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Efficacy and safety of Different Statins among Newly Diagnosed Dyslipidemic Patients

Mohammad Al Mamun[1*], Nilufar Fatema[2], Mohammod Zafor Iqbal Jamali[3], A. K. Al Miraj[4], Naveen sheikh[5], Fouzia sultana[6]

[1]Medical Officer, Department of Cardiology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.
[2]Consultant, Department of Cardiology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
[3]Medical Officer, Department of Cardiology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
[4]Research Assistant, Department of Vascular Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
[5]Associate Professor, Department of Cardiology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
[6]Medical Officer, Department of ENT, National Institute of ENT Hospital Tejgao, Dhaka, Bangladesh

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***Corresponding author**
Mohammad Al Mamun

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Abstract: ***Background:*** Cardiovascular Disease is the leading cause of death. Prevention of cardiovascular disease is the major aim of treatment of anyone who has risk. Dyslipidemia lies in the center of cardiovascular disease risk. Not only there is difference in pattern of dyslipidemia and response to statins in different ethnic groups, there is difference in mortality due to cardiovascular disease in different race and ethnic group. Atorvastatin and Rosuvastatin are the first line statins. This study is carried out to see how our population responds to these statins in terms of change in lipid profile. ***Methods:*** It is prospective real world observational study done at the Department of Cardiology BSMMU at the time July 2016 to August 2017 who were diagnosed as having dyslipidemia and indicated for statins but not already on statin were included in the study. Total of 120 patient's data was available for analysis. Out of which 68 were in atorvastatin 10 mg group and 52 were in rosuvastatin 5 mg group. Baseline demographic and lipid profile was recorded. Lipid profile sample was taken after 12 hours of fasting. All patients were counselled for dietary control and exercise and were started on either atorvastatin 10 mg once daily or rosuvastatin 5 mg once daily according to physician's discretion. Demographic profile and baseline lipid was recorded. Lipid profile was again recorded after 3 to 4 months of treatment. ***Result:*** Total of 120 patient's data was available for analysis. Out of which 68 were in atorvastatin 10 mg group and 52 were in rosuvastatin 5 mg group. There was no significant difference in variables like gender, age, BMI, smoker, Diabetic and hypertensive among both the group. Total cholesterol decreased by 22 % (p = 0.002) in Atorvastatin group and by 22.6 % (p= 0.002) in Rosuvastatin group. Low Density Lipoprotein (LDL) decreased by 22 % (p = 0.004) in Atorvastatin group and 21.3% (p=0.005) in Rosuvastatin group. There was no significant difference between two groups. ***Conclusion:*** Both Atorvastatin 10 mg and Rosuvastatin 5 mg can reduce the lipids significantly in our population. There is no difference in using Atorvastatin 10 mg or Rosuvastatin 5 mg. However, reduction was only mild to moderate with the given doses.

Keywords: Cardiovascular disease, Dyslipidemia, Total cholesterol, Triglyceride, Low Density Lipoprotein, High Density Lipoprotein.

INTRODUCTION

Prevention of CVD is the major aim in treatment of anyone who has risk. Dyslipidemia lies in the center of CVD risk. According to AHA/ACC and also ESC guidelines treatment of dyslipidemia is the one of the major goal in primary as well as secondary prevention of CVD [1,2]. Most current guidelines include LDL as a primary target for starting and adjusting dose for dyslipidemia management. Number of trials have shown that a 1.0 mmol/L (40 mg/dL) reduction in low- density lipoprotein cholesterol (LDL) is associated with an overall 21 % reduction in major vascular events and 20 % reduction in coronary death [3]. Lipitor (atorvastatin) is typically the first-line drug to treat high cholesterol because it has fewer side effects than other statins. Statins are the drug class of

choice to manage high cholesterol for people with a risk of cardiovascular disease. Cardiovascular Disease (CVD) has become the leading cause of death worldwide. In 2013, CVD caused an about 32% of all deaths and 13% of all disability adjusted life-years (DALYs) lost.[1]As with many high-income countries during the last century, low- and middle-income countries are now experiencing an alarming and accelerating increase in CVD [4]. The NMA concludes that the efficacy of rosuvastatin in LDL-C and APOA1 in APOA1 increases for the first time. Lovastatin ranked number one in the efficacy of TC and TG reduction, while fluvastatin ranked number one in the efficacy of HDL C. Not only are there differences in patterns of dyslipidemia, but the response to statins in the mortality rates of different ethnic groups due to CVD also differs between racial and ethnic variations. Most of the data on racial/ethnic differences in statin metabolism shows that some Asian subgroups metabolize statins more slowly and have higher systemic drug concentrations compared to non-Hispanic whites. It has been [5.6]. However, the statin dosage is somewhat confusing as the guidelines use medium to high-strength statins. Clinician Considerations Risk Benefit Ratios should determine whether to choose high-strength and medium-strength statins [7]. High or moderate statin strength recommendations come from studies conducted in developed countries. We know that dyslipidemia can vary depending on ethnicity, dietary habits, movement, and economic status. Statin dose recommendations for the American or European population may not apply to our population.

