

COMPARISON OF ROSUVASTATIN WITH ATORVASTATIN IN LOWERING LOW DENSITY LIPOPROTEIN CHOLESTEROL AMONG DYSLIPIDEMIC PATIENTS

Zahidullah Khan, Zahid Fida, Iqbal Haider, Abidullah Khan

Department of Medicine, Khyber Teaching Hospital, Peshawar - Pakistan

ABSTRACT

Objective: To compare the efficacy of Rosuvastatin with Atorvastatin therapy on low density lipoprotein cholesterol (LDL-C) in patients with dyslipidemia after 12 weeks of treatment in a tertiary care hospital.

Material and Methods: This parallel-group, randomized, prospective, comparative, single center trial was conducted in Department of Medicine, District Headquarter Teaching Hospital Dera Ismail Khan from June 2015 to January 2016. This study included 200 patients with dyslipidemia, having LDL-C level of ≥ 130 mg/dl. Patients from both outpatient department (OPD) and admitted were included in the study. Two groups of patients were made randomly. Patients in Group A were treated with Rosuvastatin 10 mg/day and group B were treated with Atorvastatin 10 mg/day. Fasting blood samples were collected from all designed patients in the start of study and after 12 weeks of treatment.

Results: Two hundred patients with dyslipidemia, having a serum low density lipoprotein levels ≥ 130 mg/dl were included in the study. These patients were randomly divided into Group A and Group B, 100 in each group. There were 70 male and 30 female in group A while 75 male and 25 female in group B. Mean age in group A was 53 ± 7.43 years while in group B it was 52 ± 8.12 years. The age ranged between 38 years and 70 years. Mean base LDL-C level was 160 mg/dl in the start of study. Low density lipoprotein levels were reduced by 29% with 10 mg/day of Rosuvastatin and 19% with 10 mg/day of Atorvastatin after twelve weeks treatment. The reduction in LDL-C for Rosuvastatin was more, than for Atorvastatin. The independent sample-t test showed a statistically significant difference between the efficacy of the two drugs, $t(198) = 7.6$, $P < 0.05$, Cohen's $D = 5.14$, effect size = 0.93.

Conclusion: Rosuvastatin 10 mg/day is more effective in reducing LDL-C levels as compared to Atorvastatin 10 mg/day.

Key Words: Dyslipidemia, Rosuvastatin, Atorvastatin, Low Density Lipoprotein Cholesterol.

This article may be cited as: Khan Z, Fida Z, Haider I, Khan A. Comparison of rosuvastatin with atorvastatin in lowering low density lipoprotein cholesterol among dyslipidemic patients. *J Med Sci* 2017; 25: (1) (Supplement) 137-140.

INTRODUCTION

Coronary artery disease (CAD) is one of the major causes of death all over the world. It alone caused 1 of every 6 deaths in the United States in 2009, nearly half million deaths and is the commonest cause of death in United States and puts a lot of burden on the economy of U.S., nearly \$ 142 billion.¹ Strong association has been documented between Dyslipidemia, coronary

artery disease and Cerebro-vascular accident (CVA), thus reducing LDL-C levels is the primary goal of therapy in patients with dyslipidemia.² The results of numerous epidemiologic studies and randomized controlled trials have shown marked benefits by reducing low-Density lipoproteins cholesterol (LDL-C) and cholesterol levels. A study conducted in US showed abnormal serum cholesterol levels in every 2nd person and deranged low density lipoprotein cholesterol levels in every 3rd person.³⁻⁴

Lipid lowering in patients with dyslipidemia is not only associated with favorable outcomes in patients with Coronary artery disease/ peripheral vascular disease but is also an effective intervention in primary prevention.⁵ The likelihood of major cardiac event is reduced by 1% on every 1% reduction in level of LDL Cholesterol.⁶ Thus, reducing LDL Cholesterol level by a small proportion in patients with dyslipidemia could

Dr. Zahidullah Khan (Corresponding Author)

