Original Article

Efficacy of Rosuvastatin 10mg with Atorvastatin 20mg in Lowering Low Density Lipoprotein Cholesterol in Hypercholesterolemia Patients

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ABSTRACT

Objective: To measure the effectiveness of Rosuvastatin 10mg with Atorvastatin 20mg in lowering low density lipoprotein cholesterol.

Study Design: Retrospective study

Place and Duration of Study: This study was conducted at the Jinnah Hospital, Lahore from March 2017 to December 2017.

Materials and Methods: 252 patients were enrolled having equal subjects in each group, using efficacy of Rosuvastatin 50 %(1) and efficacy of atorvastatin 39 %(1) with 95% confidence interval and 80% power of test.

Results: In Rosuvastatin group mean age was 65 years with SD ± 1.61 with male patients 51% and female patients were 49%. While in Atorvastatin Group mean age was 63 years with SD ± 1.93 with 54% patients were male and 46% patients were female. Moreover it was showed that Rosuvastatin appeared to be potent among 82% of the individuals and was not efficacious in 18% of the individuals while Atorvastatin was efficacious in 71% of the individuals and was not beneficial in 29% of the individuals.

Conclusion: In individuals having hypercholesterolemia, it was found that atorvastatin 20 mg is non-superior than Rosuvastatin 10 mg in lowering LDL-C, enabling LDL-C goal towards healthy target values.

Key Words: Rosuvastatin, Atorvastatin, Hypercholesterolemia

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INTRODUCTION

Atherosclerotic Cardiovascular disease (ASCVD) consider to be one of the common estreason for morbidity and mortality in the globe.[1] Among the risk factors for ASCVD, hyperlipidemia or dyslipidemia (in a metabolic perspective) is an important reversible predisposing factor in its pathogenesis. It has been found that risk tend to rise markedly with elevation of low-density lipoprotein cholesterol (LDL-C) & declines with elevation of high-density lipoprotein cholesterol (HDL-C). Statins are the mainstream approach that is used medically for prevention of ASCVD due to hyperlipidemia. These are HMG Co-enzyme-A inhibitors that cause lowering in intrinsic formation of cholesterol in the liver and hence down regulates the metabolic formation of LDL-C.(2-5)

The crucial need to get help of lipid lowering agents especially LDL-C, the major aim is to prevent the frequency of serious cardiovascular problems among individuals who probably have significant cardiovascular disorder in short term. Primary prevention trials with LDL-C lowering drugs enables its use. As described previously there are two trials for primary prevention, statin therapy appears as relatively effective and safer. However, LDL-C lowering drugs do not prone individuals to any major side effects if used for a low duration for primary prevention. (6-9) Prospective epidemiological studies show that there is inverse correlation between the presence of CAD and LDL-cholesterol levels. CAD complications can be reduced, along with other risk factors, provided LDL cholesterol levels are <2.58 mmol/L. Thus, an LDL cholesterol <2.58mmol/L can be referred to as ideal. If an individual has no atherosclerotic disease risk factors provided the even near optimal levels of L-cholesterol

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concentrations, i.e., 2.58–3.33 mmol/L, the 10-year risk for CAD is still relatively less.[10]

When LDL cholesterol levels are optimal i.e. <2.58 mmol/L) or near optimal (2.58–3.33 mmol/L), despite with a low risk for CAD, there is still a need for a cost benefit analysis as this kind of a clinical trials poses the health care system at risk in context of financial burden. Selecting the individuals for such clinical intervention depends on the adjustment of the therapy for the absolute risk.[11,12]

Recently, clinical trials in those individuals having established CAD revealed that patients have a lower risk for stroke as well, especially with statins. The exact role whereby statin therapy lowers the risk of stroke with CAD patients remains answerable but most likely involve slowing of progression of plaque, stabilization of plaque, so has been reducing the incidence of coronary events.[13]

However, stroke can be prevented significantly by using statin therapy in secondary prevention.[14]

The objective of this study was to measure the effectiveness of Rosuvastatin 10mg with Atorvastatin 20mg therapy in reducing Low Density Lipoprotein Cholesterol (LDL-C) in patients with Hypercholesterolemia.

MATERIALS AND METHODS

This retrospective study was conducted at Jinnah Hospital, Lahore from March 2017 to December 2017. 252 individuals in each group, using efficacy of rosuvastatin 50% and of atorvastatin 39% with 95% confidence interval and 80% power of the test, calculated by WHO software for sample size determination. The sampling technique was of non-probability consecutive type. The patients with baseline fasting LDL-C level > 3.3mmol/L and prescribed either Rosuvastatin 10mg or Atorvastatin 20mg at baseline as primary intervention for treatment of hyperlipidemia wereenrolled for the study. Those with history of ethanol abuse or cholecystectomy, chronic liver disease, other metabolic disorders were excluded from the study.

