A COMPARISON STUDY ON EFFICACY AND SAFETY OF ROSUVASTATIN VERSUS ATORVASTATIN IN REDUCTION OF LOW DENSITY LIPOPROTEIN CHOLESTEROL IN PATIENTS OF DYSLIPIDEMIA IN TYPE 2 DIABETIES MELLITUS

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ABSTRACT : Around eightieth of passings in diabetic patients are inferable from vessel upset (CVD), that therefore is deeply related to diabetic dyslipidemia. The current examination analyzes the viability and security of rosuvastatin against often utilised lipid-lowering medicine in patients of sort a pair of DM with dyslipidemia, so as to direct the current treatment methodologies within the administration of the equivalent in Indian population. Patients satisfying the incorporation criteria were randomised in 2 gatherings. Gathering I got lipid-lowering medicine (10mg) and bunch II got rosuvastatin (5mg) at sleep time orally day by day. Serum TC, bodily fluid LDL-C, bodily fluid HDL-C and serum TG were surveyed on week zero, week half dozen and week twelve. At the end of twelve weeks, the speed decrease of LDL-C levels in lipid-lowering medicine gathering was thirty three.58% whereas in rosuvastatin gathering, it was 43.12%. the speed decrease in complete sterol (TC) in lipid-lowering medicine gathering was twenty four.85% whereas in rosuvastatin gathering, it was 30.8%. Ascend in HDL-C levels in lipid-lowering medicine gathering was seven.1% tho' in rosuvastatin gathering, it was 11.16%. all of those distinctions were factually immense.
KEYWORDS:Lipid-lowering medicine, sterol, vessel ill health, Diabetes, Dyslipidemia, Rosuvastatin

I.INTRODUCTION

Diabetes mellitus is a common metabolic disorder characterized by absolute or relative deficiencies in insulin secretion and/or insulin action associated with chronic hyperglycemia and disturbances of carbohydrate, lipid and protein metabolism.1 India has earned the distinction of being called as diabetic capital of the World.[2] It is estimated that 69.2 million people aged 20-79 years live with diabetes in India. This number is expected to increase to 123.5 million by 2040. About 1 million people died from diabetes in India in 2015.[3]

Diabetes mellitus is associated with increased oxidative stress due to hyperglycemia, which plays a role in development of micro and macro vascular complications involving almost all vital organs such as heart, eyes, kidney, blood vessels, and nervous system. These complications lead to the development of obesity, hypertension, dyslipidemia and insulin resistance.[4]

To study the comparison of efficacy and safety on rosuvastatin versus atorvastatin in reduction of low density lipoprotein cholesterol in patients of dyslipidemia in type 2 diabeties mellitus. To evaluate the patients exhibiting effectiveness and safety of the drugs. To survey over all ADRs introduced from rosuvastatin and atrovastatin. To assess the recurrence of different ADRs and see which drug is more effective and safe for medication.

II. MATERIALS AND METHODS

This study was conducted at medicine department of a tertiary care hospital attached to medical college. The study was approved by Institutional Ethics Committee.

The patients were recruited from cardiovascular OPD and diabetes OPD. They were screened for participating in the study. Patients were diagnosed on the basis of history and biochemical investigations. Patients who were found fit to be included into the study were explained the aims and objectives of the study in detail. They were informed about the benefits of the study along with possible risks. After explaining the entire scope of the study, a written

informed consent was obtained from them. The written informed consent was based on the specimen informed consent document. The patients were randomly allocated to either group I or group II of the treatment group based on chit method. Patients were blinded and were not informed about the drug they were to receive.
Baseline investigations including serum TC, serum LDL-C, serum HDL-C, serum TG levels, SGOT, SGPT and serum creatine phosphokinase (CPK) levels were done at the time of enrolment of patients (0 week).
Patients from Group I received atorvastatin (10mg) at bedtime orally daily and patients from group II received rosuvastatin (5mg) at bedtime orally daily. All patients also received the other concurrently required medications such as antidiabetic, antihypertensive or antianginal drugs etc as advised by treating physician. No patient used any other lipid lowering agents like bile acid sequestrants, fibrates or niacin. For patients who were already on statin therapy, a drug wash-out period of six weeks was allowed.
Study treatment was started on the day of randomization and continued for 12 weeks. After randomization, follow up visits were scheduled at 6 and 12 weeks. At each follow up, investigations like serum TC, serum LDL-C, serum HDL-C and serum TG were estimated, and patients were interviewed and examined for occurrence of myalgia, jaundice or any other adverse effect. Also, CPK, SGOT, and SGPT estimations were done at 6 and 12 weeks in all patients from both the groups to check for hepatotoxicity or myopathy.
Statistical Analysis was done using 'Z' test, paired t-test and unpaired t-test at appropriate places. A 'p' value <0.05 was considered statistically significant.

