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Comparison of Serum Uric Acid Levels in Ischemic Heart Disease Patients Taking Atorvastatin with those on Rosuvastatin

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ABSTRACT

Objective: To compare serum uric acid levels in stable ischemic heart disease patients taking Atorvastatin versus those taking Rosuvastatin.

Study Design: Quasi-experimental study.

Place and Duration of Study: Combined Military Hospital, Sialkot Pakistan, from Dec 2022 to Dec 2023.

Methodology: A total of 42 patients with stable ischemic heart disease were included in the study. 21 patients were placed in "Atorvastatin Group" and 21 were placed in "Rosuvastatin Group". Baseline serum uric acid levels were documented. Patients received respective statin therapy and after three months, serum uric acid levels were rechecked in both Groups.

Results: Mean age was 45.73±5.01 years. There were 29(69.05%) males and 13(30.95%) females. Mean body mass index was 30.92±3.35 kg/m^2. Mean duration of stable ischemic heart disease was 8.19±1.48 months. 33(78.57%) were smokers. 34(80.95%) were diabetics. 35 (83.33%) had hypertension. In Atorvastatin Group (n = 21), mean post-therapy serum uric acid was 5.11±0.42 mg/dl while in Rosuvastatin Group (n=21) it was 5.60±0.44 mg/dl, (p=0.001).

Conclusion: Serum uric acid level was significantly lower with the use of Atorvastatin as compared to Rosuvastatin therapy.

Keywords: Atorvastatin, Ischemic heart disease, Rosuvastatin, Uric acid.

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INTRODUCTION

"Stable ischemic heart disease (IHD)" is a serious, potentially debilitating disease of the cardiovascular system that is associated with long lasting disability and high rate of mortality with an approximate annual rate reported at more than 5%.[1] This cardiovascular morbidity is the most common cause of death across the globe accounting for more than 9 million death globally and according to previous data it has been found that its prevalence is continuously on the rise with the latest reported prevalence around 200 million.[2] There are several factors that have been studied over the course of years that have the ability to increase the propensity of developing "stable ischemic heart disease (IHD)" including smoking, atherosclerosis, diabetes mellitus, metabolic syndrome and obesity.[3]

One of the highly important association of "stable ischemic heart disease (IHD)" and its outcome is with "hyperuricemia" or raised serum uric acid levels which have been reported to result in poor outcomes secondary to accentuated platelet aggregation, oxidative stress and endothelial dysfunction.[4] Therefore, its effective reduction may provide additional positive outcome benefits in stable IHD patients. Management of advanced "ischemic heart disease (IHD)" is cardiac revascularization surgery or "coronary artery bypass grafting (CABG)" that not only provides significant survival benefit but also has the potential to result in improvement of patient's overall quality of life.[5] However, in majority of patients, medical management through a variety of medications is adopted by the physicians to control the symptoms associated with "stable ischemic heart disease (IHD)" and reduce the rate of its progression.[6] One of the drug that is essential part of drug regimen of stable IHD patients who are managed medically is "statins" which primarily functions to lower the blood cholesterol levels through inhibition of "HMG-CoA reductase" resulting in reduction in the progression of "atherosclerosis.[7]

Statins, which are part and parcel of stable IHD management, have the potential to reduce serum uric acid level.[8,9] However, when it comes to comparison of

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different statins to reduce serum uric acid levels, particularly in patients with stable ischemic heart disease (IHD), which of the statin provides maximum reduction is yet to be established. In addition, to the best of knowledge, this is the first study to be conducted in Pakistan addressing this important prognostic marker of stable IHD. Therefore, this study was conducted with the aim of comparing serum uric acid levels in stable IHD patients taking "Atorvastatin" versus those taking "Rosuvastatin. This will help determining the best possible statin to be used in stable IHD patients that can provide maximal reduction of serum uric acid levels in such patients.

METHODOLOGY

The Quasi-experimental study was conducted at "Combined military hospital (CMH), Sialkot, Pakistan from December 2022-23" with the objective to compare serum uric acid levels in "stable ischemic heart disease" patients taking Atorvastatin versus Rosuvastatin after taking ethical approval (IERB #ERC/05/2024). Appropriate sample size was

$$n = \frac{2\sigma^2(z_{1-\alpha/2} + z_{1-\beta})^2}{(\mu_1 - \mu_2)^2}$$

calculated using OpenEpi sample size calculator for mean difference using following formula:

For calculations, following parameters were filled in the automated mean difference calculator: "confidence level=95%, power=80%, anticipated mean serum uric acid levels after Atorvastatin therapy=5.48±1.44 mg/dl and mean serum uric acid levels after Rosuvastatin therapy = 6.71±1.36 mg/dl".[10] This gave a sample size of 42(21 in each Group).

