DOI: https://doi.org/10.53350/pjmhs22161683

ORIGINAL ARTICLE

Comparison of Clinical Effectiveness of Atorvastatin and Rosuvastatin Among High-Risk Patients with Dyslipidaemia

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ABSTRATC

Aim: The aim of this analysis was to compare the effectiveness of rosuvastatin in lowering cholesterol with that of atorvastatin in patients at high risk of dyslipidaemia.

Place and Duration: In the Medicine department of Islam Medical College and Teaching Hospital Sialkot for six months duration from June 2021 to November 2021.

Methods: This randomized, open-label study enrolled 90 patients with high-risk dyslipidaemia and diagnosed according to the international guidelines for the prevention of adult dyslipidaemia. These patients were randomized to rosuvastatin and atorvastatin to receive rosuvastatin 20 mg / day and atorvastatin 20 mg / day, respectively, for three months. In both groups, the efficacy of atorvastatin and rosuvastatin on the concentration of LDL-C, HDL-C, total cholesterol (TC) and triglycerides (TG) was assessed. In addition, the rates of achieving LDL-C or TC target levels were assessed in both groups.

Results: Rosuvastatin caused a significantly greater reduction of LDL-C (43.2% and 38.1%, $p < 0.05$) and TC (34.8% Vs 28.1%, $p < 0.05$) than Atorvastatin. In addition, the percentage of subjects attaining the recommended target TC and LDL-C levels was higher in the group of rosuvastatin as compared to the atorvastatin group.

Conclusions: In patients at high risk of hyperlipidemia, rosuvastatin has high efficacy in decreasing lipids than atorvastatin.

Keywords: rosuvastatin, atorvastatin, dyslipidaemia, high-density lipoprotein, triglycerides.

INTRODUTCION

Coronary heart disease (CHD) is considered to be the foremost source of demise among individuals worldwide[1-2]. In 2014 alone, it causes over 7 million deaths worldwide. Coronary heart disease has been documented to be associated with numerous risk factors, counting smoking, obesity, and hyperlipidaemia[3-4]. There is a lot of evidence that cholesterol-lowering therapy is beneficial for people at high risk of coronary artery disease[5-6]. Statins are cholesterol letting down drugs that can constrain HMG-CoA reductase, then prevent cholesterol synthesis, and treat early-stage coronary artery disease. To date, many statins have been released and used clinically, including atorvastatin, rosuvastatin, and simvastatin[7]. Rosuvastatin has a special sulphur structure and has fewer side effects than other statins. Rosuvastatin has been reported to reduce the incidence of cardiovascular events. Several clinical studies have demonstrated that rosuvastatin has high efficacy in lowering cholesterol than other competitors in the statin class. At all dose ranges (10-80 mg / day), administration of rosuvastatin was significantly better than atorvastatin, pravastatin, and simvastatin in lowering total cholesterol in patients with hypercholesterolaemia[8-9]. A clinical trial in North America showed that 10 mg rosuvastatin has high efficacy than 10mg of atorvastatin in meeting the European Society of Atherosclerosis Society LDL-cholesterol levels of target among individuals with hypercholesterolemia. Another prospective multicenter study in Pakistan showed that 10 mg / day of or atorvastatin and 2.5 mg / day of rosuvastatin appeared to have a similar effect in lowering LDL-C with minimal side effect[10]. Similarly, a clinical trial in India, Bangladesh and Nepal confirmed the superiority of rosuvastatin over atorvastatin (10 mg / day) in high-risk patients of primary hypercholesterolemia and CHD[11-12]. Though, a contrast efficacy of rosuvastatin with other comparator drugs in high-risk subjects with dyslipidaemia has not been fully described[13]. Given the effect of individual variability on drug response, a comparison in high-risk patients with dyslipidaemia is needed. The aim of this analysis was to compare the effectiveness of rosuvastatin in lowering cholesterol with that of atorvastatin in patients at high risk of dyslipidaemia.