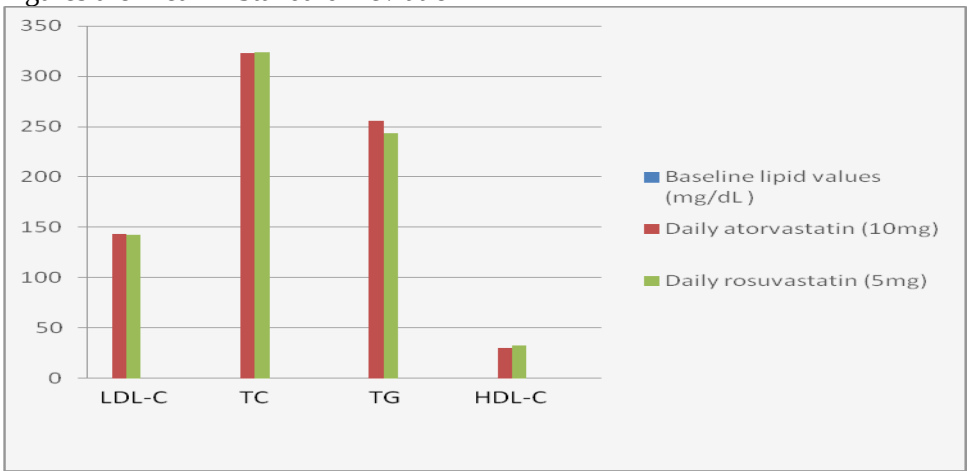
III. RESULTS AND DISCUSSION

A total 100 patients were included in the study, of which 50 patients were allocated to daily atorvastatin group and 50 patients to daily rosuvastatin group. During the study period two patient from daily atorvastatin group and one patient from daily rosuvastatin group were lost to follow up and hence excluded from the analysis. Thus 48 patients from daily atorvastatin group and 49 patients from daily rosuvastatin group were considered for the analysis of data.
The baseline characteristics of the patients of both the groups were comparable with respect to age, sex and clinical profile.

TABLE 1: BASELINE LIPID PROFILE OF PATIENTS

Baseline lipid values (mg/dL)	Daily atorvastatin (10mg)	Daily rosuvastatin (5mg)	p value
LDL-C	143.4±12.72	142.2±24.35	>0.04
TC	322.74±14.64	323.77±27.23	>0.04
TG	256.13±12.36	243.73±35.28	>0.04
HDL-C	30.37±2.47	32.45±2.27	>0.04

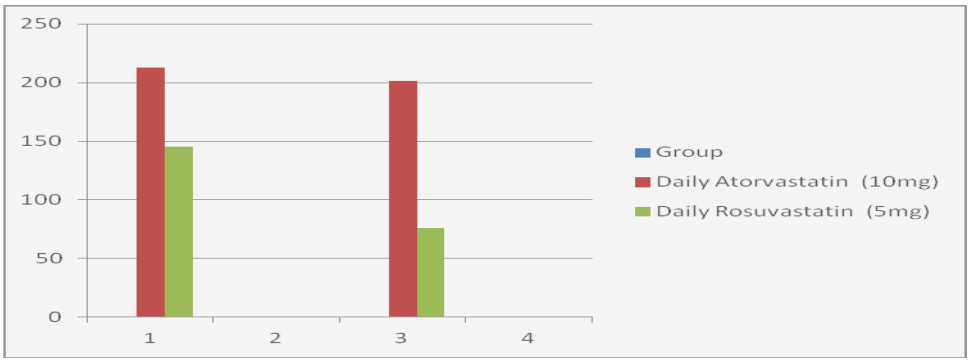
Unpaired t-test, Figures are Mean ± Standard Deviation



As Table 1 shows, the baseline mean lipid values of both the groups were comparable and there was no statistically significant difference between the two groups (p>0.05).