METHODS & MATERIALS

It is prospective real world observational study done at Department of Cardiology BSMMU at the time July 2016 to August 2017 who were diagnosed as having dyslipidemia and indicated for statins but not already on statin were included in the study. Baseline demographic and lipid profile was recorded. Lipid profile sample was taken after 12 hours of fasting. All patients were counselled for dietary control and exercise and were started on either atorvastatin 10 mg once daily or rosuvastatin 5 mg once daily according to physician's discretion. The dose being taken is the most common prescriptions found being used by treating physicians and no interference was done to change physician's decision. Patients were asked to follow up in around 3 to 4 months and repeat lipid profile was done. The baseline and repeat lipid profile was compared.

Inclusion criteria: Any patient presenting to Medicine OPD with diagnosis of Dyslipidemia and indicated for statin therapy by clinician.

Exclusion criteria: Any patient who was not willing to participate in the study or who was already on statin therapy and if the prescribed dose was different then the proposed dose in study then those patients were excluded from the study. Statistical analysis was done using SPSS 23 and paired t test was applied wherever applicable.

RESULTS

Total of 120 patient's data was available for analysis. Out of which 68 were in atorvastatin 10 mg group and 52 were in rosuvastatin 5 mg group. There was no significant difference in variables like gender, age, BMI, smoker, Diabetic and hypertensive among both the group as shown in table 1. There was no significant difference in baseline lipid profile value in both groups as shown in table 2.

Table 1: Demographic profile

	Atorvasttatin 10 mg	Rosuvastatin 5 mg	p-value
Male	33	35	0.860
Female	25	27	0.832
Age (mean +/-SD) /Years	56.23±3.05	55.97±3.62	0.350
BMI (mean +/-SD)/kg/m^2	23.54±0.56	23.72±0.71	0.415
Smoker	29	31	0.721
Diabetic	42	46	0.712
Hypertensive	58	54	0.369

Table 2: Lipid profile baseline and after treatment

	Lipids	Baseline mg/dl	After treatment mg/dl	% Change	p-value
Atorvastatin 10 mg	Total cholesterol	242±14.5	189±13.4	21.9	0.002
	Triglyceride	198±12.8	169±11.6	14.6	0.007
	LDL	158±9.6	123±9.3	22.2	0.004
	HDL	37±3.6	42±3.7	13.5	0.013
Rosuvastatin 5mg	Total cholesterol	246±15.2	191±12.8	22.3	0.002
	Triglyceride	194±12.9	170±11.2	12.3	0.008
	LDL	153±10.2	120±8.6	21.5	0.005
	HDL	36±3.9	41± 4.1	13.8	0.010

Table 3: Comparison of Atorvastatin 10 mg and Rosuvastatin 5 mg

	Lipids	Atorvastatin 10 mg	Rosuvastatin 5 mg	P value
Baseline	Total cholesterol	242±14.5	246±15.2	0.735
	Triglyceride	198±12.8	194±12.9	0.812
	LDL	158±9.6	153±10.2	0.762
	HDL	37±3.6	36±3.9	0.632
After treatment	Total cholesterol	189±13.4	191±12.8	0.532
	Triglyceride	169±11.6	170±11.2	0.645
	LDL	123±9.3	120±8.6	0.752
	HDL	42±3.7	41± 4.1	0.823

There is significant change in lipid level with treatment. Total cholesterol decreased by 22 % (p =0.002) in atorvastatin group and by 22.6 % (p= 0.002) in rosuvastatin group. Triglyceride decreased by 14.6% (p=0.007) in atorvastatin group and 12% (p= 0.008) in rosuvastatin group. LDL decreased by 22% (p = 0.004) in atorvastatin group and 21.3% (p=0.005) in rosuvastatin group. HDL increased by 14% (p=0.013) in atorvastatin group and 14% (p= 0.010) in rosuvastatin group. Atorvastatin 10 mg and rosuvastatin 5 mg had similar effect in change in lipid level.