MATERIALS AND METHODS

A prospective study included 90 patients with high-risk dyslipidaemia admitted to the Medicine department of Islam Medical College and Teaching Hospital Sialkot for six months duration from June 2021 to November 2021. According to the criteria of the Adult Dyslipidaemia Prevention Guidelines, these patients met the following criteria: high-risk dyslipidaemia: LDL-C, 3.37-4.12 mmol / L, TC, 5.18-6.19 mmol / l; Risk factors ≥1 including age (female ≥55 years, male ≥45 years), HDL-C ≤1.04 mmol / L, smoking, obesity and early-onset family history of coronary heart disease. The following patients were not included: primary hypothyroidism, secondary hyperlipidemia, renal failure or nephritic syndrome; Type I or II diabetes mellitus without satisfactory glycemic control; active liver disease, ALT and AST more than twice the normal value; Creatine kinase (CK) increased ≥ three-fold of the upper limit of normal or unexplained; allergy or intolerance to statins; long-term use of steroid hormones or thiazide diuretics in combination with statins, which may increase the risk of rehabdomyolysis; uncontrolled severe hypertension; Taking other lipid-lowering medications other than the statins used in the study. The consent was signed by each patient enrolled prior to the commencement of the study.

According to the Guidelines for the Prevention of Adult Dyslipidaemia, 5-10 mg / day of rosuvastatin and 10 mg / day of atorvastatin are recommended as appropriate doses to lower LDL-C by 30-40%. 90 patients were randomized to receive 20 mg / day of rosuvastatin (Crestor) and 20 mg / day atorvastatin (Lipitor) for three-months. In addition, none of the patients enrolled were prescribed other medications that could interfere with the effect's of statins. Venous samples of blood were withdrawn from each patient before and after treatment, respectively, after a 12 hour fast. TG, TC, HDL-C and LDL-C were analyzed using Cobas 8000 automated chemistry analyzers (Roche, Germany), respectively.

Quantitative data are articulated as standard deviation (SD) and median. Student's t-test was applied for the comparison of variances in quantitative data. The qualitative data was analyzed with chi-square test. The SPSS 21.0 software was used for statistical analysis. A difference at $p < 0.05$ was considered significant.

RESULTS

The demographic characteristics of the 90 subjects in the atorvastatin and rosuvastatin groups are shown in Table 1. There was a slight difference among the two groups in gender, age, diabetes, hypertension, smoking and body mass index. ($p > 0.05$).

Table 1: Demographic features of the patients in Atorvastatin and Rosuvastatin groups

Characteristic	Rosuvastatin group (n=47)	Atorvastatin group (n=43)	Total N=90	t-value/X^2	P-value
Age (years)	61.2±9.4	60±8.9	60.5±9.2	0.2	0.79
Male/Female [n (%)]	25 (53.2)/22 (46.8)	24(55.8)/19 (44.2)	49 (54.4)	0.11	0.72
Body weight index (kg/m^2)	25.1±2.8	24.4±3.1	24.8±2.9	<0.001	0.9
Hypertension [n (%)]	18 (38.3)	12 (27.9)	30 (33.3)	0.01	0.80
Diabetes [n (%)]	6 (12.8)	5 (11.6)	11 (12.2)	<0.001	0.8
Smoking [n (%)]	19 (40.4)	10 (23.3)	29 (32.2)	0.014	0.8

As revealed in Table 2, before treatment, a slight difference was observed in TG, TC, LDL-C and HDL-C between the atorvastatin and rosuvastatin groups ($P > 0.05$). Twelve weeks post-treatment, LDL-C decreased by 43.2% and 38.1%, respectively, in the rosuvastatin and atorvastatin groups. The amount of LDL-C reduction was different significantly in both groups (p less than 0.05). Similarly, TC in the group of rosuvastatin also decreased significantly more as compared to the atorvastatin group (34.8% Vs 28.1%, $P < 0.05$). In addition, HDL-C increased and TG decreased 12-weeks after treatment in both groups compared to before treatment. However, there was no significant difference in the magnitude of the decrease in TG or the increase in HDL-C among the two groups (P greater than 0.05).

