SHORT REPORT

Comparison of efficiency between Rosuvastatin and Atorvastatin in reducing low-density lipoprotein (LDL-C) in patients with diabetes mellitus

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Abstract

The study was designed to compare Rosuvastatin with Atorvastatin in terms of their efficacy to reduce low-density lipoproteins (LDL-C) in patients with type 2 diabetes mellitus. For this purpose, a cross-sectional analytical study was conducted in the OPD of Nishtar Medical Hospital, Multan, for six months. The study enrolled 66 patients who were consecutively allocated for double-blind therapy with 10mg Atorvastatin (n = 33) and 10mg Rosuvastatin (n = 33) for one month. The doses titration was carried up to four months in certain patients who failed to achieve 1998 European LDL-C level in the first month. A significant number of patients who were given 10mg Rosuvastatin matched the 1998 LDL-C goal in compared to the patients with 10mg dose of atorvastatin at one month (51% vs 46%, $p< 0.0001$) and at four months (94% vs 88%, $p<0.05$). Conclusively, Rosuvastatin was significantly more efficacious than Atorvastatin in its ability to reduce LDL-C.

Keywords: LDL-C, Rosuvastatin, Atorvastatin, T2DM, statins.

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Introduction

Approximately 537M adults worldwide are diagnosed with type 2 diabetes in 2021 and it is predicted that this ratio will increase by 2030 to 243M.[1] Type 2 diabetes patients are at 2-4 times the high risk of developing cardiovascular diseases than non-diabetic people.[2]

Type 2 diabetes patients are at greater risk of CVD due to the clustering of atherogenic risk factors, including abdominal obesity and hypertension.[3] In 1998 and 1999, European Diabetes Policy Group guidelines were issued for diabetic patients to prevent coronary heart diseases among them.[4] According to both these guidelines, the recommended LDL-C level is <54mg/dl (3.0 mmol/L) for diabetic patients. Later in 2003, European CVD prevention guidelines also indicated the risk of type 2 diabetes and suggested that LDL-C must be reduced to <45mg/dl (2.5 mmol/L) in such patients.

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Statins are characterised as the first line therapy for lowering cholesterol levels and a marked reduction in morbidity and mortality rates was observed upon its administration to various populations in trial studies.[5] According to studies, statin therapy has also been shown to deliver significant benefits to the diabetic patients.[6]

Although Statin therapy benefitted the patients in trial treatment, all statins do not have the capablity to modify lipids and enable patients to reach recommended lipid levels.[7,8] Rosuvastatin is more effective than Atorvastatin in lipid-lowering when studied on patients with hypercholesterolaemia;[9] however, the efficacy of the drug has not yet been proved in diabetic patients. Therefore, this study was carried out to study the therapeutic effects of both Rosuvastatin and Atorvastatin on LDL-C, other lipid profile variables, and their potential to attain LDL-C levels in diabetic patients.

Patients, Methods and Results

A cross-sectional analytical study was conducted in the Out-Patient Department of Nishtar Medical Hospital Multan for a period of six months from July 20, 2020 to December 20, 2020. The study included patients older than 18 years, diagnosed with type 2 diabetes since last three months, on oral anti-diabetic medication, and those who had a LDL-C of ≥59.4mg/dl (3.3 mmol/L) in fasting condition at the time of enrollment. Whereas, patients with deranged serum creatinine kinase (CK), had known hypersensitivity to statins, type 1 diabetes, with a body mass index >35 kg/m^2, uncontrolled type 2 diabetes, and those who underwent major cardiac surgery within three months before the beginning of the study were excluded from this study. All the patients included in the study were asked to sign an informed consent. The trial was double-blinded. Patients fulfilling the inclusion criteria were subject to a six-week dietary run-in period and two weeks before the end of this time, all lipid-lowering treatment was stopped. Among these patients the initial 33 were treated with 10mg Rosuvastatin and later 33 were treated with atorvastatin 10 mg for one month. Then dose titration, up to 40mg for Rosuvastatin and up to 40 or 80mg for Atorvastatin, was done for the next three months in patients who did not achieve the 1998 goal in first month of treatment, thus subjecting the patients to the treatment

of four months. The patients who successfully achieved the LDL-C goal after one month, continued the initial treatment.

Baseline change in the LDL-C levels within four months was considered as the primary endpoint. Whereas the following were considered as secondary endpoints: percentage variation in baseline levels of other components of lipid profile including total triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C); the non-HDL-C/HDL-C ratio; the LDL-C/HDL-C ratio; the TC/HDL-C ratio; apo A-I and the apo B/apo A-I ratio; apolipoprotein (apo) at one and four months of treatment; and the number of titrations done up till four months. Blood samples obtained for testing were after eight hours of fasting. A direct method with enzymatic colorimetry was used to measure the LDL-C levels.

SPSS software (version 18) was used for statistical analysis. Analysis of covariance was used to determine the primary and secondary endpoints, where baseline LDL-C acted as a covariate, treatment as a factor, and change in LDL-C levels as response element. Mantel-Haenzel test was used to detect patients acquiring LDL-C goals. All the calculations were two-ways with a 5% significance level.

