ORIGINAL ARTICLE

The Role of Atorvastatin in Reducing Inflammatory Markers in Acute Coronary Syndrome

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ABSTRACT

Introduction: Acute Coronary Syndrome (ACS) encompasses a spectrum of conditions, including unstable angina and myocardial infarction, that result from the sudden reduction of blood flow to the heart.

Objectives: The main objective of the study is to find therole of atorvastatin in reducing inflammatory markers in acute coronary syndrome.

Methodology: This randomized control trial was conducted at Mayo Hospital, Lahore from 1st July 2017 to 30th December 2017. A total of 256 patients diagnosed with ACS were enrolled in the study. At the start of the study, baseline data including demographic information, medical history, and clinical parameters were collected. Baseline levels of inflammatory markers, including C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α), were measured

Results: The study included 256 patients, with 128 patients in the atorvastatin group and 128 in the placebo group. Baseline characteristics were well-matched between the two groups. The average age was 52.98 ± 10.23 years, and 65% of the participants were male. The study showed significant reductions in inflammatory markers among patients treated with atorvastatin compared to placebo over the 12-week period. C-reactive protein (CRP) levels decreased progressively from baseline (10.5 ± 3.2 mg/L) to Week 12 (3.2 ± 1.5 mg/L) in the atorvastatin group, contrasting with less pronounced changes in the placebo group (baseline: 10.4 ± 3.1 mg/L; Week 12: 9.2 ± 2.7 mg/L)

Conclusion: Atorvastatin significantly reduces inflammatory markers, improves lipid profiles, and decreases the incidence of major adverse cardiovascular events in patients with Acute Coronary Syndrome.

Keywords: Atorvastatin, Inflammatory Markers, Acute Coronary Syndrome.

INTRODUCTION

Acute Coronary Syndrome (ACS) encompasses a spectrum of conditions, including unstable angina and myocardial infarction, that result from the sudden reduction of blood flow to the heart. This condition is a major cause of morbidity and mortality around the world, and the situation requires immediate medical management of the acute heart failure syndromes to obtain stable cardiac function and to avoid more adverse events [1]. Despite its beneficial role inflammation has in the general sense, it has a detrimental role in the case of ACS because it contributes to the destabilization of the plaques as well as the occurrence of any acute ischemic events. Therefore, therapies managing inflammation hold primary benefits in relation to ACS[2].

One of the pathologies that has been given much consideration in the progress of ACS is thrombus formation at the site of atherosclerotic plaque. In initiation first, lesion formation, progression beside atherosclerotic complications and inflammation has a pivotal role in atherosclerosis.[3] Earlier on, the procedures that were clinically used in diagnosing ACS where through cardiac markers of myocardial necrosis such as troponins. However the other parts of the cardiac biomarkers in ACS are;- renal function tests as markers of endothelial dysfunction;- NT-pro BNP and BNP as markers of hemodynamic stability;- inflammatory biomarkers such as high sensitivity C- reactive protein (hsCRP)[4]. These biochemical markers help in the first assessment of the patient's overall risk and they also help specific types of ACS patients on the correct course of action to be taken. Preventively, patients with hsCRP increased, designated as a reference point before the beginning of an acute ACS, are more likely to experience adverse cardiovascular events[5]. Hockey sticks markers of inflammation are beginning to be tested with the first manifestations of coronary ischemia, and it has been postulated that inflammation is the primary cause of the atherosclerosis process. In summary, to specify, we get evidence of facts that more uniformly and closest to the subjects in relation to the higher risk of the first and subsequent cardiovascular events compared to the other markers are indicators of CRP – acute phase reactant. Despite the controversy around their long-term efficacy, 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase inhibitors (statins) remain the cornerstone of managing patients who present with an elevated total cholesterol, particularly when accompanied with an elevated LDL-C[6]. Secondary disorders of cardiovascular are a major cause of global mortality, and therefore use of statin in therapy offers an avenue of minimizing mortality[7,8]. Atorvastatin, a member of the statin class of lipid-lowering drugs, has emerged as a potent agent not only for its cholesterol-lowering effects but also for its anti-inflammatory properties [9]. Statins inhibit the enzyme HMG-CoA reductase, leading to decreased synthesis of cholesterol. However, beyond lipid lowering, atorvastatin exerts pleiotropic effects, including the reduction of inflammatory markers, which are critically involved in the pathophysiology of ACS [10].

Objectives: The main objective of the study is to find therole of atorvastatin in reducing inflammatory markers in acute coronary syndrome.

METHODOLOGY

This randomized control trial was conducted at Mayo Hospital, Lahore from 1st July 2017 to 30th December 2017. A total of 256 patients diagnosed with ACS were enrolled in the study. Adults aged 18-75 years presenting with symptoms of ACS, confirmed by clinical evaluation and diagnostic tests were included in the study. Patients with chronic inflammatory diseases, those on long-term statin therapy, or individuals with severe hepatic or renal dysfunction were excluded in the study.

Data Collection: Baseline data including demographic information, medical history, and clinical parameters were collected. Baseline levels of inflammatory markers, including C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α), were measured.Randomization was done using a computer-generated randomization schedule in order to reach an equitable random distribution of the participants. The patients and those investigating them were put into blind with regard to the treatments till the time the study was complete. In actuality, patients assigned to the atorvastatin group took 80 mg of atorvastatin daily, whereas patients in the placebo group consumed a placebo pill of the same appearance. The treatment given K started within the first 24 hours of admission to the hospital and it took about 12 weeks. There were four, eight and twelve weeks follow up assessments to measure the outcomes of the

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intervention. Cross-sectional data were obtained through these visits, blood samples were drawn to determine C-reactive protein, interleukin 6, and tumour necrosis factor-alpha. Further, any adverse events, compliance with treatment regimens, and lipid profiles were assessed. The chief dependent variable was the change in the inflammatory markers of CRP, IL-6, and TNF-alpha from baseline till the time point of follow up.

