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ORIGINAL RESEARCH

ASSESSMENT OF EFFICACY AND SAFETY OF ROSUVASTATIN, ATORVASTATIN AND PRAVASTATIN AMONG DYSLIPIDEMIC DIABETIC PATIENTS

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ABSTRACT

Background: Diabetes mellitus (DM) is one of the major noncommunicable 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.

Materials & Methods: 60 diabetic patients of both genders 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.

Results: Out of 60 patients, males were 35 and females were 25. BMI group was <25 kg/m2 in 3, 4 and 4, 25–30 kg/m2 in 5, 6 and 3 and ≥30 kg/m2 in 12, 10 and 13. Smoking was seen in 3, 4 and 3. Alcoholism was seen in 2, 1 and 3 in group I, II and III respectively. The difference was significant (P< 0.05). % reduction LDL was -18.3, -29.2 and -10.7, % reduction TG was -21.5, -25.5 and -12.6, % reduction total cholesterol was -16.4, -22.2 and -15.1 and % increase HDL was -7.12, -6.3 and -5.9 in group I, II and III respectively. Statins appear to be safe in relation to hepatic and muscular functions. A slightly adverse effect of statins on renal function was found due to the new onset of microalbuminuria among some of the patients; nonetheless no case of microalbuminuria progressed to the more dangerous macroalbuminuria.

Conclusion: Rosuvastatin was the most effective statin at reducing LDL-C, triglycerides, and total cholesterol. All the 3 statins are found to be safe drugs to use for dyslipidemic diabetic patients.

Key words: Atorvastatin, Diabetes mellitus, Rosuvastatin

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I. 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.

II. MATERIALS & 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.

III. RESULTS

Table I Distribution of patients

Total- 60		
Gender	**Males**	**Females**
Number	35	25

Table I shows that out of 60 patients, males were 35 and females were 25.

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Table II Comparison of parameters

Parameters	Variables	Group I	Group II	Group III	P value
BMI group	<25 kg/m2	3	4	4	0.91
	25–30 kg/m2	5	6	3	0.81
	≥30 kg/m2	12	10	13	0.97
Smoking	Yes	3	4	3	0.12
	No	17	16	17	
Alcoholism	Yes	2	1	3	0.05
	No	18	19	17	

Table II shows that BMI group was <25 kg/m2 in 3, 4 and 4, 25–30 kg/m2 in 5, 6 and 3 and ≥30 kg/m2 in 12, 10 and 13. Smoking was seen in 3, 4 and 3. Alcoholism was seen in 2, 1 and 3 in group I, II and III respectively. The difference was significant (P< 0.05).

