Original Article

Role of Rosuvastatin in Preventing Risk of Cardiovascular Disease in Patients with Chronic Obstructive Pulmonary Disease

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ABSTRACT

Objective: This study aims to evaluate and treat dyslipidemia in COPD patients and to calculate cardiovascular disease risk before and after treating dyslipidemia.

Study Design: This prospective cohort study

Place and Duration of Study: This study was conducted at the Pharmacology, Khyber Medical College Peshawar KMC Peshawar for eighth months started from February 2022 to October 2022.

Materials and Methods: This prospective cohort study enrolls 140 COPD patients according to the inclusion/exclusion criteria. After proper consent, Body mass index (BMI), LDL/HDL ratio and AIP were calculated as per protocols and 3cc blood was withdrawn from each patient to calculate lipid profile. Patients having dyslipidemia were treated with rosuvastatin 10mg and were followed for 12 weeks. Lipid profile, LDL/HDL ratio and AIP were re-calculated post follow-up and the data were recorded and analyzed using SPSS version 22.0.

Results: The mean age was 56.95 ± 10.21 years. The distribution of male and females were 39.3% and 60.7% respectively. Dyslipidemia was prevalent in 47.9% COPD patients. Based on LDL/HDL ratio, 66.4% patients were in low risk group, 31.4% were in moderate risk and 2.1% were in high CVD risk group. Atherogenic index of plasma (AIP) calculations shows that 5% patients have low CVD risk, 4.3% have intermediate while 90.7% patients have high CVD risk. Post follow-up analysis reveals significant differences in dyslipidemia (p-value 0.01), AIP categories (p-value <0.001) and LDL/HDL ratio (p-value <0.001).

Conclusion: COPD patients are at high risk of developing CVDs due to dyslipidemia. Management of dyslipidemia successfully reduced CVD risk in COPD patients and subsequently results in the reduction of CVD related morbidity and mortality.

Key Words: COPD, dyslipidemia, atherogenic index, LDL/HDL ratio, cardiovascular diseases

Citation of article: Shah MA, Nizamuddin, Subhan Z, Khawaja TM, Mehmood I, Sami Ullah. Role of Rosuvastatin in Preventing Risk of Cardiovascular Disease in Patients with Chronic Obstructive Pulmonary Disease. Med Forum 2023;34(9):37-40. doi:10.60110/medforum.340909.

INTRODUCTION

Dyslipidemia is a medical disorder characterized by elevated levels of total cholesterol (TC), low density lipoprotein (LDL), serum triglycerides (TG) and decrease high density lipoprotein (HDL)[(1)]. Dyslipidemia is routinely investigated to determine the cardiovascular risk and the presence of dyslipidemia alongside other metabolic disorders further enhances the development of cardiovascular diseases (CVDs)[(2)]. COPD is a disease of lungs characterized by limitation in airflow and abnormal increment of inflammatory response to noxious particles. Globally COPD is the 4th leading cause of mortality[(3)]. CVDs are very common in COPD and are considered as independent cause of morbidity and mortality in these patients. Patients with COPD are more prone to develop CVDs than non-COPD patients due to pulmonary hypertension, dysrhythmia and ventricular dysfunction[(4)]. The prevalence of CVDs in COPD is variable ranges from 14% to 33%[(5)]. COPD and CVD are associated and both shares common risk factors including dyslipidemia[(6)]. Dyslipidemia is very prevalent in COPD[(7)] that leads to atherosclerosis; a common risk factor to CVDs development. The cardiovascular risk is often estimated by LDL/HDL ratio and atherogenic index of plasma (AIP)[(8)]. Thus treating dyslipidemia in patients with COPD will results in the reduction of CVD risk and will leads to decrease morbidity and mortality in these patients. This study was designed to evaluate dyslipidemia and cardiovascular risk by calculating

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Received: April, 2023
Accepted: June, 2023
Printed: September, 2023

LDL/HDL ratio and AIP and to find the impact of treating dyslipidemia on CVD risk in COPD patients.

MATERIALS AND METHODS

Enrolment of patients: This single centered prospective study was conducted in the pulmonology and cardiology clinic Khushal Medical Center (KMC) Peshawar. The study was approved by the ethical board KMC Peshawar via letter number KMC/EB01/001. The total duration of the study was eighth months started from February 2022. After proper patient consent, 140 COPD patients of either gender were enrolled in the study. The sample size was calculated using web based tool open epi
(https://www.openepi.com/Menu/OE_Menu.htm),
where proportional model was followed keeping recent prevalence of dyslipidemia in our ethnicity as 29.3%[9] with 95% confidence interval. All the patients were interviewed and the demographics were recorded on pre-designed proforma. After patient history, 3cc blood was extracted from each patient in gel tube and readily centrifuged at 4000rpm for 10 minutes for separation of plasma. The plasma underwent lipid profile analysis using cobas 6000 analyzer c501.

