EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 4
Issue: 01
329-332
Year: 2017

EFFECT OF ROSUVASTATIN ON DYSLIPIDEMIA IN HEMODIALYSIS PATIENTS

Ashwini A. Balode and Z. H. Khan*

Department of Biochemistry, Shri Shivaji College, Akola.

Corresponding Author: Dr. Z. H. Khan
Department of Biochemistry, Shri Shivaji College, Akola.

Article Received on 02/11/2016 **Article Revised on 23/11/2016** **Article Accepted on 14/12/2016**

ABSTRACT
Lipid disorders are one of the known metabolic changes associated with chronic renal failure (CRF).The prominent features of uremic dyslipidemia are an increase in plasma triglycerides and cholesterol in nearly all lipoproteins, and a reduction in high-density lipoprotein (HDL) cholesterol. Cardiovascular disease (CVD) is a major cause of mortality in patients with chronic renal failure (CRF). One of the risk factors for cardiovascular disease is dyslipidemia as it accelerates atherosclerosis. Therefore it is essential to study uremic dyslipidemia, since optimal treatment is essential for the prevention or delay of cardiovascular complications in patients on hemodialysis. Statins bind to and inhibit the enzyme 3-hydroxy-3- methyl-glutaryl coenzyme A Reductase, the rate limiting step in cholesterol biosynthesis. The inhibition of HMG-CoA reductase activity results in a drop in intracellular cholesterol production, thus improving the lipoprotein pattern. This study aims to evaluate the effect of Rosuvastatin on lipid parameters in hemodialysis patients in Akola district. A total of 200 hemodialysis patients were included: 150 were Rosuvastatin group and 50 were controls. As efficacy variables, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol and triglyceride levels were determined at the start of the study and at post treatment. The parameters were estimated using commercially available kits on semiautoanalyser. The results showed that in the Rosuvastatin group there was a significant decrease from baseline to the study end in the mean total cholesterol (228.76± 19.80 mg/dL to 144.26± 17.81 mg/dL), in triglyceride level (172.09 28.44 mg/dL to 91.12 19.28 mg/dL) and in LDL- cholesterol from (152.20± 22.27 mg/dL to 76.17±18.38mg/dL). There was an effective increase in HDLcholesterol from 42.14± 5.80 mg/dL to 49.86± 3.43mg/dL. In the control group no significant decrease was observed. Rosuvastatin at 10 mg/day was associated with significant improvement in lipid profile in patients on regular hemodialysis.

KEYWORDS: Rosuvastatin, Dyslipidemia, Cardiovascular disease, Hemodialysis.

INRODUCTION
Patients with end-stage renal disease (ESRD) undergoing Hemodialysis have substantially higher cardiovascular disease mortality rates than the general population (Brown JH *et al.*, 1994; Parfrey PS. 2000) Accelerated atherosclerosis has been observed in Hemodialysis patients (Levey AS, 1998) and may contribute to this increased cardiovascular event rate. Although cardiovascular mortality is decreasing in the general population, cardiovascular disease (CVD) still accounts for the largest proportion of fatalities in dialysis patients by far (Foley 2007). Dyslipidaemia (including increased total cholesterol, triglycerides, and LDL cholesterol and low HDL cholesterol levels) is one of several factors (hypertension, diabetes, hyperphosphataemia and smoking) that have been implicated in the increased cardiovascular risk associated with chronic kidney disease (CKD) (Ganesh *et al.*, 2001; Mallamaci *et al.*, 2002). Treatment of ESRD and its cardiovascular consequences places a large burden upon healthcare providers, and the cost and prevalence are expected to increase greatly over the next decade [US Renal Data System Annual Data Report). Therefore, controlling risk factors for atherosclerosis may play an important role in preventing cardiovascular events in these individuals. Optimal management of dyslipidemia, in particular reduction of LDL, is therefore anticipated to result in cardiovascular and overall mortality benefits.

