EFFECT OF EARLY INTENSIVE TREATMENT WITH ROSUVASTATIN ON SERUM HYPERSENSITIVE C-REACTIVE PROTEIN, IL-6 LEVEL AND CARDIAC FUNCTION IN PATIENTS WITH ACUTE CORONARY SYNDROME AFTER PCI

HONGGUANG ZHU, QINGYAN WANG, XIN HUANG*
Department of Cardiology, Yantai Harbour Hospltal, Yantai, 264000,Shandong Province, China

ABSTRACT

Objective*: The purpose was to explore the effect of early intensive treatment with rosuvastatin on serum hypersensitive C-reactive protein, IL-6 level and cardiac function in patients with acute coronary syndrome (ACS) after PCI.*

Methods: *100 ACS patients treated by PCI in our hospital from May 2018 to March 2020 were selected as the study subjects, and divided into routine group (n=50) and intensive group (n=50) according to their order of admission. Both groups of patients underwent PCI in a routine manner and were treated with rosuvastatin 7 days before surgery. The routine group was treated with 10mg/d of rosuvastatin while the intensive group was treated with 20mg/d of rosuvastatin to analyze the serum hypersensitive C-reactive protein, IL-6 level, cardiac function (LVEF, LVSD, LVDD and E/A) and adverse event rate after PCI in two groups of patients.*

Results: *After operation, the hs-CRP level of the intensive group was significantly lower than that of the routine group, with statistical significance (T=8.10, P<0.001). The IL-6 level of the intensive group was significantly lower than that of the routine group, with statistical significance (T=7.32, P<0.001). LVEF and E/A levels of the intensive group were significantly higher than those of the routine group while LVSD and LVDD levels of the intensive group were significantly lower than those of the routine group, with statistical significance (T=3.91, 4.01, 3.68, 3.72; P<0.001). The adverse event rate of the intensive group was significantly lower than that of the routine group, with statistical significance (X^2=13.56, P<0.001).*

Conclusion: *Early intensive treatment with rosuvastatin in ACS patients with PCI can effectively improve inflammatory factors, enhance cardiac function and reduce the occurrence of adverse events, which is worthy of popularization and application in clinical practice.*

Keywords: *Rosuvastatin, early, intensive, acute coronary syndrome, PCI, after operation, serum hypersensitive C-reactive protein, IL-6; cardiac function.*

DOI: 10.19193/0393-6384_2021_4_397

Received *March 15, 2020;* ***Accepted*** *October 20, 2020*

Introduction

Nowadays, relevant reports have confirmed that coronary plague instability is related to the production of ACS which is commonly caused by smoking, hyperlipidemia, hypertension, diabetes and other predisposing factors[1-3]. ACS patients are mostly middle-aged and elderly people with clinical manifestations as arrhythmia, chest tightness, etc. If they are not treated as soon as possible, they will cause heart failure and other diseases, which seriously affect the life safety of patients. At present, how to improve patient survival and clinical symptoms has become one of the focuses in clinical research. The main treatment method of ACS is PCI, which dredges occluded and narrow arterial vessels by cardiac catheterization to restore blood perfusion, thereby reducing further myocardial damage and avoiding disease progression[4-6]. However, clinical findings found that some ACS patients will have

adverse events such as arrhythmia and arterial stenosis again after PCI. Currently, some scholars believe that lipid-regulating drugs for PCI patients can improve the occurrence of adverse events and play a positive role in improving the survival rate of patients. Statins are strong lipid-lowering drugs with high drug safety, and rosuvastatin is one of statins[7-9].

This study aims to explore the effect of early intensive treatment with rosuvastatin on serum hypersensitive C-reactive protein, IL-6 level and cardiac function in ACS patients with PCI, providing a favorable reference for the clinical treatment of ACS, specifically reported as follows.

Materials and methods

General information

100 ACS patients who received PCI in our hospital from May 2018 to March 2020 were selected as the study subjects, and divided into routine group and intensive group according to their order of admission.

