International Journal of Pharmacology and Clinical Research
Online ISSN: 2664-7621, Print ISSN: 2664-7613
Received: 12-05-2019, Accepted: 15-06-2019, Published: 03-07-2019
www.pharmacologyjournal.in
Volume 1; Issue 2; 2019; Page No. 09-12

Evaluation of efficacy and safety profile of rosuvastatin, simvastatin and atorvastatin in newly diagnosed type 2 diabetic patients with dyslipidemia

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DOI: https://10.33545/26647613.2019.v1.i2a.24

Abstract

Background: Diabetes mellitus (DM) is one of the major non-communicable diseases with increasing prevalence in both the developed and developing world. The present study was conducted to assess efficacy and safety of Rosuvastatin, Atorvastatin and Pravastatin among dyslipidemic diabetic patients. Atorvastatin documented to be the most potent statin at reducing LDLC levels. Alternatively, pravastatin which is available at the higher doses of 20 mg and 40 mg is found to be slightly less effective; the main reason for its prescription in patients is put down to its hydrophilic properties which make it more tolerable to patients with greater risk factors in addition to CVD. The present study was conducted to assess efficacy and safety of Rosuvastatin, Atorvastatin and Pravastatin among dyslipidemic diabetic patients.

Materials and Methods: The present study comprised of 60 diabetic patients of both genders. All were informed regarding the study and their written consent was obtained.

Data such as name, age, sex, height, weight, and BMI was recorded. Patients were divided into 3 groups of 20 each. Group I received 40 mg Atorvastatin, group II received 10 mg Rosuvastatin and group III received 20 mg Pravastatin. Lifestyle habits like smoking and alcohol intake, type of DM, its duration, and presence of hypertension was recorded. Fasting blood glucose, glycated hemoglobin (HbA1C), total cholesterol, HDL and LDL cholesterol levels, triglycerides, creatine kinase level, serum creatinine, bilirubin, LFTs, GGT, and serum albumin, microalbuminuria and macroalbuminuria was recorded. Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

Result: In Group 'A' the mean difference of Total Cholesterol between baselines versus after 6 months was 84.43 mg/dl, 66.98 mg/dl and 54.29 mg/dl in Group B and Group C respectively. The mean difference of Triglycerides between baselines versus after 6 months was 67.08 mg/dl in Group A, 41.99 mg/dl in Group B and 39.08 mg/dl in Group C. The mean difference of HDL between baselines versus after 6 months was 12.08 mg/dl in Group A, 12.31 mg/dl in Group B and 11.19 mg/dl in Group C. The mean difference of LDL between baseline versus after 6 months was 81.6 mg/dl in Group A, 69.8 mg/dl in Group B and 35.88 mg/dl in Group C. The mean difference of VLDL between baselines versus after 6 months was 15.03 mg/dl in Group A, 9.64 mg/dl in Group B and 9.45 mg/dl in Group C.

Conclusion: The present study confirmed that rosuvastatin therapy in commonly prescribed doses is the most effective statin for low-density lipoprotein cholesterol goal achievement and for improving the lipid profile in hypercholesterolemic diabetic patients with and without MetS.

Keywords: Rosuvastatin, atorvastatin, simvastatin, pravastatin, dyslipidemic diabetic patients

Introduction

Diabetes mellitus (DM) is one of the major noncommunicable diseases with increasing prevalence in both the developed and developing world. Middle East region has seen some of the largest growth in DM in the world [1]. Diabetes is now commonly recognized as a 'coronary heart disease risk equivalent'. This is mainly attributed to the high rates of dyslipidemia among diabetic patients which is believed to be one of the major factors accounting for the high percentage of deaths among diabetics due to cardiovascular disease (CVD) [2]. The differences in the lipid profile between diabetics (especially type 2 diabetics) and nondiabetics account for the increased CVD risk [3]. Essentially, T2DM lipid profiles consist of elevations in triglyceride (TG) levels (>2 mmol/L) and reductions in high-density lipoprotein cholesterol (HDLC). While low-density lipoproteins cholesterol (LDL-C) concentration levels are normal, the particles are denser and smaller in size, which is believed to enhance their atherogenic potential [4].

Atorvastatin documented to be the most potent statin at reducing LDLC levels. Alternatively, pravastatin which is available at the higher doses of 20 mg and 40 mg is found to be slightly less effective; the main reason for its prescription in patients is put down to its hydrophilic properties which make it more tolerable to patients with greater risk factors in addition to CVD [5]. The present study was conducted to assess efficacy and safety of Rosuvastatin, Atorvastatin and Pravastatin among dyslipidemic diabetic patients.

Materials and Methods

The present study comprised of 60 diabetic patients of both genders. All were informed regarding the study and their written consent was obtained.

