Comparison between rosuvastatin and atorvastatin for the prevention of contrast-induced nephropathy in patients with STEMI undergoing primary percutaneous coronary intervention

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Introduction
The leading cause of mortality worldwide, coronary artery disease is on the rise owing to higher sanitary levels, urbanization, and aging populations.1-3 Coronary artery disease is responsible for 6.4 deaths per 10000 Iranian population, and 35% of all mortalities are due to cardiac diseases.4,5 Coronary artery bypass grafting and percutaneous coronary interventions (PCI) are the principal revascularization approaches.6-8 Early PCI is the method of choice for myocardial infarction with ST-segment elevation undergoing primary percutaneous coronary intervention (PCI) in a training referral hospital in 2015. Patients were randomly assigned to receive either atorvastatin 80 mg at admission and daily or rosuvastatin 40 mg at admission and daily. CIN was defined based on serum creatinine elevation after 48 hours from the PCI.

Results: The incidence of CIN was observed in 63 patients (21.4%) After 48 hours from primary PCI. Of those, 17% (n = 50) were grade 1 CIN, while 4.4% (n = 13) were grade 2 CIN. There was no significant difference between rosuvastatin group compared with atorvastatin group, regarding the CIN grading (P = 0.14).

Conclusion: Our results indicate that atorvastatin and rosuvastatin have similar efficacy for the prevention of CIN.

Abstract
Introduction: There is some controversy over the efficacy of statins for the prevention of contrast-induced nephropathy (CIN). There have also been reports on varying efficacies of different statins. Hence, in this study the efficacy of atorvastatin and rosuvastatin for the prevention of CIN was assessed.

Methods: This single-blind randomized clinical trial was performed on 495 random patients with myocardial infarction with ST-segment elevation undergoing primary percutaneous coronary intervention (PCI) in a training referral hospital in 2015. Patients were randomly assigned to receive either atorvastatin 80 mg at admission and daily or rosuvastatin 40 mg at admission and daily. CIN was defined based on serum creatinine elevation after 48 hours from the PCI.

Results: The incidence of CIN was observed in 63 patients (21.4%) After 48 hours from primary PCI. Of those, 17% (n = 50) were grade 1 CIN, while 4.4% (n = 13) were grade 2 CIN. There was no significant difference between rosuvastatin group compared with atorvastatin group, regarding the CIN grading (P = 0.14).

Conclusion: Our results indicate that atorvastatin and rosuvastatin have similar efficacy for the prevention of CIN.

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on varying efficacies of various statins. Accordingly, in this study the efficacy of atorvastatin and rosvastatin for the prevention of CIN was assessed among patients undergoing primary PCI.

Materials and Methods

This single-blind randomized clinical trial was performed on 302 random patients with myocardial infarction with ST-segment elevation undergoing primary PCI in a training referral hospital in 2015. The patients with known hypersensitivity to statins, those with cardiogenic shock status, pregnant and lactating females, and those who had received a contrast agent within the preceding week were excluded from the study.

The patients were randomly assigned to receive either atorvastatin (n = 150) or rosvastatin (n = 152). Unfortunately, 7 patients died before 48 hours from presentation. Thus, 144 patients in atorvastatin group and 151 patients in rosvastatin were evaluated. Atorvastatin dose was 80 mg at admission and daily up to 48 hours later, and rosvastatin dose was 40 mg at admission and daily up to 48 hours after the procedure. Before the PCI procedure, hemoglobin, lipid profile, baseline blood urea nitrogen (BUN), creatinine, and glomerular filtration rate (GFR) were assessed. The Mehran CIN-Risk score was calculated based on Mehran et al study. Thereafter, BUN, creatinine, and GFR were assessed for 48 hours. The prediction of creatinine clearance (in mL/min) by the Cockcroft-Gault formula was calculated as 
\[
(140 – \text{age}) \times \frac{\text{body weight}}{\text{serum creatinine}} \times 72 \times (0.85 \text{ if female})
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Statistical Analysis

The continuous variables are expressed as mean ± standard deviation, and they were compared using the Student t-test or the Mann-Whitney U-test, as appropriate. The categorical variables are expressed as frequencies and percentages, and they were compared between the aforementioned groups applying the χ² test or the Fisher exact test. All \( P \) values <0.05 were considered statistically significant. All the data analyses were conducted using SPSS (version 19.0) (Chicago, Illinois, US).

Results

A total of 295 patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary PCI were enrolled in the study. The patients were randomized to 80 mg atorvastatin (n = 144) or 40 mg rosvastatin (n = 151), respectively, prior to primary PCI. The baseline characteristics were not difference between 2 groups (Table 1). Also, Mehran’s CIN risk score was not different

