A COMPARATIVE STUDY TO MEASURE EFFECTIVE REDUCTION IN LDL CHOLESTEROL USING ROSUVASTATIN 10 mg & ATORVASTATIN 20 mg THERAPY IN HYPERLIPIDEMIA PATIENTS IN HARYANA POPULATION

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BACKGROUND

Atherosclerosis is a killer disease and is a major cause of death throughout the world. **Hyperlipidemia** is a major cause of atherosclerosis and atherosclerosis-induced conditions, such as coronary heart disease , ischemic cerebrovascular disease and peripheral vascular disease.[1]Recently World Health Organization (WHO) has declared that by 2020, 60% of cardiovascular cases will be of Indian origin[2] and from years 2000 to 2020 disability-adjusted life years lost (DALYs) from CHD in India shall double in both men and women from 7.7 and 5.5 million, respectively[3].The etiology of Cardiovascular diseases (CVD) is complex and multifactorial and is influenced by various modifiable (**hyperlipidemia,** obesity, hypertension, diabetes, smoking, physical inactivity, diet) and non-modifiable(family history, age)**risk factors**.[4]A high concentration of lipids i.e. hyperlipidemia and the increase in concentration of low density lipoprotein (LDL-C) has been closely linked to pathophysiology of **CAD.**[5]

Statins have now become one of the most widely used therapeutic classes in clinical practice because the cardiovascular benefits of statins that reduce concentrations of LDL-C and inflammatory markers in primary and secondary prevention have already been confirmed in several randomised studies or meta-analysis.[6,7]

METHODS:

Trial design

This 12 weeks trial was conducted from september 2012 to March 2013 at MMIMSR ,MMU, Mullana in Haryana state of India. After diagnosing the patient as hyperlipidemic, 60 eligible patients were randomised to receive rosuvastatin 10 mg and atorvastatin 20 mg once daily Patient randomised to rosuvastatin treatment were given a 12 week supply of rosuvastatin 10 mg and similarly the other group was given 12 week supply of atorvastatin 20 mg. Levels of LDL were monitored at 0,6 and 12 weeks for assessment of effective reduction in the same using , rosuvastatin 10 mg and atorvastatin 20 mg**.**

Patients

Men and women aged between 40-75 years of age with documented (NCEP: THIRD REPORT:JAMA(2001) hyperlipidemia were eligible for randomization to the study if LDL-C levels was≥ 100 mg/dl. Exclusion criteria included history of statin-induced myopathy or a serious hypersensitivity reaction to statins, concurrent liver, renal, gastro intestinal tract or myopathic diseases , women who were pregnant, breast-feeding or of child-bearing potential and not using a reliable form of contraception were excluded.

Objectives

The primary endpoint was the percentage change from baseline (at randomization, week 0) in LDL-C levels after 6 and 12 weeks of treatment with rosuvastatin 10 mg and atorvastatin 20 mg.

Assessments

Fasting blood samples were obtained from patients at 0,6 and 12 weeks, and lipid profiles analyzed at laboratory (Maharishi Markendeshwar Institute Of Medical Science and Research). Fasting concentrations of LDL-C was determined at 0,6 and 12 weeks. Fasting LDL-C concentrations were calculated from TC, TG, and HDL-C using the Friedewald equation.[8] (LDL-C = Total Cholesterol (-) HDL-C (-) TG/5 whereTG/5= VLDL)

Statistical analyses and Results:

The present study was conducted on sixty patients of dyslipidemia attending the in – and out- patient department of Medicine of M.M.I.M.S.R., Mullana. All patients of both sexes (M= 29; F = 31) and within the age group of 40-75 years (Mean age of 59.74 years and 68.88 years for Group A and B respectively) were considered. The patients with deranged lipid levels were assessed for eligibility criteria for enrolment in the study. The selected patients were randomised into two groups – Group A & Group B. **Group A :** (n=30) It included the eligible patients diagnosed with dyslipidemia and were administered *Atorvastatin 20mg*, once a day for 12 weeks. **Group B :** (n=30).It included the eligible patients diagnosed with dyslipidemia and were administered Rosuvastatin *10mg* once a day for 12 weeks. Complete medical history, clinical examination and investigations (as per Performa) were carried out for each case. The results of the lipid profile of individual patients were consolidated at the end of twelve weeks after treatment for both groups. Continuous variables were expressed as Mean ± SD and categorical variables were expressed as percentage. For comparison between pre- and post treatments, the Student's paired't' test was used. Difference between groups or independent variables was compared by an unpaired t test for normally distributed variables.

