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Efficacy and safety of Rosuvastatin versus Atorvastatin in patients with Hypercholestrolemia

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ABSTRACT

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The objective of the study was to measure efficacy and safety of Rosuvastatin-10mg versus Atorvastatin-20mg in patients with Hypercholesterolemia. We conducted a single centre retrospective study, involving 117 hypercholesterolemia patients between age group of 45-80 years. Data of both diabetic and non-diabetic patients with LDL-C: ⩾ 140 - < 250 mg/dl, HDL-C: < 40 - >60 mg/dl, Total Cholesterol: 200-240 mg/dl, Triglyceride: ⩾ 165-⩽ 400 mg/dl and VLDL: <5->40 mg and who were prescribed either Rosuvastatin 10mg or Atorvastatin 20mg were included in the study. A statistically significant reduction in LDL-C, TG, TC and VLDL was seen in both the groups. Similarly a statistically significant increase in HDL-C levels was observed in both the groups. Rosuvastatin showed a statistically significant reduction in TG at week 12 as compared to Atorvastatin. Decrease in LDL-C, TC, TG and VLDL was 22.3%, 16.3%, 30.1% and 31% respectively in Rosuvastatin group while the reduction was 15.5%, 13.7%, 19.2% and 23.4% respectively in Atorvastatin group. Rosuvastatin showed a greater improvement in lipid parameters as compared to Atorvastatin though this difference was not statistically significant. Both treatments were well tolerated with similar incidence of adverse events (Rosuvastatin 10 mg: 6.25% as compared to Atorvastatin 20 mg: 7.55%).Rosuvastatin was more effective than Atorvastatin in reducing LDL-C, Total Cholesterol, Triglyceride and VLDL. It was also better in increasing HDL-C as compared to Atorvastatin. Rosuvastatin therefore seems to be a better alternative from other statins in patients having Hypercholesterolemia.

Keywords: Rosuvastatin, Atorvastatin, Hypercholesterolemia

INTRODUCTION

Hypercholesterolemia is defined as either a low high density lipoprotein (HDL) cholesterol value or elevations in atherogenic lipoprotein particles, including cholesterol, cholesterol esters, and triglycerides. Hyperlipidemia can be caused by primary causes (genetic predisposition) or secondary causes (diet, underlying disease, or medications). Primary Hyperlipidemia is associated with high morbidity and mortality. A defect often occurs in lipid metabolism or transport in primary hyperlipidemia, resulting in reduced LDL receptor activity and accumulation of LDL cholesterol in the plasma, leading to atherogenesis.[1] Diseases such as diabetes mellitus, hypothyroidism, Growth hormone deficiency, Cushing's syndrome, obstructive liver disease, nephrotic syndrome, and alcoholism are all common causes of high cholesterol.[2] Age in Men is ⩾ 45 years and Women is ⩾ 55 years, major risk factor for hypercholesterolemia.[2] This condition is defined by elevated LDL-C, CHOLESTEROL and Triglycerides and decreased level of HDL-C,[1] classified based on Framingham Risk Assessment scale (Table. No 1).

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Table 1: Framingham Risk Assessment Scale

LDL-C	Total cholesterol	HDL-C	Triglyceride	Indication
<100	< 200	< 40	< 150	Optimal
100-129	-	-	-	Near/above optimal
130-159	200-239	-	150-199	Borderline
160-189	> 240	60 >	200-499	High
>190-	-	-	> 500	Very high

To treat the hypercholesterolemic patients, various pharmacological approaches are used, but in last few years statins are used more in comparison with other class of drugs. Atorvastatin, Rosuvastatin, Simvastatin, Lovastatin & fluvastatin are used in this class. The statins share a common mechanism of action: they bind to and inhibit the enzyme HMG-CoA Reductase, the rate-limiting step in cholesterol biosynthesis. The inhibition of HMG-CoA reductase activity results in a drop in intracellular cholesterol production, thus activating primarily hepatic LDL receptors and increasing the clearance of LDL from the bloodstream. Atorvastatin and Rosuvastatin are highly prescribed drugs in hypercholesterolemia.[1] Rosuvastatin is more effective than atorvastatin even after reducing the dose to half.[21] Some studies indicated that rosuvastatin 10mg dose was more effective than atorvastatin 20mg and 40 mg.[20] Major side effects of statins are myalgia, liver enzyme elevation, muscle

breakdown.[1] Hence, in this study efficacy and safety of rosuvastatin 10mg versus atorvastatin 20mg was measured in hypercholesterolemia patients.

