Research Article

A Comparative study on the Effect of Atorvastatin and Rosuvastatin on Cholesterol level and Liver Enzyme Elevation in Patients Undergoing CABG

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ABSTRACT

In this paper we report a comparative study of the effect of dyslipidemic drugs Atorvastatin and Rosuvastatin in patients who underwent coronary artery bypass graft surgery (CABG), to evaluate the effect of cholesterol levels and liver enzymes, its adverse effects and quality of life associated with myopathy. The method of study includes, identifying 60 patients of all age groups who underwent CABG and a prospective observational study was conducted on these patients for a period of six months. The effect of statins on cholesterol level as well as liver enzyme were analysed from laboratory reports of patients and compared with the normal value. The adverse effect of statins and quality of life (QOL) associated with myopathy were analysed using standard questionnaires. Total cholesterol level of patients before and after treatment were compared and found that the cholesterol level checked after the treatment were found to be statistically significant, i.e., P <0.002. The QOL checked after the treatment were found to be statistically significant, i.e., the P <0.028. From the prospective observational study, we found that the Atorvastatin is better to lower the LDL cholesterol and Rosuvastatin is better to increase the HDL cholesterol. So by comparing the drugs we concluded that Rosuvastatin was recommended for younger patients and patients with post – operative liver enzyme elevation and Atorvastatin was recommended for older patients and patients who had complaints of myopathy.

Keywords: Coronary artery bypass graft surgery, Total cholesterol, liver enzymes, low density lipoprotein, high density lipoprotein, Atorvastain, Rosuvastatin, Quality of life.

INTRODUCTION

Coronary Artery Disease (CAD) is a serious medical problem that affects about seven million peoples annually. It causes nearly three quarters of a million deaths in the US each year and is the leading cause of death for both men and women. CAD results from the effect of the accumulation of atherosclerotic plaques in coronary arteries, which leads to a reduction in blood flow to the myocardium. Some individuals have no signs or symptoms, others experience angina pectoris and still others suffer heart attack [1,12].

Myocardial revascularization represents an effective treatment strategy shown to prolong survival. Techniques of revascularization include Percutaneous Coronary Intervention (PCI) and Coronary Artery Bypass Graft Surgery (CABG), which can be performed with or without cardiopulmonary bypass. Current techniques for CABG can be carried out with low perioperative morbidity and mortality, with excellent long term outcomes despite an increasing risk profile [2]. Coronary artery bypass graft surgery (CABG) with cardiopulmonary bypass remains the standard by which the other techniques (ie PCI, Off pump CABG) are measured [3,4.] It is expected that it will continue to be a cornerstone in the management of CAD in the foreseeable future [8].

The main symptoms of CAD are tightness, heaviness, pressure and /or pain in the chest radiating behind the arms, shoulders, jaw, neck and or/back shortness of breath, fatigue and weakness [5]. Diagnosis of CAD is done by techniques such as Electrocardiogram (ECG), Echocardiography, Electron Beam Computerized Tomography, Cardiac Catheterization and Coronary Angioplasty[1]. Treatment of CAD includes life style changes; controlling risk factors of CAD and Pharmacological therapy include the use of Anti-platelet agent and Anti-hypertensive drugs, Percutaneous Transluminal Coronary Angioplasty and Coronary Artery Bypass Surgery [6.]

CABG is a surgical procedure in which one or more blocked coronary arteries are bypassed by a blood vessel graft to restore normal blood flow to the heart. These grafts usually came from patients own arteries and veins located in the leg, arm or chest [9]. Goals of CABG may include improving quality of life and reducing angina and other CAD symptoms, lowering the risk of heart attacks, improving pumping action of heart if it has been damaged by a heart attack [7]. The main indications for CABG are Left main artery disease or equivalent Triple vessel left ventricular function, Failed PTCA immediately after myocardial infarction, Life threatening arrhythmias caused by a previous myocardial infarction, Occlusion of grafts from previous CABGs [12]. The main types of CABG's are Traditional coronary artery bypass grafting, Off-pump coronary artery bypass grafting [4], Minimally invasive direct coronary artery bypass grafting and Totally endoscopic coronary artery bypass surgery [2,3,9].

Atorvastatin is a member of the drug class known as statins generally used for lowering cholesterol.

