Original Article

Effectiveness of High Dose Statins among Acute Coronary Syndrome Patients Presenting at a Tertiary Care Hospital

Muhammad Aqib Javed, Fahar Adnan, Syed Naseem Bukhari, Zubair Zaffar, Muhammad Shoaib Abid and Asif Zarif

ABSTRACT

Objective: The study aimed to determine the effectiveness of high dose statin after four weeks of therapy among patients with acute coronary syndrome (ACS) presenting to a tertiary care hospital.

Study Design: Cross-sectional study.

Place and Duration of Study: This study was conducted at the Department of Cardiology, Ch. Pervaiz Elahi Institute of Cardiology in Multan and Jinnah Hospital in Lahore, from January 2020 to July 2020.

Materials and Methods: About 160 ACS patients fulfilling the inclusion criteria were enrolled. All patients underwent a fasting serum lipid profile for measuring the serum low-density lipoprotein (LDL) level on the baseline. Then at the end of four weeks after obtaining treatment with high dose statin. The patients were treated with Rosuvastatin (40 mg) orally once daily and Atorvastatin (80 mg) on an alternate basis for four weeks. The effectiveness of high dose statins in lowering the serum LDL levels was measured.

Results: The mean age of the enrolled patients was 41.88 ± 11.05 years, and more female patients presented at the study site during this period. The minimum serum LDL level observed after treatment was 103 mg/dl, and the mean hemoglobin level was 121.95 ± 11.83 mg/dl, where it maximally reached 140 mg/dl. 51.2% of patients were hypertensive, and the high-dose of statins effectively reduced the serum LDL levels among 71% of cases. It was found that the efficacy was significantly associated with the age, gender and presence of hypertension ($p<0.05$).

Conclusion: The administration of the high dose of statins for four weeks (Rosuvastatin + Atorvastatin) effectively lowered the serum LDL levels among the ACS patients.

Key Words: Acute Coronary Syndrome, STEMI, Non-STEMI, High Dose Statin Therapy, Hypertension

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INTRODUCTION

CVD is the leading cause of death worldwide, accounting for 31% of the overall death rate where heart attack and strokes are the prominent contributors. According to the World Health Organization (WHO), in 2016, 17.9 million people died from CVDs and three-quarters of these deaths were reported in low- and middle-income countries [1]. Advancing age is the most potent independent risk factor for CVD, while other factors closely associated with advanced age include frailty, obesity, and diabetes [2].

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Although females tend to have a comparatively more extended life expectancy than males, elderly females or those > 80 years of age make up the most significant percentage of CVD diagnoses [3].

ACS refers to a group of clinical presentations, including ST-segment elevation myocardial infarction (STEMI) and non–ST-segment elevation myocardial infarction (NSTEMI) or unstable angina [4]. It is associated with partial or complete thrombosis of the infarct-related artery. Atherosclerosis is among the primary etiological factors of ACS. Palpitations, pain, shortness of breath (exertional), diaphoresis, nausea, and decreased exercise tolerance are the most common complaints among ACS patients. Potential complications include Ischemia and Myocardial infarction (MI). According to current guidelines, secondary prevention typically includes lifestyle modifications and therapeutic management to control risk factors [5,6]. For acute ACS, anti-thrombotic, anti-ischemic medications, and revascularization procedures, including percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG), are highly recommended [5,6].

Statins have anti-thrombotic effects; they are primarily used to lower the cholesterol levels among CVD

patients [7] and are often used for secondary prevention of ACS. High-dose statin treatment effectively improves the long-term outcomes of ACS, reducing the risk of cardiovascular complications and associated death, which is also supported by many clinical studies and randomized controlled trials (RCTs) [8-12]. Therefore, the present study aimed to determine the effectiveness of high dose statins after four weeks of therapy among ACS patients presenting to tertiary care hospital.

MATERIALS AND METHODS

This cross-sectional study was conducted from 4th January to 3rd July 2020 at the cardiology and medical unit of CPEIC-Multan and Jinnah hospital-Lahore. A sample size of 160 was calculated using a 95% confidence level, 6.5% margin of error and taking expected efficacy at the end of 4 weeks of treatment 78.6%[5]. Both male and female ACS patients between 25 to 60 years of age were included in the study. While under exclusion, all patients with alanine aminotransferase (ALT) levels > 3 upper limits of normal (ULN), serum creatine kinase (CK) level > 3 ULN, serum creatinine > 2 mg/dl, receiving lipid-lowering therapy for > 3 months before admission and those with history of hypersensitivity to statins were kept.

Written informed consent was obtained before inclusion in the study. The fasting serum lipid profile was estimated for measuring the baseline serum LDL level. The patients were treated with Rosuvastatin (40 mg) orally once daily and Atorvastatin (80 mg) on an alternate basis for four weeks. At the end of 4 weeks of treatment with high dose statin, the fasting serum lipid profiles were again assessed to observe the effectiveness of high dose statin in lowering the serum LDL level.

Effectiveness of High Dose Statin: A significant reduction in serum LDL level (40 or more) on comparing baseline and after four weeks of high dose statin administration.

The following formula calculated percentage reduction:

$$\frac{(\text{LDL at baseline}) - (\text{LDL at four weeks})}{\text{LDL at baseline}} \text{ X } 100$$

Data were analyzed using SPSS version 17.0; continuous variables including age and serum LDL level were summarized as mean and standard deviation. Categorical variables like gender and efficacy were presented as frequency and percentages. Data was stratified for age, gender and presence of hypertension (BP > 160/90). Post-stratification chi-square test was applied, taking p-value < 0.05 statistically significant.

