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Comparison between Loading Dose of Atorvastatin and Loading Dose of Rosuvastatin Prior to Percutaneous Coronary Intervention in Patient with ST Elevation Myocardial Infarction for the Prevention of Contrast Induced Nephropathy

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Early percutaneous coronary intervention (PCI) is the method of choice for myocardial infarction with ST-elevation, and a shorter interval between event and hospital arrival can result in lower mortality rates. The aim of the study was to compare the efficacy of loading dose atorvastatin defined as 80 milligrams versus loading dose rosuvastatin defined as 40 milligrams for the prevention of contrast induced nephropathy (CIN) in ST elevation myocardial infarction patients undergoing primary percutaneous coronary intervention.
Methods: This prospective randomized study was carried out on 150 patients with clinical features of ST elevation myocardial infarction who randomly assigned to receive either atorvastatin (80 mg) or rosuvastatin (40 mg) before undergoing the primary PCI and diagnosed according to the 2018 European society of cardiology guidelines. Patients were divided into two equal groups: Atorvastatin group: experienced PCI accepting 80 mg Atorvastatin and Rosuvastatin group: experienced PCI getting high portion (40 mg) of Rosuvastatin.

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Results: CIN was insignificantly different between atorvastatin and Rosuvastatin groups. Procedural duration, contrast volume, hydration volume and number of vessels were insignificantly different between atorvastatin and rosuvastatin group. Culprit vessel was significantly different between atorvastatin and rosuvastatin group (P value= 0.0003). Number of stents was significantly different between atorvastatin and rosuvastatin group (P value= 0.013).
Conclusions: The CIN was insignificantly different between the atorvastatin and rosuvastatin groups. Thus, the antioxidant properties of both statins could protect against the CIN.

Keywords: Atorvastatin; rosuvastatin; percutaneous coronary intervention; ST elevation myocardial infarction; contrast induced nephropathy.

1. INTRODUCTION

"Early percutaneous coronary intervention (PCI) is the method of choice for myocardial infarction with ST elevation, and a shorter interval between event and hospital arrival can result in lower mortality rates. Coronary angiography is the most common heart procedure worldwide and contrast-induced nephropathy (CIN) has shown increased rates in those undergoing this modality" [1].

"CIN is defined as an increase of more than 25% or more than 0.5 mg/dl (44 μmol/l) of serum creatinine from baseline within 48 − 72 h following intravenous injection of contrast material if other etiologies of renal impairment can be excluded, usually peaking on the third to fifth day, and returning to baseline values within 10–14 days. The overall incidence of CIN in the general population has been estimated to be 1–6%. The incidence is higher in patients undergoing PCI leading to increased mortality, morbidity, and in-hospital stay" [2].

"CIN is commonly observed among patients undergoing primary PCI, even in those with a normal renal function. Chronic kidney alterations may affect those with previous renal insufficiency up to 12%; however, the symptoms are seen in less than 1%. CIN is an acute decreased renal function after an intravenous infusion of iodine contrast media, which is the third cause of hospital-acquired acute renal failure and is due to cardiac procedures in half of the cases. furthermore, it may increase the risk of hemodialysis and death" [3].

"CIN may be secondary to direct tubular toxicity, vasoconstriction, and oxidative stress. Statins may lessen atherosclerosis, inflammation, endothelial dysfunction, and platelet hyperactivity. Good effects of statins such as atorvastatin and rosuvastatin on oxidative stress, nitric oxide synthesis, and endothelial function constitute some of the mechanisms responsible for the reno- protective effects in those with chronic kidney disease. Nevertheless, not only is there controversy surrounding the efficacy of statins for the prevention of CIN, but also there have been reports on varying efficacies of various statins" [4]. "Statins work by competitively blocking the active site of the first and key rate-limiting enzyme in the mevalonate pathway, HMG-CoA reductase, inhibition of this site prevents substrate access, thereby blocking the conversion of HMG-CoA to mevalonic acid" [5].

"Within the liver, this reduces hepatic cholesterol synthesis, leading to increased production of microsomal HMG-CoA reductase and increased cell surface LDL receptor expression. This facilitates increased clearance of LDL-c from the bloodstream and a subsequent reduction in circulating LDL-c levels by 20% to 55%. In addition to reducing LDL-c and cardiovascular morbidity and mortality, statins may have additional non–lipid-related pleiotropic effects. These include improvements in endothelial function, stabilization of atherosclerotic plaques, anti-inflammatory, immunomodulatory and antithrombotic effects, effects on bone metabolism, and reduced risk of dementia" [6].