Hydroxy-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors (statins) which are hypolipidaemic drugs have been demonstrated to reduce coronary heart disease morbidity and mortality in several landmark trials (Shepherd *et al.*, 2002 ; Sever PS *et al.*, 2003). The reductions in cardiovascular events also occur in patients with average to lower than average baseline low-density lipoprotein cholesterol (LDL-C) levels and the benefits of statin therapy can be independent of lipid lowering (Laufs U, 2003). Hemodialysis patients have other lipid abnormalities such as lower levels of high-density lipoprotein cholesterol (HDL-C) and elevated intermediate-density lipoprotein (IDL). Both small dense

LDL and triglyceride-rich lipoproteins have been implicated in the development of cardiovascular disease (Sacks FM *et al.,* 2000, Alaupovic *et al.,* 2000) and are common in patients with ESRD and on hemodialysis.

Statins (or HMG-CoA reductase inhibitors) are a class of drug used to lower cholesterol levels by inhibiting the enzyme HMG-CoA reductase, which plays a central role in the production of cholesterol in the liver. Rosuvastatin is a potent inhibitor of HMG-CoA reductase that has demonstrated efficacy for various lipid disorders. (Blasetto JW *et al.,* 2003) Rosuvastatin appears to exhibit a favourable pharmacodynamics and pharmacokinetic profile, which includes low lipophilicity, high hepatocyte selectivity, along with minimal metabolism. (Chapman *et al.,* 2003)

Although the efficacy of statins is well established in conditions associated with increased cardiovascular risk, dialysis patients have generally been excluded from statin outcome trials because of their related co-morbidities and as a result of pharmacokinetic and safety issues. Thus there is a need to investigate the benefit risk profile of Rosuvastatin especially in this population.

AIMS AND OBJECTIVES

Dyslipidemia is a prevalent condition in chronic renal disease, but is often left untreated. Statin treatment constitutes an effective way to improve lipid abnormalities. The present study aims to evaluate the effects of Rosuvastatin on lipid profile and various Biochemical parameters in subjects on regular hemodialysis.

MATERIAL AND METHODS

A total of 200 hemodialysis patients from Akola district who had been regularly treated with 4-hr hemodialysis sessions were considered for research study. Patients were randomly divided into two groups according to the study. Group A (Control group) included patients who did not take any lipid lowering drug and Group B included patients who took Rosuvastatin 10mg/day for 12 weeks (Rosuvastatin group). In this study, at first a questionnaire was used to collect clinical and demographic characteristics, including age, sex, and the classical risk factor for CVD, namely smoking status, alcohol consumption, the presence of hypertension, peripheral vascular disease, eating habits, a family history of vascular disease , and any other diseases such as Hepatitis B, or HIV etc. A well-defined follow up visit was scheduled at the interval of 4 weeks. Five ml of venous blood was drawn from the considered hemodialysis patients (200) from Dialysis Centre, Akola and have been analyzed in Research laboratory of Biochemistry Department, Shri. Shivaji College, Akola, Maharashtra. Biochemical parameters like urea, creatinineand serum electrolytes along with the lipid parameters - total cholesterol, triglycerides, LDL and HDL cholesterol were analyzed. All the parameters were estimated using commercially available kits on semiautoanalyser – Robonik. The total cholesterol and high density lipoprotein cholesterol (HDL) were analyzed using cholesterol oxidase CHOD-PAP method, triglyceride by GPO-PAP method while low density lipoprotein cholesterol (LDL) was obtained using Frieldwald formula: LDL cholesterol= Total cholesterol − TGL÷5 – HDL. Latex Turbidemetry was employed for measuring the hs-CRP.