Table 2: Serum lipid variations of Atorvastatin and Rosuvastatin groups

Parameters	Rosuvastatin group (n=47)			Atorvastatin group (n=43)			
	0 week	12 weeks	Change	0 week	12 weeks	Change	
TC (mmol/L)	5.98±1.18	4.18±0.94	↓34.8	6.60±0.64	4.21±0.73	↓28.1	<0.05
LDL-C (mmol/L)	4.01±0.59	2.21±0.80	↓43.2	3. 88±0.50	2.37±0.81	↓38.1	<0.05
HDL-C (mmol/L)	1.34±0.49	1.57±0.51	↑5.9	1.41±0.60	1.37±0.46	↑4.8	>0.05
TG (mmol/L)	2.83±0.45	1.67±0.48	↓20.1	2.67±0.67	1.13±0.80	↓17.8	>0.05

The proportion of patients achieving the recommended TC target in the rosuvastatin group was greater as compared to the atorvastatin group (51.1% vs. 32.6%, $p > 0.05$) (Table 3). However, the changes in the success rates of LDL-C and TC were insignificant ($P > 0.05$).

Table 3: Goal achievement rates of Atorvastatin and Rosuvastatin groups

Parameters	Rosuvastatin group (n=47)	Atorvastatin group (n=43)	X2	P-value
LDL-C	27(57.4%)	19(44.2%)	1.8	0.2
TC	24(51.1%)	14(32.6%)	1.5	0.21

A slight change among the two groups was observed for liver enzymes, creatinine, CK and glucose compared before and after 12 weeks of treatment ($P > 0.05$). There was one patient in the rosuvastatin group who endured rise in aspartate aminotransferase (AST) to 63 U / L and two patienta experienced an increase in AST to 63 U / L and an increase in alanine aminotransferase (ALT) up to 45 U / L. These abnormal increases returned to normal within two weeks without changing test medications. Also, in only two patients in the atorvastatin group, AST increased to 45 U / L, which was then lowered to normal with the prescribed drug atorvastatin. Both drugs showed similar tolerability and safety during the study.

DISCUSSION

Rosuvastatin is a member of the statins, a class of inhibitors of HMG-CoA reductase. It is extremely operative in decreasing cholesterol[14]. To better understand the safety and efficacy of atorvastatin and rosuvastatin, this study looked at comparing the lipid lowering effects of atorvastatin and rosuvastatin in Pakistani patients with high-risk hyperlipidaemia[15]. The study showed that rosuvastatin 20 mg daily for 12 weeks produced better LDL-C reduction than the same dose of atorvastatin. The findings will increase the weight of the superiority of rosuvastatin over atorvastatin in patients with

hyperlipidaemia. The benefits of therapy to lower LDL-C have been confirmed in patients with high-risk hyperlipidaemia, which means a reduction in the incidence of cardiovascular disease and a better life quality for patients. Based on the convincing results of a series of randomized, controlled trials with a large sample size, NCEP ATP III published in 2014 a set of guidelines for the management of blood cholesterol[16-17]. The ATP III recommendations have been widely accepted in research and clinical trial. on cholesterol management. Therefore, it was also accepted in this study. However, there is another view that argues that in the absence of robust clinical evidence, elevation of LDL-C should not be considered as the primary target of ATP III cholesterol lowering therapy. The study showed a better decrease in LDL-C and TC with a daily dose of 20 mg rosuvastatin for 12 weeks compared to the same dose of atorvastatin[18]. Additionally, the drug rosuvastatin resulted in a higher percentage of patients achieving the recommended target LDL-C and TC levels compared to the drug atorvastatin. Our study found that patients with high-risk dyslipidaemia were also more sensitive to rosuvastatin than atorvastatin. These findings were in line with a previous study that found that more patients taking rosuvastatin (10 to 40 mg) achieved LDL-C levels[19-20]. There is evidence that rosuvastatin (10 mg and 20 mg) reaches the total ATP III cholesterol target in 63.95% of dyslipidaemia patients in India. Similarly, atorvastatin (10 mg) and rosuvastatin (5-10 mg) are sufficient to lower LDL-C by 30-40%, so in this study, based on clinical experience, either atorvastatin or 20 mg rosuvastatin was used[21-22].