The aim of the study was to compare the efficacy of loading dose atorvastatin defined as 80 milligrams versus loading dose rosuvastatin defined as 40 milligrams for the prevention of CIN in ST elevation myocardial infarction patients undergoing primary percutaneous coronary intervention.

2. PATIENTS AND METHODS

This prospective randomized study was carried out on 150 patients with clinical features of ST elevation myocardial infarction who randomly assigned to receive either atorvastatin (80 mg) or rosuvastatin (40 mg) before undergoing the primary PCI and diagnosed according to the 2018 European society of cardiology guidelines.

Exclusion criteria were patients aged > 80 years or <18 years, patients with other forms of acute coronary syndrome, patient with moderate to severe renal impairment (creatinine clearance ≤ 60 ml/min), cardiogenic shock, heart failure on admission, current treatment with statins, those who had received a contrast agent within the preceding week, malignancy, myositis, myopathy, patient with hepatic disease and patient with known hypersensitivity to statins.

Patients were divided into two equal groups: Atorvastatin group: experienced PCI accepting 80mg Atorvastatin and Rosuvastatin group: experienced PCI getting high portion (40mg) of Rosuvastatin.

All patients were subjected to history taking (age, sex, HTN, DM, Dyslipidemia, HF, chronic kidney disease, ischemic heart disease and medication history), demographic data (height and weight), general and local examination and laboratory investigations (CBC, cholesterol, LDL-Cholesterol, triglycerides, CK, CKMB, troponin, serum urea and creatinine) and resting 12 ECG leads.

Coronary angiography: Primary percutaneous coronary intervention was done -according to the European society of cardiology guidelines- within 12 hours from symptoms onset. Before the procedure patients were randomly assigned to receive either atorvastatin (80 mg) or rosuvastatin (40 mg) and were maintained on either drug after the procedure. All patients received the loading dose of aspirin and clopidogrel. Before the PCI procedure CBC, cholesterol, LDL-Cholesterol, triglycerides, CK, CKMB, troponin, serum urea and creatinine were evaluated, thereafter serum urea, creatinine and creatinine clearance were followed up for 72 hours, all interventions were performed with a non-ionic, low- osmolar, iodinated contrast agent.

Percutaneous coronary intervention: Aspirin (300 mg) and clopidogrel (600 mg) were loaded in all patients before the procedure. An intravenous bolus of 5000 U unfractionated heparin was given to keep up activated coagulating time >300 seconds during the procedure. Coronary angiography and stent implantation were performed utilizing standard interventional techniques. Platelet glycoprotein IIb/IIIa inhibitor was administrated in some elective cases. Aspirin (100 mg/day), clopidogrel (75 mg/day), and statins were recommended to all patients after the procedure. Hydration treatment (0.9%NaCl, 1 mL/kg/h) was performed during the pre-and post-PCI periods.

Measurements: Demographic data (Age, gender, height, weight and body mass index [BMI]), risk factors (smoking, DM, hypertension, IHD, family history and hyperlipidemia), serum creatinine at baseline and after 48hr, difference in serum creatinine levels, CrCl at baseline and after 48hr, difference in CrCl, angiographic and procedural characteristics (Procedural duration, contrast volume, hydration volume, Culprit vessel and number of vessels) and medication (angiotensin-converting enzyme (ACE) or angiotensin receptor blockers (ARB), Beta blocker (BB), Calcium channel blockers (CCB) and Antihyperglycemic).

Statistical analysis: Statistical analysis was done by SPSS v26 (IBM Inc., Chicago, IL, USA). Quantitative variables were presented as mean and standard deviation (SD) and compared between the two groups utilizing unpaired Student's t- test. Qualitative variables were presented as frequency and percentage (%) and were analyzed utilizing the Chi-square test or Fisher's exact test when appropriate. A two tailed P value < 0.05 was considered statistically significant.

3. RESULTS

Demographic data (age, gender, height, weight and BMI) and risk factors (smoking, DM, hypertension, IHD, family history and hyperlipidemia) were insignificantly different between atorvastatin and rosuvastatin groups Table 1.

Serum creatinine was significantly higher after 48hr compared to baseline in atorvastatin group (P value<0.001). was insignificantly different between baseline and after 48hr in rosuvastatin group. Serum creatinine was insignificantly different between baseline in both groups. was significantly higher after 48 hr in atorvastatin group compared to after 48hr in rosuvastatin group (P value=0.008). The difference in creatinine level was significantly higher in atorvastatin group compared to rosuvastatin group (P value<0.001) Table 2.