TABLE 2: LDL-C (MG/DL) IN BOTH TREATMENT GROUPS.

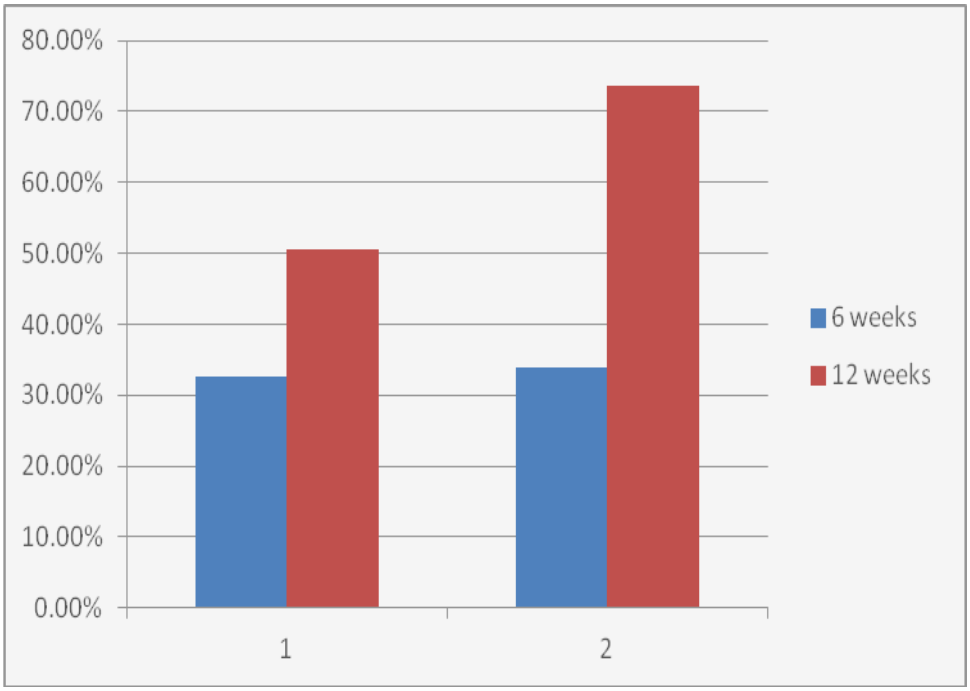
Group	Daily Atorvastatin (10mg)	Daily Rosuvastatin (5mg)	p value
6 weeks	212.75±28	145.49±33.24	<0.0002
12 weeks	201.46±25.21	76.1±22.57	<0.0002



As Table 2 shows, there was significantly greater reduction in levels of LDL-C in patients treated with rosuvastatin therapy as compared to those treated with atorvastatin (p<0.0001). The percentage reduction of LDL-C levels in atorvastatin group at 6 and 12 weeks was 21.1% and 33.58% respectively (Figure 1). The percentage reduction of LDL-C levels in rosuvastatin group at 6 and 12 weeks was 30.51% and 43.12% respectively.

TABLE 3: PERCENTAGE OF PATIENTS WHO ACHIEVED LEVELS OF LDL-C <100 MG/DL.