DISCUSSION

The association between LDL levels and cardiovascular events and mortality is well established in the literature and relevant guidelines, whereby the classification of high-intensity statins is based on LDL reduction of ≥50% to reduce risk of ASCVD [6]. Evidence has also shown that compared with moderate- or low-intensity statins, high-intensity statins decrease CVD risk more effectively [7,8]. Cardiovascular disease (CVD) is the most common cause of mortality in industry and most developing countries. The World Health Organization estimates that dyslipidemia is associated with more than half of the global cases of ischemic heart disease and more than 4 million deaths per year. It is known that there are differences in prevalence, patterns, and responses to treatment of dyslipidemia in various racial and ethnic groups around the world [8.9]. Compared to previous reports, rosuvastatin did not significantly reduce lipid parameters. The possible reason is that each group has a different sample size and may also be related to variation in drug responses associated with ethnic groups. Ethnic differences in statin efficacy regarding different responses of LDL-C to statin therapy have been documented in several pharmacological studies of African Americans, Indians, Hispanics and South Asians [10, 11]. Our study shows that lipid profiles vary significantly in treatment. LDL value decreased by 20 to 25%. However, there was no significant difference between 10 mg of Atorvastatin and 5 mg of rosuvastatin. ASCOTT-LLA trial was done in 10,305 patients with atorvastatin 10 mg which found a 34.6% reduction LDL from baseline of 133 mg/ dl. In our study we found a reduction of 22% in LDL from baseline of 158 mg/dl with atorvastatin 10 mg [12]. The difference could have been due to the selection of patients as the ASCOTT-LLA included patients with lower-than-average cholesterol and also was done in Anglo-Scandinavian population which is has very different race and ethnic group and also has different dietary habit than our population. 2823 patients of UK and Ireland were included in CARDS trial where they also used 10 mg of atorvastatin 10 mg and found 40% reduction in LDL [13]. The difference with our study could have been due to different population. Both ASCOTT-LA and CORDIS trial has long term follow up more than three years. ASPEN trial showed 29 % reduction in LDL with 10 mg of Atorvastatin [14]. It was done in diabetic patients only. Though both study showed significant reduction in LDL but because of difference in dose we cannot make a comparison. URANUS trial compared atorvastatin 10 mg and rosuvastatin 10 mg and found rosuvastatin significantly reduced LDL in comparison to atorvastatin [15]. In our study there was no difference between atorvastatin and rosuvastatin but we used Atorvastatin 10 mg and rosuvastatin 5 mg. If we had used equal dose of Atorvastatin and rosuvastatin probably we could have got similar results. Pedersen TR et al. [16] compared atorvastatin 10 mg and rosuvastatin 5 mg in Pakistani population and found reduction of total cholesterol of 14.0% with atorvastatin and 20% with rosuvastatin. In our study total cholesterol reduction was 22% and 22% with Atorvastatin and rosuvastatin respectively. Similarly, they found TG reduction by 6% and 3.3% whereas we found 14.6% and 12% reduction with atorvastatin 10 mg and rosuvastatin 5 mg respectively. In their study they found LDL reduction of 13.3% and 24% and we found LDL reduction of 22% and 21.3% with atorvastatin and rosuvastatin respectively. HDL increased by 7.3% and 6% in their study where as our study showed an increase of 13.3% and 14% with atorvastatin and rosuvastatin respectively. Their study showed significant difference in LDL reduction whereas there was no significant difference in Total Cholesterol, TG and HDL. In our study there was no significant difference in change in Total cholesterol, TG, LDL and HDL [17]. Cannon CP et al, Hodkinson A et al and Bener A et al. did meta-analysis and found that all statins had class effect in reducing cardiovascular disease outcome and atorvastatin and rosuvastatin were most effective [18-20]. Abdul

Rehman et al did comparative study between atorvastatin 10 mg and rosuvastatin 10 mg and found that there was greater reduction in Total cholesterol and LDL in rosuvastatin group as compared to atrorvastatin group [21]. Abdulbari Bener et al did study in Indian population and found that atorvastatin 10 mg reduced Lipids by 24.16% which is very similar to our study [22]. We could not find many studies where comparison was made between atorvastatin 10 mg and rosuvastatin 5 mg. And we could find lot of variation in reduction of LDL by statins. So, this difference could be due to multifactorial reasons like the racial, ethnic, cultural, individual characteristics, food habit, life style and even quality of drugs being used. So, it is important for us to know our own data and how our population responds to different statins. However, we could not find any studies to compare our finding. In our studies we found that both atorvastatin and rosuvastatin were effective in reducing lipids especially LD. 10 mg of atorvastatin and 5 mg of rosuvastatin were equally effective but the reduction was only mild to moderate. Mild reduction considered as <30% reduction in LDL, moderate reduction as 30 to 49% and high intensity as ≥50% reduction in LDL [23]. Although the studies included in the meta-analysis are different in the follow-up period and population, the overall benefit of rosuvastatin did not change upon performing the sensitivity analysis. The study looks at the lipid value as parameter rather than the outcome like atrherosclerotic cardiovascular events which requires long term follow up and beyond scope of this study.

CONCLUSION

This review further confirms that high-intensity statins reduce LDL by ≥50%, favoring rosuvastatin over atorvastatin. Additional data are needed to confirm the clinical significance on cardiovascular outcomes using real-world studies. According to these guidelines, LDL cholesterol levels are no longer considered as a major risk factor for coronary events. Both atorvastatin 10 mg and rosuvastatin 5 mg can significantly reduce lipids in our population. There is no difference between using atorvastatin 10 mg or rosuvastatin 5 mg. However, at a given dose, the reduction was slow. Higher doses are required for moderate to high reductions in LDL. Large-scale randomized controlled studies are required to draw final conclusions.

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