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Clinical Efficacy Study of Atorvastatin, Simvastatin and Pravastatin in Hyperlipidemic Patients

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ABSTRACT

This study was undertaken to evaluate the effective role of atorvastatin, simvastatin and pravastatin in hyperlipidemia patients. In this prospective study, study population contained 60 subjects (32 men and 28 women, mean age of 45.9 ± 8.4) with hyperlipidemia. Twenty patients were selected in each group who was taking atorvastatin 10 mg, simvastatin 10 mg and pravastatin 10 mg according to the inclusion and exclusion criteria. The demographic profiles, clinical data, therapies and other information needed for the study were collected by using individually designed data entry form and questionnaire. Lipid profile and cardiac markers were screened 3 months and 5 months after statin therapy. Results of our study indicate the percentage reduction in LDL-C levels was more in atorvastatin 36.0%. While in simvastatin it was 21.1% and pravastatin 24.8%. The percentage reduction in TC and VLDL–C are found to be more in atorvastatin itself. The percentage elevation in HDL–C was also found to be more in atorvastatin 38.4%. Atorvastatin therapy also effectively reduces the level of CK and CK-MB. Atorvastatin can be more effective in reducing hyperlipidemia compared to the simvastatin and pravastatin and thus further reduce the risk of cardiovascular disease in such patients.

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INTRODUCTION

Hyperlipidemia is a disorder of lipoprotein metabolism, which includes a number of abnormalities such as hypercholesterolemia and hypertriglyceridemia. It is one of the major risk factors associated with atherosclerosis and atherosclerosis induced - conditions, such as coronary heart disease, ischaemic cerebrovascular disease and peripheral vascular disease. World Health Organization (WHO) has reported that approximately 60% of Indians will be affected by cardiovascular diseases by 2020[1]. The Coronary heart disease (CHD) incidences are correlated with elevated levels of low-density lipoproteins (LDL) cholesterol and triacylglycerols and with low levels of high-density lipoproteins (HDL) cholesterol[2].

Risks factors for dyslipidemia are smoking, alcohol intake, hypertension (BP> 140/90), diabetes mellitus; family history of premature coronary heart disease (CHD). The global burden of disease study has estimated that cardiovascular disorder was currently the second leading worldwide cause of disability-adjusted life year. The major emphasis of dyslipidemia management was focused on the reduction of LDL-C levels. Understanding the pathophysiology of dyslipidemia has led to the evolvement of effective treatment strategies [3, 4].

Currently, five major classes of medications have been reported to treat people with detrimental lipid levels that include statins, nicotinic acid derivatives, fibric acid derivatives, bile acid binding resins and cholesterol absorption inhibitors[5]. Among these statins are first line therapies for lowering lipid levels. Statins are a class of drug used to lower cholesterol levels by inhibiting the enzyme HMG-CoA reductase, which plays a central role in the production of cholesterol in the liver. Increased cholesterol levels have been associated with cardiovascular diseases (CVD), and therefore statins exert their beneficial effects primarily by reducing the level of LDL cholesterol[6], and the reductions in the relative risk of cardiovascular events achieved by statins therapy appear to be similar regardless of baseline cholesterol levels[7, 8, 9].

There are multiple statins are available in the market like atorvastatin, simvastatin, pravastatin, pitvastatin, fluvastatin, cerivastatin and rosuvastatin. Indications of statins have been greatly extended over the last five years subsequent to publication of many multicenter prospective trails[10]. Efficacy and safety of different statins in the hyperlipidemia patients differs considerably. These are the things made our interest towards the statins study. So in this present

study, we have evaluated the comparative efficacy of atorvastatin, simvastatin and pravastatin in hyperlipidemia patients.

MATERIALS AND METHODS

Study design

The study population consists of 60 patients (32 men and 28 women) had evidence of hyperlipidemia. Twenty patients were selected in each group who was taking atorvastatin 10 mg, simvastatin 10 mg and pravastatin 10 mg according to the inclusion and exclusion criteria. The inclusion criteria for the study were described as; patients who had total cholesterol level of >220 mg/dl or triglycerides concentration >200 mg/ dl, or receiving lipid lowering statin drugs like atorvastatin, simvastatin and pravastatin. Our exclusion criteria were; having a lipid lowering drug therapy for last two months, primary hypothyroidism, nephritic syndrome, type 1 or uncontrolled type 2 diabetes mellitus; hepatic dysfunction, serum creatine phosphokinase levels > 3 times the upper limit of normal, uncontrolled hypertension, myocardial infarction, coronary angioplasty, coronary artery bypass graft, or severe or unstable angina pectoris within the 3 months before the study, known hypersensitivity to HMG-CoA reductase inhibitors or significant that the investigator believed could compromise the patient's safety or successful participation in the study. Medications known to affect lipid levels; interact with study medication, or affect clinical laboratory parameters were not allowed during the study[11].