The study has limitations. First, your samples are relatively small. Large-scale studies should be carried out to validate and extend the research results. Second, it should be noted that there was an imbalance in the number of withdrawals from treatment despite slight differences in baseline data and demographics between the two groups, which may be a potential source of bias between the atorvastatin and rosuvastatin groups.

CONCLUSION

Overall, rosuvastatin may provide a better lipid-lowering effect than the same dose of atorvastatin in patients with high-risk hyperlipidemia and a higher success rate in LDL-C and TC studies. The study provided additional evidence supporting the superior therapeutic efficacy of rosuvastatin over atorvastatin.

REFERENCES

1. Lorenzi M, Ambegaonkar B, Baxter CA, Jansen J, Zoratti MJ, Davies G. Ezetimibe in high-risk, previously treated statin patients: a systematic review and network meta-analysis of lipid efficacy. Clinical Research in Cardiology. 2019 May;108(5):487-509.
2. Zhao S, Peng D. Efficacy and safety of rosuvastatin versus atorvastatin in high-risk Chinese patients with hypercholesterolemia: a randomized, double-blind, active-controlled study. Current medical research and opinion. 2018 Feb 1;34(2):227-35.
3. Rallidis LS. The changing landscape of lipid-lowering therapy after the new ESC/EAS guidelines for the management of dyslipidaemias: Launching the era of triple hypolipidaemic therapy in very high risk patients. Atherosclerosis. 2020 Jan 1;292:231-3.
4. De Luca L, Arca M, Temporelli PL, Meessen J, Riccio C, Bonomo P, Colavita AR, Gabrielli D, Gulizia MM, Colivicchi F, START Investigators. Current lipid lowering treatment and attainment of LDL targets recommended by ESC/EAS guidelines in very high-risk patients with established atherosclerotic cardiovascular disease: Insights from the START registry. International journal of cardiology. 2020 Oct 1;316:229-35.
5. Hager MR, Narla AD, Tannock LR. Dyslipidemia in patients with chronic kidney disease. Reviews in endocrine & metabolic disorders. 2017 Mar 1;18(1):29.
6. Dyrbuś K, Osadnik T, Desperak P, Desperak A, Gąsior M, Banach M. Evaluation of dyslipidaemia and the impact of hypolipidemic therapy on prognosis in high and very high risk patients through the Hyperlipidaemia Therapy in tERtiary Cardiological cEnTer (TERCET) Registry. Pharmacological research. 2018 Jun 1;132:204-10.
7. Kuo TT, Huang YB, Hsieh CJ. Consumption and market share of cholesterol-lowering drugs in high-risk patients before and after the release of the 2013 ACC/AHA cholesterol guidelines: a retrospective observational study. BMJ open. 2020 Nov 1;10(11):e036769.
8. Kim JB, Song WH, Park JS, Youn TJ, Park YH, Kim SJ, Ahn SG, Doh JH, Cho YH, Kim JW. A randomized, open-label, parallel, multi-center Phase IV study to compare the efficacy and safety of atorvastatin 10 and 20 mg in high-risk Asian patients with hypercholesterolemia. PloS one. 2021 Jan 22;16(1):e0245481.
9. Gitt AK, Lautsch D, Ferrières J, De Ferrari GM, Vyas A, Baxter CA, Bash LD, Ashton V, Horack M, Almahmeed W, Chiang FT. Cholesterol target value attainment and lipid-lowering therapy in patients with stable or acute coronary heart disease: results from the Dyslipidemia International Study II. Atherosclerosis. 2017 Nov 1;266:158-66.
10. Marazzi G, Campolongo G, Pelliccia F, Quattrino S, Vitale C, Cacciotti L, Massaro R, Volterrani M, Rosano G. Comparison of low-dose statin versus low-dose statin+ armolipid plus in high-intensity statin-intolerant patients with a previous coronary event and percutaneous coronary intervention (ADHERENCE trial). The American journal of cardiology. 2017 Sep 15;120(6):893-7.
11. Ganda OP, Bhatt DL, Mason RP, Miller M, Boden WE. Unmet need for adjunctive dyslipidemia therapy in hypertriglyceridemia management. Journal of the American College of Cardiology. 2018 Jul 17;72(3):330-43.
12. Szymański FM, Barylski M, Cybulska B, Wożakowska-Kapłon B, Krasiński Z, Mamcarz A, Widecka K, Płatek AE, Dudek D, Mickiewicz A, Kobayashi A. Recommendation for the management of dyslipidemia in Poland—third declaration of Sopot. Interdisciplinary expert position statement endorsed by the Polish Cardiac Society working group on cardiovascular pharmacotherapy. Cardiology journal. 2018;25(6):655-65.
13. Li YH, Ueng KC, Jeng JS, Charng MJ, Lin TH, Chien KL, Wang CY, Chao TH, Liu PY, Su CH, Chien SC. 2017 Taiwan lipid guidelines for high risk patients. Journal of the Formosan Medical Association. 2017 Apr 1;116(4):217-48.
14. Mikolasevic I, Žutelija M, Mavrinac V, Orlic L. Dyslipidemia in patients with chronic kidney disease: etiology and management. International journal of nephrology and renovascular disease. 2017;10:35.
15. Cannon CP, de Lemos JA, Rosenson RS, Ballantyne CM, Liu Y, Yazdi D, Elliott-Davey M, Mues KE, Bhatt DL, Kosiborod MN, GOULD Investigators. Getting to an ImprOved Understanding of Low-Density Lipoprotein-Cholesterol and Dyslipidemia Management (GOULD): Methods and baseline data of a registry of high

