COMPARISON OF LIPID LOWERING EFFECTS OF ROSUVASTATIN AND ATORVASTATIN IN TYPE 2 DIABETIC PATIENTS WITH PRIMARY HYPERLIPIDEMIA

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ABSTRACT

Objective: To evaluate & compare the mean change in fasting serum total cholesterol and LDL-C levels from baseline, after 12 weeks of oral treatment with oral Rosuvastatin and with Atorvastatin in type 2 diabetic patients with primary hyperlipidemia.

Study Design: Cross sectional comparative study.

Place and Duration of Study: The present study was conducted in the Medicine Department, Pakistan Naval Ship, Shifa Hospital, Karachi, from Mar to Sep 2016.

Methodology: The sample was collected by non- probability convenient sampling. The total of 114 DM type 2 patients were randomly divided into two equal groups. Group A was given Rosuvastatin whereas group B was given Atorvastatin orally daily for 12 weeks along with oral treatment for diabetes. After 12 weeks, Fasting Serum Total Cholesterol and Serum LDL-C were estimated, and noted as final levels.

Results: There was greater reduction in terms of mean change in serum total cholesterol levels and low-density lipoprotein – cholesterol (LDL-C) levels with Rosuvastatin as compared to Atorvastatin in type 2 diabetic patients with hyperlipidemia.

Conclusion: Rosuvastatin can significantly improve lipid profile as compared to Atorvastatin in type 2 diabetic patients with hyperlipidemia.

Keywords: Rosuvastatin, Diabetes mellitus, Hyperlipidemia, Rosuvastatin.

INTRODUCTION

Diabetes mellitus is an intricate metabolic disorder characterized by the hyperglycemia due to impaired insulin secretion, defective insulin action or both¹. The number of people suffering from diabetes mellitus has elevated rapidly in the past three decades, Asia being a major area of the rapidly evolving type 2 DM global epidemic². According to International Diabetic Federation (IDF) 415 million people were suffering from type 2 DM² and the number is expected to rise to 642 million by the year 2040³. The prevalence of DM in Pakistan is 26.3% as documented by the freshly published National Diabetes Survey of Pakistan (NDSP)⁴. Approximately five million direct deaths occurred due to DM in 2015; implying that in every six seconds a patient dies because of the impediments of Type 2 DM.

Cardiovascular disease (CVD) is a chief source of mortality and disability in type-2 diabetics⁵. The CVD affects approximately 32.2% of all patients suffering from type 2 DM⁶ with 68% mortality⁷. Among middle-age individuals with type 2 DM living in mediocre financial conditions, up to 27 individuals out of 1,000 die from CVD every year; one 3rd of them die from stroke, and one fourth expire from coronary artery disease⁸.

DM aggravates core mechanisms responsible for atherosclerosis and heart failure⁹. Long standing hyperglycemia and insulin resistance play an vital role in the initiation and progression of macro and micro vascular impediments of DM. Number of mechanisms including; increased glucose flux to polyol pathway; increased formation...
of advanced glycation end products (AGEs); stimulation of the receptor for advanced glycation end products (RAGE); oxidative stress; excited inflammation and immune responses and micro RNAs are held responsible for the diabetic vasculopathy. Which is exhibited as endothelial dysfunction, vascular inflammation, arterial remodelling, atherosclerosis and dyslipidemia via increased lipid peroxidation. There is well established positive correlation between the incidence of CVD and levels of low-density lipoprotein cholesterol (LDL-C) concentration.

Decreasing atherosclerotic cardiovascular disease (ASCVD) prevalence in diabetes mellitus is a foremost clinical imperative that should be lined up to prevent premature death, improve quality of life, and reduce individual and economic burdens of concomitant morbidities, diminished work efficiency, and extraordinary cost of medical care provision. Unfortunately, these mechanisms are not effectively restrained by therapeutic approaches aiming solely on ideal glycemic control with available drugs or treatment options at present. Multi dimensional CVD threats, with statins and other lipid-lowering drugs, antihypertensive therapies, life style modifications and anti-hyperglycemic treatment approaches, cardiovascular impediment rates are dropping, yet remain greater for patients with diabetes mellitus as compared to non-diabetics, hence proving the significance of more research in this direction.

Statins are widely used safer Lipid-lowering therapy (LLT) which escalates the clearance of atherogenic lipoproteins and hence reduces plasma cholesterol levels, primarily through decrease in LDL cholesterol. The lowered LDL levels results in a significantly reduced risk of ASCVD with the comparative advantage associated to the total reduction in LDL cholesterol. They are also known to significantly prevent cardiovascular complications of different disease. Statins have a significant role in preventing the long term complications in type 2 diabetic patients. Different drugs from statins group are widely used for treating hyperlipidemia in high risk patients like diabetes, hypertension, stroke and myocardial infarction. Atorvastatin and Rosuvasstatin are commonly used statins for this purpose. Multiple studies have compared their efficacy in wide variety of medical conditions. As the genetic and ethnic diversity has great influence the effectiveness of treatment options among certain population, it is essential to carry out the comparison among various treatment options and their efficacy in our diabetic population, in order to evaluate/compare the benefits of these drugs. The objective of this study was to compare the mean change in fasting Serum Total Cholesterol and LDL-C levels from baseline, after 12 weeks of oral treatment with oral Rosuvasstatin from Atorvastatin in type 2 diabetic patients with primary hyperlipidemia. This study will also be beneficial in suggesting new protocol for management of hyperlipidemia in diabetic population.