MATERIALS AND METHOD

The study was single center, retrospective study to evaluate the safety and efficacy of Rosuvastatin and Atorvastatin in patients of Hypercholesterolemia.

Patients were divided in two groups:

1) Patient receiving rosuvastatin alone, (Code-R)

2) Patient receiving atorvastatin alone, (Code-A)

Table 2: Drug and Intervention

Arm	Assigned Interventions
1. Rosuvastatin	10 mg OD for 12 week
2. Atorvastatin	20 mg OD for 12 week

Study Population

Patient population in study : 100-150

Age eligible for study : 45 Years to 80 Years

Genders eligible for study : Both

Healthy Volunteers : No

Inclusion criteria

1. LDL-C : ⩾140 - <250 mg/dl

2. TG : ⩾165- <400 mg/dl

3. TC : 200 - 240 mg/dl

4. Minimum 12 weeks data must available.

Exclusion criteria

1. History of hypersensitivity to statins

2. Overt proteinuria

3. Pregnant or lactating mothers

4. Diagnosis to have any other endocardial or Metabolic disease other than Type 2 DM

5. Type-1 Diabetes Mellitus

6. History of alcohol consumption > 2 drinks/day or 10 drink per week.

7. Patients having renal disease having serum creatinine > 1.5 mg/dL

8. Documented case of homozygous familial hypercholesterolemia

9. Recent ongoing inter current infection

10. Use of concomitant medication (cyclosporine, systemic Glucocorticoids or Ketoconazole, Erythromycin or Clarithromycin, Glucocorticoids or Verapamil) known to affect the lipid profile or with potency safety concern.

Assessment

To measure the LDL-C, HDL-C, TG, TC and VLDL.

To measure any adverse event reported during treatment.

Data Collection

Data collection was done from case files at Lifecare Hospital, Ahmedabad and recorded in case record form.

The following information was collected for each patient.

I. Demographic profile

II. Any significant past history

III. Concomitant medication

IV. Physical examination

V. Lipid profile at baseline and at 12 weeks.

Statistical Analyses

Data was evaluated using student t- test by using Graph pad 5.04 software.

RESULT AND DISCUSSION

Data of 117 patients was collected in this retrospective study i.e. those who had received rosuvastatin and atorvastatin. There were 64 patients in rosuvastatin group and 53 patients in atorvastatin group.

Table 3: Baseline Demographic Characteristics

	Rosuvastatin 10mg (n= 64)	Atorvastatin 20mg (n= 53)
Age in years Mean ±SD	55.17±6.95	55.79±7.09
Sex		
Male n (%)	48(75%)	36(67.9%)
Female n (%)	16(25%)	17(33.3%)
Type 2 Diabetes n (%)	25(39%)	20(37.7%)
Non Diabetic n (%)	39(60.9%)	33(62.2%)

The baseline demographic characteristics of patients are shown in Table 3. The mean age of patients was similar in both groups (55.17±6.95 and 55.79±7.09) for rosuvastatin and atorvastatin groups respectively. There were 48 male and 16 female in rosuvastatin group as compared to 36 male and 17 female in atorvastatin group. We also included diabetic patients. There were 25 diabetic patients in rosuvastatin group as compared to 20 diabetic patients in atorvastatin group.

Table 4: Summary of Lipid Profile at Baseline and at 12 weeks.

Lipid profile	Rosuvastatin		Atorvastatin	
	Week 0 (n=64) Mean±SD	Week 12 (n=64) Mean±SD	Week 0 (n=53) Mean±SD	Week 12 (n=53) Mean±SD
LDL-C(mg/dl)	165.08±15.8	128.2±11.73*	153.9±10.7	130±11.5*
HDLC(mg/dl)	41.5±8.68	48.9±5.14*	42.9±7.47	48.4±4.68*
TGs(mg/dl)	214.3±35.2	147.7±29.8*	182.5±21.4	157.4±15.2*
TC(mg/dl)	214.03±20	173.1±29.8*#	226.1±21.7	182.6±19.9*
VLDL(mg/dl)	53.4±5.88	36.8±3.82*	49.2±4.60	37.7±3.18*

*p value <0.0001 (at week 12 compared to week 0), paired t-test, # p value <0.05 (at week 12 compared to week 12),unpaired t-test.
LDL= Low Density Lipoprotein, HDL-C= High Density Lipoprotein Cholesterol,
TC= Total Cholesterol, TG= Triglyceride, VLDL= Very Low Density Lipoprotein