The study protocol was approved by Institutional Ethical Committee of Vivekananda Medical Care Hospital, Namakkal, Tamilnadu, India and all patients signed written informed consent.

Blood sample collection

Blood samples were collected by venous puncture in heparinized tubes and the plasma was separated by centrifugation at 1000g for 15 min.

Biochemical evaluation

Fasting blood samples are obtained from patients, fasting concentration of the Lipid Profile – low density lipoprotein (LDL-C), very low density lipoprotein (VLDL-C), total cholesterol (TC), high density lipoprotein (HDL-C) and triglycerides (TG) were analyzed at the beginning, at the

third month and fifth month of the therapy. Cardiac Markers creatine kinase (CK), creatine kinase-MB (CK –MB) are measured after 5th month of the initial treatment. The lipid profile and the cardiac markers levels were measured by Roche- Cobas C11 autoanalyser by using standard laboratory diagnostic trading kits.

Statistical analysis

The data were represented as mean ± SD. Results were analyzed statistically by one way ANOVA followed by post hoc Dunnett's test and unpaired t-test by using SPSS V.17 statistical package. The statistical difference was considered significant when $P < 0.05$.

RESULTS

The Demographic characteristics of hyperlipidemia subjects are shown in Table1. The mean age limit was 45.9 ± 8.4 and the mean body mass index was 28.22 ± 1.9 in hyperlipidemia patients. Mean systolic blood pressure was 130 ± 10 and Diastolic blood pressure was 93 ± 5.

Table 1. Demographic characteristics of Hyperlipidemia study subjects.

Demographic characteristics	Hyperlipidemia patients
Age Range (Years)	30 to 60
Age (Mean ± SD) years	45.9 ± 8.4
Body mass index (Mean ± SD), kg/m^2	28.22 ± 1.9
Systolic blood pressure (mm of Hg)	130 ± 10
Diastolic blood pressure (mm of Hg)	93 ± 5

Effects of statins on Lipid and Lipoprotein cholesterols

It has been seen that the LDL cholesterol, VLDL cholesterol, total cholesterol and triglyceride levels got significant decreased at the third and fifth month consistently after the statins therapy in hyperlipidemic patients. Atorvastatin 10 mg produces greater reduction in LDL cholesterol 36% than simvastatin 10 mg (21.1%) and pravastatin 10 mg (24.8%); VLDL cholesterol (46.0%) than simvastatin (38.2%) and pravastatin (35.1%); total cholesterol (28.0%) than simvastatin (20.6%)and pravastatin (22.0%); TG (46.1%) than simvastatin (38.2%) and pravastatin (35.2%)

after 5 months treatment. Atorvastatin 10 mg also produces greater increases in HDL cholesterol 38.4% than simvastatin (13.0%) and pravastatin (16.0%). (Table 2 and 3)

Table 2. Mean (± SD) Lipid and Lipoprotein cholesterol changes in Hyperlipidemia study subjects.

Parameters [mg/dl]	Atorvastatin -10mg			Simvastatin-10mg			Pravastatin-10mg		
	Baseline	After 3rd month	After 5th month	Baseline	After 3rd month	After 5th month	Baseline	After 3rd month	After 5th month
LDL Cholesterol	161.6 ±22.99	112.9 ±22.80 **	103.5 ±18.7 **	176.2±22.9	156.1±20.2 **	139.0 ±14.4 **	183.1 ±17.0	172.1 ±25.4 **	137.7±13.0 **
VLDL Cholesterol	56.1±8.90	32.1±5.32**	30.3±2.38**	55.5±6.60	37.5±7.0**	34.3±6.7**	57.2±6.0	46.5±4.9**	37.1±3.2**
HDL Cholesterol	34.6±3.63	45.2±7.31 **	47.9±7.96 **	31.5±3.9	35.6±3.6 **	35.6±4.1 **	31.3±9.5	35.4±3.2 **	36.3±6.5 **
Total Cholesterol	252.3±27.6	190.3±20.0 **	181.6±16.3 **	263.2±29.3	227.3±20.6 **	209.0±13.7 **	271.7±18.0	242.9±23.3 **	211.9±9.5 **
Triglyceride	280.5±44.5	160.7±26.6 **	151.3±11.9 **	277.8±33.0	187.5±35.4 **	171.8±33.9 **	286.4±30.2	232.5±24.7 **	185.5±16.4 **

Table 3. Mean Percentage changes in Lipid and Lipoprotein concentrations consistently.