Data collection procedure:

This study was done after the research and ethical committees approval from the hospital. Patient data records from hospital(s) and medical centers were collected. Patients fulfilling all the inclusion and exclusion criteria were selected. Baseline homogeneity was ensured for the primary variable LDL-C and for the secondary variables like age, gender, diabetes (HbA1C≥5.5%), dietary intake of lipids, intake pattern of antioxidants/fruits and vegetables. Groups sorted on the bases of lipid lowering treatment prescribed (Rosuvastatin 10mg or Atorvastatin 20mg) were compared in terms of the aforementioned variables at baseline, to ensure homogeneity of groups.

Detailed history, clinical investigations and demographic information were gathered upon data collection form (Annexure) and later on tabulated using spreadsheet software; Microsoft Excel. Methods used for assay of LDL-C were confirmed from relevant lab(s) for both baseline and 6 months after treatment values. If the treatment has resulted in 30% lowering of the LDL-C value at 6thweek of the treatment from the baseline value, it was considered to produce desired efficacy. For every patient, efficacy was calculated and labelled as “efficacious” or “non-efficacious”.

Data Analysis procedure: The data was analyzed by using statistical package for social sciences (SPSS) version 20 after data entry. Mean and standard deviation were calculated for continuous variables like age and fasting serum LDL-C levels. Other variables like gender, diabetes (HbA1C≥5.5%) and efficacy were expressed as frequencies and percentages. For comparisons among groups, Chi-Square test was used to compare the efficacy. P value of ≤ 0.05 was considered as significant. All the results are presented in the form of graphs and tables. Age and gender that ae effect modifiers were controlled through stratification/ post stratification.

RESULTS

252 were the number of individuals included in our study having 126 individuals in each of the group. Patients were observed for the reduction of levels of Low Density Lipo`protein Cholesterol for the effectiveness of either Rosuvastatin or Atorvastatin with Hypercholesterolemia and the outcome was analyzed:

Age distribution among two groups was analyzed as in Rosuvastatin Group 25(20%) patients having age range 41-50 years, 70(55%) patients having age range 51-60 years, 31(24%) patients having age range 61-70 years. Mean age was 65 years with SD ± 33.0. While in Atorvastatin Group 34(33%) patients having age range 41-50 years, 42(41%) patients having age range 51-60 years, 50(26%) patients having age range 61-70 years. Mean age was 63 years with SD ± 20.5. (Table-1).

Gender distribution among two groups was analyzed as in Rosuvastatin Group 64(51%) patients were male while 62(49%) patients were female where as in Atorvastatin Group 68(54%) patients were male and 58(46%) patients were female. (Table-2).

Baseline fasting serum LDL-C Level among two groups was analyzed as in Rosuvastatin group 24(19%) patients had baseline serum LDL-C Level ranged from 3.36-4.11 mmol/L, 82(65%) patients had baseline serum LDL-C Level ranged from 4.12-4.88 mmol/L, 20(16%) patients had baseline serum LDL-C Level ranged from ≥ 4.89 mmol/L. Mean baseline serum LDL-C Level was 4.88 mmol/L with SD ± 0.06. While in Atorvastatin Group 26(21%) patients had baseline serum LDL-C Level ranged from 3.36-4.11 mmol/L,

77(61%) patients had baseline serum LDL-C Level ranged from 4.12-4.88 mmol/L, 23(18%) patients had baseline serum LDL-C Level ranged from ≥ 4.89 mmol/L. Mean baseline serum LDL-C Level was 4.78 mmol/L with SD ± 0.07. (Table-3).

Fasting Serum LDL-C Level after 6 weeks among two groups was analyzed as in Rosuvastatin group 92(73%) patients had serum LDL-C Level ranged from < 2.58 mmol/L, 19(15%)patients had serum LDL-C Level ranged from 2.59-3.33mmol/L, 11(9%) patients had serum LDL-C Level ranged from 3.34-4.11mmol/L, 4(3%) patients had serum LDL-C Level ranged from ≥ 4.12mmol/L. Mean serum LDL-C Level was 2.58 ± 0.02mmol/L. While in Atorvastatin Group 88(70%) patients had serum LDL-C Level ranged from < 2.58mmol/L, 21(16%) patients had serum LDL-C Level ranged from 2.59-3.33mmol/L, 12(10%) patients had serum LDL-C Level ranged from 3.34-4.11mmol/L, 5(4%) patients had serum LDL-C Level ranged from ≥ 4.12mmol/L. Mean serum LDL-C Level was 2.71 ± 0.04mmol/L. (as shown in Table-4).