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Results: The present study was carried out in collaboration with the Department of Medicine, and Department of Pharmacology, Tertiary Care Teaching Hospital. A total 90 patients were enrolled. Patients were randomly divided into three groups of 30 each.

Table 1: Distribution of Age of the subjects

Age in years	Group A	Group B	Group C
30-40	07	07	08
41-50	09	08	08
51-60	09	10	09

In table 1 depicts the age distribution of the subjects in all 3 groups under study. All the three groups consisted of 25 subjects each.

Table 2: Distribution of patients according to Gender

	Group A		Group B		Group C	
	No	Percentage	No	Percentage	No	Percentage
Male	15	60%	14	56.%	16	64%
Female	10	40%	11	44%	09	36%
Total	25	100%	25	100%	25	100%

In Table 2 shows the sex distribution of the subjects in 3 groups under study. Three groups consisted of 25 subjects each. Group A consisted of 15 male and 10 female patients. In Group B patients were 14 Male and female 11. In Group C patients were 16 Male and female 09.

Table 3: Comparison of Mean Lipid profile in three Groups at baseline versus 6 months of treatment by unpaired "t" test

Parameters		Group A Mean ±SD	Group B Mean ±SD	Group C Mean ±SD
Total Cholesterol (mg/dl)	Baseline	306.85±51.59	309.54±50.53	306.85±51.26
	After 6 months	224.49±34.64	244.62±34.64	254.62±35.85
	p-value	<0.0001	<0.0001	<0.0001
Triglycerides (mg/dl)	Baseline	293.25±51.53	286.52±50.51	299.25±51.16
	After 6 months	228.20±43.80	246.54±34.64	258.22±48.80
	p-value	<0.0001	<0.0001	<0.0001
HDL (mg/dl)	Baseline	39.46 ± 6.72	38.29 ± 6.51	38.29 ± 6.59
	After 6 months	49.51 ± 7.71	48.54 ± 7.54	47.41 ± 7.74
	p-value	<0.0001	<0.0001	<0.0001
LDL (mg/dl)	Baseline	211.18 ± 37.11	216.85 ± 36.89	191.85 ± 36.91
	After 6 months	131.79 ± 20.64	149.24 ± 22.65	157.99 ± 20.84
	p-value	<0.0001	<0.0001	<0.0001
VLDL (mg/dl)	Baseline	60.28 ± 11.88	58.53 ± 11.75	60.70 ± 11.88
	After 6 months	47.29 ± 10.41	50.74 ± 8.55	53.29 ± 11.41
	p-value	<0.0001	<0.0001	<0.0001

P value < 0.05 is significant & P value > 0.05 is not significant

Table 4: Overview of Mean Differences between Baseline Vs after 6 months of the Therapy

Parameters	Group A	Group B	Group C
Total Cholesterol	84.43	66.98	54.29
Triglycerides	67.08	41.99	39.08
HDL	12.08	12.31	11.19
LDL	81.6	69.8	35.88
VLDL	15.03	9.64	9.45

In Group 'A' the mean difference of Total Cholesterol between baselines versus after 6 months was 84.43 mg/dl, 66.98 mg/dl and 54.29 mg/dl in Group B and Group C respectively. The mean difference of Triglycerides between baselines versus after 6 months was 67.08 mg/dl in Group A, 41.99 mg/dl in Group B and 39.08 mg/dl in Group C. The mean difference of HDL between baselines versus after 6 months was 12.08 mg/dl in Group A, 12.31 mg/dl in Group B and 11.19 mg/dl in Group C. The mean difference of LDL between baseline versus after 6 months was 81.6 mg/dl in Group A, 69.8 mg/dl in Group B and 35.88 mg/dl in Group C. The mean difference of VLDL between baselines versus after 6 months was 15.03 mg/dl in Group A, 9.64 mg/dl in Group B and 9.45 mg/dl in Group C.

Discussion

The State of Qatar in the Middle East region is predicted to have one of the highest prevalences of T2DM in the world. However, data are lacking regarding the efficacy and safety of the 4 most commonly prescribed statins (rosuvastatin, atorvastatin, pravastatin, and simvastatin) for managing dyslipidemia among diabetic patients [6]. In the current study, rosuvastatin was found to be the most effective statin at reducing LDL-C when compared with atorvastatin and simvastatin. The findings of this study are consistent with the previous reported studies in that rosuvastatin at its lowest dose in this study (10 mg) was more effective in reducing LDL-C levels than atorvastatin and pravastatin at their highest doses (40 mg). Indeed, it should be noted that

rosuvastatin, which is the latest statin to receive approved labeling by the Food and Drug Administration, has been consistently found to be the most effective at reducing LDL-C levels in the most recent studies comparing its efficacy with other statins [7].