**METHODOLOGY**

This randomized control trial study was conducted in the Medicine Department, Pakistan Naval Ship (PNS) Shifa Hospital Karachi, from March 2016 to September 2016. After approval by the ethics committee, PNS Shifa Hospital, written informed consent was taken from the patient’s prior to inclusion in the study. Subjects fulfilling the inclusion criteria, underwent complete systemic examination, along with confirmation of type 2 diabetes mellitus by fasting blood sugar levels. Fasting Serum Total Cholesterol and Serum LDL-C were advised, and noted as baseline. All examination and analysis of labs were done by same researcher to exclude observer bias. The sample size was calculated using World Health Organization sample size calculator by using 5% error, 95% confidence interval and anticipated population 8%. Hence the sample size, n=114 (57 in each group). Sample was collected by non-probability convenient sampling.

The total 114 patients were randomly divided in two groups by lottery method. Group A was the Rosuvasstatin group, prescribed with oral Rosuvasstatin, 5mg at bed time, daily for 12 weeks along with oral treatment for diabetes. Group B
was Atorvastatin group, prescribed with oral Atorvastatin, 10 mg at bed time, daily for 12 weeks along with oral treatment for diabetes. After 12 weeks, Fasting Serum Total Cholesterol and Serum LDL-C were advised, and noted as final levels.

**Statistical Analysis**

Data was evaluated and analyzed using SPSS version 17.0. Mean and Standard deviation was reported for continuous variables (Age, Serum Blood sugar fasting, Fasting Total Serum Cholesterol, Fasting Serum LDL-C) while frequency and percentage for nominal/ordinal data like gender. Mean reductions in Serum Cholesterol and Serum LDL-C in two treatment groups over 12 weeks were calculated and compared using Independent sample t-test. A \( p<0.05 \) was considered as statistically significant.

**RESULTS**

Total 114 patients were included were randomly divided into two equal groups. Group A was given Rosuvastatin whereas group B was given Atorvastatin. Mean age (years) in the study was 49.61 ± 6.39, there were 79 (63.9) male and 41 (36.3) female patients. Mean serum total cholesterol fasting (mmol/L) was 4.85 ± 0.47 in the study whereas mean serum total LDL-C fasting (mmol/L) was 4.08 ± 0.49 in the study (fig-1). Mean change in serum total cholesterol fasting (mmol/L) in group A was 0.88 ± 0.51 and in group B it was 0.05 ± 0.08 which was statistically significant (\( p\)-value 0.000) whereas mean change in serum total LDL-C fasting (mmol/L) in both the groups was 1.42±0.92 and 0.94±0.54 which was again statistically significant (\( p\)-value 0.001) (table-I).

**DISCUSSION**

Dyslipidemia is a well-recognized risk reason for the development & progress of diseases associated with atherosclerosis, including ischemic heart disease (IHD) and stroke. It has been estimated that in USA the prevalence of abnormal raised serum cholesterol is very high and about every 3\(^{rd}\) adult person has raised serum LDL-C levels. The lipid lowering is the most powerful intervention in primary prevention of these diseases. For treating high lipid levels,
Statins drugs are the first-line of therapy used all over the world. The statin drugs in addition to the numeric decrease of lipid profile, they expressively decrease vascular events and all-cause mortality through their pleiotropic properties. It has already been verified & proved that statins drugs have anti-inflammatory, antioxidant properties and anti-thrombotic effects, which further increase their clinical utility. Statin drugs improve endothelial dysfunction and diminish the growth & development of atherosclerotic plaque. Available data & evidence does not powerfully propose clear clinical benefit of other lipid-lowering agents & drugs in such situations.

All of the currently available statins drugs in market have small differences & variation in terms of pharmacodynamic & pharmacokinetics; hence in clinical efficiency, efficacy and side effects profile. Atorvastatin & Simvastatin are the most commonly used statin drugs. It has been evidenced from the Western countries research in dyslipidemia patients that rosuvastatin attains greater reductions & drops in LDL-C and has a higher rate of attaining therapeutic milestones than other statins drugs used currently in market. However, such data from our country Pakistan is inadequate and it is well known that Asians population may respond in a different way from western population because of genetic differences in drug metabolism at the hepatic enzyme and drug transporter level.

In a study conducted in 2014, total serum cholesterol was 0.77 ± 0.85 mmol/L in Atorvastatin group and 1.09 ± 1.010 mmol/L in Rosuvastatin group. Similarly, in our study, mean change in serum total cholesterol fasting (mmol/L) was 0.88 ± 0.51 and 0.05 ± 0.08 in Rosuvastatin and Atorvastatin groups respectively. In our study, mean change in serum total LDL-C fasting (mmol/L) was 1.42 ± 0.92 & 0.94 ± 0.54 in Rosuvastatin and Atorvastatin groups respectively. Whereas, in a study carried out by Arshad AR observed that the mean Low Density Lipoprotein – Cholesterol (LDL-C) levels with Rosuvastatin as compared to Atorvastatin were 0.96 and 0.54 mg/dL respectively.

The findings in the present study are consistent with those reported by Tsutomu Yamazak et al. (2009), by comparing the effects of Rosuvastatin and Atorvastatin in Japanese hypercholesterolemic patients. Momin et al. (2015), studied the effects of these two drugs on type-2 DM stroke patient and concluded that lipid lowering effects of Rosuvastatin is better than Atorvastatin.

**CONCLUSION**

The study concludes that there was a greater reduction in terms of mean change in serum total cholesterol levels and low-density lipoprotein-cholesterol (LDL-C) levels with rosuvastatin 5mg daily as compared to atorvastatin 10 mg daily in type 2 diabetic patients with primary hyperlipidemia.

**CONFLICT OF INTEREST**

This study has no conflict of interest to be declared by any author.

**REFERENCES**