Routine group included 27 males and 23 females with a total of 50 cases aged 46-75 years old with an average age of (60.58±12.23) years old and an average body mass index of (24.86±2.08) kg/m^2. There were 7 patients with diabetes mellitus, 23 patients with hypertension, 21 patients with STEMI (ST-segment elevation myocardial infarction) and 29 patients with NSTEMI (non-ST-segment elevation myocardial infarction). Intensive group included 26 males and 24 females with a total of 50 cases aged 47-76 years old with an average age of (60.78±12.32) years old and an average body mass index of 24.79±2.11) kg/m^2.

There were 8 patients with diabetes mellitus, 23 patients with hypertension, 22 patients with STEMI (ST-segment elevation myocardial infarction) and 28 patients with NSTEMI (non-ST-segment elevation myocardial infarction).

There was no significant difference in general clinical data such as age and average body mass index between the two groups of patients (P>0.05), which was comparable.

Inclusion/exclusion criteria

Inclusion criteria:

• They met the criteria of ACC/AHA (American College of Cardiology and American Heart Association);

• All patients had persistent or paroxysmal chest pain;

• This study was approved by the hospital ethics committee, and all the patients and their families knew the treatment and signed a consent form.

Exclusion criteria:

• The patients had immune and chronic connective tissue diseases;

• The patients had severe arrhythmia, malignant tumor, liver injury and acute left heart failure;

• The patients were in lactation and pregnancy;

• The patients took other statins or lipid-regulating drugs within 30 days.

Methods

Usage of rosuvastatin

Both groups of patients underwent PCI in a routine manner and were treated with rosuvastatin (SFDA approval number: J20170008, manufacturer: China Branch of AstraZeneca Pharmaceutical Co Ltd) 7 days before surgery.

The routine group was treated with 10mg/d of rosuvastatin while the intensive group was treated with 20mg/d of rosuvastatin. Both groups of patients were treated with rosuvastatin for at least 30 days after PCI.

PCI operation method

Both groups of patients received PCI according to the conventional way, in which guiding catheters with 5-8F diameter of XB, Judkins, EBU and Amplatz models were used. Appropriate guidewire and guiding catheters were selected according to the specific conditions of patients.

Some patients used the guiding catheters with insufficient support, including 1 case with the fourth, 6 cases with the third and 13 cases with the second.

There were 28 patients with non-hydrophilic coated guidewire of medium-hardness (Traverse), and 72 patients with hard or relatively hard guidewire or hydrophilic coated guidewire (PT Craphix inermediate, Cross-It 100-300, Choice PT inermediate, Shinobi and Wisper). VIVA, Maverick, Stomer, Crosssail, NM and Sprinter were balloon catheters used during PCI.

After local anesthesia of patients, the femoral artery was punctured. After artery sheath was inserted, the guiding catheter was placed at the opening of the coronary artery. Then coronary angiography was performed to confirm the range, location and degree of lesions. Then the guidewire was placed at the the coronary artery lesions. After 1-2 times of pre-expansion, intracoronary stent was implanted.

Evaluation indexes

hs-CRP

4ml of fasting venous blood was taken in the early morning before and after operation. After serum was separated, AU5800 automatic biochemical analyzer (Beckman Coulter, USA) was used to detect the hs-CRP level.

IL-6 level

4ml of fasting venous blood was taken in the early morning before and after operation. After serum was separated, GC-1200 radiation immunity arithmometer was used to detect the IL-6 level according to radioimmunoassay.

Cardiac function

GE-E9 color echocardiography was used to detect the cardiac structure and function of all patients before and after operation to statistically analyze the LVEF (left ventricular ejection fraction), LVSD (left ventricular end systolic diameter), LVDD (left ventricular end diastolic diameter) and E/A (early ventricular diastolic peak flow velocity of the left atrioventricular valve/late ventricular diastolic peak flow velocity of the left atrioventricular valve).