Statistical analysis was performed using computer software - SPSS version 16.0 The level of significance was determined by probability value ($p<0.05$-significant)

TABLE 1
Baseline characteristics in Study Groups

Characteristic	Group A	Group B
Number of patients	30	30
Age Range (years) **Mean Age**	40 – 75 59.74	40 – 75 68.88
Sex (Male / Female)	17/ 13	12/ 18
TC (mg/dl)	288.24	333.50
TG (mg/dl)	164.64	170.31
LDL(mg/dl)	212.01	255.09
HDL (mg/dl)	432.96	443.43

There were no statistical differences regarding baseline characteristics between the two groups including age, sex, and the lipid profiles. The parameters were normally distributed and were comparable. ($p>0.05$).

Comparison of Percent change of LDL (mg/dl) from baseline to 6 weeks

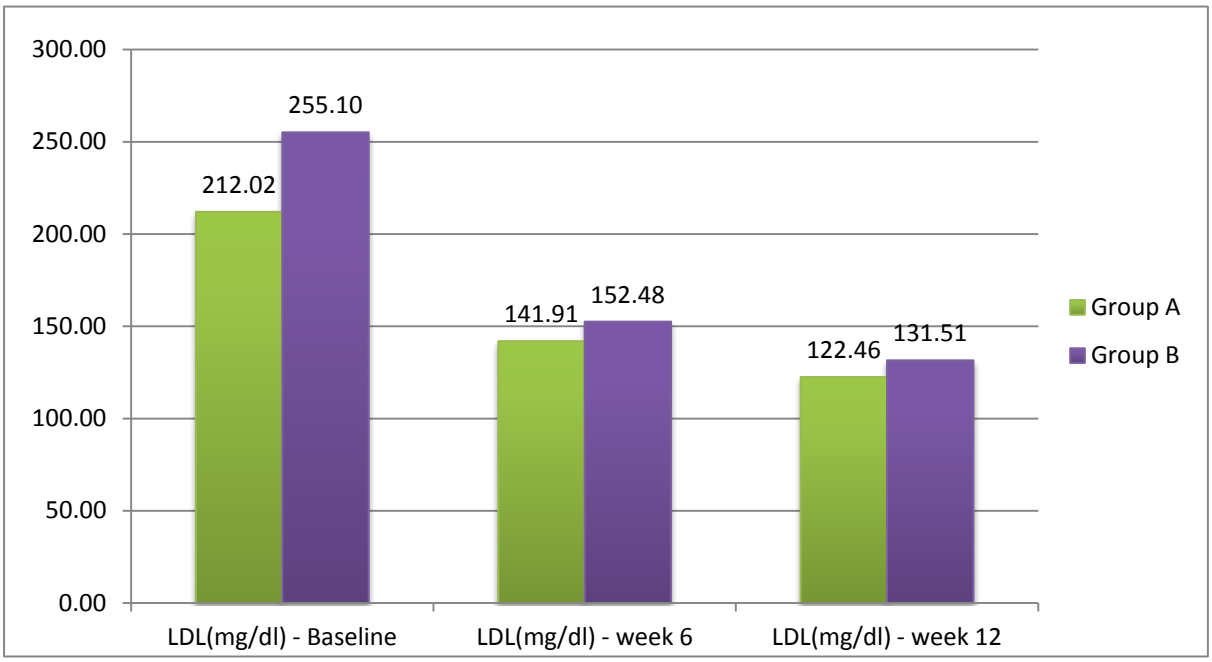
LDL (mg/dl)	Baseline value (Mean ± SD)	At 6 weeks (Mean ± SD)	Percentage change (%)
Group A	212.01±60.9	141.90±46.8	-33.1
Group B	255.09±88.5	152.48±62.0	-40.2

The Mean ± SD for LDL decreased from 212.01±60.9 to 141.90±46.8 in Group A accounting for a 33.1 % decrease in the LDL levels at 6 weeks with 20 mg daily day dosing. In Group B Rosuvastatin 10 mg /day dosing, LDL decreased by 40.2 % i.e. from 255.09±88.5 at baseline to 152.48±62.0 at 6 weeks.