Senior Registrar

Department of Medicine, Khyber Teaching Hospital,
Peshawar - Pakistan

Cell: +92-333-917-3901

Email: zahidullahmarwat@gmail.com

Date Received: December 19, 2016

Date Revised: January 22, 2017

Date Accepted: February 10, 2017

reduce many CAD related morbidity and mortality. Remarkable progress has been made regarding lipid lowering therapy. Currently, the most commonly used agents for lowering LDL-C levels are hydroxymethylglutaryl-coenzyme A reductase inhibitors (HMG-CoA reductase) or Statins. HMG-CoA reductase is an enzyme in cholesterol synthesis pathway.⁷⁻⁹

Numerous local and international trials have been conducted to compare the efficacy and side effect profile of various lipid lowering drugs in comparable as well as higher doses in patients with impaired cholesterol levels. A major trial, Statin Therapies for Elevated Lipid Levels compared Across doses to Rosuvastatin (STELLAR), compared the efficacy of Rosuvastatin with atorvastatin, simvastatin, and pravastatin in different doses and results showed that Rosuvastatin was more efficacious than other commonly used statins in lowering high cholesterol levels¹⁰. In Atorvastatin Versus Revascularization Treatment Trial (AVERT), Atorvastatin significantly lowered low density lipoprotein cholesterol level by 46% and thus ischemic event was reduced by Atorvastatin therapy.¹¹

The purpose of current study is to compare the efficacy of two commonly used statins, Rosuvastatin with Atorvastatin in similar doses because they have different pharmacokinetics and pharmacodynamics and hence may have different efficacy.

MATERIAL AND METHODS

This parallel-group, randomized, prospective, comparative, single center trial was conducted in Medical Department of District Headquarter Teaching Hospital, Dera Ismail Khan. This study was conducted on 200 patients (both male and female) with dyslipidemia who were taking either Rosuvastatin or Atorvastatin 10mg/day. Informed, written consent was taken from all patients undergoing the trial. Fasting lipid profile of all patients included in the study was performed before start of statin treatment (June 2015) and end of study (January 2016). All patients having fasting low density lipoprotein cholesterol levels of ≥ 130 mg/dl and aged ≥ 20 year were included in the study. Patients from both medical OPD and medical ward were enrolled. Patients already taking statins before start of trial, pregnant ladies, alcohol abuse, patients with any genetic disorder, patients with hypothyroidism or nephropathy, active liver disease, patients taking immunosuppressants like steroids or other agents, patients who are physically inactive or taking any hormonal replacement therapy were excluded from the study.

After taking thorough history and clinical examination, all patients were subjected to relevant investigations like peripheral blood smear, liver enzymes, thyroid function tests were performed from the hospital laboratory to exclude the diseases mentioned in exclusion criteria. Tests which could not be performed in hospital laboratory were sent to a reliable laboratory outside the

hospital.

Two groups of patients were formed randomly. Group A patients was given Rosuvastatin 10 mg/day and Group B patients was given Atorvastatin 10 mg/day. Fasting blood samples from the all patients in the start of study and after 12 weeks of therapy were analyzed in hospital laboratory under supervision of single expert biochemist. The patient detailed history, clinical examination with physical findings and results of relevant investigations were noted on questionnaires, devised in accordance with the objectives of the study. Informed, written consent was taken from all patients. Data analysis was performed using SPSS Version 16.

RESULTS

Efficacy data of 200 patients was obtained through randomized sampling, 100 in the Rosuvastatin group (Group A) and 100 in Atorvastatin group (Group B). Group A comprised of 70 male and 30 female while Group B comprised of 75 male and 25 female as shown in Fig 1. Mean ages were 53 ± 7.43 years and 52 ± 8.12 years in Group A and Group B respectively. The age range in study population was 38-70 years.