| Variables | Drugs | Atorvastatin (n = 144) | p value |
|-----------|-------|------------------------|---------|
| Age > 75 years old, No. (%) | Rosuvastatin (n = 151) | 15 (9.9%) | 8 (5.6%) | 0.161 |
| Male gender, No. (%) | 130 (86.1%) | 118 (81.9%) | 0.330 |
| Cigarette smoking, No. (%) | 65 (43.0%) | 75 (52.1%) | 0.120 |
| Diabetes mellitus, No. (%) | 42 (27.8%) | 38 (26.4%) | 0.783 |
| Hypertension, No. (%) | 60 (39.7%) | 72 (50.0%) | 0.076 |
| Hypercholesterolemia, No. (%) | 8 (5.3%) | 14 (9.7%) | 0.148 |
| Prior CABG, No. (%) | 13 (8.6%) | 7 (4.9%) | 0.201 |
| Prior PCI, No. (%) | 25 (16.6%) | 18 (12.5%) | 0.324 |
| Total cholesterol | 166.4 ± 42.4 | 168.8 ± 42.0 | 0.638 |
| Low-density lipoprotein | 104.2 ± 76.2 | 102.0 ± 33.6 | 0.372 |
| High-density lipoprotein | 42.4 ± 8.9 | 40.7 ± 7.9 | 0.117 |
| Triglycerides | 123.6 ± 56.7 | 136.2 ± 77.0 | 0.342 |
| Hemoglobin | 14.5 ± 1.6 | 14.4 ± 1.5 | 0.567 |
| Angiotensin-converting enzyme-inhibitor, No. (%) | 103 (68.2%) | 94 (65.3%) | 0.593 |
| Angiotensin II receptor blocker use, No. (%) | 27 (17.9%) | 33 (22.9%) | 0.283 |
| Beta-blocker use, No. (%) | 118 (78.1%) | 115 (79.9%) | 0.718 |
| Diuretic use, No. (%) | 55 (36.4%) | 50 (34.7%) | 0.760 |
| Calcium channel blocker, No. (%) | 11 (7.3%) | 11 (7.6%) | 0.908 |
| Angiography data, No. (%) | | | |
| Multi-vessel | 85 (56.3%) | 81 (56.3%) | 0.994 |
| Single-vessel | 65 (43.0%) | 61 (42.4%) | 0.905 |
| Ejection fraction < 30% | 36 (23.8%) | 31 (21.5%) | 0.635 |
| Mehran’s contrast-induced nephropathy risk score, No. (%) | | | |
| ≤5 | 57 (37.7%) | 58 (40.3%) | |
| 6–10 | 67 (44.4%) | 62 (43.1%) | 0.966 |
| 11–16 | 23 (15.2%) | 21 (14.6%) | |
| ≥ 16 | 4 (2.6%) | 3 (2.1%) | |
between statin groups.

Totally, 36 patients (12.2%) had eGFR lower than 60 mL/min/1.73 m², which was not different between groups (P value: 0.36). After 48 hours from primary PCI, the CIN were observed in 63 patients (21.4%). Of those, 17% (n = 50) were grade 1 CIN, while 4.4% (n = 13) were grade 2 CIN. There was no significant between statin groups regarding the CIN grading (P value: 0.14) (Table 2; Figure 1).

Discussion

The present study revealed that high doses rosuvastatin in setting of STEMI patients who underwent primary PCI on preventing CIN is effective compared with high dose atorvastatin. Muñoz et al compared the efficacy of simvastatin and pravastatin for CIN prophylaxis among 261 patients and reported rates of 17.9% and 8.6% in the simvastatin and pravastatin groups, respectively, with the difference constituting statistical significance. There was no dialysis-requiring case in their study, similar to our study. However, the authors found that 14.5% and 6.9% of their patients in the simvastatin and pravastatin groups, correspondingly, had acute renal failure - with a significant difference. Totally, they concluded that pravastatin had better efficacy for CIN prophylaxis.

Leoncini et al had 2 groups of patients with and without rosuvastatin and reported that 15.1% and 6.7% had CIN in the control and drugs groups, respectively, showing a statistically significant difference. In addition, their rosuvastatin group experienced lower death and re-infarction rates.

Toso et al compared 2 groups of patients with and without atorvastatin and reported that 11% in the control group and 10% in the drugs group had CIN, showing no statistically significant difference. The investigators concluded that atorvastatin had no effect on CIN prevention. Pappy et al revealed in their meta-analysis that statins were effective drugs for CIN prophylaxis, which is concordant with our results. The results of our study are reliable because of the use of group matching and reduction of the effects of confounding factors.

Figure 1. The frequency of CIN was not significant difference found between statin treatment groups.

Table 2. Baseline and 48 hour laboratory data and frequency of CIN between groups

|                          | Rosuvastatin (n=151) | Atorvastatin (n=144) | P value |
|--------------------------|----------------------|----------------------|---------|
| Baseline creatinine (mg/dL) | 1.02±0.41           | 0.93±0.42            | <0.001  |
| Baseline BUN (mg/dL)       | 18.5±8.02           | 16.9±8.3             | 0.002   |
| Baseline eGFR (mL/min/1.73 m²) | 94.06±33.1       | 107±39.01            | 0.002   |
| Baseline eGFR <60 mL/min/1.73 m², No. (%) | 21 (13.9)       | 15 (10.4)            | 0.362   |
| 48 hours creatinine (mg/dL)    | 1.08±0.54           | 1.03±0.57             | 0.009   |
| 48 hours BUN (mg/dL)         | 21.2±10.5           | 20.4±13.1             | 0.028   |
| 48 hours eGFR (mL/min/1.73 m²) | 90.2±33.6         | 98.9±40.0             | 0.053   |
| Creatinine, ∆ (from baseline to 48 hours) (mg/dL)| 0.07±0.28         | 0.11±0.34             | 0.300   |
| Contrast induced nephropathy, No. (%) | 125 (19.4)     | 107 (74.3)            |         |
| Grade 1                    | 22 (14.6)           | 28 (19.4)             |         |
| Grade 2                    | 4 (2.6)             | 9 (6.3)               | 0.144   |

Ethical approval

Informed consent was received from all the patients, and the Helsinki Declaration was observed throughout the study. The local ethics committee of the center approved this study.

Competing interests

None.
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