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Atorvastatin is a competitive inhibitor of hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase, the rate determining enzyme in cholesterol biosynthesis *via* the mevalonate pathway. HMG-CoA reductase catalyses the conversion of HMG-CoA to mevalonate. Atorvastatin acts primarily in the liver. Decreased hepatic cholesterol levels increases hepatic uptake of cholesterol and reduces plasma cholesterol levels.

The mechanism of action is Atorvastatin selectively and competitively inhibits the hepatic enzyme HMG-CoA reductase. As HMG-CoA reductase is responsible for converting HMG-CoA to mevalonate in the cholesterol biosynthesis pathway, this results in a subsequent decrease in hepatic cholesterol levels. Initial Dose: 10 or 20mg once a day; an initial dose of 40mg may be used in patients who require a reduction in LDL more than 45%, Maintenance dose:10 mg to 80mg orally once a day [10-12].

Rosuvastatin is an anti-lipidemic agent that competitively inhibits hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase. HMG-CoA reducuase catalyses the conversion of HMG-CoA to mevalonic acid, the rate-limiting step in cholesterol biosynthesis. Rosuvastatin belongs to a class of medications called statin. The mechanism of action of Rosuvastatin is a competitive inhibitor of HMG-CoA reductase [13,14,15]. HMG-CoA reductase catalyses the conversion of HMG-CoA to mevalonate, an early rate-limiting step in cholesterol biosynthesis. Rosuvastatin acts primarily in the liver. Decreased hepatic cholesterol concentrations stimulate the upregulation of hepatic low density lipoprotein (LDL) receptors which increases hepatic uptake of LDL. Initial dose: 10mg to 20 mg once a day, Maintenance dose: 5mg to 40mg orally once a day[10-12].

MATERIALS AND METHODS

A prospective observational 6 month study was conducted in the Department of Cardiothoracic and Vascular Surgery, Pushpagiri Medical College Hospital, Thiruvalla. The patients undergoing CABG were the study subjects and are selected on the basis of inclusion and exclusion criteria.

Inclusion Criteria

- Both male and female patients.
- Patients of all age groups.
- Patients undergoing CABG.
- Patients administering Atorvastatin/Rosuvastatin as Dyslipidemic drug.

Exclusion criteria

- Intra- operative mortality.
- Patients undergoing cardiac surgery other than CABG.
- Patients with previous deranged liver enzymes.
- Patients with congenital abnormalities in heart.

Procedure

After taking approval from Institutional ethical committee, a hospital based prospective observational study was carried out to compare the lipid lowering property and liver enzyme elevation of Atorvastatin and Rosuvastatin in patients undergoing CABG. The study was conducted in the department of Cardiothoracic and Vascular Surgery at Pushpagiri Medical College Hospital. 60 patients including both male and female of all age groups were selected for the follow-up study. The patients for prospective observational study were selected on the basis of inclusion and exclusion criteria. All the patients selected were given brief introduction regarding the study and a written informed consent form was collected from each patient or caregiver. Information regarding demographic details of patient, past medical history, medication history, current medications, laboratory values, co-morbidities, adverse drug reactions were noted from the hospital case report. Liver enzyme levels and cholesterol levels of patients were noted from laboratory reports and follow-up procedure is adopted. The results obtained were compared with normal range of cholesterol and liver enzymes. Quality of life associated with CABG and myopathy were determined using WHO QOL BREF Questionnaire and Statin Experience Assessment Questionnaire (SEAQ) respectively and the information's collected were used to compare and evaluate the ADRs of Atorvastatin and Rosuvastatin by using Narinjo causality assessment scale.

RESULTS AND DISCUSSION

In the six month study, 60 patients were enrolled as per the inclusion and exclusion criteria. The results are as follows:

Comparison of drugs on total cholesterol

The effect of drugs Atorvastatin and Rosuvastatin on total cholesterol for 60 patients enrolled are presented in Table 1 and its graphical representation in Figure 1.

