ORIGINAL ARTICLE

A Randomized, Open Label, Comparative, Prospective Study Evaluating Efficacy, Safety and Compliance of Rosuvastatin Versus Atorvastatin in Overweight and Obese Dyslipidemic Patients

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Abstract

The present study was conducted to study the efficacy and safety of rosuvastatin and atorvastatin in dyslipidemic patients. It was demonstrated that rosuvastatin 10 mg and atorvastatin 10 mg produced a significant decrease from their respective baseline value of TC, LDL-C, TG, VLDL-C, LDL/HDL ratio and a dose dependent significant increase from their baseline value of HDL-C level from 4 week onwards till the end of study. At 12 weeks the statistically significant difference was observed between the two groups at 8 and 12 weeks and with regard to their effect on lipid profile. Hence, rosuvastatin in addition to diet control and life style modification can be a useful measure to reduce the lipid profile in case of overweight and obese dyslipidemic individuals. No significant adverse effects were observed in any of the study groups. Myalgia, headache, fatigue, dyspepsia and pharyngitis they were the most common adverse effects in both the study groups.

Key Words

Aatorvastatin , dyslipidemia , rosuvastatin, CVD

Introduction

Cardiovascular diseases (CVD) are the most prevalent causes of death and disability in both developed as well as in developing countries affecting and is responsible for 17.1 million deaths globally each year (1). By 2015 in India and of these, 23 million would be patients younger than 40 years of age (2). The various modifiable risk factors for CAD are hypertension, diabetes mellitus, dyslipidemia, obesity and smoking and the non modifiable risk factors include age, sex, race and family history for CAD (3). Among all the risk factors, dyslipidemia has been found to be one of the important and modifiable risk factor for atherosclerosis related vascular events like CAD, ischemic cerebrovascular disease and peripheral vascular disease which are important among the leading causes of morbidity and mortality (4, 5).

There are several statins available in Indian market like Atorvastatin, Simvastatin, Pravastatin, Pitavastatin, Fluvastatin, Rosuvastatin etc. Many studies suggest that efficacy and safety of various statins varies considerably and it is difficult for medical practitioners to select suitable statins for dyslipidemic patients (6).

Atorvastatin is the most widely used statin. Rosuvastatin, a newer drug has been proven in various studies to be the most potent and well tolerated among all statins in hypercholesterolemia (7). There is paucity of existing data rega rding the effect of rosuvastatin and atorvastatin on lipid profile in the India. In the present study the efficacy and safety profile of rosuvastatin and atorvastatin has been evaluated in patients of dyslipidemia.

Materials and Methods

The present prospective randomized, comparative, open-label parallel study was conducted for a period of one year after the approval of Institutional Ethics Committee of the institution. Written informed consent was obtained from all patients after explaining them the nature and purpose of the study. All the principles of bioethics were followed. A total of 102 patients attending the cardiology OPD were enrolled in the study. Out of 102 patients, 82 patients fulfilled the eligibility criteria and were subsequently included in the study. Out of these only 81 patients completed the study. The main aim and objective of the study was to see the effect of rosuvastatin

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and atorvastatin on lipid parameters in Overweight and Obese dyslipidemic patients and to compare the safety of rosuvastatin versus atorvastatin in the same patients. To study the compliance of these drugs in the given patients population. Patients of either sex: >18 year, Total cholesterol: >240mg/dl, low density lipoprotein: >130mg/dl, Triglycerides: >200 mg/dl, Overweight: BMI: 25-29.9 kg/m², Obese: BMI>30 kg/m² were included in the study.

Whereas, patients with diabetes mellitus, thyroid dysfunction, renal disorders (serum creatinine >2.5 mg/dl), congestive heart failure, patients with active arterial disease over the last 6 months (myocardial infarction, unstable angina, stroke, coronary intervention) convulsive disorders, patients with hepatic disorders, patients with malignancy, infection, trauma and acute infection were excluded.

Pregnant and lactating mothers and those taking hormonal preparation., history of hypersensitivity to statins and patients using any drug which modifies the lipid profile, patients with fatty liver, alcohol intake, smoking, rheumatologic disorders were excluded from the study.

The Clinical evaluation with complete medical history, general physical and systemic examination was done. Hb, TLC, DLC, ESR ,Blood sugar (F/PP), Liver function tests, Renal function tests, Lipid profile, Urine R/E, ECG Chest x-ray, CPK enzyme, Weight/ Height, Body Mass Index and Waist Circumference were noted at 0,4, 8 & 12 weeks. These patients were registered after obtaining an informed written consent from them.

The old patients who were already on other hypolipidemic drugs underwent a drug washout period for 3 weeks. Enrolled patients were randomized into 2 groups for a period of 12 weeks. They were given following medication along with dietary restriction and exercise. Randomization was done by random table method. *Group 1*- Tab. rosuvastatin 10mg. orally once a day.*Group -2*- Tab. atorvastatin 10 mg. orally once a day.