Inclusion exclusion criteria: The global initiative of COPD guidelines (GOLD) was used as diagnostic criteria to enroll COPD patients[3]. Patients with dyslipidemia according to the criteria described previously and willing to participate in the study were included. Patients having other metabolic disorders including chronic kidney disease, chronic liver disease and known cardiovascular disease were excluded from the study. Furthermore, patients on anti-hyperlipidemic drugs and/or not willing to participate in the study were also excluded.

Determination of Body mass index (BMI), LDL/HDL ratio and AIP

The BMI was calculated by dividing patients weight (kg) by their height (meter squared) and classified the patients having normal BMI (18-24.9), pre-obese (25-29.9) and obese (>30)[8]. The LDL/HDL ratio was calculated by dividing LDL value by the HDL value of the patients while AIP was determined as logarithmic transformation of TG to HDL ratio using methods previously described[10]. The LDL/HDL ratio <3 is considered lower risk, 3-5 moderate risk and >5 as high CVD risk. Similarly, the AIP values between 0.3-0.1 is considered lower risk, 0.-0.24 intermediate risk and >0.24 as high CVD risk.

Treatment of dyslipidemia and follow-up: The dyslipidemia was treated with rosuvastatin 10mg for 12 weeks as rosuvastatin is the most efficacious with lower adverse events profile among statins (11). All the patients were followed for 12 weeks interval and after 12 weeks, the patients were reassessed for dyslipidemia and subsequent analysis of LDL/HDL ratio and AIP to determine the CVD risk.

Statistical analysis: Descriptive statistic model was used to determine the frequency and distribution of study parameters including age, gender, BMI, dyslipidemia, LDL/HDL ratio and AIP. Chi-square test/fisher exact test was applied to determine the difference between dyslipidemia, LDL/HDL ratio and AIP before and after follow-up. All the considered test values were 2 tailed. P-value <0.05 were considered significant. SPSS version 22.0 was used for analysis of data while graph-pad prism version 8 was used for construction of graphs.

RESULTS

Demographic characteristics of COPD patients: The mean age of the COPD patients were 56.95 ± 10.21 years. In total 140 enrolled patients, 39.3% were males while 60.7% were females. The BMI was categorized as normal, pre-obese and obese where 38.6% patients having normal BMI, 47.1% were categorized as pre-obese while 14.3% were obese. Dyslipidemia was prevalent in 47.9% COPD patients. Based on AIP categories, 5% patients were classified as lower CVD risk, 4.3% had intermediate risk while 90.7% patients have high CVD risk. Similarly, based on LDL/HDL ratio, 66.4% patients were in low risk categories, 31.4% in moderate risk while 2.1% were in high risk categories. All the details are shown in table 1 below.

Table No. 1: Demographics of study population

Variable		Frequency/Mean	% / SD
Age	-	56.95	10.21
Gender	Male	55	39.3
	Female	85	60.7
BMI	Normal	54	38.6
	Pre-obese	66	47.1
	Obese	20	14.3
Dyslipi-demia	No	73	52.1
	Yes	63	47.9
AIP	Lower risk	7	5
	Intermediate risk	6	4.3
	High risk	127	90.7
LDL/HDL ratio	Low risk	93	66.4
	Moderate risk	44	31.4
	High risk	3	2.1

Impact of rosuvastatin treatment on CVD risk determinants: The CVD risk determinants including dyslipidemia, AIP and LDL/HDL ratio were determined at the initiation of the therapy and after 12 weeks follow-up. The dyslipidemia was prevalent in 47.9% COPD patients initially while it was reduced to 8.6% after treatment. Significant differences were observed before and after treatment with p-value 0.01. Based on AIP categorization, patients with low, intermediate and high CVD risk before treatment were 5%, 4.3% and 90.7% respectively while after treatment, there were 70.7% patients in low risk group, 18.6%

were in intermediate risk group while only 10.7% were in high risk group. The risk of CVD development in COPD patients were significantly reduced with rosuvastatin treatment (p-value <0.001). Furthermore, the LDL/HDL ratio is also significantly reduced (p-value <0.001) with subsequent reduction in CVD risk. The details of each variable are given in table 2 and graphically shown in figure 1 below.