Graph I Comparison of parameters

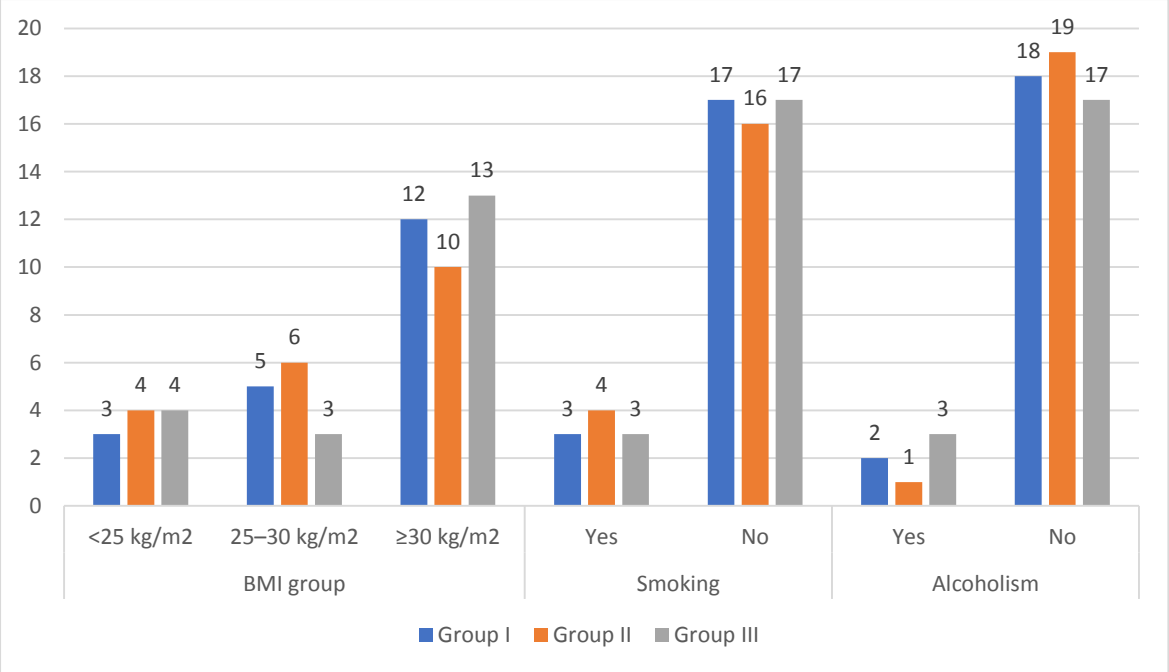

Table III Efficacy of statins

Variables	Group I	Group II	Group III	P value
% reduction LDL	-18.3	-29.2	-10.7	0.03
% reduction TG	-21.5	-25.5	-12.6	0.05
% reduction TC	-16.4	-22.2	-15.1	0.02
% increase HDL	-7.12	-6.3	-5.9	0.17

Table III shows that % reduction LDL was -18.3, -29.2 and -10.7, % reduction TG was -21.5, -25.5 and -12.6, % reduction total cholesterol was -16.4, -22.2 and -15.1 and % increase HDL was -7.12, -6.3 and -5.9 in group I, II and III respectively.

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Table IV: Safety comparison on hepatic, renal, and muscular functions: adverse events after 2 years of statin use.

Variables	40 mg Atorvastatin (n=20)	10 mg Rosuvastatin (n=20)	20 mg Pravastatin (n=20)
Hepatic function ALT > 3 × ULN	0	0	0
Renal function			
Normal (eGFR ≥ 90 mL/min/1.73 m^2)	15 (75.0)	16 (80.0)	15 (75.0)
Mild (eGFR 60–89 mL/min/1.73 m^2)	4 (20.0)	3 (15.0)	5 (25.0)
Moderate (eGFR 30–59 mL/min/1.73 m^2)	1 (5.0)	1 (5.0)	0 (10.0)
Severe (eGFR 15–29 mL/min/1.73 m^2)	0	0	0
Kidney failure (eGFR < 15 mL/min/1.73 m^2)	0	0	0
Microalbuminuria			
At baseline without ACE inhibitors and/or ARBs	1 (5.0)	0 (0.0)	0
At 2 years after without ACE inhibitors and/or ARBs	1 (5.0)	1 (5.0)	1 (5.0)
At baseline with ACE inhibitors and/or ARBs	3 (15.0)	2 (10.0)	4 (20.0)
At 2 years after with ACE inhibitors and/or ARBs	3 (15.0)	20 (40.0)	4 (20.0)
Macroalbuminuria	0	0	0
CK level >10 × ULN	0	0	0

Table IV showed the safety profile of each of the statins at their various doses among patients. Statins appear to be safe in relation to hepatic and muscular functions. A slightly adverse effect of statins on renal function was found due to the new onset of microalbuminuria among some of the patients; nonetheless no case of microalbuminuria progressed to the more dangerous macroalbuminuria.