Table 1: Baseline characteristics of the patients

Variables	Group A Control (Patients without Rosuvastatin) N=50		Group B Rosuvastatin (Patients with Rosuvastatin) N=150	
	Mean	Std .Dev	Mean	Std .Dev
Age (year)	54.2	7.98	53.2	8.2
Male/Female	Male-33/ Female-17			
Time on dialysis (months)	27.2	7.11	24.5	7.4
Total Cholesterol (mg/dl	172.56	16.14	228.76	19.8
Triglyceride (mg/dl)	132.98	28.21	172.09	28.44
LDL-C (mg/dl)	101.184	18.7	152.2	22.26
HDL-C (mg/dl	44.78	4.06	42.14	5.8
C-Reactive Protein	9.11	1.98	11.35	6.34
Albumin (g/l)	3.44	0.338	3.48	0.314
Urea(mg/dl)	117.08	26.92	113.45	27.77
Creatinine (mg/dl)	10.434	2.34	10.46	2.36
Haemoglobin (g/dl	9.51	1.28	9.64	1.06
Causes of end stage renal disease-no. (%)				
Diabetic nephropathy	15 (30)		42 (28)	
Hypertension	12 (24)		33 (22)	
Glomerulonephritis	8 (16)		19 (12.6)	
Tubulointerstitial disease	3 (6)		12 (8)	
Nephrosclerosis	7(14)		17 (11.3)	
Polycystic Kidney			3 (2)	

Others	5(10)	24 (16)