Table 1 shows efficacy of both statins in comparable doses (10 mg/day) at the end of study duration (12 weeks of treatment). More reduction in LDL-C was seen in patients treated with Rosuvastatin 10 mg/day (29.6%) as compared to patients used Atorvastatin 10 mg/day

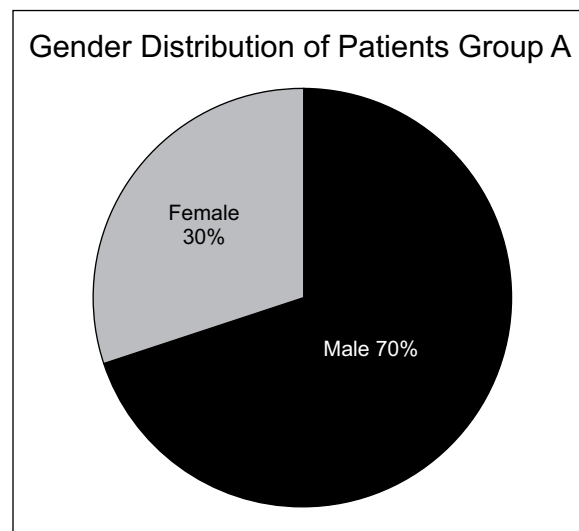


Figure 1:

Table 1: Reduction In LDL-C Level After 12 Weeks Of Treatment With Statins (%)

	Mean Baseline	Rosuvastatin	Atorvastatin	t-test p-value
LDL-C	160 mg/dl	29.6% (-47.4 mg/dl)	19.1% (-30.6 mg/dl)	t-test = 7.6 p \leq 0.05

(19.1%). The reduction in LDL-C for Rosuvastatin was more, than for Atorvastatin. The independent sample-t test showed a statistically significant difference between the efficacy of the two drugs, $t(198) = 7.6$, $P < 0.05$, Cohen's $D = 5.14$, effect size = 0.93.

DISCUSSION

In modern era, preventive medicine is the main focus of primary care practitioners. Diagnosing and managing hyperlipidemia is the prime responsibility of primary care physician and is a simple way of preventing cardiovascular disease. According to data received from Center for Disease Control (CDC), hyperlipidemia is 2nd only to hypertension in list of 10 most common chronic illnesses.¹² High levels of low density lipoprotein cholesterol (LDL-C) increases the risk of cardiovascular diseases while high levels of high-density lipoprotein cholesterol (HDL) decrease the risk of cardiovascular diseases.¹³ Well-balanced diet, exercise are compulsory components along with statins that have been proven to lower the risk of coronary artery disease and stroke, lessen the need for invasive cardiac procedures and reduce the mortality significantly.¹⁴⁻¹⁷

The Third Report of National Cholesterol Education Program Adult Treatment Panel and the Third Joint Task force of European have recommended Low density lipoprotein cholesterol levels $< 100\text{mg/dl}$ in patients with coronary artery disease patients^{18,19}.

Rosuvastatin 10 mg/day lowered Low density lipoprotein levels by 29.6% after 12 weeks of treatment in our study. The results of our study were matching with results of Barakat L, in which LDL-C level were reduced by 29%.¹⁹ This study was conducted on diabetic population. Another study conducted by Arshad AR showed reduction of 24% in LDL-C levels in 6 weeks trail. This result nearly coincides with our result.²⁰ In a local study conducted by Fahim Ullah, LDL-C level was reduced by 24% after six weeks of treatment with Rosuvastatin 5mg/day.²¹ A Study conducted by Nicholls SJ documented that 10 mg of Rosuvastatin reduced LDL-C level by 44% which is higher than our study. In this study Nicholls SJ also found that doubling statins dose brought more reduction in LDL-C by 4-6%.²² Adsule SM also showed 44% reduction LDL-C in patients taking Rosuvastatin 10 mg/day. This study was conducted on a small population (sample size $n=60$).²³ A similar study conducted by Khan S showed 44.3% reduction from baseline in Rosuvastatin group.²⁴

Atorvastatin reduced LDL-C levels by 19% after 12 weeks of treatment. A 6 week trial conducted abroad compared the efficacy of three commonly used statins (Atorvastatin, Simvastatin, Pravastatin) with Rosuvastatin for lowering plasma low-density lipoprotein cholesterol (LDL-C) levels. In this trial, comparable and higher doses of above 3 statins were compared with Rosuvastatin. Atorvastatin 10 mg/day reduced LDL-C levels by 18% while Rosuvastatin 10 mg/day reduced it by 53%.¹⁰