For estimation of plasma lipids (TC, HDL-C, LDL-C, TG, VLDL-C) a semi automatic analyser was used. Out of 102 patients, a total of 82 patients were randomized in to two groups and only 81 patients completed the study. Forty patients received tab Rosuvastatin 10 mg/day and forty one patients received tab Atorvastatin 10 mg /day. In addition both the groups were advised diet restriction, exercise and to walk for at least 30 minutes on most days of the week. The demographic profile of patients was taken.

Results

The base line characteristics were comparable in both the groups (*Table 1*) & other results in (*Table-2-4*)

The age (Mean±SD) of patients was 55.07±12.57 in the rosuvastatin group and 53.63±13.76 in the atorvastatin group. There were 27(67.5%) males and 13(32.5%) females in rosuvastatin group as compared to 25(60.97%) males and 16(39.03%) females in atorvastatin group. The ratio of urban- rural population in rosuvastatin group was 28:12 and in atorvastatin group was 27:14.The Weight (Mean±SD) of patients was 77.95±7.60 in rosuvastatin group and 78.43±5.86 in the atorvastatin group. The no. of overweight patients were 25(62.5%) and 15(37.5%) obese patients in the rosuvastatin group as compared to no. of overweight and obese patients in the atorvastatin group were 23(56.09%)and 18(44.90%).

The mean WC and in rosuvastatin group as well as atorvastatin group was 39.69±1.69 and 39.27±1.75 and BMI was 29.99±3.55 VS 30.03±2.97.

Baseline biochemical levels were normal in both the groups. Highly significant reduction was seen in total cholesterol (TC) in both the treatment groups but on comparative analysis decrease was more pronounced in rosuvastatin group. Rosuvastatin and atorvastatin produced a highly significant decrease in LDL-C with in the group when compared to baseline value. On comparing LDL-C in two treatment groups, pronounced decrease was seen in rosuvastatin group. Both rosuvastatin and atorvastatin arm produced highly significant effect on HDL-C within the group. On comparing HDL-C between two groups, pronounced increase was shown by rosuvastatin group. Both treatment groups produced highly significant effect on serum triglycerides on comparing to baseline value but there was more percentage reduction in rosuvastatin group. No statistical significant difference was seen between two groups throughout the period ($p>0.05$). On serum VLDL-C levels, both rosuvastatin and atorvastatin groups produced highly significant effect ($p<0.001$) but on comparison no significant difference was seen (table 2&3). Compliance rate was 100% but objectively it was 95% and 97% in rosuvastatin and atorvastatin group by pill count method. Adverse events reported were in accordance to the previous studies and were clinically insignificant (*Table 4*).

Discussion

With regard to our total cholesterol results, they are in accordance with those put forth by Olsson AG *et al*, 2001; Prakash B *et al*, 2012; Sanket SS and Anand IS, 2013; Raju RS *et al*, 2014 (8, 2, 9, 10) who also showed a significant decrease in TC with rosuvastatin 10 mg. However, Davidson M *et al*, 2002; Olsson AG *et al*, 2002; Brown WV *et al*, 2002; Blasetto JW et al, 2003; and shephered J *et al*, 2004; Gleuk *et al*, 2006 (11, 8, 12, 13,

Table 1. Demographic Profile of Study Population

Parameters	Rosuvastatin (N=40)	Atorvastatin (N=40)
Age (years) MEAN ± SD	55.07±12.57	52.63±13.76
Male :Female	27:13:00	25:16:00
Height(cm)mean ±SD	161.7±6.21	161.80±7.98
waist circumference(inches)	39.6±1.79	39.09±1.88
BMI (Kg/m²)±SD	29.98 ±3.55	30.07±1.88
TC(mg/dl Mean±SD	268.50±18.62	273.58±25.40
LDL (mg/dl) Mean± SD	181.12±18.66	179.75±26.32
HDL(mg/dl) Mean±SD	38.10±2.95	39.14±2.44
TG(mg/dl) Mean±SD	245.95±77.51	242.34±63.95
VLDL mg/dl)Mean± SD	48.07±12.05	54.78±14.92
LDL/HDL	4.50±1.25	4.59±.68

n = number of patients ** = highly significant, p value < 0.001 (Paired t - test) as compared to baseline

Table 4. Adverse Events of Study Population

Adverse Events	Rosuvastatin N=40	Atorvastatin N=41
Myalgia	3	1
Headache	1	1
Fatigue	3	1
Dyspepsia	2	1
Nausea	2	1
Backache	3	2
Pharyngitis	2	1

Table.2 Effect of Atorvastatin on Lipid Profile (Mean±Sd) in Overweight and Obese Dyslipidemia Patients (N= 41)

Parameter	0 Week	4 week	8 week	12 week
TC	273.58±25.40	262.51±25.36**	232.07±20.87**	196.80±9.89**
LDL	179.75±26.32	168.90±26.99**	141.46±24.28**	106.21±21.54**
HDL	39.14±2.44	40.09±1.95**	41.31±1.72**	44.51±1.01**
TG	242.34±63.95	220.07±54.19**	181.51±32.76**	151.68±19.06**
VLDL	53.73±13.88	53.70±13.56	50.29±15.41	42.41±12.38**
LDL/HDL	4.59±.68	4.04±1.07**	3.40±.64**	2.45±.31**