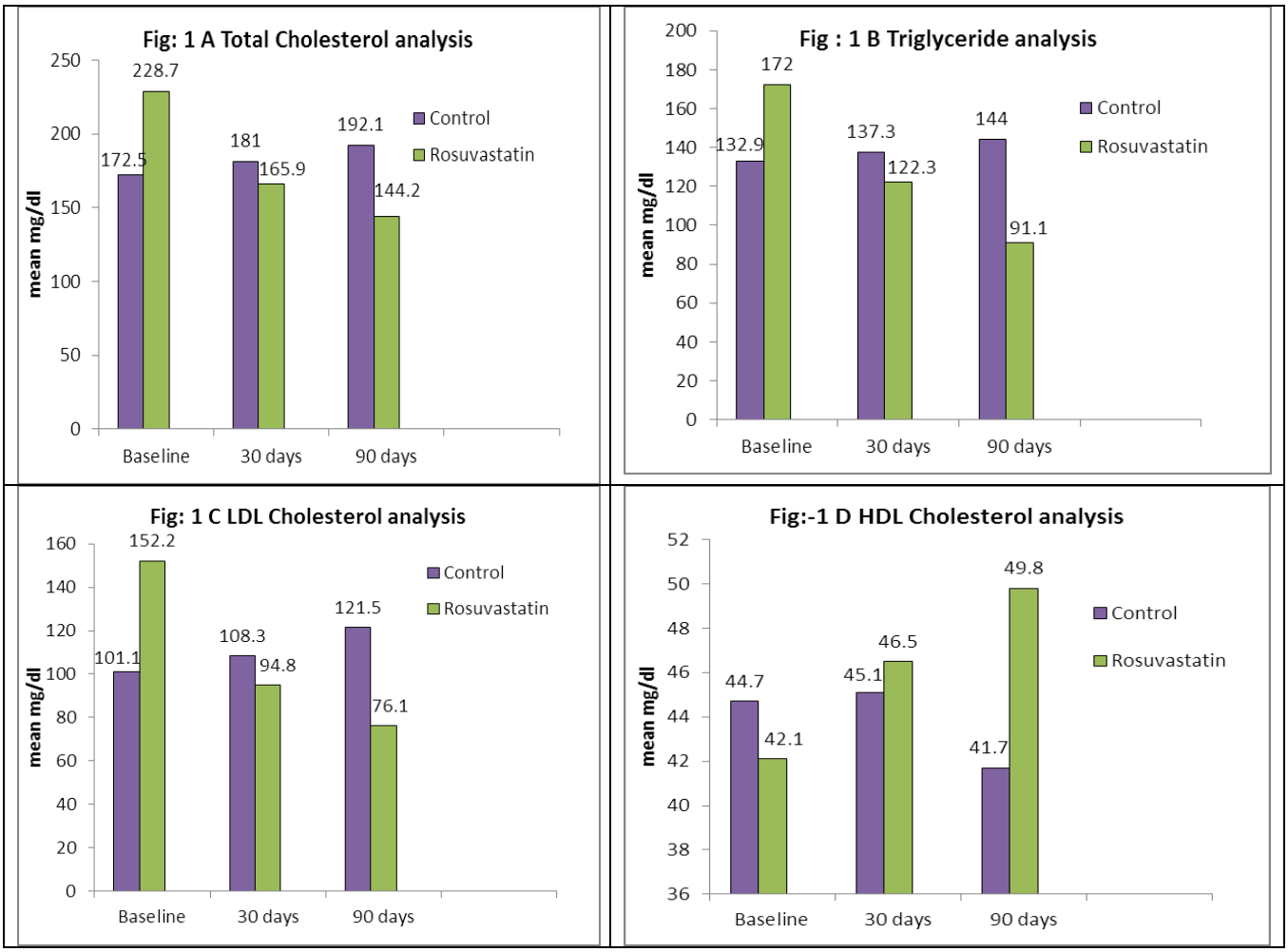

Figure 1: Changes in lipid parameters

RESULTS AND DISCUSSION

Two hundred patients were enrolled for this study and randomly allocated them to the Rosuvastatin group (n=150, male 89 and female 61) and control group i.e. patients without Rosuvastatin (n=50, male 33 and female 17). The baseline characteristics of the patients in the 2 groups are shown in Table 1. The age range of patients in Rosuvastatin group and control group was 53.2 ± 8.2 and 54.2 ± 7.98 years respectively. The primary cause of End stage renal disease in the study population was Diabetic nephropathy. Baseline lipid levels are depicted in Table 1. Changes in the various lipid parameters from the baseline are shown in Fig. 1. Patients in the Rosuvastatin treatment group showed significant improvement in lipid parameters at week 12 as compared to control group. Fig: 1A shows that total cholesterol after administration of Rosuvastatin fell from 228.76 ±19.80 mg/dL to 144.26± 17.8 mg/dL while the patients not taking Rosuvastatin showed an increase in total cholesterol from 172.56 mg/dL to 192.14 mg/dL. Triglyceride level and LDL- cholesterol markedly decreased from 172.09± 28.44 mg/dL to 91.12± 19.28 mg/dL and 152.20± 22.27 mg/dL to 76.17 ±18.38 mg/dl respectively as compared with an increase of 132.98 mg/dL to 144.06 mg/dL and 101.18 mg/dL to 121.54 mg/dL in the control group at the end of the study (Fig: B and Fig: 1C). There was a significant increase in HDL-cholesterol from 42.14± 5.80 mg/dL to 49.86± 3.43 mg/dL (Fig: 1 D).

Taking into consideration of the above retrieved results, it was found that at the interval of 3 months, the cholesterol level in the patients getting Rosuvastatin therapy was 37 % lower than the baseline level. Similarly, triglyceride level was reduced by approximate 47% in three months during Rosuvastatin therapy. The study has revealed that HDL cholesterol level gets increased by 18.33 % than the baseline HDL cholesterol level. The LDL cholesterol level has reduced significantly by a major percentile of (49%) after the Rosuvastatin therapy. This is of great significance as reduction in lipid profile (LDL) signifies positive impact of Rosuvastatin for renal failure patients on regular hemodialysis. In general the level of serum lipids showing both quantitative and qualitative abnormalities worsens with decreasing kidney function, being more pronounced in subjects in end stage renal disease. Statins have revolutionized the treatment of high plasma cholesterol and atherosclerosis, confirming their benefits

in vascular disease. They are effective in correcting dyslipidemia and are relatively safe.

It may imply that long term use of lipid lowering treatment may be important, especially for the patients with chronic inflammatory stress, such as CKD or dialysis.