Changes from baseline in the various lipid parameters are shown in Table 4, Figure 1 Patients in both the groups showed statistically significant improvement in LDL-C, HDL-C, TGs, TC and VLDL at week 12. A statistically significant reduction in TC level was observed with rosuvastatin as compared to atorvastatin at week 12. Although rosuvastatin showed a better improvement in all other lipid parameter as compared to atorvastatin at week 12, this difference was not statistically significant. The percentage decreased in lipid parameter like LDL-C, TG, TC and VLDL were 22.3%, 30.1%, 16.3% and 31% in patients of rosuvastatin group as compared to 15.5%, 19.2%, 13.7% and 23.4% in atorvastatin group. The increase in HDL-C level was 17.3% in rosuvastatin group as compared to 12.8% in atorvastatin group.

Fig. 1: Percentage change in lipid parameters.

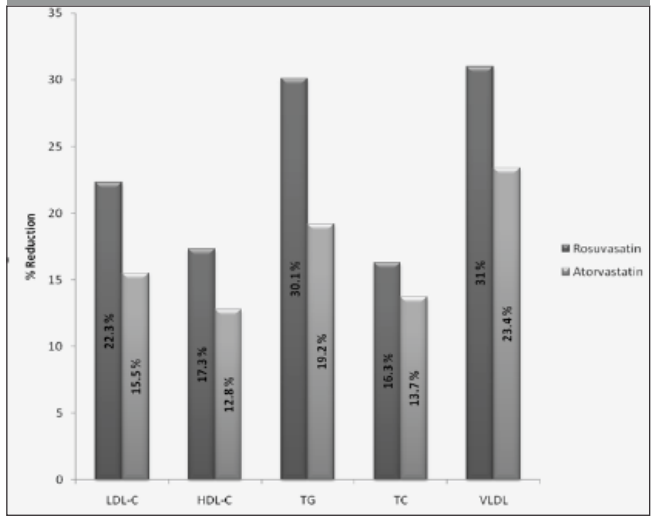

Table 5: Lipid Profile in Male and Female Patients in Rosuvastatin Group

	MALE (n=48) Mean±SD		FE MALE (n=16) Mean±SD	
Weeks	0	12	0	12
LDL-C(mg/dl)	163.5±15.2	127.5±10.9*	169.7±17.2	132.7±13.3*
HDL-C(mg/dl)	41.0±7.96	48.3±4.38*	42.9±10.7	50.8±6.13*
TGs(mg/dl)	210.3±29.2	152.1±30.2*	220.2±48.1	142.7±28.3*
TC(mg/dl)	214.5±19.6	173.3±21.3*	212.5±21.9	172.2±21.8*
VLDL (mg/dl)	53.6±5.77	37.5±3.71*	54.5±4.99	35.7±3.95*

*p value <0.0001 (at week 12 compared to week 0), paired t-test, # p value <0.05 (at week 12 compared to week 12),unpaired t-test.
LDL= Low Density Lipoprotein, HDL-C= High Density Lipoprotein Cholesterol,
TC= Total Cholesterol, TG= Triglyceride, VLDL= Very Low Density Lipoprotein

Changes from baseline in various lipid parameters in male and female of rosuvastatin group are shown in Table No 5 and Figure No 2. In this group, there were 48 male and 16 female. A statistically significant decreased in LDL-C, HDL-C, and TC was seen in both the groups. A statistically significant deceased in TG and VLDL were seen in female as compared to male consuming atorvastatin.

Fig. 2: Percentage change in lipid profile in Male and Female

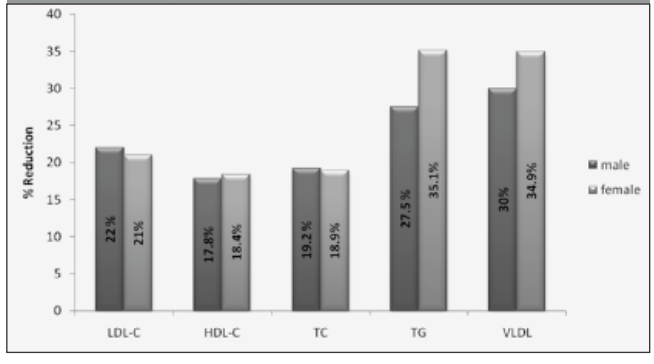

Table 6: Lipid Profile in Male and Female Patients in Atorvastatin group.