Adverse event rate

The adverse events such as arrhythmia, angina pectoris, death and heart failure in the two groups of patients were statistically analyzed.

Statistical processing

The research data were processed and analyzed by the data software SPSS20.0. The measurement data were measured by t test, expressed by ($\bar{x}\pm s$), and the count data were tested by X^2, expressed by [n(%)]. The difference was statistically significant when $p<0.05$.

Results

Analysis on changes of hs-CRP levels in two groups of patients

Before operation, there was no significant difference in hs-CRP level between two groups of patients (P>0.05).

After operation, the hs-CRP levels in both groups increased significantly, and the hs-CRP level of the intensive group was significantly lower than that of the routine group, with statistical significance (T=8.10, P<0.001), as shown in Figure 1.

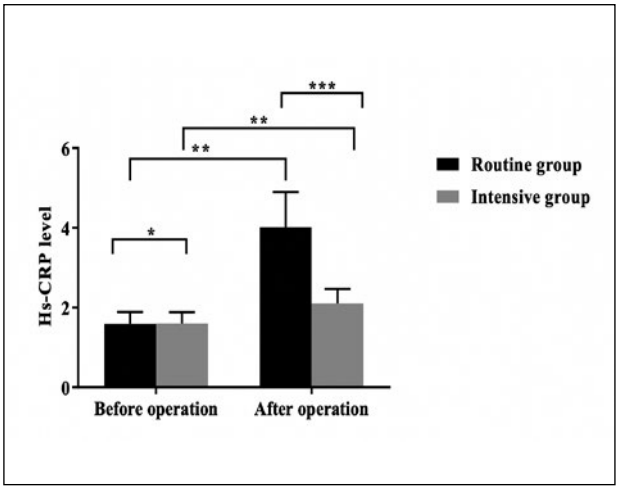

Figure 1: Analysis on changes of hs-CRP levels in two groups of patients.

*Note: The abscissa of Figure 1 represents before operation and after operation, the ordinate represents the hs-CRP level, black represents routine group and gray represents intensive group. Before operation, hs-CRP was (1.38±0.42) in the routine group and (1.39±0.41) in the intensive group; After operation, hs-CRP was (3.39±1.25) in the routine group and (1.84±0.52) in the intensive group; *Indicated that there was no significant difference in hs-CRP levels between the routine group and the intensive group before operation (T=0.12, P=0.90); **indicated that the hs-CRP levels of the routine group and the intensive group after operation were significantly higher than those before operation, with statistical significance (T=10.77, 4.81, P<0.001); ***indicated that after operation, the hs-CRP level of the intensive group was significantly lower than that of the routine group, with statistical significance (T=8.10, P<0.001).*

Analysis on changes of IL-6 levels in two groups of patients

Before operation, there was no significant difference in IL-6 level between two groups of patients (P>0.05).

After operation, the IL-6 levels in both groups decreased significantly, and the IL-6 level of the intensive group was significantly lower than that of the routine group, with statistical significance (T=7.32, P<0.001), as shown in Figure 2.

Analysis on changes of cardiac function levels in two groups of patients

Before operation, there was no significant difference in the levels of LVEF, LVSD, LVDD and E/A between two groups of patients (P>0.05).

After operation, LVEF and E/A levels of the intensive group were significantly higher than those of the routine group while LVSD and LVDD levels of the intensive group were significantly lower than those of the routine group, with statistical significance (T=3.91, 4.01, 3.68, 3.72; P<0.001), as shown in Figures 3-6.