RESULTS

A total of 160 ACS patients were treated at the study site; the mean age of these patients was 41.88±11.05 years. There was a female majority, i.e. the sample included 51.9%, female patients and 48.15 male patients. Moreover, 51.2% of patients were hypertensive. The mean hemoglobin levelwas 121.95±11.83 mg/dl, and it maximally reached up to 140 mg/dl. The mean serum LDL level was reduced up to 103.00 mg/dl.

Table No.1: Demographic & clinical characteristics of the study patients

Variables		**N=160**
Age (years)		41.88±11.05
Hemoglobin Level (mg/dl)		121.95±11.83
Gender	Male	96(60)
	Female	64(40)
Hypertension	Yes	82(51.2)
	No	78(48.8)
Efficacy	Yes	115(71.9)
	No	45(28.1)

The efficacy of high dose statin was stratified with respect to age, gender and hypertension. It was found that efficacy is significantly associated with the age group, gender and hypertension with p-value<0.05.

Table No.2: Stratification of Efficacy with respect to age, gender and hypertension

Variables		**Efficacy n(%)**		**Total**	**p-value**
		Yes (n=115)	**No (n=45)**		
Age	≤ 40 years	64(83.11)	13(16.8)	77	0.002*
	>40 years	51(61.44)	32(38.5)	83	
Gender	Male	83(86.45)	13(13.5)	96	0.000*
	Female	32(50)	32(50)	64	
Hypertension	Yes	44(53.6)	38(46.3)	82	0.001*
	No	71(91.02)	07(87.5)	78	

**p<0.05 is considered statistically significant*

DISCUSSION

As CVDs are known to add significant social and financial burden globally, research focusing on the primary and secondary prevention of these cardiovascular events is necessary to control this public health hazard. Following RCTs, statins have effectively gained popularity for both primary and secondary prevention among CVD patients. The present research objective was to determine the effectiveness of high dose statin after four weeks of therapy among ACS patients presenting at a tertiary care hospital.

In this study, with the administration of high dose statins, i.e. Rosuvastatin (40 mg) + Atorvastatin (80 mg), we found that the percentage reduction in the serum LDL level was 103 mg/dl and the maximum hemoglobin level observed was 140 mg/dl with a mean value of 121.95 ± 11.83 mg/dl. A significant reduction in the serum LDL level was observed among 71% of patients, efficacy derived via comparing the baseline

LDL levels with the one after four weeks (after administration of high dose statins). A meta-analysis including 11 articles displayed that Rosuvastatin's loading dose significantly reduced the hs-CRP level after PCI, TG and TC ($p<0.05$). Compared with the conventional dose, Rosuvastatin's loading dose was more beneficial to patients with ACS in China and is suitable for clinical application [13].

Existing literature showed that 27%(n=46,675) of 174,149 randomly assigned participants were women [14]. Allocation to a statin had similar absolute effects on the 1-year lipid concentrations among both men and women (LDL cholesterol reduced by about 1.1 mmol/L in statin vs control trials and roughly 0.5 mmol/l for more-intensive vs less-intensive therapy). Women were generally at lower cardiovascular risk than men. The proportional reductions per 1.0 mmol/l reduction in LDL cholesterol in major vascular events were similar overall for women (rate ratio [RR] 0.84, 99% CI 0.78-0.91) and men (RR 0.78, 99% CI 0.75-0.81, adjusted p-value for heterogeneity by sex=0.33)[14]. The present study had a high frequency of females as compared to males. Therefore, the effectiveness of a high-dose of statins as observed might be influenced by the gender-based differences in the study sample.

Kasai et al. conducted a small study including PCI patients (n = 575). It was found that the mortality rate was significantly reduced among patients treated with a statin compared to the counterparts during an 11-year follow-up[15]. Another study explained how the mortality rate was raised among post-MI patients due to low adherence to the statin treatment [16]. Although the high statin dose effectively reduced the serum LDL levels, but the outcomes were significantly affected by modifiers, including age, gender and hypertension. It is known that cardiovascular health is interlinked to several other factors, including comorbidities, stress and depression, etc[17,18]. Studies report an increased risk of death for diabetics of either gender that may or may not be associated with CVD. One of the reasons for this might be that diabetes itself is linked to several other complications [19]. However, the current study doesn't involve comorbid history except for hypertension, which is also one of the limitations.

No serious adverse effects were observed among the present study participants. In contrast, a previous study reported myalgia among ACS patients treated with statins. Apart from the positive effects of statins among ACS patients documented in the literature, it has also been associated with diabetes on set [20], worsening insulin resistance, and effects the secretion and metabolic control [21]. Rocco et al. suggested that the positive effects of statins on the serum LDL levels outweigh the negative effects associated with metabolic control [20,22]. However, the statin treatment showed a significant impact on the serum LDL levels among the ACS patients in the present study, which is also in support of several existing studies, but there are certain limitations to the present findings. First and foremost, the patient's medical history that might have altered the treatment efficacy during the course was not inquired. Moreover, outcomes like repeated hospitalization and mortality rate must also be considered for future inferences.

CONCLUSION

The findings of the present study add to the pre-existing evidence that statin treatment has a beneficial effect on the serum LDL level among patients with CVD. The significant association of statin treatment efficacy with age, gender and hypertension highlights the need to identify the relation, impact and risk caused by these correlates. As it is essential to identify patients with a high-risk secondary modifier to confirm treatment effect.

Author's Contribution:

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

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