Table No.1: Age distribution in treatment groups

Age	Frequency and percentages	
	Rosuvastatin 10 mg/day (Group A)	Atorvastatin 20mg/day. (Group B)
41-50 Years(1)	25(20%)	34(33%)
51-60 Years(2)	70(55%)	42(41%)
61-70 Years(3)	31(24%)	50(26%)
Total	126(100%)	126(100%)
Mean±SD	65 ± 33.0	63 ± 20.5

Table No.2:Gender distribution in treatment groups

Gender	Frequency and percentages	
	Rosuvastatin 10 mg/day (Group A)	Atorvastatin 20mg/day. (Group B)
Male	64(51%)	68(54%)
Female	62(49%)	58(46%)
Total	126(100%)	126(100%)

Table No.3: Baseline LDL-C Levels in treatment groups

Baseline LDL level (mmol/L)	Frequency and percentages	
	Rosuvastatin 10 mg/day (Group A)	Atorvastatin 20mg/day. (Group B)
3.36-4.11	24(19%)	26(21%)
4.12-4.88	82(65%)	77(61%)
≥ 4.89	20(16%)	23(18%)
Total	126(100%)	126(100%)
Mean±SD	4.88 ± 0.06	4.78 ± 0.07

Efficacy of Rosuvastatin vs Atorvastatin was analyzed by calculating 30% of the baseline level of the LDL-C for each patient and evaluating that reduction of LDL-C after 6 weeks treatment was less than equals to or more than the determined value. A less than or equal to the determined reduction was efficacious. Rosuvastatin was effective in 103(82%) however in 23(18%) of the individuals it was effective while Atorvastatin was effective in 89(71%) patients and it was non-superior in 37(29%) patients. (as shown in Table-5).

To compare the efficacy of the two groups Chi Square test applied and the p value obtained was 0.000 for the whole data as well as upon stratification according to gender (Table-6), which was statistically significant, hence there is a statistically significant difference between the low-density lipid lowering efficacy of Rosuvastatin 10 mg and Atorvastatin 20 mg.

Table No.4: LDL Levels after 6 weeks in both treatment groups

LDL level after 6 weeks (mmol/L)	Frequency and percentages	
	Rosuvastatin 10 mg/day (Group A)	Atorvastatin 20mg/day (Group B)
< 2.58	92(73%)	88(70%)
2.59-3.33	19(15%)	21(16%)
3.34-4.11	11(9%)	12(10%)
≥ 4.12	4(3%)	5(4%)
Total	126(100%)	126(100%)
Mean ± SD	2.58 ± 0.02	2.71 ± 0.04

Table No.5: Efficacy in both treatment groups

Efficacy	Frequency and percentages		Total
	Rosuvastatin 10 mg/day (Group A)	Atorvastatin 20mg/day. (Group B)	
Effective	103(82%)	89(71%)	192
Not effective	23(18%)	37(29%)	60
Total	126(100%)	126(100%)	252(100%)

Chi square test was applied in which P value was 0.000. (Annexure)

Table No.6: Stratification with respect to gender

Gender	Groups	Efficacy		Total	P-Value
		Effective	Not effective		
Male	Rosuvastatin 10 mg/day (Group A)	52	12	64	0.000
	Atorvastatin 20mg/day. (Group B)	48	20	68	
Total		100	32	132	
Female	Rosuvastatin 10 mg/day (Group A)	49	13	62	0.000
	Atorvastatin 20mg/day. (Group B)	40	18	58	
Total		89	31	120	

DISCUSSION

This study was conducted at Jinnah Hospital, Lahore and the aim of this study was to compare the effectiveness of Rosuvastatin 10mg in comparison with Atorvastatin 20mg therapy inlowering Low Density Lipoprotein Cholesterol (LDL-C) in individuals having raised blood cholesterol levels.