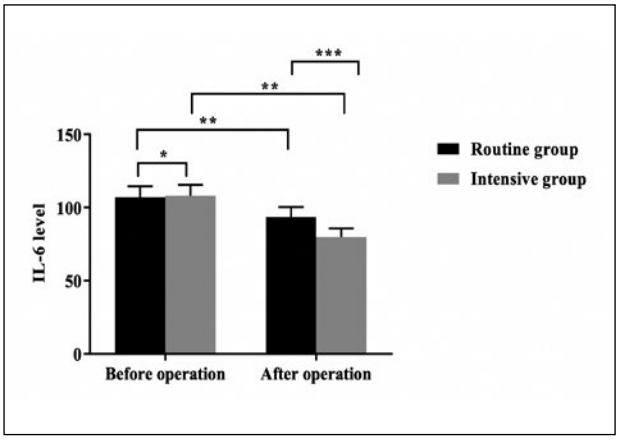

Figure 2: Analysis on changes of IL-6 levels in two groups of patients.

*Note: The abscissa of Figure 2 represents before operation and after operation, the ordinate represents the IL-6 level, black represents routine group and gray represents intensive group. Before operation, IL-6 was (101.58±10.68) in the routine group and (102.55±10.72) in the intensive group; After operation, IL-6 was (88.72±9.58) in the routine group and (75.59±8.32) in the intensive group; *Indicated that there was no significant difference in IL-6 levels between the routine group and the intensive group before operation (T=0.45, P=0.65); **indicated that the IL-6 levels of the routine group and the intensive group after operation were significantly lower than those before operation, with statistical significance (T=6.34, 14.05, P<0.001); ***indicated that after operation, the IL-6 level of the intensive group was significantly lower than that of the routine group, with statistical significance (T=7.32, P<0.001).*

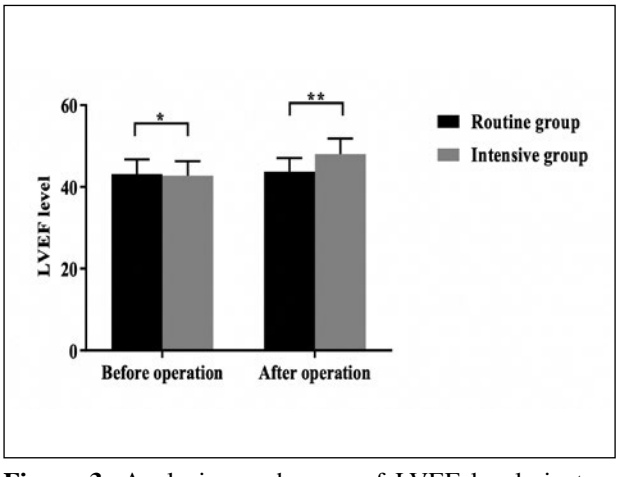

Figure 3: Analysis on changes of LVEF levels in two groups of patients.

*Note: The abscissa of Figure 3 represents before operation and after operation, the ordinate represents LVEF level, black represents routine group and gray represents intensive group. Before operation, LVEF was (40.58±5.11) in the routine group and (40.21±5.08) in the intensive group; After operation, LVEF was (41.35±4.76) in the routine group and (45.32±5.38) in the intensive group; *Indicated that there was no significant difference in LVEF levels between the routine group and the intensive group before operation (T=0.36, P=0.72); **indicated that after operation, the LVEF level of the intensive group was significantly higher than that of the routine group, with statistical significance (T=3.91, P<0.001).*

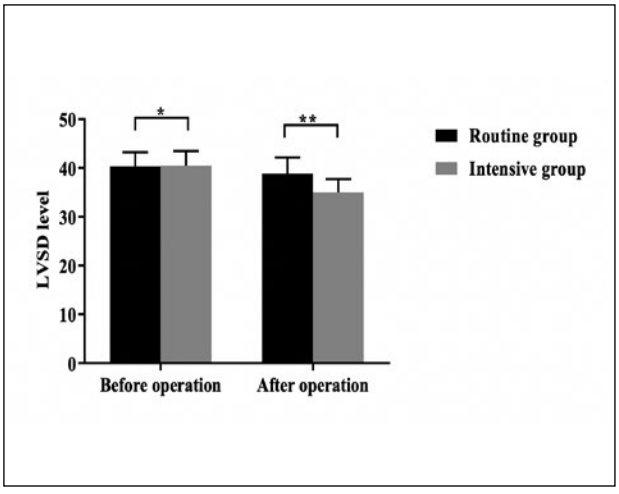

Figure 4: Analysis on changes of LVSD levels in two groups of patients.