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IV. DISCUSSION

Statins are considered the first line pharmacological treatment of dyslipidemia in diabetic patients. However, various studies reported randomized trials among various ethnicities have documented that rosuvastatin is the most effective statin at reducing LDL-C, TGs, and at raising HDL-C levels.[6] Although, previously atorvastatin was considered best potent in reducing LDL-C before the approval of rosuvastatin.[7,8] The present study was conducted to assess efficacy and safety of Rosuvastatin, Atorvastatin and Pravastatin among dyslipidemic diabetic patients.

We found that out of 60 patients, males were 35 and females were 25. Bener et al[9] determined efficacy safety and the cost effectiveness, of the four most commonly prescribed statins (rosuvastatin, atorvastatin, pravastatin, and simvastatin) in the treatment of dyslipidemia among diabetic patients. The study included 1,542 consecutive diabetes patients above 18 years of age diagnosed with dyslipidemia and prescribed any of the indicated statins. The effective reductions in total cholesterol using rosuvastatin with atorvastatin, simvastatin, and pravastatin in achieving cholesterol goals and improving plasma lipids in dyslipidemic diabetic patients were measured. Serum lipid levels measured a 1 week before the treatment and at the end 2 nd year. Rosuvastatin (10 mg) was the most effective in reducing low-density lipoprotein cholesterol (LDL-C; 28.59%), followed by simvastatin 20 mg (16.7%), atorvastatin 20 mg (15.9%), and pravastatin 20 mg (11.59.3%). All statins were safe with respect to muscular and hepatic functions. Atorvastatin was the safest statin as it resulted in the least number of patients with microalbuminuria (10.92%) as compared to other statins. Treatment with rosuvastatin 10 mg was more effective in allowing patients to reach European and Adult Treatment Plan (ATP) III LDL-C goals as compared to other statins ($P < 0.0001$) and produced greater reductions in LDL-C, total cholesterol, and non-HDL-C, produced similar or greater reductions in triglycerides (TGs) and increased in HDL-C.

We found that BMI group was <25 kg/m2 in 3, 4 and 4, 25–30 kg/m2 in 5, 6 and 3 and ≥30 kg/m2 in 12, 10 and 13. Smoking was seen in 3, 4 and 3. Alcoholism was seen in 2, 1 and 3 in group I, II and III respectively. Barakat et al[10] investigated the efficacy and the safety of the three most commonly prescribed statins (rosuvastatin, atorvastatin, and pravastatin) for managing dyslipidemia among 350 diabetic patients. Rosuvastatin (10 mg) was the most effective at reducing LDL-C (29.03%). Atorvastatin reduced LDL-C the most at a dose of 40 mg (22.8%), and pravastatin reduced LDL-C the most at a dose of 20 mg (20.3%). All three statins were safe in relation to muscular and hepatic functions. In relation to renal function, atorvastatin was the safest statin as it resulted in the least number of patients at the end of 2 years of treatment with the new onset of microalbuminuria (10.9%) followed by rosuvastatin (14.3%) and then pravastatin (26.6%).

We found that % reduction LDL was -18.3, -29.2 and -10.7, % reduction TG was -21.5, -25.5 and -12.6, % reduction total cholesterol was -16.4, -22.2 and -15.1 and % increase HDL was -7.12, -6.3 and -5.9 in group I, II and III respectively. Barter et al[11] 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

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related to dose with atorvastatin. The analysis also revealed that the HDL-C raising achieved by all three 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.

In the present study, the three statins did not significantly affect the serum creatinine and GFR after 2 years and proven to be relatively safe for patients with microalbuminuria at baseline, as the number of those whose microalbuminuria increased was very minimal. The literature relating to the effect of statins on microalbuminuria is somewhat controversial. While some statin trials have reported a reduction in proteinuria [12] or no effect [13], some of the literature supports the findings in the current study that statins do have negative effects relating to the onset of proteinuria.[14]

The limitation the study is small sample size.

V. CONCLUSION

Authors found that Rosuvastatin was the most effective statin at reducing LDL-C, triglycerides, and total cholesterol. All the 3 statins are found to be safe drugs to use for dyslipidemic diabetic patients.

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