CrCl was significantly lower after 48hr compared to baseline in atorvastatin group (P value<0.001), was insignificantly different between baseline and after 48hr in rosuvastatin group. CrCl baseline and after 48hr were insignificantly

different between atorvastatin and rosuvastatin group. The difference in CrCl in atorvastatin group was significantly lower than rosuvastatin group (P value<0.001) Table 3.

Procedural duration, contrast volume, hydration volume and number of vessels were insignificantly different between atorvastatin and rosuvastatin group. Culprit vessel was significantly different between atorvastatin and rosuvastatin group (P value= 0.0003). Number of stents was significantly different between atorvastatin and rosuvastatin group (P value= 0.013) Table 4.

Table 1. Demographic data and risk factors of the studied groups

			Atorvastatin group (n=75)	Rosuvastatin group (n=75)	P-value
Demographic data	**Age (years)**		52.65 ± 10.74	53.60 ± 10.40	0.584
	Gender	**Male**	63 (84%)	65 (87%)	0.818
		Female	12 (16%)	10 (13%)	
	Height(m)		1.74 ± 0.09	1.72 ± 0.08	0.208
	Weight (Kg)		83.52 ± 14.469	86.24 ± 11.889	0.210
	BMI (kg m^2)		25.764 ± 4.464	26.616 ± 3.670	0.204
Risk factors	**Smoking**		46 (61%)	38 (51%)	0.246
	DM		30 (40%)	24 (32%)	0.395
	Hypertension		35 (47%)	41 (55%)	0.414
	IHD		8 (11%)	5 (7%)	0.562
	Family history		16 (21%)	15 (20%)	0.840
	Hyperlipidaemia		29 (39%)	30 (40%)	0.867

Data are presented as mean ± SD or frequency (%), BMI: body mass index, DM: diabetes mellitus, IHD: ischemic heart disease

Table 2. Serum creatinine baseline and after 48 hr and difference in serum creatinine level of the studied groups

	Atorvastatin group		P-value
Creatinine (mg/dL)	**Baseline**	**After 48hr**	
	0.93 ± 0.17	1.06 ± 0.24	<0.001*
	Rosuvastatin group		
	0.90 ± 0.22	0.94 ± 0.31	0.092
	P value 0.305	**P value** 0.008*	
	Atorvastatin group	**Rosuvastatin group**	
Difference in serum creatinine level	0.13 ± 0.15	0.04 ± 0.21	<0.001*

*Data are presented as mean ± SD or frequency (%), *: significant as p value <0.05*

Table 3. CrCl baseline and after 48 hr and difference in CrCl of the studied groups

	Atorvastatin group		P-value
CrCl (mg/dL)	**Baseline**	**After 48hr**	
	124.99 ± 37.68	111.03 ± 39.05	<0.001*
	Rosuvastatin group		
	121.64 ± 42.86	119.01 ± 41.97	0.131
	P value 0.611	**P value** 0.230	
	Atorvastatin group	**Rosuvastatin group**	
Difference in CrCl	-13.97 ± 13.52	-2.62 ± 14.86	<0.001*

*Data are presented as mean ± SD or frequency (%), *: significant as p value <0.05*

Table 4. Angiographic and procedural characteristics of the studied groups

		Atorvastatin group (n=75)	Rosuvastatin group (n=75)	P-value
Procedural duration (min)		43.2 ± 10.738	40.2 ± 10.215	0.082
Contrast Volume (ml)		184 ± 46.615	172 ± 32.08	0.068
Hydration Volume (ml)		1000 ± 0	1000 ± 0	---
Number of vessels	**I**	54 (72%)	44 (59%)	0.203
	II	18 (24%)	28 (37%)	
	III	3 (4%)	3 (4%)	
Culprit vessel	**Diagonal**	7 (9%)	14 (19%)	0.0003*
	LAD	24 (32%)	44 (59%)	
	LCX	14 (19%)	8 (11%)	
	PDA	4 (5%)	2 (3%)	
	RCA	26 (35%)	7 (9%)	
Number of stents	**I**	59 (79%)	45 (60%)	0.021*
	II	16 (21%)	30 (40%)	

*Data are presented as mean ± SD or frequency (%), LAD: left anterior descending artery, LCX: left circumflex artery, PDA: Patent ductus arteriosus, RCA: Right coronary artery, *: significant as p value <0.05*

Table 5. Medication and contrast induced nephropathy of the studied groups

		Atorvastatin group (n=75)	Rosuvastatin group (n=75)	P-value
Medication	**ACE or ARB**	27 (36%)	24 (32%)	0.730
	BB	27 (36%)	21 (28%)	0.412
	CCB	17 (23%)	14 (19%)	0.687
	Antihyperglycemic	30 (40%)	24 (32%)	0.395
Contrast induced nephropathy	**Developed**	6 (8%)	6 (8%)	1
	Not developed	69 (92%)	69 (92%)	

Data are presented as mean ± SD or frequency (%), ACE: Angiotensin-converting enzyme, ARB: Angiotensin receptor blockers, BB: Beta blocker, CCB: Calcium channel blockers

Medication (ACE ARB, BB, CCB and Antihyperglycemic) and CIN were insignificantly different between atorvastatin and rosuvastatin groups Table 5.