*Note: The abscissa of Figure 4 represents before operation and after operation, the ordinate represents LVSD level, black represents routine group and gray represents intensive group.Before operation, LVSD was (38.24±4.15) in the routine group and (38.32±4.28) in the intensive group; After operation, LVSD was (36.53±4.65) in the routine group and (33.11±3.83) in the intensive group; *Indicated that there was no significant difference in LVSD levels between the routine group and the intensive group before operation (T=0.09, P=0.92); **indicated that after operation, the LVSD level of the intensive group was significantly lower than that of the routine group, with statistical significance (T=4.01, P<0.001).*

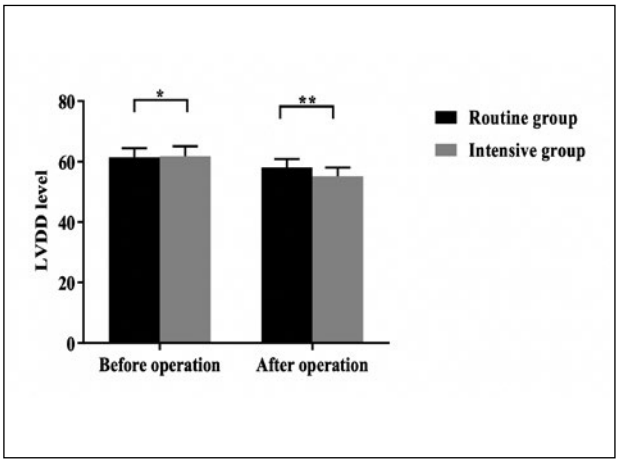

Figure 5: Analysis on changes of LVDD levels in two groups of patients.

*Note: The abscissa of Figure 5 represents before operation and after operation, the ordinate represents LVDD level, black represents routine group and gray represents intensive group. Before operation, LVDD was (59.28±4.28) in the routine group and (59.46±4.65) in the intensive group; After operation, LVDD was (56.08±4.02) in the routine group and (53.08±4.13) in the intensive group; *Indicated that there was no significant difference in LVDD levels between the routine group and the intensive group before operation (T=0.20, P=0.84); **indicated that after operation, the LVDD level of the intensive group was significantly lower than that of the routine group, with statistical significance (T=3.68, P<0.001).*

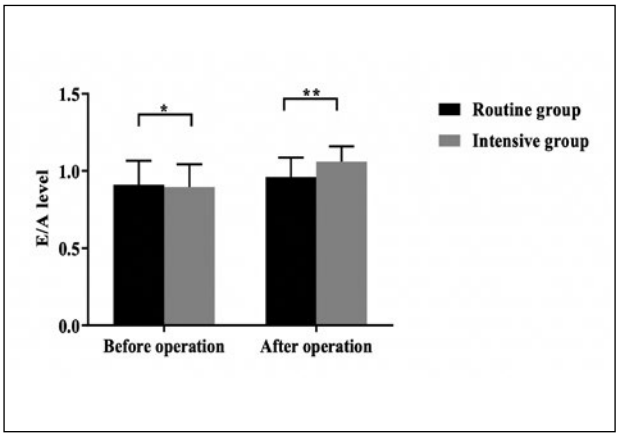

Figure 6: Analysis on changes of E/A levels in two groups of patients.