Inclusion Criteria: Patients who were over the age of 30 years, both males and females who had stable ischemic heart disease, defined as "ischemic cardiomyopathy on echocardiography with preserved ejection fraction of 55-60%", were included in the study.

Exclusion Criteria: Patients who had previous history of CABG, already taking statin therapy, had history of statin induced liver injury/myopathy, chronic liver disease, familial hypercholesterolemia, amino acid metabolic disorders, cancer, myeloproliferative disorder, chemotherapy and radiotherapy, known case of gout and those with history of intake of urocosoric drugs were excluded from the study.

Patients were selected by using "non-probability consecutive sampling technique". Baseline characteristics of the patients including age, gender, body mass index (BMI), history of smoking, diabetes (HbA1C% ≥6.5%), hypertension (BP >130/90), duration of IHD (in months), fasting lipid profile and baseline serum uric acid levels (in mg/dl) were documented. To assess the patient's fasting lipid profile and serum uric acid levels in the patients, a 5ml blood sample was taken by an expert phlebotomist (having a minimum of one year experience) and was sent to in-hospital laboratory before statin therapy. Patients were then divided into two equal Groups randomly using mobile randomizer application. In "ATV Group", patients received tablet Atorvastatin 80 mg once at night for a period of three months. In "ROS Group", patients received tablet Rosuvastatin 20mg once at night for a period of three months. After completion of 03 months, patients were reassessed to check their serum uric acid levels. In addition, fasting lipid profile was also assessed at completion of therapy.

Data analysis was performed using Statistical package for Social Sciences version 20. Quantitative data was represented using Mean±SD. Qualitative data was represented by using percentage and frequency. The independent samples t test (for quantitative variables) and chi square (for qualitative variables) were used. The $p \leq 0.05$ was taken as significant.

RESULTS

In present study, 42 patients (21 in ATV Group and 21 in ROS Group) were included in this study. Mean age was 45.73±5.01 years. There were 29(69.05%) male and 13(30.95%) female patients. Mean BMI was 30.92±3.35 kg/m^2. Mean duration of IHD was 8.19±1.48 months. 33(78.57%) were smokers while 9(21.43%) were non-smokers. 34(80.95%) were diabetics while 8(19.05%) were non-diabetics. 35(83.33%) had hypertension while 7(16.67%) did not had hypertension. Comparison of baseline demographics and pre-treatment lipid profile & uric acid levels between Groups are summarized in Table-I

In ATV Group (n=21), mean post-therapy serum uric acid was 5.11±0.42 mg/dl while in ROS Group (n=21) it was 5.60±0.44 mg/dl, (p=0.001). This comparison, in addition to post-therapy lipid profile parameters is tabulated in Table-II.

DISCUSSION

Statins is a Group of pharmaceutical agents that play an important role in lowering the cholesterol levels of patients having dyslipidemia.[11,12] These do so by inhibiting an important enzyme involved in synthetic process of cholesterol named as "3-hydroxy-3-methyl-glutaryl-CoA reductase (HMG-CoA)".[13,14] An additional effect of statins that have been considered in previous literature to provide additional benefits in patients with cardiovascular disease in their ability to lower the uric acid levels in serum.[15,16] Present study focused on comparing the serum uric acid levels in patients taking two different statins.

Table-I: Comparison of Pre-Treatment Parameters Between Groups (n = 42)

