ORIGINAL ARTICLE

Effect of Atorvastatin on Hematological Parameters in Patients with Dyslipidemias

NASIR FAROOQ BUTT[1], RABIA RATHORE[2], HINA LATIF[3], *HASSAN MEHMOOD[4], HAFIZ SALEEM FAISAL[5], ADIL IQBAL[6].*

ABSTRACT

Aim: To determine the effect of atorvastatin on hematological parameters in patients with dyslipidemia in order to reduce the cardiovascular risk.

Study Design: Quasi-experimental study.

Place & Duration of Study: Department of Medicine, Mayo Hospital Lahore from January 2017 to December 2017.

Methods: 100patients with treatment naïve dyslipidemia were included in the study.We investigated the effect of atorvastatin on hematological parameters i.e. mean platelet volume (MPV), red cell distribution width(RDW) and Neutrophil Lymphocyte ratio (NLR), which havean association with increased cardiovascular risk.Patients were prescribed 20mg of atorvastatin per day and were evaluated for above mentioned hematological parameters after 12 weeks. Paired t test was applied to compare pre- and post-treatment values of hematological parameters i.e., MPV, RDW and NLR. P-value less than 0.05 was considered significant.

Results: Total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL) and triglycerides levels decreased significantly from baseline to 12 weeks after treatment with atorvastatin. Levels of MPV showed reduction from 10.37±1.27 fl at baseline to 9.35 ± 0.38 fl after treatment. ($p<0.001$). RDW levels fall from 14.46 ±0.51% at baseline to 14.24 ± 0.46 % after treatment. ($p<0.001$). NLR decreased from 2.82 ± 0.25 at baseline to 2.73 ± 0.25 after treatment. ($p<0.001$).

Conclusion: Atorvastatin treatment significantly decreased cardiovascular risk makers like RDW,MPV and NLR in patients with dyslipidemia.

Keywords: Atorvastatin, mean platelet volume, red cell distribution width, neutrophil Lymphocyte ratio.

INTRODUCTION

Cardiovascular disease (CVD) is a group of diseases affecting blood vessels and heart muscles.CVD is one of the major cause of death in the world. An estimated 17 million people die of CVD[1]. In United States about 1.5 million people suffer from acute myocardial infarction annually[2], while in Pakistan 19% of deaths are attributed to CVD[3].

Hyperlipidemia is a disorder which is considered to be due to an abnormally high levels of one or all of the lipids in blood including cholesterol, cholesterol esters and triglycerides[4]. Abnormal lipid metabolism is one of the risk factors for CVD[5]. Hematological parameters like white blood cell count, plateletcount, mean platelet volume (MPV), erythrocyte sedimentation rate red cell distribution width (RDW) and neutrophil lymphocyte ratio(NLR) have been described to be substantial and individual predictor of adverse cardiovascular outcomes[6]. Platelets represent an important linkage between inflammation, thrombosis and atherogenesis[7]. Platelets go through a dramatic change in shape from disc to swollen spheres with greater MPV during activation process. Large platelets are more adhering and liableto clump than smaller ones[8]. Large platelets contain more dense granules which are active both metabolically as well as enzymatically as they contain more prothrombotic material. They show greater clumping in response to Adenosine diphosphate and reduced inhibition of clumping by prostacyclin in vitro[9]. Also large platelets have alpha granules which release prothrombotic substance. When activated under pathological circumstances such as disruption of an atherosclerotic plaque, exaggeratedplatelet activation and clumping may result in thrombosis and vessel blockage. This may lead to myocardial infarction or ischemic stroke, the major causes of mortality and morbidity worldwide[10]. Platelet volume, a marker of platelet activation is measured by MPV.[11]ThusMPV is potentially a useful indicator of platelet function and cardiovascular diseases[12].

RDW describes the variability in size of circulating erythrocytes and is indicated as the coefficient of disparity in the size of red blood cells[13]. Study done by Skjelbakken et al[14] investigated the association between RDW and the risk of first-ever event of Myocardial infarction (MI) in 25,612 participants recruited from a general population. During a median follow-up time of 15.8 years, 1799 participants in total experienced a first-ever MI. They also found a linear association between RDW levels and the risk of first-ever event of MI, for which a 1% increment in RDW level was associated with a 13% increased risk.

The Neutrophil lymphocyte ratio (NLR) is a marker of inflammation and is predictive of death, myocardial infarction, and coronary artery disease.[15]A high NLR is prognostic of atherosclerotic progression. Furthermore, many epidemiological studies have shown that chronic low-grade inflammation, as indicated by the NLR, plays roles in diabetes, hypertension, metabolic syndrome, obesity, dyslipidemia, and endothelial dysfunction[16].