*Note: The abscissa of Figure 6 represents before operation and after operation, the ordinate represents E/A level, black represents routine group and gray represents intensive group. Before operation, E/A was (0.80±0.22) in the routine group and (0.79±0.21) in the intensive group; After operation, E/A was (0.87±0.18) in the routine group and (0.99±0.14) in the intensive group; *Indicated that there was no significant difference in E/A levels between the routine group and the intensive group before operation (T=0.23, P=0.82); **indicated that after operation, the E/A level of the intensive group was significantly higher than that of the routine group, with statistical significance (T=3.72, P<0.001).*

Analysis of adverse event rate after PCI in two groups of patients

The adverse event rate of the intensive group was significantly lower than that of the routine group, with statistical significance (X^2=13.56, P<0.001), as shown in Table 1.

Group	Number of cases	Arrhythmia	Angina pectoris	Death	Heart failure	Adverse event rate
Routine group	50	7	6	1	4	36% (18/50)
Intensive group	50	2	1	0	0	6% (3/50)
X^2						13.56
P						0.00

Table 1: Analysis of adverse event rate after PCI in two groups of patients.

Discussion

PCI is currently the most important treatment for ACS[10-12]. PCI mainly uses catheters to dilate stenotic coronary artery to improve the obstructed coronary artery, restore the blood supply to the lesions and reduce the clinical symptoms of patients[13]. However, ACS patients often have adverse events such as arrhythmia, angina pectoris, death and heart failure after PCI, which are related to factors such as myocardial remodeling, vascular stenosis and angiogenesis, and the pathological mechanism may be related to the inflammatory response induced by plaque rupture after PCI[14-16]. Therefore, cardiac function and inflammation-related indicators of ACS patients must be measured.

Statins are widely used to prevent grade I and II of coronary heart disease in clinic. They not only regulate blood lipids, but also play a positive role in improving the functions of cardiomyocytes and endothelium, and reducing inflammatory response. Rosuvastatin is one of statins, characterized by high selectivity, which inhibits the action of HMG-CoA reductase by selectivity[17-19]. Adverse phenomena of ACS patients after PCI may be related to inflammation response produced by endothelial injury caused by balloon compression during PCI. In addition, postoperative plaque extrusion can also cause microvascular occlusion and lead to myocardial cell necrosis at the lesion locations[20]. This study aims to explore the effect of early intensive treatment with rosuvastatin on serum hypersensitive C-reactive protein, IL-6 level and cardiac function in ACS patients with PCI, and showed that cardiac function indexes such as LVEF and E/A levels of the intensive group were significantly higher than those of the routine group while LVSD and LVDD levels of the intensive group were significantly lower than those of the routine group, with statistical significance (P<0.001). This suggests that early intensive treatment with rosuvastatin has better effect on cardiac function and structure in intensive group. The reason is that rosuvastatin significantly inhibits the process of ventricular remodeling and left ventricular dilatation, so that the cardiac function of the intensive group was significantly better than that of the routine group.

With the development of the disease, ACS patients will release a large number of inflammatory factors, and inflammatory response is not only conducive to the formation of coronary atherosclerotic plaques, but also further aggravates myocardial damage and promote ventricular remodeling[21-23]. Hs-CRP is an acute inflammatory response time-phase protein that not only reflects the level of systemic inflammatory response but also is a factor predicting the risk of cardiovascular events. The results of this study showed that the hs-CRP levels in both groups increased significantly after operation, and the hs-CRP level of the intensive group was significantly lower than that of the routine group, with statistical significance (P<0.001). This was

consistent with the conclusions of Paul Guedeney[24] et al., which demonstrated that the early intensive treatment with rosuvastatin in ACS patients had better hs-CRP levels after PCI. The reason for this is that rosuvastatin reduces the number of Rho proteins on the cell membrane, reducing their activity and thus lowering the level of inflammatory factors.

According to the findings of Otake[25] et al., statin therapy can improve the prognosis of patients with PCI and reduce the occurrence of adverse events. The results of this study showed that the adverse event rate of the intensive group was significantly lower than that of the routine group, with statistical significance ($P<0.001$). This indicates that early intensive treatment with rosuvastatin can reduce the activity of HMG-CoA reductase, inhibits the synthesis of cholesterol, and reduce lipoprotein concentration and cholesterol levels, thus having a lipid-lowering effect. Meanwhile, rosuvastatin can inhibit the production of oxygen free radicals and prevent thrombus. Therefore, adverse event rate of the intensive group was lower than that of the routine group.