Group	Daily Atorvastatin (10 mg)	Daily Rosuvastatin (5 mg)	p value
6 weeks	32.73% (12/58)	33.9% (33/37)	<0.04
12 weeks	50.63% (38/36)	73.66%(41/49)	<0.04



Z test for difference between two proportions

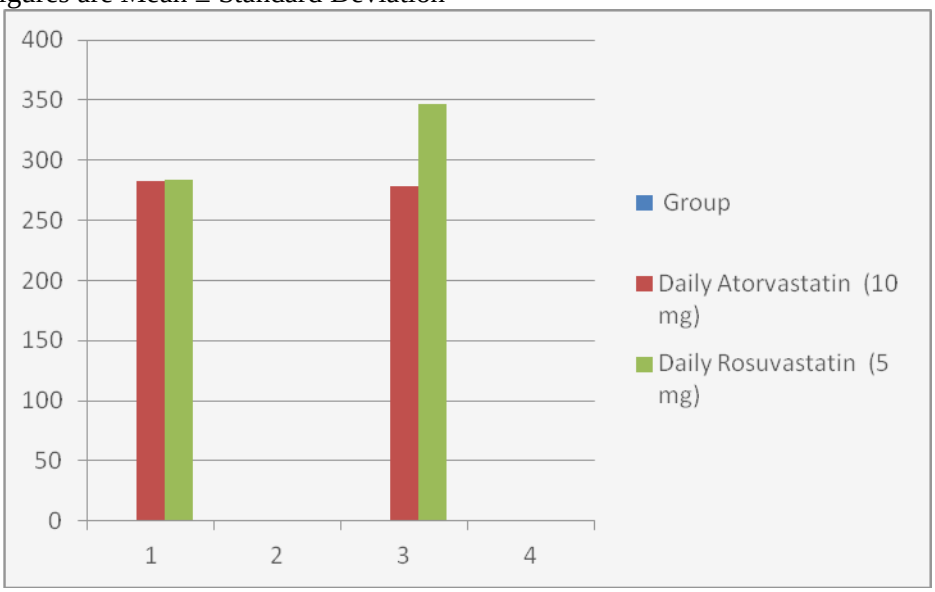
As Table 3 shows, significantly higher number of patients from rosuvastatin group achieved levels of LDL-C

<100mg/dL at 6 and 12 weeks (p<0.05).

TABLE 4: LEVELS OF TOTAL CHOLESTEROL (TC) MG/DL IN TWO TREATMENT GROUPS

Group	Daily Atorvastatin (10 mg)	Daily Rosuvastatin (5 mg)	p value
6 weeks	283.12±30.22	284±24.27	<0.0002
12 weeks	278.47±28.24	346.48±23.66	<0.0002

Unpaired t-test, Figures are Mean ± Standard Deviation

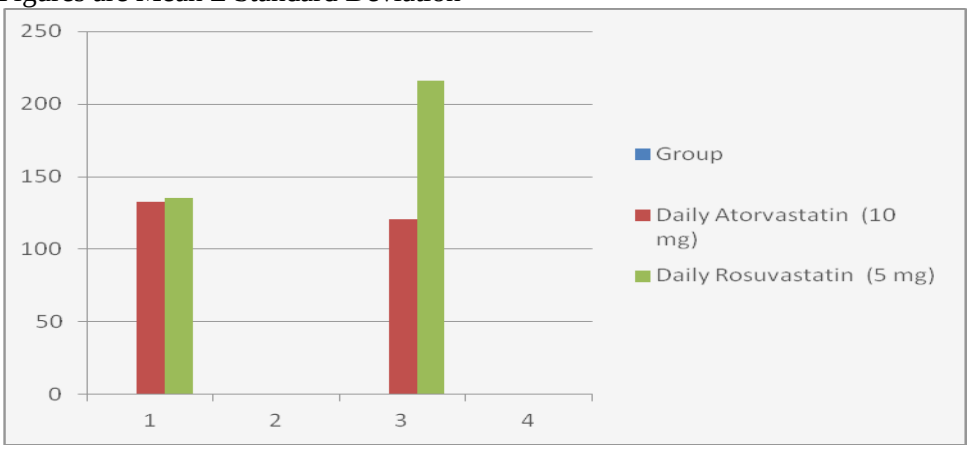


As Table 4 shows, reduction in levels of total cholesterol in rosuvastatin group was significantly higher than in the atorvastatin group (p<0.0001). The percentage reduction in total cholesterol in atorvastatin group at 6 and 12 weeks was 15.71% and 24.85% respectively. In rosuvastatin group the percentage reduction in total cholesterol at 6 and 12 weeks was 22.37% and 30.8% respectively.