[1,2]Associate Professor Medicine, K. E. Medical University, Lahore
[3]Assistant Professor of Medicine, K. E Medical University, Lahore.
[4]Assistant Professor Pathology, K. E. Medical University, Lahore.
[5]Senior Registrar Medicine, Mayo Hospital, Lahore.
[6]Professor of Medicine, King Edward Medical University, Lahore.
Correspondence to Dr. Rabia Rathore Email: doctorrabia77@gmail.com, cell:0333-4265869

Statins are lipid lowering drugs that inhibits cholesterol biosynthesis by down regulation of hydroxymethylglutaryl co-enzyme A reductase.[17]A wide spectrum of statin mediated actions like reduction in inflammation, plaque stabilization and improvement of endothelial dysfunction may contribute to potential benefits of statins. This manifold action of statins other than cholesterol lowering has been collectively called as pleiotropic effect.[18]The effect of atorvastatin as antiplatelets and anti-inflammatory could play a major part in decreasing cardiovascular risk by reducing the levels of MPV[19].

Recent studies demonstrate that statins have inhibitory activity on platelets, this effect is seen by lower blood levels of inflammatory mediators like IL-6 and IL-8, while statins activate platelet receptors peroxisome proliferator-activated receptorswhich causes attenuation of platelet activation[20]. Study done by Akin etal[21] showed Atorvastatin may effectively decrease MPV levels and neutrophil to lymphocyte ratio. This anti-inflammatoryand anti-platelet effect of treatmentwith atorvastatin could play a leading part in diminishing the cardiovascular risk.

We conducted this study to find out the effect of Atorvastatin on hematological parameters i.e., MPV, RDW and NLR, considering them as the markers of cardiovascular risk.

MATERIAL AND METHODS

This Quasi-experimental study was carried out at Department of Medicine, Mayo Hospital Lahore from January 2017 to December 2017.

Ethical approval was obtained from the institutional review board (IRB) of King Edward Medical University, Lahore.100patients with dyslipidemia were included in the study after taking informed consent.Patients of either gender with base line low-density lipoprotein (LDL) cholesterol above 130mg/dl, total cholesterol above 200mg/dl and triglycerides level above 150mg/dl were included.Patients were excluded from the study if they were hypersensitive toStatins, familialhypercholesterolemia, chronic liver disease,elevated phosphokinase (more than twice the upper limit of normal range), high serum creatinine level, myositis and pregnant females. Patients were prescribed 20mg of Atorvastatin per day and were evaluated for hematological parameters i.e. MPV, RDW and NLR which are linked with heightened cardiovascular risk after 12 weeks of therapy.

All the data was entered and analyzed using SPSS version 23. Continuous data like age, Cholesterol, LDL, high-density lipoprotein (HDL), triglycerides, MPV, RDW and NLR was expressed as Mean ± Standard Deviation. Frequency and percentages were calculated for gender, hypertension, diabetes mellitus and smoking. Continuous variables were evaluated for their normal distribution by applying Kolmogorov-Smirnov test, and those that did not found fit in the criteria were log transformed to acquire normal distribution. Paired t test wasapplied to compare pre- and posttreatment values of hematological parameters i.e. MPV, RDW and NLR. P-value less than 0.05 was considered significant.

RESULTS

Mean Age of the patients was 56.46±3.40 years. There were 55(55%) females and 45(45%) males. 33(33%) patients were smokers, 36(36%) had hypertension and 23(23%) were found to be diabetic (Table 1).

Total Cholesterol levels decreased from 252.48±14.78 mg/dl at baseline to 174.15±14.83 mg/dl after treatment. (p<0.001). High-density lipoprotein (HDL) levels increased from 40.76±3.95 mg/dl at baseline to 46.02±2.41 mg/dl after treatment. (p<0.001). Values of Low-density lipoprotein (LDL) fall from 165.10±14.68 mg/dl at baseline to 113.50±7.89 mg/dl after treatment. (p<0.001). Triglycerides levels also decreased from 178.79±14.04 mg/dl at baseline to 153.82±8.07 mg/dl after treatment. (p<0.001). Levels of Mean platelet volume (MPV) showed reduction from 10.37±1.27 fl at baseline to 9.35±0.38 fl after treatment. (p<0.001). Red cell distribution width (RDW) levels fall from 14.46±0.51% at baseline to 14.24±0.46% after treatment. (p<0.001). Neutrophils–lymphocytes ratio (NLR) decreased from 2.82±0.25 at baseline to 2.73±0.25 after treatment. (p<0.001) (Table 2).

Table 1: Patient Characteristics

Age (Years) Mean ± SD	56.46 ± 3.40
Male	45 (45%)
Female	55 (55%)
Hypertension	36 (36%)
Diabetes mellitus	23 (23%)
Smoker	33 (33%)

Table 2: Effect of Atorvastatin on Hematologic Parameters in Patients WithDyslipidemia.