4. DISCUSSION

Coronary angiography and percutaneous coronary intervention (PCI) are the gold standard for the treatment of obstructive lesions in ST-segment–elevation myocardial infarction (STEMI) [7]. “However, some life-threatening complications such as contrast-induced nephropathy (CIN) are observed after primary-PCI. Evidence shows a strong correlation between CIN and high mortality and morbidity in patients with STEMI” [8].

The present study reported that serum creatinine was significantly higher after 48 hrs of PCI compared to the baseline in atorvastatin group. While its level was insignificantly different between baseline and after 48hr in the rosuvastatin group. Additionally, our results are in agreement with Sadawi et al. [9] who demonstrated that no significant difference was recorded between the atorvastatin group, rosuvastatin.

Moreover, the serum creatinine was significantly higher after 48hr in the atorvastatin group compared to the rosuvastatin group.

These results are matched with Zhou et al. [10] reported in their meta-analysis a highly elevated creatinine levels after 48 hrs in the atorvastatin compared to the rosuvastatin group. Furthermore, our results revealed that creatinine clearance (CrCl) was significantly lower after 48 hrs compared to baseline in the atorvastatin group however, the CrCl level was insignificantly different between baseline and after 48hr in rosuvastatin group.

Similarly, the difference in CrCl in the atorvastatin group was significantly lower than the rosuvastatin group. Firouzi et al. [4] recorded similar results in his study where the CrCl level in

the atorvastatin group after 48 hrs was lower than the baseline. In addition, the difference in CrCl in the atorvastatin group was significantly lower than the rosuvastatin group. Hence, the strong anti-inflammatory and antioxidant properties of rosuvastatin may play a role in improving the renal function.

Our study showed that the culprit vessel was significantly different between atorvastatin and rosuvastatin group. The obtained result is similar to Rahhal et al. [11] who enrolled "a retrospective cohort study included patients diagnosed with acute coronary syndrome to compare between the 2 high-intensity statin therapies (rosuvastatin vs atorvastatin) in terms of a primary composite outcome of CVD-associated death. The results showed that the culprit vessel in atorvastatin was significantly higher than the rosuvastatin group".

Moreover, we found that the number of stents was significantly different between atorvastatin and rosuvastatin groups. The results are in the same line with Dai et al. [12] who enrolled his observational cohort study on STEMI patients undergoing PCI to evaluate the preventive efficacy of rosuvastatin versus atorvastatin in post-contrast acute kidney injury in patients with STEMI undergoing PCI. A total of 1300 included patients were divided into two groups according to the statin type (atorvastatin: n = 1040; rosuvastatin: n = 260). The results demonstrated insignificant differences regarding the number of stents between both groups.

Furthermore, the different medications administered by both groups (ACE, ARB, BB, CCB and antihyperglycemic) were recorded and the results showed statistically insignificant difference between atorvastatin and rosuvastatin groups.

These results are compatible with Firouzi et al. [10] who demonstrated that "there was statistically insignificant difference between atorvastatin and rosuvastatin groups regarding the different medications such as angiotensin-converting enzyme-inhibitor, angiotensin II receptor blocker, beta-blocker, diuretic and calcium channel blocker".

Finally, our results demonstrated that the CIN was insignificantly different between atorvastatin and rosuvastatin groups. Our results are similar to Firouzi et al. [10] they showed that according to the obtained results the atorvastatin and rosuvastatin have similar efficacy for preventing CIN with no significant difference between statin groups regarding the CIN grading.

5. LIMITATIONS

the small sample size, the control group that did not receive any drug was missed in the study, the mortality rate was not included in the statistical analysis and the study did not perform complete renal function analysis.

6. CONCLUSIONS

Creatinine level and creatinine clearance were significantly different between atorvastatin and rosuvastatin groups. However, the contrast induced nephropathy was insignificantly different between the atorvastatin and rosuvastatin groups. Thus, the antioxidant properties of both statins could protect against the CIN.

CONSENT AND ETHICAL APPROVAL

The study was done after approval from the Ethical Committee Tanta University Hospitals. An informed written consent was obtained from the patient or relatives of the patients.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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