Table.3 Effect of Rosuvastatin on Lipid Profile (Mean±Sd) in Overweight and Obese Dyslipidemia Patients (N= 41)

Parameters	0 Week	4week	8week	12week
TC	268.5O±18.62	254.45±17.55**	215.30±18.07**	185.37±14.26**
LDL	181.12±18.66**	167.27±17.74**	130.80±22.07**	97.80±12.51**
HDL	38.10±2.95	40.10±2.14**	42.70±2.24**	47.75±3.80**
TG	245.95±60.39	230.62±64.40**	173.72±32.71**	141.90±19.50**
VLDL	48.07±12.05	47.75±13.40	41.50±16.86	38.82±11.05**
LDL/HDL	4.50±1.25	4.17±0.49	3.07±.59**	2.05±0.32**

14, 15) demonstrated a decrease in TC even with lower doses of rosuvastatin.

In concordance with the results of present study, Jones PH *et al*, 2003; Park JS *et al*, 2009; Sanket SS and Anand IS, 2013; Prakash B *et al*, 2012; Jyoti N *et al*, 2013; Adsule SM *et al*, 2009 (16, 17, 9, 2, 18, 19) reported a decrease in LDL-C with 10 mg of rosuvastatin. Similarly Glueck CJ *et al*, 2006; Arshad, 2014 (15, 20) reported a decrease in LDL-C with lower doses of rosuvastatin. Stein EA *et al*, 2003 (21) reported a decrease in LDL-C with higher doses of rosuvastatin. Although, a number of previous studies have compared atorvastatin with

rosuvastatin in patients with hypercholesterolemia, some did not include high-risk patients, some were local studies conducted in a single country, and many were not powered to study efficacy in terms of lowering of LDL-C levels. PULSAR was the The results of the PULSAR study; the first prospective, large-scale, multinational study designed to compare low doses of rosuvastatin and atorvastatin for their LDL-C-lowering efficacy in high-risk patients, demonstrated that rosuvastatin 10 mg was significantly more effective than atorvastatin 20 mg at reducing LDL-C levels in high-risk patients with hypercholesterolemia. This is consistent with our finding in which Rosuvastatin reduced LDL levels which were statistically significant at the end of the study. These results are also consistent with the STELLAR trial where rosuvastatin, atorvastatin and simvastatin reduced LDL levels by 45.8, 36.8, and 28.3%, respectively.

HDL-C is thought to have a protective role against the development of atherosclerotic plaques and a low HDL-C level is considered a risk factor for CHD. Agents that improve HDL-C as well as lower LDL-C may offer additional benefits for CHD-risk reduction.(15-20) In the present study, increases in HDL-C were significantly greater with both rosuvastatin 10 as well as atorvastatin 10 mg per day. In concordance with the results of the present, Sanket SS and Anand IS, 2013; Raju RS *et al*, 2014 (9, 10) demonstrated an increase in HDL-C with rosuvastatin 10 mg/day. However, Gleuk et al, 2006 (15) demonstrated a dose dependent increase in HDL-C with doses of 5 and 10mg rosuvastatin and Stein EA *et al*,2003; Pit B *et al*,2013 (21, 22) reported a dose dependent Increase in the HDL-C with higher doses of rosuvastatin.

With regard to TG, the results of our study are supported by Schneck DW *et al*, 2003; Deedwania PC *et al*, 2005 and Stein EA *et al*, 2003 (23, 24, 21).

Ratio of LDLC-HDL-C provides a composite marker of risk of CAD. In the present study a decrease of 52.44% and 44.88% by rosuvastatin 10 mg and atorvastatin 10 mg at the end of 12 weeks of therapy was seen. Hence both the drugs are effective in decreasing the risk of CAD.

No clinically significant adverse effects were observed in any of the study groups. Myalgia, headache, fatigue, dyspepsia and pharyngitis they were the most common adverse effects in both the study groups. The other effects recorded were constipation, backache, nausea. Particular attention was focused on the presence of myopathy or elevated serum transaminase levels because these condition have been associated with the use of HMG Co A reductase inhibitors.

Patients were asked for the compliance subjectively as well as objectively. Subjectively the compliance was 100% in both the groups but objectively by pill count method, only 38(95%) patients have shown the compliance in rosuvastatin group and 40 (97.56%) patients in atorvastatin group by pill count method. The present study was conducted for short duration. All the lipid parameters were not taken like apo A1, apo B, HDL2-C. Only subjective and objective compliance was seen and no attempt was made to analyze compliance by measuring drug levels.

Conclusion

The current study demonstrated that rosuvastatin has shown highly significant effect on TC, LDL-C HDL-C, and non significant effect on VLDL-C, and TG on comparing to atorvastatin hence, rosuvastatin in addition to diet control and life style modification can be a useful measure to reduce the lipid profile in case of overweight and obese dyslipidemic individual.

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