	MALE (n=36) Mean±SD		FE MALE (n=17) Mean±SD	
Weeks	**0**	**12**	**0**	**12**
LDL-C (mg/dl)	156.4±9.9	133.4±6.12*	141.1±33.9	120.8±29.1#
HDL-C (mg/dl)	42.4±6.38	47.1±4.16*	41.3±12	47.8±11.5*
TGs(mg/dl)	177±9.68	155.6±11.2*	182.6±25.8	166.4±43.5*
TC(mg/dl)	220.8±9.42	182.6±14.2*	220.7±59.2	166.4±43.5*
VLDL(mg/dl)	49.0±4.56	37.7±3.09*	49.7±4.81	37.8±3.46*

*p value <0.0001 (at week 12 compared to week 0), paired t-test, # p value <0.05 (at week 12 compared to week 12),unpaired t-test.
LDL= Low Density Lipoprotein, HDL-C= High Density Lipoprotein Cholesterol,
TC= Total Cholesterol, TG= Triglyceride, VLDL= Very Low Density Lipoprotein

Changes from baseline in various lipid parameters in males and females of Atorvastatin group are shown in Table 6, Figure 3. In this group, there were 36 male and 17 female. A statistically significant decreased in LDL-C, TG, TC and VLDL was seen in both the groups. Similarly a statistically significant increased HDL-C level was seen in both the groups. A statistically significant decreased in LDL-C was seen in female as compared to male consuming atorvastatin.

Fig. 3: Percentage change in lipid Parameters in Male and Female Patients

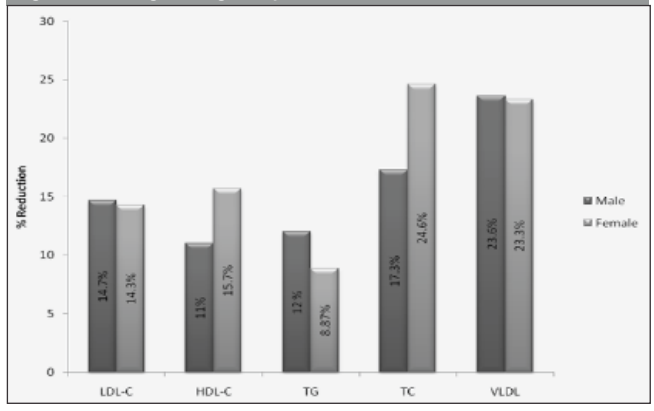

Table 7: Lipid Profile in Diabetic and Non-Diabetic Patients in Rosuvastatin group.

	DM (n=25) Mean±SD		NDM (n=39) Mean±SD	
Weeks	**0**	**12**	**0**	**12**
LDL-C (mg/dl)	160.7±14.2	125.5±12.8*	153±38.4	120.6±31.6*
HDL-C (mg/dl)	42.3±9.64	49.6±5.44*	39.7±11.8	46.6±11.9*
TGs(mg/dl)	209.3±27.3	148.4±29*	207.4±60.3	142±39.2*
TC(mg/dl)	214.1±21.8	167.2±20.6*	201.8±51.6	159.4±41.3*
VLDL(mg/dl)	49.2±12.2	33.9±8.36*	54.4±5.57	37.2±3.11*

*p value <0.0001 (at week 12 compared to week 0), paired t-test, # p value <0.05 (at week 12 compared to week 12),unpaired t-test.
LDL= Low Density Lipoprotein, HDL-C= High Density Lipoprotein Cholesterol,
TC= Total Cholesterol, TG= Triglyceride, VLDL= Very Low Density Lipoprotein

Changes from baseline in various lipid parameters in diabetic and non-diabetic patients of rosuvastatin group are shown in Table 7, Figure 4. In this group, there were 25 diabetic and 39 non-diabetics. Reduction in lipid parameters like LDL-C, TG, TC and VLDL were 21.9%, 29%, 21.9% and 31.1% in diabetic as compared to 21.1%, 31.5%, 21.8% and 36.6% in non-diabetic patients. Whereas increase in HDL-C level was 17.2% in diabetic as compared to 17.3% in non-diabetic patients. Results showed no much difference in LDL-C and HDL-C, but there was more percentage decreased in TC, TG and VLDL in non-diabetic as compared to diabetic patients. This data indicated no statistically significant difference in diabetic patients as compared to non-diabetic patients in rosuvastatin group.