The Stellar trial, Mercury trial, and Pulsar are the major open-label, randomized, multicenter trials to compare rosuvastatin (10, 20, 40, or 80 mg) with atorvastatin (10, 20, 40, or 80 mg), pravastatin (10, 20, or 40 mg), and simvastatin (10, 20, 40, or 80 mg) across dose ranges for reduction of LDL-C.15 The results of the Stellar trial revealed that rosuvastatin was consistently, across all doses, the most effective at reducing LDL-C levels in comparison to all of the other statins. The Mercury and Stellar studies reported that rosuvastatin therapy is effective in achieving LDL-C goal and in improving the lipid profile in hypercholesterolemic and high-risk diabetic patients. This is consistent with the current study performed in Qatar.

Despite the proven benefits of LDL-C reduction, lipid management is suboptimal and many patients fail to achieve recommended LDL-C goals [8]. Perhaps the most likely reason for this is the use of agents with a poor efficacy for LDL-C lowering and suboptimal dose titration. The most effective statin at the lowest dose would represent a simple, effective treatment strategy, enabling more patients to achieve goals without the need for dose titration. 19 The effective statin at the lowest dose in current study is consistent with the previous reported studies [9].

It has been reported by several studies that the lowering of TG is another important goal in reducing CVD risk among diabetic patients. In the current study, the greatest reduction in TG was -20.6% and was achieved by patients taking rosuvastatin. However, it is important to note that atorvastatin both achieved the second highest reduction in TG among those with and without MetS. These findings are similar to the majority of studies in the literature, which have shown a slightly higher reduction in TG in patients taking rosuvastatin in comparison with atorvastatin [10]. It thus appears that in relation to this factor (TG) that both rosuvastatin and atorvastatin are effective at reducing TG.

Additionally, in most cases raising HDL-C levels is another major factor known to reduce CVD risk as reported by some studies. In the current study, all the statins appear to have reduced rather than raised HDL-C levels. Rosuvastatin had the least reduction of and would thus be regarded as the most effective; however, none of the values for the statins were significant. The current study is consistent with the previous studies and trials such as the Mercury trial,7,19 Stellar trial, 13, 15, 18 and Pulsar,19 which investigated starting doses of rosuvastatin and atorvastatin and found that the increase in HDL-C was significantly greater statistically with low dosage rosuvastatin than with high dose of atorvastatin.

Furthermore, more recently, the Voyager Database study11 investigated the effects of different statins on HDL-C levels, relationships between changes in HDL-C and changes in LDL-C, and meta-analysis of 32 258 dyslipidemic patients included in 37 randomized studies using rosuvastatin, atorvastatin, and simvastatin. The HDL-C raising ability of rosuvastatin and simvastatin was comparable, with both being superior to atorvastatin. Increases in HDL-C were positively related to statin dose with rosuvastatin and simvastatin but inversely related to dose with atorvastatin. The analysis also revealed that the HDL-C raising achieved by all 3 statins was totally independent of the reduction in LDL-C. And finally, it has been found that baseline concentrations of HDL-C and plasma TG and the presence of diabetes are robust, independent predictors of statin-induced elevations of HDL-C [11].

More recently, various studies reported that patients with MetS had greater reductions in TG and somewhat greater percentage increases in HDL-C with statin treatment, as expected. The comparisons between statin treatment groups showed consistent advantages of rosuvastatin treatment, compared with atorvastatin, simvastatin, and pravastatin, in LDL-C goal achievement and in LDL-C, total cholesterol, and non-HDL-C reduction. As in the main study analysis, rosuvastatin 10 mg provided benefits comparable to a higher dose of atorvastatin in the MetS population. It is worth noting that a pharmacoeconomic analysis of the primary MERCURY results showed that treatment with rosuvastatin 10 mg was more cost-effective compared with equivalent or higher doses of atorvastatin, simvastatin, and pravastatin, and that switching patients from a comparator statin to rosuvastatin improved LDL-C goal attainment at relatively little additional cost, with equivalent (or lower) associated drug costs. Thus, rosuvastatin may have pharmacoeconomic advantages, compared with atorvastatin, while providing comparable efficacy.

Finally, rosuvastatin at a low dose has demonstrated high efficacy for LDL-C lowering, enabling patients with hypercholesterolemia to achieve their lipid goals.13,18 In addition, rosuvastatin has beneficial effects on other components of the lipid profile, including HDL-C,13,24-27 which is a major, independent risk factor for CVD [12]. Safety data from several large-scale clinical and pharmacoepidemiologic studies have shown that the safety of rosuvastatin and results from the current recent study also support these findings [13-23].

Conclusion

The present study confirmed that rosuvastatin therapy in commonly prescribed doses is the most effective statin for LDL-C goal achievement and for improving the lipid profile in hypercholesterolemic diabetic patients with and without MetS.

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