Characteristics	Atorvastatin Group (n = 21)		Rosuvastatin Group (n=21)	*p*-value
Mean age	45.57±5.35 years		45.90±4.77 years	0.832
Gender	Male	15(71.43%)	14(66.67%)	0.739
	Female	6(28.57%)	7 (33.33%)	
Mean Body Mass Index	30.94 ± 3.41 kg/m2		30.90±3.37 kg/m2	0.968
Mean Duration of Ischemic Heart Disease	7.66 ± 0.91 months		8.71±1.76 months	0.020
Smoking	Yes	14(66.67%)	19 (90.48%)	0.060
	No	7(33.33%)	2 (9.52%)	
Diabetes (DM)	Yes	18(85.71%)	16 (76.19%)	0.432
	No	3(14.29%)	5 (23.81%)	
Hypertension (HTN)	Yes	17(80.95%)	18 (85.71%)	0.679
	No	4(19.05%)	3 (14.29%)	
Mean Serum Uric Acid (UA)	6.08±0.42 mg/dl		5.96±0.43 mg/dl	0.375
Total Cholesterol (TC)	254.09±11.71 mg/dl		256.23±10.55 mg/dl	0.537
Triglycerides (TG)	220.71±19.98 mg/dl		219.76±19.24 mg/dl	0.876
Low Density Lipids (LDL)	191.90±8.79 mg/dl		191.23±8.97 mg/dl	0.809
High Density Lipids (HDL)	33.04±5.78 mg/dl		33.04±5.66 mg/dl	1.000

In this study, majority of patients who had IHD had male gender which corresponded with the fact reported globally that men are much more likely to suffer from cardiovascular disease primarily due to differences in expression of certain genes located on sex chromosomes between genders.[17] Majority of the IHD patients who were part of present study were smokers and had co-morbid conditions (like hypertension and diabetes). All these factors have been well-known to play central role in the pathogenesis of "ischemic heart disease (IHD)".[18,19] There was no difference between the two study Groups in terms of baseline lipid profile and serum uric acid levels. However, it was observed that both Atorvastatin as well as Rosuvastatin effectively reduced serum uric acid levels as compared to the baseline levels. This uric acid lowering ability of statins has been reported by Zhang *et al*.,[20] and Ogata *et al*.[21] both of which reported that statins used in present study effectively reduce the levels of uric acid levels. This may be attributed to the ability of statins to enhance renal tubular excretion of uric acid by reduction of its reabsorption.[22] When it comes to comparison of post-therapy uric acid levels, Atorvastatin reduced the levels much more as compared to Rosuvastatin and the difference between the two statin Groups was of statistical significance. This was congruent with the findings of a study conducted by Kose *et al*.,[10] who found Atorvastatin to be much more effective than Rosuvastatin. This uric acid lowering ability of Atorvastatin was also reported by Palikhey *et al*.,[23] Contrarily, Chen *et al*.,[24] reported that both the statins reduce serum uric acid levels without any difference between the two agents. In addition, there was no difference between both statins in terms of post-therapy lipid profile components except for HDL elevation of which was significantly higher with rosuvstatin therapy. Despite extensive research of PubMed, Cochrane library and Medline, limited number of clinical comparison studies were found. Those found were made part of the discussion to make comparison with the findings of present study.

Table II: Comparison of Post-Therapy Parameters Between Groups (n = 42)

Characteristic	Atorvastatin Group (n = 21)	Rosuvastatin Group (n = 21)	*p*-value
Mean serum uric acid (UA)	5.11±0.42 mg/dl	5.60±0.44 mg/dl	0.001
Total cholesterol (TC)	186.66±5.69 mg/dl	186.57±6.78 mg/dl	0.961
Triglycerides (TG)	178.00±12.15 mg/dl	176.42±13.95 mg/dl	0.699
Low density lipids (LDL)	144.28±8.21 mg/dl	138.85±5.86 mg/dl	0.018
High density lipids (HDL)	53.47±7.00 mg/dl	67.19±7.83 mg/dl	< 0.001

Findings of this study exhibit that Atorvastatin may be a better choice for stable IHD patients as compared to Rosuvastatin due to higher reduction of serum uric acid levels being achieved with the use of Atorvastatin. A few limitations of present study were smaller sample size, shorter period of follow up and lack of comparative clinical trials to compare findings

of present study which made it difficult to make extensive comparison of results of present study and observe long term benefits of this uric acid lowering. Therefore, it is recommended that long term cohort studies should be conducted in this regard in future.

CONCLUSION

In conclusion, corresponding to the study finding that serum uric acid level was significantly lower with the use of Atorvastatin as compared to Rosuvastatin therapy, serum uric acid level reduction is significantly greater with the use of Atorvastatin as compared to Rosuvastatin therapy.

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Authors' Contribution

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

AA & TBT: Data acquisition, data analysis, critical review, approval of the final version to be published.

FZ & AT: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

JI & HMU: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

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.

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