Fig. 4: Percentage change in Lipid Parameters in DM and NDM in Rosuvastatin group

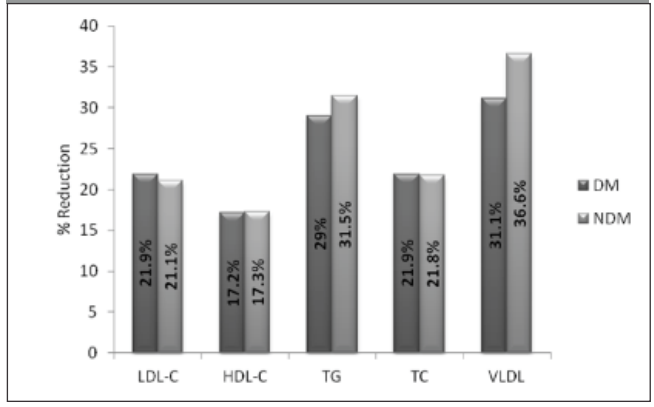

Table 8: Lipid Profile in Diabetic and Non-Diabetic Patients in Atorvastatin group.

	MALE (n=20) Mean±SD		FE MALE (n=33) Mean±SD	
Weeks	**0**	**12**	**0**	**12**
LDL-C (mg/dl)	154.4±11.0	132.1±6.07*	153.6±10.7	130.6±6.99*
HDL-C (mg/dl)	42.0±7.08	48.8±4.97*	43.5±7.5	48.3±4.55*
TGs(mg/dl)	182.5±11.2	159.7±10.7*	182.55±11.2	153.3±17.5*
TC(mg/dl)	226.5±11.2	184.7±21.8*	226.58±26.3	181.7±18.9*
VLDL(mg/dl)	47.3±3.61	36.7±3.11*	50.4±4.77	38.4±3.08*

*p value <0.0001 (at week 12 compared to week 0), paired t-test, # p value <0.05 (at week 12 compared to week 12),unpaired t-test.
LDL= Low Density Lipoprotein, HDL-C= High Density Lipoprotein Cholesterol,
TC= Total Cholesterol, TG= Triglyceride, VLDL= Very Low Density Lipoprotein

Changes from baseline in various lipid parameters in diabetic and non-diabetic of atorvastatin group are shown in Table 8 Figure 5. In this group, there were 20 diabetic and 33 non-diabetics. Reduction in lipid parameter like LDL-C, TG, TC and VLDL were 14.4%, 12.5%, 18.8% and 22.4% in diabetic as compared to 14.8%, 16%, 19.8% and 23.8% in non-diabetic patients. Whereas increased in HDL-C level was 16.2% in diabetic as compared to 11.5% in non-diabetic patients. There were no statistically significant improvements in lipid parameter in these groups of patients. Results showed no much difference in LDL-C, TC and VLDL but there was more percentage increased in HDL-C in diabetic as compared to non-diabetic patients and more increase in TG in diabetic patients as compared to non-diabetic patients

Fig. 5: Percentage change in lipid Parameters in Male and Female Patients

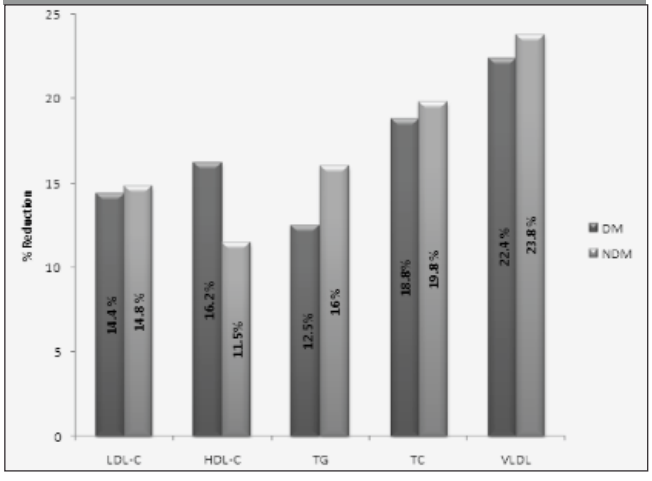

Table 9: Adverse Events

Adverse Effect	Rosuvastatin(N=64)	Atorvastatin(N=53)
Headache	1(1.5%)	1(1.8%)
Nausea	1(1.5%)	1(1.8%)
Myalgia	2(3.1%)	2(3.7%)

Both rosuvastatin and atorvastatin were well tolerated with only a few incidences of mild adverse events. The common adverse events repotted in both group were headache, nausea and myalgia as shown in Table no 9.

CONCLUSION

Rosuvastatin was more effective than atorvastatin in reducing LDL-C, Total Cholesterol, Triglyceride and VLDL. It was also better in increasing HDL-C as compared to atorvastatin. rosuvastatin therefore seems to be a better alternative from other statins in patient having hypercholesterolemia .

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