Table No. 2: Association of risk determinants before and after treatment

Variables		Before treatment N(%)	After treatment N(%)	p-value
Dyslipidemia	No	73 (52.1)	128 (91.4)	0.01
	Yes	63 (47.9)	12 (8.6)	
AIP	Low risk	7 (5)	99 (70.7)	<0.001
	Intermediate risk	6 (4.3)	26 (18.6)	
	High risk	127 (90.7)	15 (10.7)	
LDL/HDL ratio	Low risk	93 (66.4)	132 (94.3)	<0.001
	Moderate risk	44 (31.4)	8 (5.7)	
	High risk	3 (2.1)	0 (0)	

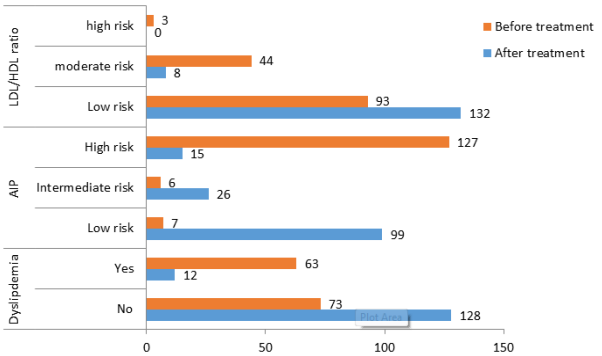

Figure No. 1: Differences in values before and after treatment

DISCUSSION

In our study, the mean age of the COPD patients was 56.95 ± 10.21 years. Female gender was prevalent in our research study with 60.7% as compared to males (39.3%). In consisting with our study, a recent conducted in the same vicinity reported mean age of COPD patients 57.34 ± 9.6 years [9]. Female gender was dominant in our study. According to the previous reports published shows conflicting results regarding gender and COPD while some articles shows no differences between gender and COPD development [12]. In our study, dyslipidemia was prevalent in 47.9% COPD patients. A recent study published in 2023, conducted in Iran reported that dyslipidemia was prevalent in 68.9% COPD patients[13]. Similarly, another report published in 2023 in Pakistan reported 29.3% prevalence of dyslipidemia in COPD patients[9]. Furthermore, many researchers in the past also reported that dyslipidemia is prevalent in COPD patients[7]. The exact mechanism of dyslipidemia in COPD is still ambiguous however, systemic inflammation, oxidative stress and corticosteroids treatment is related to the development of dyslipidemia in COPD[14]. The treatment intervention in our patients significantly reduces dyslipidemia with p-value 0.01. Extensive epidemiological data demonstrated that dyslipidemia increases the risk of CVDs and treating dyslipidemia results in significant reduction in the risk of CVDs and overall cardiovascular deaths[15]. The LDL/HDL ratio is a recent valuable tool to evaluate the CVD risk particularly in COPD patients[16]. In our study based on LDL/HDL ratio, 66.4% patients were at low CVD risk, 31% at moderate risk and 2.1% were at high CVD risk at the initiation of the therapy. The CVD risk was significant reduced post treatment with p-value <0.001, where 94.3% were in low risk while only 5.7% patients have moderate risk, no patients poses high CVD risk post treatment. High levels of low density lipoprotein (LDL) is independently responsible for the atherosclerotic CVDs. reduction in LDL levels greatly reduces the risk of cardiovascular events[11]. In contrast to LDL, high levels of high density lipoprotein (HDL) have positive impact on CVD risk reduction[18]. Thus the overall reduction in LDL/HDL ratio greatly reduced CVD risk[19], consistent with these results, our treatment intervention significantly reduce LDL/HDL ratio and results in subsequent reduction in CVD risk. In our COPD patients, based on AIP categories, 90.7% patients were on high risk, 4.3% were at intermediate risk and 5% patients were a low CVD risk. In consistent with our findings, a report published in the past shows that AIP were increased in COPD patients and at higher risk of developing CVDs[14]. Similar findings were also reported by a recent study representing our ethnicity, where COPD patients were found be at higher risk of CVD development[9]. In our study, the risk of cardiovascular events were significantly decreases post treatment follow-up with p-value <0.001. A meta-analysis published in 2018 reported that dyslipidemia was prevalent in COPD patients and thus these patients are highly prone to CVDs[20]. Thus treating dyslipidemia in COPD provided successful reduction in cardiovascular events. The evaluations of dyslipidemia in COPD patients are very prevalent in many studies around the world but there is very limited information available in treating dyslipidemia in COPD patients. This study is of great importance that not only evaluates the prevalence of dyslipidemia and CVD risk in COPD patients but also successfully treat dyslipidemia in

COPD patients resulting in the reduction of cardiovascular events.

CONCLUSION

Our study concluded that dyslipidemia is very prevalent in COPD patients. Such patients are at high risk of cardiovascular related morbidity and mortality. In our study, management of dyslipidemia results in significant reduction of CVD risk. Clinicians should screen and treat COPD patients for dyslipidemia to reduce the risk of cardiovascular related morbidity and mortality in our settings.

Author's Contribution:

Concept & Design of Study:	Muhammad Abid Shah
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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