TABLE 5: SERUM TRIGLYCERIDES (MG/DL) IN TWO TREATMENT GROUPS.

Group	Daily Atorvastatin (10 mg)	Daily Rosuvastatin (5 mg)	p value
6 weeks	132.57±28.24	135.17±13.21	>0.04
12 weeks	120.40±28.17	216.34±12.81	>0.04

Unpaired t test, Figures are Mean ± Standard Deviation

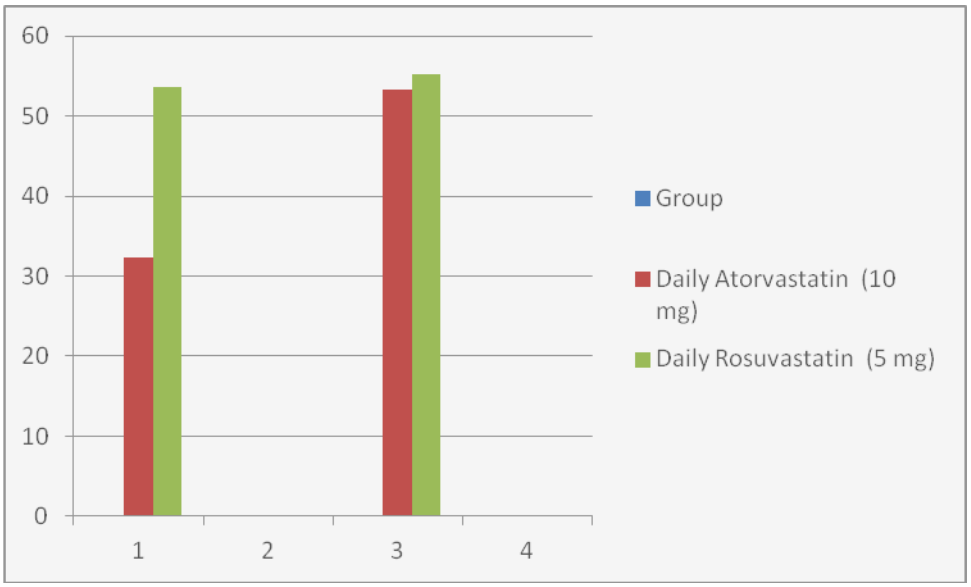


As Table 5 shows, though there was greater reduction in levels of triglycerides in patients treated with rosuvastatin therapy as compared to those treated with atorvastatin, the difference was not statistically significant (p>0.05). The percentage reduction in levels of triglyceride in atorvastatin group at 6 and 12 weeks was 15.72% and 22.92%

respectively. In rosuvastatin group the percentage reduction in triglyceride levels at 6 and 12 weeks was 18.44% and 24.92% respectively.

TABLE 6: CHANGES IN MEAN VALUES OF HDL-C (MG/DL) IN TWO TREATMENT GROUPS.

Group	Daily Atorvastatin (10 mg)	Daily Rosuvastatin (5 mg)	p value
6 weeks	32.35±3.56	53.66±4.26	>0.04
12 weeks	53.23±4.37	55.22±4.43	<0.04



As Table 6 shows, at 6 weeks, the difference between the two therapies was not statistically significant (p>0.05) whereas at 12 weeks, there was significantly more increase in HDL-C levels with rosuvastatin therapy as compared to atorvastatin therapy (p<0.05).

Total 7 patients of atorvastatin group and 9 patients from rosuvastatin group reported mild and self-limiting adverse effects like nausea, headache, bodyache or abdominal pain. There was no statistically significant difference in the incidence of these adverse effects in the two treatment groups (p>0.05). There was no occurrence of any serious adverse event in any patient during this study. During this study no patient from either group showed significant increase in serum CPK, SGOT, SGPT levels at 12 weeks.

In the present study, patients received either atorvastatin (10mg) or rosuvastatin (5mg) as daily therapy. Similar doses had been used in several studies comparing the efficacy and safety of atorvastatin therapy with that of rosuvastatin. In studies such as URANUS, ANDROMEDA, Adsule et al and Barakat et al investigators had used 10mg atorvastatin.19-22 In the LISTEN trial and the trial by Arshad et al 10mg atorvastatin was compared against 5mg rosuvastatin.23,24 Besides, the FDA recommends a starting dose of rosuvastatin 5mg in Asians while the starting dose of atorvastatin is 10mg.