	Baseline	**After Treatment**	**p-value**
Total Cholesterol (mg/dL)	252.48 ± 14.78	174.15 ± 14.83	0.0001
HDL (mg/dL)	40.76 ± 3.95	46.02 ± 2.41	0.0001
LDL (mg/dL)	165.10 ± 14.68	113.50 ± 7.89	0.0001
Triglycerides (mg/dL)	178.79 ± 14.04	153.82 ± 8.07	0.0001
MPV (fl)	10.37 ± 1.27	9.35 ± 0.38	0.0001
RDW (%)	14.46 ± 0.51	14.24 ± 0.46	0.0001
NLR	2.82 ± 0.25	2.73 ± 0.25	0.0001

Abbreviations: LDL, low-density lipoprotein; RDW, red cell distribution width; MPV. Mean platelet volume; NLR, neutrophils–lymphocytes ratio; HDL, high-density lipoprotein.

DISCUSSION

The relationship between lipids, lipoproteins, and atherosclerotic cardiovascular disease has been known for more than a half a century. Exceptional development in understanding the correlation between lipoproteins and cardiovascular disease (CVD) has taken place during the past 3 decades that includes leading advances in the prevention and management of CVD. By far the most successful of the therapeutic approach has been the use of statins.[22]. Atherosclerosis, the underlying cause of ischemia, has inflammatory origin. Increased serum inflammatory marker levels chiefly, white blood cells, platelets, C-reactive protein, MPV and RDW have been affiliated with a higher possibility of cardiovascular events in many studies[23]. RDW is a measure of the variation in size of circulating erythrocytes normally used for the diagnosis of anemia, has recently drawn increased attention as a potential biomarker of CVD risk. In the study of Patel et al., the RDW values above 14% were significantly related to a decreased red blood cell deformability, which can impair the blood flow through microcirculation. The resultant diminution of oxygen supply at the tissue level may help to explain the increased risk of adverse cardiovascular events associated with elevated RDW.[24]Arbel et al. showed the RDW level of 12% and above is associated with an increased risk of cardiovascular morbidity and all-cause mortality in both anemic and nonanemic patients[25]. In their study, Lippi et al. showed that the combined measure of RDW and cardiac troponin T (cTnT) increased diagnostic sensitivity to 99%, which meant that the combined measure was more effective in diagnosing ACS than the measure of cTnT alone[26]. Moreover, it was proved that RDW is an essential predictor of CAD severity among patients with acute myocardial infarction (AMI)[27].

Regardless of their role in the systemic inflammatory response, platelets have been closely related to the activation and coordination of endothelium. It has recently been observed that there is a close relation between cardiovascular mortality and the number of platelets or their ability to aggregate. Platelets are considered to be important factor inthe development of Ischemic heart disease. Compounded with fibrin, platelets form coronary thrombus[28]. Vagdatli and colleagues showed that MPV and Platelet distribution width are important and simple markers which significantly increase during platelet activation.[29] Furthermore, these indices are helpful in the evaluation of thromboembolic diseases.

Kucera M, et al did a study on 40 hyperlipidemic patients to see the association between the atherosclerotic biomarkers (MPV and RDW) and lipoprotein sub fraction.They also checked the role of atorvastatin on these atherosclerotic biomarkers of cardiovascular risk. Result of this study showed that there was a significant fall in MPV and RDW values after 12 weeks of atorvastatin therapy.Our study also showed the similar results, showing significant decrease in MPV, NLR and RDW values after use of atorvastatin.

Akin Fand associates[21] did a trial in 2013 and analyzed the impact of atorvastatin on hematological parameters in dyslipidemic patients. They used atorvastatin in a dose of 10 -80 mg for 6 months. The results showed noteworthy reduction in levels of MPV and platelet values and NLR.They concluded that atorvastatin has favorable effect on hematological parameters in addition to reduction in lipid levels. The results of our study are consistent with their results, however, we used atorvastatin in a dose of 20mg for only 3 months.

The results of the study done by Sivri and colleagues[31]showed that statins considerably decreased MPV regardless of their effect on lipid profile, and Atorvastatin and Rosuvastatin have similar efficacy regarding this effect. WhileAnand et al showed a notable decrement in the level of inflammatory markers like white blood cells, RDW and MPV with Rosuvastatin as compared to Atorvastatin treatment. Our study was done with Atorvastatin. However, a new research can be done in which we can compare the effects of different statins, like Atorvastatin, Simvastatin, Rosuvastatin and Fluvastatin, so that we can find out the most effective statin which can help control the inflammatory markers in hyperlipidemic patients causing cardiovascular disease[32].

CONCLUSION

The main advantage of hematological indices is that they are relatively inexpensive and thus widely and easily available in daily clinical practice. They have also proven their diagnostic and prognostic value in many cardiovascular diseases including coronary artery disease. Thus, any patient with these raised hematological indices can be treated with Statins, as Statins significantly reduce hematological indices, irrespective of Lipid levels.

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