Table 1: Effect of drugs on total cholesterol

Drugs	Parameter	Maximum	Mean	SD	P-Value
Atorvastatin	Before	298	242.57	24.88	<0.002
	After	200	194.77	8.823	
Rosuvastatin	Before	296	246.93	24.48	
	After	200	188.57	10.855	

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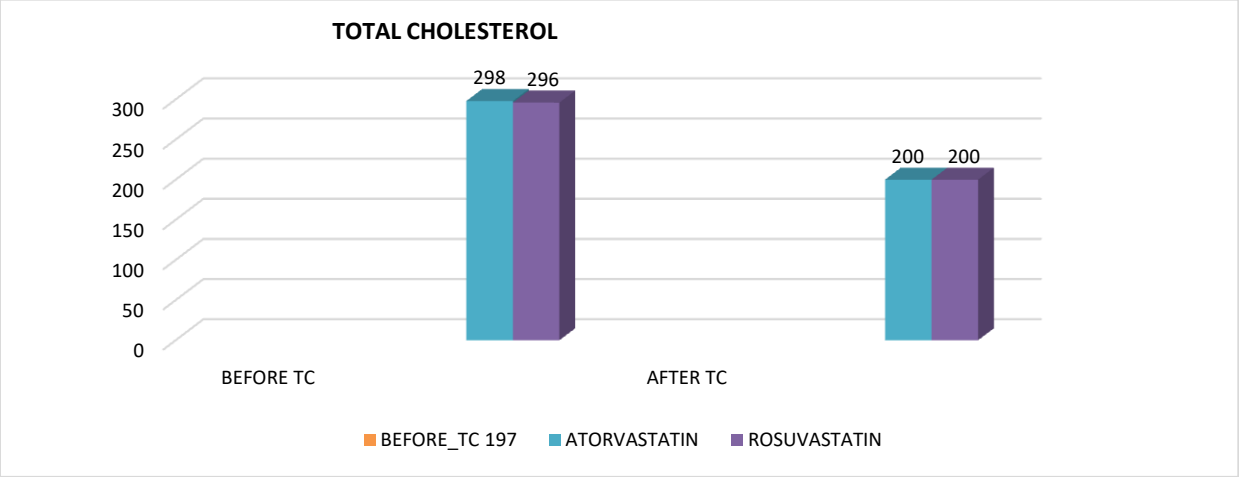


Figure 1: The effect of drugs on total cholesterol

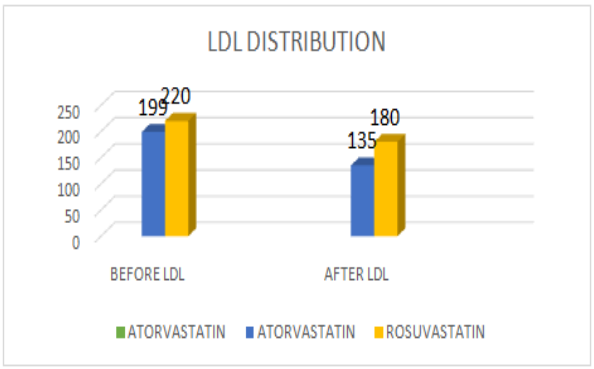
In Table 1, the total cholesterol levels of patients before and after treatment were compared. The cholesterol level checked after the treatment were found to be statistically significant, i.e., P <0.002.

Effect of drugs on LDL Cholesterol

The effect of drugs Atorvastatin and Rosuvastatin on LDL cholesterol for 60 patients enrolled are presented in Table 2 and its graphical representation in Figure 2.

Table 2: Effect of drugs on LDL cholesterol

Drugs	Parameter	Maximum	Mean	SD	P-Value
Atorvastatin	Before	199	168.07	25.421	<0.001
	After	135	119.13	6.791	
Rosuvastatin	Before	220	173.77	23.48	
	After	180	119.27	19.818	



In Table 2, the LDL cholesterol levels of patients before and after treatment were compared. The LDL cholesterol level checked after the treatment were found to be statistically significant, i.e., P <0.001.

Effect of drugs on HDL cholesterol

The effect of drugs Atrovastatin and Rosuvastatin on HDL cholesterol for 60 patients enrolled are presented in Table 3 and its graphical representation in Figure 3.

Figure 2: The effect of drugs on LDL cholesterol

Table 3: Effect of drugs on HDL

Drugs	Parameter	Maximum	Mean	SD	P-Value
Atorvastatin	Before	53	30.07	6.448	<0.003
	After	60	37.80	6.332	
Rosuvastatin	Before	38	28.77	4.431	
	After	245	44.60	38.045	

In Table 3, the HDL cholesterol levels of patients before and after treatment were compared. The HDL cholesterol level checked after the treatment were found to be statistically significant, i.e., P<0.003.

Effect of drugs on Liver Enzymes-SGPT

The effect of drugs Atorvastatin and Rosuvastatin on liver enzyme SGPT for 60 patients enrolled are presented in Table 4 and its graphical representation in Figure 4.