In the present study, at the end of 12 weeks, it was found that there was statistically significant difference between atorvastatin and rosuvastatin therapy in reduction of LDL-C levels. Also, the percentage reduction of LDL-C levels in rosuvastatin group was significantly higher. These findings are consistent with those of ANDROMEDA, URANUS, CORALL and LISTEN trials, all of which were done on diabetic dyslipidemic patients.

In the double blind ANDROMEDA study, the percentage reduction of LDL-C levels from the baseline at 8 weeks in atorvastatin group (10mg) was 39% whereas in rosuvastatin group (10mg) it was 51%.20 In the URANUS study comparing atorvastatin and rosuvastatin, both started at 10mg daily, and the dose titrated up periodically till specific LDL-C goals were achieved, the percentage reduction of LDL-C levels from the baseline in atorvastatin group was 45.5% whereas in rosuvastatin group it was 52.3% at the end of 16 week study.19 Similar results were obtained in the CORALL study where 45.6% and 50.6% were the percent reductions in LDL-C levels in the atorvastatin 20mg and rosuvastatin 10mg group respectively at the end of 12 weeks.27 In these studies, the difference in the percent reductions of LDL-C levels in

atorvastatin and rosuvastatin groups was statistically significant. In the LISTEN trial too, the rosuvastatin group

showed greater percent reductions in LDL-C levels as compared to atorvastatin group considering the overall results at the end of 3, 6 and 12 months.
STELLAR trial comparing rosuvastatin with atorvastatin, simvastatin, and pravastatin, in which non-diabetics were also included, revealed that rosuvastatin produced a significantly greater reduction in LDL-C levels as compared to its competitors. These findings are similar to the one seen in the present study.
However, in the prospective, randomized study by Adsule et al, though the percentage reduction of LDL-C was more in the rosuvastatin group (44.25%) as compared to the atorvastatin group (35.56%), this difference was not statistically significant ($p>0.05$), which may be attributable to the smaller sample size.
In the present study, after 12 weeks, significantly higher number of patients from rosuvastatin group achieved <100mg/dL LDL-C levels (Table 3). A similar finding was seen in CORALL study where 76.5% patients from atorvastatin group and 83.1% patients from rosuvastatin group achieved LDL-C levels <100 mg/dL at the end of 12 weeks.
In the present study, at the end of 12 weeks significantly higher percentage reduction in total cholesterol (TC) was seen in rosuvastatin group. Similar findings had been reported by URANUS trial and CORALL study.
However, the study by Adsule et al, notes that although rosuvastatin caused greater percentage reduction of TC as compared to atorvastatin (30.83% vs 25.75%), there was no statistically significant difference, which may be attributable to the smaller sample size.
The results of our study hence indicate that treatment with rosuvastatin 5mg causes greater reduction in LDL-C and TC and comparable reduction of TG when compared with atorvastatin 10mg therapy. Rosuvastatin therapy also led to greater rise in HDL-C levels at the end of 12 weeks compared to atorvastatin therapy, the inter-group difference being statistically significant. Considering the overall changes to lipid variables, the findings of the present study indicate that a less atherogenic lipid profile was achieved with rosuvastatin. The safety and tolerability elicited by both regimens in present study were consistent with the previous studies.

IV.CONCLUSION

Rosuvastatin 5mg is more efficacious than atorvastatin 10 mg in reducing LDL-C and TC levels and in increasing HDL-C levels and showed a comparable safety profile with atorvastatin 10mg after 12 weeks of therapy in patients of type 2 diabetes mellitus with dyslipidemia. The greater efficacy of rosuvastatin will enable more patients to achieve recommended treatment goals in clinical practice and may provide further reductions in the risk of CVD. However, long-term economic analyses of rosuvastatin are needed to determine its potential as a more cost-effective therapy compared with atorvastatin.

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