 211-218.

27. Wiklund O, Mattsson-Hulten L, Hurt-Camejo E, Oscarsson J. Effects of simvastatin and atorvastatin on inflammation markers in plasma. Journal of internal medicine. 2002; 251: 338-347.

28. Barbarash O, Gruzdeva O, Uchasova E, Belik E, Dyleva Y, Karetnikova V. Dose-dependent effects of atorvastatin on myocardial infarction. Drug Design, Development and Therapy. 2015; 9: 3361.

29. Qu H-y, Xiao Y-w, Jiang G-h, Wang Z-y, Zhang Y, Zhang M, et al. Effect of atorvastatin versus rosuvastatin on levels of serum lipids, inflammatory markers and adiponectin in patients with hypercholesterolemia. Pharmaceutical research. 2009; 26: 958-964.

30. Sirtori CR, Calabresi L, Pisciotta L, Cattin L, Pauciullo P, Montagnani M, et al. Effect of statins on LDL particle size in patients with familial combined hyperlipidemia: A comparison between atorvastatin and pravastatin. Nutrition, metabolism and cardiovascular diseases. 2005; 15: 47-55.

31. Sadeghi M, Razavi NS, Sarrafzadegan N, Saeedifar M, Talaee M. Early And Late Effect Of High Dose Atorvastatin And Low Dose Atorvastatin On Serum C-Reactive Protein Reduction In Non St Elevation Myocardial Infarction. Arya Atherosclerosis. 2010; 4.