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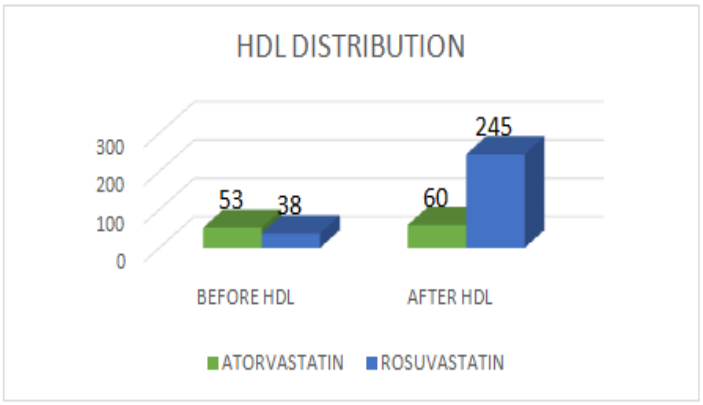

Figure 3: The effect of drugs on HDL cholesterol

Table 4: Effect of drugs on Liver enzymes SGPT

Drugs	Parameter	Maximum	Mean	SD	P-Value
Atorvastatin	Before	32	26.20	4.16	<0.001
	After	79	42.30	20.03	
Rosuvastatin	Before	30	24.37	3.643	
	After	52	29.20	5.189	

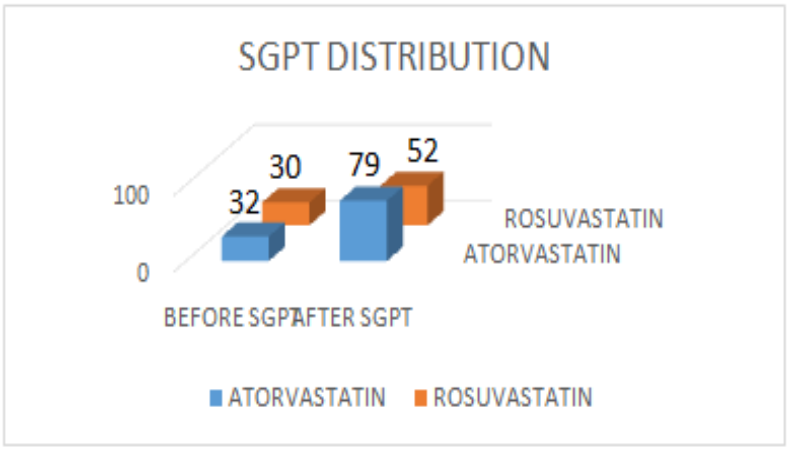

Figure 4: Effect of drugs on Liver enzyme SGPT

In Table 4, the SGPT levels of patients before and after treatment were compared. The SGPT level checked after the treatment were found to be statistically significant, i.e., P<0.001.

Effect of drugs on Liver enzymes-SGOT

The effect of drugs Atorvastatin and Rosuvastatin on Liver enzymes -SGOT for 60 patients enrolled are presented in Table 5 and its graphical representation in Figure 5.

Table 5: Effect of drugs on Liver enzymes -SGOT

Drugs	Parameter	Maximum	Mean	SD	P-Value
Atorvastatin	Before	32	26.10	4.656	<0.034
	After	82	42.67	20.033	
Rosuvastatin	Before	30	26.43	3.070	
	After	54	30.37	5.720	

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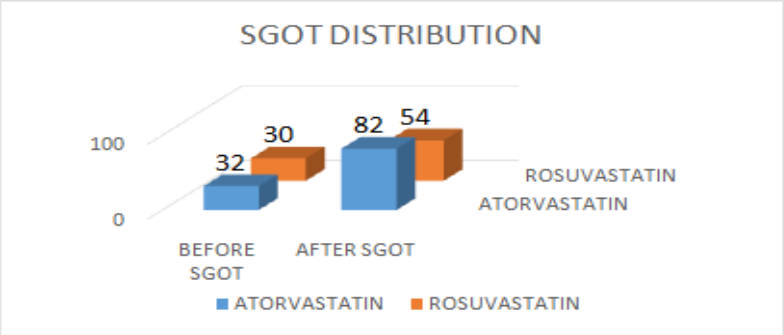

Figure 5: Effect of drugs on Liver enzymes –SGOT

In Table 5, the SGOT levels of patients before and after treatment were compared. The SGOT level checked after the treatment were found to be statistically significant, i.e., P<0.034.