Comparison of Percent change of LDL (mg/dl) from 0 weeks to 12 weeks

LDL (mg/dl)	At 0 week (Mean ± SD)	At 12 weeks (Mean ± SD)	Percentage change (%)
Group A	212.01±60.9	122.46±43.4	-42.2
Group B	255.09±88.5	131.51±56.8	-48.4

The Mean ± SD for LDL decreased from 141.90±46.8 to 122.46±43.4 in Group A accounting for a 42.2 % decrease in the LDL levels at 12 weeks with 20 mg daily day dosing. In Group B Rosuvastatin 10 mg /day dosing, LDL decreased by 48.4 % i.e. from 255.09±88.5 at baseline to 131.51±56.8 at 12 weeks



LDL Comparison

Comparison of Mean of LDL (mg/dl) for Group A and Group B

LDL (mg/dl)	Group A	Group B	't'	'p'	Sig
At Baseline	212.01±60.9	255.09±88.5	2.195	0.032*	S
At 6 weeks	141.90±46.8	152.48±62.0	0.745	0.459	NS

Comparison of Mean of LDL (mg/dl) for Group A and Group B

LDL (mg/dl)	Group A	Group B	't'	'p'	Sig
At Baseline	212.01±60.9	255.09±88.5	2.195	0.032*	S
At 12 weeks	122.46±43.4	131.51±56.8	0.693	0.491	NS

Discussion

The study results were consistent with those of the individual studies confirming that rosuvastatin is efficient in lowering LDL-C than atorvastatin.

In the present study using Rosuvastatin 10 mg and atorvastatin 20 mg, we found that both the regimens were effective in improving the levels of atherogenic LDL. When we compared the two drugs amongst themselves to determine the superiority of one therapy over the other, we found that both the therapies are equally effective in improving the LDL of the patients with dyslipidemias.

LDL-C is a well-established risk factor for cardiovascular disease, and there is considerable evidence that lowering LDL-C reduces the risk of both cardiovascular events and mortality [(5,9)] The real clinical benefits of statins are due to their LDL-C lowering effects and this benefit has been observed in clinical trial. Rosuvastatin and Atorvastatin is a **competitive inhibitor** of the enzyme **HMG-Co A Reductase** with half-life of 19 and 14 hours,respectively.[10]Action of HMG is maximum at night so these drugs are administered at night. Rosuvastatin(RSV) and Atorvastatin (ATV) are long-acting drugs hence administered at any time of the day. In our study we found that when Rosuvastatin and atorvastatin was used daily for twelve weeks, there was a significant reduction of 48.4% and 42.2% in the LDL levels, respectively. Results from the LUNAR study showed that RSV more effectively decreased LDL cholesterol, increased HDL cholesterol, and improved other blood lipid parameters than ATV in patients with acute coronary syndrome.[11,12,13]

Hence the finding of present study is consistent with findings from previous studies that have compared rosuvastatin 10 mg and atorvastatin 20 mg in patients with hypercholesterolemia. In three separate studies, one with 2431 patients with hypercholesterolemia (LDL-C $\geq$ 160 and < 250 mg/dL [4.1 and 6.5 mmol/L]), one with 461 patients (aged 40–80 years) with CHD and low HDL-C, and one with 263 patients with type 2 diabetes, rosuvastatin 10 mg was more effective at reducing LDL-C than atorvastatin 20 mg after 6 weeks of treatment (45.8% vs. 42.6%, 44.0% vs. 38.4%, 45.9% vs. 41.3%, respectively; all $p < 0.05$). [14,15,16] Furthermore, in an 8-week study of 3140 high-risk patients with hypercholesterolemia and CHD, atherosclerosis, type 2 diabetes, or a 10-year CHD risk > 20%, rosuvastatin 10 mg was also significantly more efficacious than atorvastatin 20 mg at reducing LDL-C (47.0% vs. 43.7%, $p < 0.001$). [17]

Conclusion

In conclusion, at recommended starting doses, rosuvastatin (10 mg) was more efficacious than atorvastatin (20 mg), in terms of LDL-C lowering, LDL-C goal achievement, and improving the atherogenic lipid profile. The greater efficacy of rosuvastatin at starting dose should help to reduce the need for dose titration and enable more patients to achieve recommended treatment goals in clinical practice.

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