Chaudhry A found in his study that Atorvastatin 10 mg/dl reduced LDL-C by 35%.²⁵ This result is in accordance with our study. A study conducted by Shah M showed that Atorvastatin reduced LDL-C level by 35%.²⁶ These two local studies showed higher levels of reduction as compared to our study. Two studies conducted in United States showed 26% and 28% reduction in LDL-C levels. These results are nearly comparable to our study.^{27,28} Pharmacokinetics and pharmacodynamics properties of all statins are different from each other and hence differ in clinical efficacy and side effects too. Two most commonly statins are simvastatin and atorvastatin. Evidence from local as well as abroad studies show that Rosuvastatin is more efficacious in reducing LDL-C levels and thus has a greater effect on overall morbidity and mortality due to cardiovascular diseases as discussed above.

CONCLUSION

In treating dyslipidemia, Rosuvastatin is superior to Atorvastatin in efficacy in comparable doses.

RECOMMENDATIONS

However large multi-center trials across the country are the need of time.

LIMITATIONS

One limitation of our study was that only one center was involved in study with small catchment area. Secondly, patients admitted to medical ward or seen in OPD only were included in the study.

REFERENCES

1. American Heart Association. Heart disease and stroke statistics update, 2005.
2. Go AS, Mozaffarian D, Roger LV, Lloyd-Jones DM, Benjamin EJ, Berry JD, et al. Heart disease and stroke statistics—2011 update: report from the American Heart Association. *Circulation*. 2013; 127(6):245-49.
3. Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart diseases using risk factor categories. *Circulation*. 1998; 97: 1837-47.
4. Gould AL, Rossouw JE, Santanillo NC, Heyse JF, Furberg CD. Cholesterol reduction yields clinical benefit: impact of statin trails. *Circulation*. 1998; 97: 946-52.
5. Last AR, Ference JD, Falleroni J. Pharmacologic treatment of hyperlipidemia, *American Family Physician*. 2011; 84(5): 551-58.
6. Grundy SM, Cleeman JI, Merz CN, Brewer HB, Jr, Clark LT, Hunninghake DB, et al. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III Guidelines. *J Am Coll Cardiol*. 2004; 44(3): 720-32.
7. Blumenthal RS. Statins: Effective atherosclerotic therapy. *Am Heart J*. 2000; 139: 577-83.
8. Maron DZ, Fazio S, Linton MF. Current prospectives on statins. *Circulation*. 2000; 101: 207-13.
9. Cziraky MJ, Watson KE, Talbert RL. Targeting low HDL-cholesterol to decrease residual cardiovascu-