Quality of life (QOL) of patients undergoing CABG

The effect of drugs Atorvastatin and Rosuvastatin on Quality of Life of patients undergoing CABG for 60 patients enrolled are presented in Table 6 and its graphical representation in Figure 6.

Table 6: QOL of patients undergoing CABG

Drugs	Parameter	Maximum	Mean	SD	P-Value
Atorvastatin	Before	51	43.33	4.26	<0.028
	After	75	65.03	13.063	
Rosuvastatin	Before	64	47.13	5.853	
	After	81	67.73	7.492	

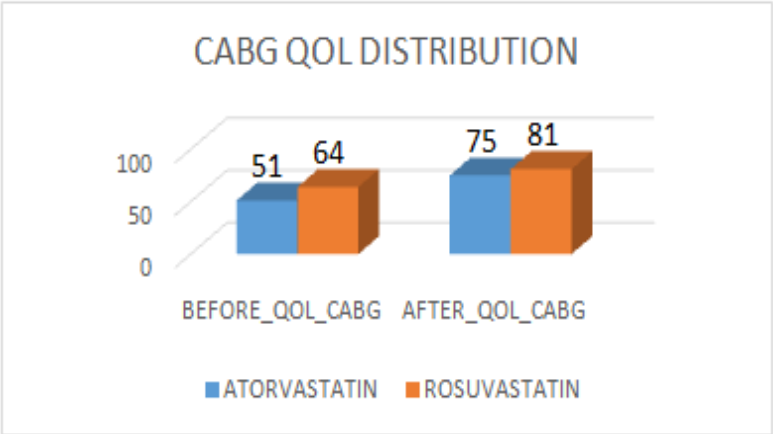

Figure 6: Quality of Life of patients undergoing CAB

In Table 6, the CABG QOL of patients before and after treatment was compared. The QOL checked after the treatment were found to be statistically significant, i.e., P <0.028.

QOL associated with Myopathy

The effect of drugs Atorvastatin and Rosuvastatin on Quality of Life associated with Myopathy for 60 patients enrolled are presented in Table 7 and its graphical representation in Figure 7.

Table 7: QOL associated with Myopathy

Drugs	Parameter	Maximum	Mean	SD	P-Value
Atorvastatin	Before	0	0	0	<0.073
	After	0	0	0	
Rosuvastatin	Before	0	0	0	
	After	4	.41	1.240	

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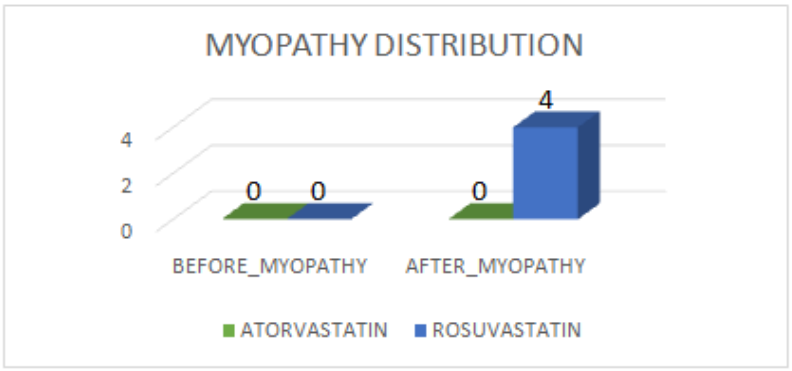

Figure 7: QOL associated with Myopathy

In Table 7, QOL associated with myopathy before and after treatment were compared. The QOL checked after the treatment were found to be statistically significant, i.e., P <0.073.

Cholesterol and liver enzyme levels of patients were monitored and follow-up was conducted during the study period. From the results we found that the patients having high cholesterol and normal liver enzyme levels before the treatment, their cholesterol levels are reduced and liver enzymes are elevated in some patients significantly during the treatment with the drugs.

CONCLUSION

In conclusion, Atorvastatin and Rosuvastatin have potent lipid lowering effect, but the spectrums of adverse effects are different in both the drugs. Hence Atorvastatin is better to lower the LDL cholesterol than Rosuvastatin. Rosuvastatin is better to increase the HDL cholesterol than Atorvastatin, but both the drugs have their own limitations. So by comparing the effect of both drugs, Rosuvastatin was recommended for younger patients and patients with post–operative liver enzyme elevation and Atorvastatin was recommended for older patients and patients who had complaints of myopathy.

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