In conclusion, early intensive treatment with rosuvastatin in ACS patients with PCI can effectively improve inflammatory factors, enhance cardiac function and reduce the occurrence of adverse events, which is worthy of popularization and application in clinical practice.

References

1) Jigneshkumar Vaghasiya, Satyam Patel, Sudhir Patel, et al. Non-clinical safety evaluation of a novel pharmaceutical salt, rosuvastatin ethanolamine, in Wistar rats[J]. Interdisciplinary Toxicology, 2019, 12(1): 7-14.
2) Weiliang He, Xiaochao Tian, Bilin Yuan, et al. Rosuvastatin improves neurite extension in cortical neurons through the Notch 1/BDNF pathway[J]. Neurological Research, 2019, 41(7): 658-664.
3) Marco Previsdomini, Elisa Graziano, Laurent Decosterd, et al. Severe rosuvastatin accumulation with rhabdomyolysis due to drug interactions and low cardiac output syndrome[J]. British Journal of Clinical Pharmacology, 2019, 85(7): 1616-1618.
4) Chemical Weekly group. Sun Pharma launches advanced rosuvastatin formulation in US market[J]. Chemical Weekly, 2019, 64(51): 156.
5) Elkady MA, Shalaby S, Fathi F, et al.Effects of quercetin and rosuvastatin each alone or in combination on cyclophosphamide-induced premature ovarian failure in female albino mice[J]. Human & Experimental Toxicology, 2019, 38(11): 1283-1295.
6) F. Abdollahimajd, F. Rajabi, M. Shahidi-Dadras, et al. Pachyonychia congenita: a case report of a successful treatment with rosuvastatin in a patient with a KRT6A mutation[J]. British Journal of Dermatology, 2019, 181(3): 584-586.
7) Sarah Billington, Steven Shoner, Scott Lee, et al. Positron Emission Tomography Imaging of [11C]Rosuvastatin Hepatic Concentrations and Hepatobiliary Transport in Humans in the Absence and Presence of Cyclosporin A[J]. Clinical Pharmacology & Therapeutics, 2019, 106(5): 1056-1066.
8) Sandra J. Lewis, Temitope Olufade, Deborah A. Anzalone, et al. LDL cholesterol levels after switch from atorvastatin to rosuvastatin[J]. Current Medical Research and Opinion, 2018, 34(10): 1717-1723.
9) Aghajanzadeh Mozhgan, Ghannad Farhang, Zamani Mostafa, et al. Anti-inflammatory effect of rosuvastatin using diblock amphiphilic copolymer: Synthesis, characterization, in vitro and in vivo study[J]. Journal of Biomaterials Applications, 2019, 34(2): 229-238.
10) Ibraheem Husain, Sana Khan, Saba Khan, et al. Unfolding the pleiotropic facades of rosuvastatin in therapeutic intervention of myriads of neurodegenerative disorders[J]. Clinical and Experimental Pharmacology and Physiology, 2019, 46(4): 283-291.
11) Hayder. Al-Kuraishy, Ali. Al-Gareeb. Effects of rosuvastatin on metabolic profile: Versatility of dose-dependent effect[J]. Journal of Advanced Pharmaceutical Technology & Research, 2019, 10(1): 33-38.
12) Naoyuki Otani, Hirokazu Wakuda, Hiromitsu Imai, et al. No Effect of Digoxin on Rosuvastatin Pharmacokinetics in Healthy Subjects: Utility of Oita Combination for Clinical Drug-Drug Interaction Study[J]. Clinical and Translational Science, 2019, 12(5): 513-518.
13) Ayuko Kondo, Katsuya Narumi, Keisuke Okuhara, et al. Black tea extract and theaflavin derivatives affect the pharmacokinetics of rosuvastatin by modulating organic anion transporting polypeptide (OATP) 2B1 activity[J]. Biopharmaceutics & Drug Disposition, 2019, 40(8): 302-306.
14) R. Donald Harvey, Noemi Reguart Aransay, Nicolas Isambert, et al. Effect of multiple-dose osimertinib on the pharmacokinetics of simvastatin and rosuvastatin[J]. British Journal of Clinical Pharmacology, 2018, 84(12): 2877-2888.
15) He, Weiliang, Tian, Xiaochao, Yuan, Bilin, et al. Rosuvastatin improves neurite extension in cortical neurons through the Notch 1/BDNF pathway[J]. Neurological Research: An Interdisciplinary Quarterly Journal, 2019, 41(7): 658-664.
16) Cheynne C. McLean, Wendy A. Teft, Bridget L. Morse, et al. Food Effect on Rosuvastatin Disposition and Low-Density Lipoprotein Cholesterol[J]. Clinical Pharmacology & Therapeutics, 2018, 104(3): 525-533.
17) Wang, Lijun, Zhou, Baihua, Zhou, Xue, et al. Combined Lowering Effects of Rosuvastatin and L. acidophilus on Cholesterol Levels in Rat[J]. Journal of microbiology and biotechnology, 2019, 29(3): 473-481.