In this study Rosuvastatin 10 mg/day given to 126 individuals having baseline LDL-C levels with a mean of 4.88 ± 0.06mmol/L. After treatment those patients who had their mean LDL-C Levels of 2.58 ± 0.02mmol/L with mean reduction in LDL-C levels of 2.3mmol/L. Out of 126 patients 103 i.e. 82%, acquired the target LDL-C Levels. Whereas Atorvastatin (20mg/day) was given to 126 patients having baseline LDL-C levels with mean of 4.78 ± 0.07mmol/L. After treatment those patients had mean LDL-C Levels of 2.71 ± 0.04 mmol/L with mean reduction in LDL-C levels of 2.07mmol/L. Out of 126 patients 89 i.e. 71%, achieved the target LDL-C Levels. On application of the chi square test the p-value of the outcome between the two groups was 0.00, which is less than alpha value (0.05) thus statistically significant. Results were also significant when stratification done based on gender (Table-6). The one tailed fischer exact test also gave a significant p-value (0.000) as shown in Annexure. Hence it was concluded that the efficacy of Rosuvastatin 10mg was better than atorvastatin 20 mg in patient having hypercholestrolemia. The result of the study was similar to comparative studies doneto measure the effectiveness of Rosuvastatin and atorvastatin in lowering lipids, done internationally. Side effect profile of both drugs was similar and both drugs were well tolerated with no major side effects observed in any of the treatment group. My results are consistent with many previous investigations carried out.

The study conducted by B. H. R. Wolffenbuttel et al., compared the efficacy of the rosuvastatin with atorvastatin in subjects having type 2 diabetes over 24 weeks. A multicenter randomized, study in parallel group conducted in Netherlands upon 263 patients. The study observed apolipoprotein B (apoB) and apoB/ apolipoprotein A1 (apoA1) ratio in the subjects. However, there were changes in other lipid parameters in secondary outcomes. Baseline LDL-C in both groups was comparable i.e. 4.23 ± 0.98 mmol/ L and 4.43 ±0.99 mmol/ L in Rosuvastatin and atorvastatin groups. Greater number of patients had a marked lowering level of LDL-C in rosuvastatin group (82%) in comparison with atorvastatin group (74%) according to The American Diabetes Association (ADA) criteria. Significantly greater reductions in apoB/apoA1 ratio seen in Rosuvastatin cases in comparison with atorvastatin treated cases in this study.[15]

Another study by Keith C. Ferdinand et al. matched my study in terms of duration of treatment and dosage. It studied African-Americans adult patients for the lipid-lowering ability of statin therapy in hypercholes-terolemic for 6 weeks treatment. End points were marked lowering in low-density lipoprotein cholesterol, total cholesterol, non–high-density lipoprotein cholesterol, and apolipoprotein B concentrations, as well as lipoprotein and apolipoprotein ratios. The results did not only show significant reduction of LDL-C; rosuvastatin was also found to increase HDL-C more than atorvastatin. Overall African-Americans lipid profile of hypercholesterolemic patients was better improved by treatment with rosuvastatin with the same dose of atorvastatin.[16]

Allevidences as mentioned above are aligned with the results found in the carried study and thus it could be recommended that rosuvastatin could be used as first line therapy in treatment of hypercholesterolemia.

Another study by Calza et al. investigated the use of various statins including the ones I studied, in Highly active antiretroviral therapy (HAART) therapy. HAART including protease inhibitors (PIs) have been independently associated with an abnormal lipid profile. The study concluded that although all used statins showed a significant efficacy and a good tolerability in the treatment of diet-resistant hyperlipidaemia, but rosuvastatin was more effective in reducing total and LDL cholesterol levels.[17]

Another study by J Wouter Jukema et al., investigated LDL-C/HDL-C ratio. This study compared the effects of rosuvastatin and atorvastatin on the LDL-C/HDL-C ratio in patients while treatment with either rosuvastatin or atorvastatin. In this study patients with established cardiovascular disease and HDL-C < 1.0 mmol/L were included. After randomization, each group was treated with rosuvastatin 10 mg or atorvastatin 20 mg for 6 weeks the doses were increased afterwards to rosuvastatin 40mg and atorvastatin 80mg during 18 week treatment. This escalating dose study too, resulted with similar results i.e. Rosuvastatin 10, 20 and 40 mg to be significantly more effective than atorvastatin 20, 40 and 80 mg, respectively, in improving the LDL-C/HDL-C ratio.[18]

CONCLUSION

It was concluded that individuals having hypercholesterolemia, Rosuvastatin 10 mg was better as compared to those taking atorvastatin 20 mg in lowering LDL-C, leading to LDL-C to a desirable limits. Both treatments were well tolerated.

Author's Contribution:

Concept & Design of Study:	Shahid Iqbal
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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