Parameters [mg/dl]	Atorvastatin -10mg		Simvastatin-10mg		Pravastatin-10mg	
	After 3rd month	After 5th month	After 3rd month	After 5th month	After 3rd month	After 5th month
LDL Cholesterol	30.2	36.0	11.4	21.1	6.0	24.8
VLDL Cholesterol	42.7	46.0	32.4	38.2	18.7	35.1
HDL Cholesterol	30.6	38.4	13.0	13.0	13.1	16.0
Total Cholesterol	24.6	28.0	13.6	20.6	10.6	22.0
Triglyceride	42.7	46.1	32.5	38.2	18.8	35.2

Table 4. Mean (± SD) changes of cardiac markers in Hyperlipidemia study subjects.

Markers (IU/L)	Atorvastatin -10mg			Simvastatin-10mg			Pravastatin-10mg		
	Baseline	After 5th month	% reduction	Baseline	After 5th month	% reduction	Baseline	After 5th month	% reduction
CK	133.1 ±22.5	80.5 ±41.4	39.5	141.8 ±55.34	111.6 ±33.8	21.3	177.0 ±50.8	145.4 ±55.33	17.9
CK-MB	36.5 ±2.1	22.4 ±7.3	39.6	32.6 ±1.3	22.3 ±4.0	31.6	34.9 ±4.9	23.2 ±3.5	33.5

Effects of statins on cardiac markers

Table 4 shows that percentage reduction of cardiac markers CK and CK-MB was higher 39.5 % and 39.6% respectively in atorvastatin than the simvastatin (21.3% & 31.6%) and pravastatin (17.9% & 33.5%) after 5 months treatment in hyperlipidemia patients.

DISCUSSION

Hyperlipidemia is a critical condition characterized by elevated serum LDL-C levels and low level of HDL-C in the body that ultimately lead to the development and progression of various CVDs. Presently, ischemic cardiovascular and cerebrovascular events are leading cause of morbidity and mortality[12,13,14]. The efficacy and safety of various HMG-CoA reductase inhibitors differ considerably. In this present study, we have investigated the effect of atorvastatin, simvastatin and pravastatin in hyperlipidemia patients. The study included 60 patients diagnosed as hyperlipidemia. Among the 60 hyperlipidemic patients, males accounted for 53.3% and females 46.7% most of the patients were in the age group of 30-60 years.

In this study, we are included hyperlipidemic patients who are taking dose of atorvastatin 10mg, simvastatin 10mg and pravastatin 10mg. Lipid profile and cardiac markers were analyzed in all the cases. The effect of atorvastatin, simvastatin and pravastatin therapy on lipid profile of the patients examined post 3 months and 5 months of treatment. Our study revealed that the atorvastatin 10mg showed greater percentage of reduction in LDL-C (30.2 %) than simvastatin 10mg (11.4%) and pravastatin 10mg (6%) after three months of therapy. After five months of treatment atorvastatin 10mg also showed greater reduction in LDL-C (36.0%) than simvastatin (21.1%) and pravastatin (24.8%).

In VLDL profile atorvastatin 10mg showed greater reduction (42.7%) than simvastatin 10mg (32.4%) and pravastatin 10mg (18.7%) after three months of treatment. After five months treatment atorvastatin 10 mg also showed greater reduction in VLDL (46.0%) than simvastatin 10mg (38.2%) and pravastatin 20mg (35.1%). Apart from that atorvastatin 10mg also showed greater reduction in total cholesterol profile and triglycerides level than simvastatin 10mg and pravastatin 10mg after three months as well as fifth of the treatment.

In HDL-C profile atorvastatin 10mg showed greater elevation (30.6%) than simvastatin 10mg (13.0%) and pravastatin 10mg (13.1%) after 3 months of therapy. After five month atorvastatin 10 mg showed greater consistent elevation in HDL-C (38.4%) than simvastatin 10 mg (13.0%) and pravastatin 20mg (16.0%).

Wierzbicki *et al*. reported that treatment of hyperlipidemia with statins has become an integral part of the management of vascular diseases. Statins efficaciously decrease plasma levels of apoB containing lipoprotein, primarily LDL, VLDL, and VLDL remnants. In addition, statins induce minor increase in the HDL-C levels (by 5% - 10%). Statins (HMG-CoA reductase inhibitor's) efficacy in hyperlipidemia is measured by its ability to lower lipid profile (LDL-C, VLDL- C and TG) and significant increases in HDL-C [16, 17]. Among these three statins treatment in hyperlipidemia with atorvastatin showed greater reduction in LDL-C, total cholesterol and triglycerides than simvastatin and pravastatin. Our study consistent with the study carried out by Jones *et al*. and Wierzbicki *et al*. Atorvastatin also markedly reduce the level of CK and CK-MB isoenzymes than the simvastatin and pravastatin, which are considered as efficient markers of CVDs.

CONCLUSION

It might be concluded that atorvastatin 10 mg can be more effectively reduces the LDL-C, VLDL-C, TC, TG, and increases the HDL-C in patients with hyperlipidemia than simvastatin 10 mg and pravastatin 10 mg. and thus further reduces the risk of cardiovascular diseases in hyperlipidemic patients.

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