18) Sivanan Sivasinprasasn, Naruemon Wikan, Jiraporn Tocharus, et al.Synergistic effects of the capsaicinoid nonivamide and rosuvastatin on obesity-related endothelial dysfunction in rat fed a high-fat diet[J]. Phytotherapy Research, 2019, 33(7): 1815-1826.
19) Chenfei Wang, Dan Huang, Xingmei Feng, et al. Rosuvastatin Regulates Odontoblast Differentiation by Suppressing NF-ϰB Activation in an Inflammatory Environment[J]. Cellular reprogramming, 2019, 21(1):18-25.
20) Maged, Amr, Abdelkhalek, Abdelfattah A., Mahmoud, Azza A., et al. Mesenchymal stem cells associated with chitosan scaffolds loaded with rosuvastatin to improve wound healing[J]. European journal of pharmaceutical sciences, 2019, 127: 185-198.
21) Husain Ibraheem, Khan Sana, Khan Saba, et al. Unfolding the pleiotropic facades of rosuvastatin in therapeutic intervention of myriads of neurodegenerative disorders[J]. Clinical and experimental pharmacology & physiology, 2019, 46(4): 283-291.
22) Misari Patel, Charmy Kothari. A simple, rapid and fully validated HPLC method for simultaneous quantitative bio-analysis of rosuvastatin and candesartan in rat plasma: Application to pharmacokinetic interaction study[J]. Biomedical Chromatography, 2019, 33(10): n/a-n/a.
23) Bin Zhang, Jia-Li Li, Shi-Long Zhong, et al. Simultaneous Determination of Rosuvastatin, Rosuvastatin-5 S-lactone, and N-desmethyl Rosuvastatin in Human Plasma by UPLC-MS/MS and Its Application to Clinical Study[J]. Drug research, 2018, 68(6): 328-334.
24) Paul Guedeney, Usman Baber, Bimmer Claessen, et al. Temporal trends, determinants, and impact of high-intensity statin prescriptions after percutaneous coronary intervention[J]. The American heart journal, 2019, 207:10-18.
25) Otake, Hiromasa, Sugizaki, Yoichiro, Toba, Takayoshi, et al. Efficacy of alirocumab for reducing plaque vulnerability: Study protocol for ALTAIR, a randomized controlled trial in Japanese patients with coronary artery disease receiving rosuvastatin[J]. Journal of cardiology, 2019, 73(3/4): 228-232.

Corresponding Author:
Xin Huang
Department of Cardiology, Yantai Harbour Hospltal, No.100 Xingfu Road, Zhifu District, Yantai, 264000, Shandong Province, China
(China)