- lar risk in the managed care setting. *J Manag Care Pharm.* 2008; 14: 3-10.
10. McKenney JM, Jones PH, Adamczyk AM, Cain VA, Bryzinski BS, Blasetto JW. Comparison of the Efficacy of Rosuvastatin versus Atorvastatin, Simvastatin, and Pravastatin in Achieving Lipid Goals: Results From the STELLAR Trial. *Curr Med Res Opin.* 2003;19(8): 689-98.
 11. Pitt B, Waters D, Brown WV, van Boven AJ, Schwartz L. Aggressive lipid-lowering therapy compared with angioplasty in stable coronary artery disease. *Atorvastatin versus Revascularization Treatment Investigators. N Engl J Med.* 1999; 341(2):70-76.
 12. Nelson RH. Hyperlipidemia as a Risk Factor for Cardiovascular Disease. *Prim Care.* 2013; 40(1): 195-211.
 13. Bashore TM, Granger CB, Hranitzky P, Patel MR. Heart disease. In: McPhee SJ, Papadakis MA, Rabow MW, editors. *Current Medical Diagnosis and Treatment.* 54th ed. New York: McGraw-Hill Medical; 2015: 350.
 14. Fedder DO, Koro CE, L'Italien GJ. New National Cholesterol Education Program III Guidelines for Primary Prevention Lipid-Lowering Drug Therapy. Projected Impact on the Size, Sex, and Age Distribution of the Treatment-Eligible Population. *Circulation* 2002; 105: 152-56.
 15. Heart Disease and Stroke Statistics-2015 Update. A Report From the American Heart Association. *Circulation* 2015; 131: 29-322.
 16. LaRosa JC, Hunninghake D, Bush D, Criqui MH, Getz GS. The cholesterol facts. A summary of the evidence relating dietary fats, serum cholesterol, and coronary heart disease. A joint statement by the American Heart Association and the National Heart, Lung, and Blood Institute. The Task Force on Cholesterol Issues, American Heart Association. *Circulation.* 1990; 81(5): 1721-33.
 17. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 2001; 285: 2486-97.
 18. De Backer G, Ambrosioni E, Borch-Johnsen K, Brotons C, Cifkova R. European guidelines on cardiovascular disease prevention in clinical practice. Third Joint Task Force of European and Other Societies on Cardiovascular Disease Prevention in Clinical Practice. *Eur Heart J.* 2003; 24(17): 1601-10.
 19. Barakat L, Jayyousi A, Bener A, Zuby B, Zirie M. Comparison of Efficacy and Safety of Rosuvastatin, Atorvastatin and Pravastatin among Dyslipidemic Diabetic Patients. *ISRN Pharmacol.* 2013;14(6) 579-82.
 20. Arshad AR. Comparison of Low-Dose Rosuvastatin with Atorvastatin in Lipid-Lowering Efficacy and Safety in a High-Risk Pakistani Cohort: An Open-Label Randomized Trial. *Journal of Lipids* 2014: 87(5) 907-10.
 21. Fahim Ullah, Afridi AK, Rahim F, Rahman SU, Ashfaq M. Efficacy of 5mg and 10 mg of Rosuvastatin in Type 2 Diabetes Mellitus with Hypercholesterolemia. *J Ayub Med Coll Abbottabad* 2015; 27(3): 564-68.
 22. Nicholls SJ, Brandrup-Wognsen G, Palmer M, Barter PJ. Meta-analysis of comparative efficacy of increasing dose of Atorvastatin versus Rosuvastatin versus Simvastatin on lowering levels of atherogenic lipids (from VOYAGER). *Am J Cardiol.* 2010; 105 (1): 69-76.
 23. Adsule SM, Baig MS, Gade PR, Khandelwal PN. A Comparative Evaluation of Safety and Efficacy of Rosuvastatin, Simvastatin, and Atorvastatin in Patients of Type 2 Diabetes Mellitus with Dyslipidemia. *Int J Diabetes Dev Ctries.* 2009; 29(2):74-79.
 24. Khan S, Abrar A, Rafique A, Abid AR, Jan T. Efficacy and Safety of Rosuvastatin Compared to Simvastatin in Coronary Artery Disease. *Gomal J Med Sci* 2010; 8(1): 64-69.
 25. Chaudhry A, Mashoori GR, Zehra T, Naz N, Laghari J. Comparative dose efficacy study of Atorvastatin versus Simvastatin and Lovastatin in primary hyperlipidemic patients; *Med Channel* 2008; 14(1): 40-44.
 26. Shah M, Wagan MA, Shah S, Bhurgri AN. Efficacy of statins and fibrates in altering the lipid profile in hypertensive patients. *Medical Channel* 2012; 19(3): 74-77.
 27. Jones PH, Hunninghake DB, Ferdinand KC, Stein EA, Gold A. Effects of rosuvastatin versus atorvastatin, simvastatin, and pravastatin on non-high-density lipoprotein cholesterol, apo-lipoproteins, and lipid ratios in patients with hypercholesterolemia: additional results from the STELLAR trial. *Clin Ther.* 2004; 26(9): 1388-99.
 28. Ohsfeldt RL, Gandhi SK, Fox KM, Stacy TA, McKenney JM. Effectiveness and cost-effectiveness of rosuvastatin, atorvastatin, and simvastatin among high-risk patients in usual clinical practice. *Am J Manag Care.* 2006; 12: S412-23.

CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE NIL

AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

Khan Z: Main idea.

Fida Z: Data collection.

Haider I: Bibliography.

Khan A: Bibliography.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.