cardiovascular risk patients in the United States. American heart journal. 2020 Jan 1;219:70-7.
16. Yang YS, Yang BR, Kim MS, Hwang Y, Choi SH. Low-density lipoprotein cholesterol goal attainment rates in high-risk patients with cardiovascular diseases and diabetes mellitus in Korea: a retrospective cohort study. Lipids in health and disease. 2020 Dec;19(1):1-3.
17. Yan BP, Chiang FT, Ambegaonkar B, Brudi P, Horack M, Lautsch D, Vyas A, Gitt AK. Low-density lipoprotein cholesterol target achievement in patients surviving an acute coronary syndrome in Hong Kong and Taiwan-findings from the Dyslipidemia International Study II. International journal of cardiology. 2018 Aug 15;265:1-5.
18. Katzmann JL, Sorio-Vilela F, Dornstauder E, Fraas U, Smieszek T, Zappacosta S, Laufs U. Non-statin lipid-lowering therapy over time in very-high-risk patients: effectiveness of fixed-dose statin/ezetimibe compared to separate pill combination on LDL-C. Clinical Research in Cardiology. 2020 Sep 19:1-0.
19. Boutari C, Karagiannis A, Athyros VG. Rosuvastatin and ezetimibe for the treatment of dyslipidemia and hypercholesterolemia. Expert Review of Cardiovascular Therapy. 2021 Jul 3(just-accepted).
20. Zhang X, Xing L, Jia X, Pang X, Xiang Q, Zhao X, Ma L, Liu Z, Hu K, Wang Z, Cui Y. Comparative lipid-lowering/increasing efficacy of 7 statins in patients with dyslipidemia, cardiovascular diseases, or diabetes mellitus: systematic review and network meta-analyses of 50 randomized controlled trials. Cardiovascular therapeutics. 2020 Apr 23;2020.
21. Machado-Duque ME, Gaviria-Mendoza A, Machado-Alba JE. Real-World Effectiveness of Therapy With Rosuvastatin Combined With Fenofibric Acid in a Sample of Colombian Patients With Mixed Dyslipidemia. Journal of Primary Care & Community Health. 2020 Nov;11:2150132720977733.
22. da Silva PM, Aguiar C, Morais J, DISGEN-LIPID study investigators. Suboptimal lipid levels in clinical practice among Portuguese adults with dyslipidemia under lipid-lowering therapy: Data from the DISGEN-LIPID study. Revista Portuguesa de Cardiologia (English Edition). 2019 Aug 1;38(8):559-69.