Table-1: Demographics of Participants of the Two Analysed Groups (n=66).

	Rosuvastatin (n=33)	**Atorvaststin** (n=33)
Gender (men/women)%	18/15 (54.5/45.4)	20/13 (60.6/39.3)
Mean age (years)	64.5±9.9	65.5±9.1
Mean weight (kg)	85.5±15.3	83.0±14.0
Mean BMI, kg/m^2	30.2±4.8	29.4±4.8
Mean initial LDL-C, mg/dl	81±0.84	81±.81
Mean initial HDL-C, mg/dl	23.4±0.28	23.4±0.28
Mean initial TG, mg/dl	36±1.0	36±0.97

Sixty-six patients were randomly selected and their efficacy data were analysed, 33 patients in Rosuvastatin groups while the other 33 were in Atorvastatin groups. Table-1 presents the demographic data for both groups.

Following the titrations till the achievement of goal, Rosuvastatin was found to be significantly more effective than Atorvastatin since LDL-C was reduced by 52% in the Rosuvastatin group while the patients treated with Atorvastatin showed 46% LDL-C reduction (p<0.0001) (Table-2). Additionally, 31 patients out of 33 patients treated with Rosuvastatin was able to reach the LDL-C goal of 1998 European criteria after four months more as compared to patients treated with Atorvastatin (29 patients) (94% against 88%, p< 0.05). The better efficacy of Rosuvastatin was also demonstrated by the limited titrations level required by the patients of this group to reach the LDL-C goal (70 vs 150 in the Atorvastatin group).

Rosuvastatin also greatly reduced other variables in lipid profile more than Atorvastatin after one month of treatment. However, both statins were effective in increasing HDL-C and reducing TG levels (Table-3).

Table-2: Percentage change in Initial Levels of lipid variables at four months upon Titration (n=66).

Variables	**Least-squares mean percentage variation from baseline up till four months**		**Difference (95% Confidence interval)**	***p*-value**
	Rosuvastatin 10–40mg (n=33)	**Atorvastatin 10–80mg** (n=33)		
LDL-C	-51.4	-44.4	-7.0 (-8.7,-4.6)	< 0.0001
TC	-36.5	-32.4	-4.1 (-5.5,-2.2)	< 0.0001
HDL-C	5.5	4.2	1.2 (-1.4,3.9)	>0.05
TG	-20.2	-20.1	-0.1 (-5.7,5.4)	>0.05
Non-HDL-C	-44.0	-38.5	-5.4 (-7.5,-3.6)	< .001
LDL-C/HDL-C ratio	-55.2	-48.0	-7.2 (-9.4,-5.0)	< 0.001
Non HDL-C/HDL-C ratio	-46.2	-39.8	-6.4 (-8.5,-3.8)	< 0.0001
TC/HDL-C ratio	-37.0	-32.2	-4.8 (-7.0,-2.9)	< 0.0001
Apo B	-46.3	-41.3	-5.0 (-7.1,-3.0)	< 0.0001
Apo A-I	2.5	-.1	2.6 (1.1,4.5)	0.024
Apo B/Apo A-I ratio	-45.2	-38.5	-6.7 (-9.0,-4.5)	< 0.0001

Table-3: Percentage variation from initial levels of lipid profile variables at one month (n=66).

Variables	**Least-squares mean percentage variation from baseline at one month**		**Difference (95% Confidence interval)**	***p*-value**
	Rosuvastatin 10–40mg (n=33)	**Atorvastatin 10–80mg** (n=33)		
LDL-C	-46.5	-37.6	-8.9(-10.4,-7.7)	< 0.0001
TC	-34.5	-28.8	-5.7(-7.5,-4.4)	< 0.0001
HDL-C	4.3	2.7	1.6(1.0,-4.5)	NS
TG	-20.3	-16.6	-3.7(-8.5,2.5)	NS
Non-HDL-C	-43.5	-34.0	-9.5(-7.5,-5.5)	< 0.0001
LDL-C/HDL-C ratio	-50.2	-40.3	-9.9(-10.2,-8.0)	< 0.0001
Non HDL-C/HDL-C ratio	-45.5	-37.8	-7.7(-9.9,-7.2)	< 0.0001
TC/HDL-C ratio	-34.9	-30.0	-4.9(-7.0,-5.2)	< 0.0001
Apo B	-43.0	-36.2	-6.8(-8.5,-5.7)	< 0.0001
Apo A-I	2.7	0.7	2.0(0.1,3.3)	0.05
Apo B/Apo A-I ratio	-44.8	-36.5	-8.3(-10.1,-6.5)	< 0.0001

Conclusion

In conclusion, Rosuvastatin proved more beneficial in decreasing LDL-C levels in diabetes type 2 patients and enabled them to achieve European goals, when given fixed-dose and also when followed by dose titrations than Atorvastatin.

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Conflict of Interest: None to declare.

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