CONCLUSION

In the present study Rosuvastatin significantly improved total cholesterol, triglycerides, LDL-C and HDL-C when compared with the values at baseline and in the control group. Patients appear to benefit from statin therapy by their lipid lowering effects. The mechanism of action of statins based on binding at the active site of the enzyme 3-hydroxy-3- methyl-glutaryl coenzyme reductase A leads to increased expression of Low –Density Lipoprotein receptors and a subsequent decrease in LDL-C levels. This beneficial effect has also been observed in this study. The reduction in LDL and increase in HDL lipid profile due to Rosuvastatin therapy signifies the subsequent reduction in cardiovascular risk (CVR) and also affirms safety and effective consideration of Rosuvastatin. No drug-related serious adverse events were reported. This study suggests that Rosuvastatin with its enhanced efficacy may provide adequate therapy for a large number of dyslipidemia patients undergoing hemodialysis.

REFERENCES

1. Blasetto JW, Stein EA, Brown WV, Chitra R, Raza A. *et al.* Efficacy of rosuvastatin compared with other statins at selected starting doses in hypercholesterolemic patients and in special population groups. Am J Cardiol. 2003; 91: 3C–10C.
2. Brown JH, Hunt LP, Vites NP, Short CD, Gokal R, Mallick NP. Comparative mortality from cardiovascular disease in patients with chronic renal failure. Nephrol Dial Transplant. 1994; 9: 1136-1142.
3. Chapman MJ, Caslake M, Packard C, McTaggart F. New dimension of statin action on apoBatherogenicity. ClinCardiol. 2003
4. Foley RN. Collins AJ. End-stage renal disease in the United States: an update from the United States Renal Data System. Journal of the American Society of Nephrology 2007; 18(10): 2644-8.
5. Ganesh SK, Stack AG, Levin NW, Hulbert-Shearon T, Port FK. Association of elevated serum PO (4), Ca x PO (4) product, and parathyroid hormone with cardiac mortality risk in chronic hemodialysis patients.Journal of the American Society of Nephrology 2001.
6. Laufs U. Beyond lipid-lowering: effects of statins on endothelial nitric oxide. Eur J ClinPharmacol. 2003; 58: 719-731.
7. Levey AS, Beto JA, Coronado BE, Eknoyan G, Foley RN, Kasiske BL, Klag MJ, Mailloux LU, Manske CL, Meyer KB, Parfrey PS, Pfeffer MA, Wenger NK, Wilson PW, Wright JT. Controlling the epidemic of cardiovascular disease in chronic renal disease. National Kidney Foundation Task Force on Cardiovascular Disease.Am J Kidney Dis. 1998; 32: 853- 906.
8. Mallamaci F, Zoccali C, Tripepi G, Fermo I, Benedetto FA, Cataliotti A, *et al.* Hyperhomocysteinemia predicts cardiovascular outcomes in hemodialysis patients. Kidney International 2002.
9. Parfrey PS. Cardiac disease in dialysis patients: diagnosis, burden of disease, prognosis, risk factors and management. Nephrol Dial Transplant. 2000; 15(Suppl 5): 58–68.
10. Sacks FM, Alaupovic P, Moye LA, Cole TG, Sussex B, Stamfer MJ, Pfeffer MA, Braunwald E. VLDL, apolipoproteins B, CIII, and E, and risk of recurrent coronary events in the Cholesterol Recurrent Events (CARE) trial.Circulation. 2000
11. Sever PS, Dahlöf B, Poulter NR, Wedel H, Beevers G, Caulfield M, Collins R. for the ASCOT investigators Prevention of coronary and stroke events with atorvastatin in hypertensive patients in the Anglo-Scandinavian Cardiac Outcomes Trial-Lipid Lowering Arm (ASCOT-LLA): a multicentrerandomised controlled trial. Lancet. 2003.
12. Shepherd J, Cobbe SM, Ford I, Isles CG, Lorimer AR, MacFarlane PW, McKillop JH, Packard CJ. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. N Engl J Med. 1995; 333: 1301-1307.
13. US Renal Data System Annual Data Report. Bethesda, MD. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases 2000.