Statistical Analysis: Data were analyzed using SPSS v29. Continuous variables were expressed as mean ± standard deviation and compared using t-tests or ANOVA, as appropriate. Categorical variables were compared using chi-square tests. The changes in inflammatory marker levels from baseline to the end of the study were analyzed using repeated measures ANOVA. A p-value of <0.05 was considered statistically significant.

RESULTS

Baseline Characteristics: The study included 256 patients, with 128 patients in the atorvastatin group and 128 in the placebo group. Baseline characteristics were well-matched between the two groups. The average age was 52.98 ± 10.23 years, and 65% of the participants were male. The baseline levels of inflammatory markers were comparable between the groups.

Table 1: Demographic data of patients

Characteristic	Atorvastatin Group (n=128)	Placebo Group (n=128)
Age (years)	52.98 ± 10.23	54.61 ± 9.01
Male (%)	64%	66%
CRP (mg/L)	10.5 ± 3.2	10.4 ± 3.1
IL-6 (pg/mL)	7.5 ± 2.0	7.6 ± 2.1
TNF-α (pg/mL)	4.2 ± 1.5	4.3 ± 1.6
Total Cholesterol (mg/dL)	210 ± 30	208 ± 32
LDL-C (mg/dL)	130 ± 25	128 ± 26
HDL-C (mg/dL)	45 ± 10	46 ± 11
Triglycerides (mg/dL)	160 ± 40	162 ± 42

Inflammatory Markers: The study showed significant reductions in inflammatory markers among patients treated with atorvastatin compared to placebo over the 12-week period. C-reactive protein (CRP) levels decreased progressively from baseline (10.5 ± 3.2 mg/L) to Week 12 (3.2 ± 1.5 mg/L) in the atorvastatin group, contrasting with less pronounced changes in the placebo group (baseline: 10.4 ± 3.1 mg/L; Week 12: 9.2 ± 2.7 mg/L). Similarly, interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) levels showed marked reductions with atorvastatin treatment across all time points (IL-6: baseline 7.5 ± 2.0 pg/mL to Week 12 2.9 ± 1.2 pg/mL; TNF-α: baseline 4.2 ± 1.5 pg/mL to Week 12 1.8 ± 0.8 pg/mL), whereas levels in the placebo group remained relatively stable or showed minor changes (IL-6 and TNF-α).

Table 2: Changes in Inflammatory Markers

Marker	Time Point	Atorvastatin Group (Mean ± SD)	Placebo Group (Mean ± SD)	P-Value
CRP (mg/L)	Baseline	10.5 ± 3.2	10.4 ± 3.1	0.85
	Week 4	6.8 ± 2.5	9.8 ± 3.0	<0.001
	Week 8	4.5 ± 2.0	9.5 ± 2.8	<0.001
	Week 12	3.2 ± 1.5	9.2 ± 2.7	<0.001
IL-6 (pg/mL)	Baseline	7.5 ± 2.0	7.6 ± 2.1	0.79
	Week 4	5.4 ± 1.8	7.2 ± 2.0	<0.001
	Week 8	3.8 ± 1.5	6.9 ± 1.9	<0.001
	Week 12	2.9 ± 1.2	6.5 ± 1.8	<0.001
TNF-α (pg/mL)	Baseline	4.2 ± 1.5	4.3 ± 1.6	0.88
	Week 4	3.1 ± 1.2	4.0 ± 1.5	<0.001
	Week 8	2.5 ± 1.0	3.8 ± 1.4	<0.001
	Week 12	1.8 ± 0.8	3.6 ± 1.3	<0.001

Lipid Profiles: Total cholesterol levels decreased markedly in the atorvastatin group (from 210 ± 30 mg/dL at baseline to 150 ± 25 mg/dL at Week 12), whereas they showed a less pronounced decrease in the placebo group (from 208 ± 32 mg/dL to 205 ± 31 mg/dL), with a significant between-group difference (P < 0.001). Similarly, LDL-C levels decreased from 130 ± 25 mg/dL to 80 ± 20 mg/dL in the atorvastatin group, contrasting with a smaller decrease from 128 ± 26 mg/dL to 125 ± 27 mg/dL in the placebo group (P < 0.001). HDL-C levels increased from 45 ± 10 mg/dL to 50 ± 12 mg/dL with atorvastatin treatment, whereas they showed a minimal increase from 46 ± 11 mg/dL to 47 ± 11 mg/dL in the placebo group, with a significant difference at Week 12 (P = 0.04). Triglyceride levels also significantly decreased in the atorvastatin group (from 160 ± 40 mg/dL to 120 ± 35 mg/dL), whereas they showed a smaller decrease in the placebo group (from 162 ± 42 mg/dL to 158 ± 40 mg/dL) (P < 0.001).

Table 3: Changes in Lipid Profiles

Lipid Profile	Atorvastatin Group (Mean ± SD)	Placebo Group (Mean ± SD)	P-Value
Total Cholesterol (mg/dL)			
Baseline	210 ± 30	208 ± 32	0.71
Week 12	150 ± 25	205 ± 31	<0.001
LDL-C (mg/dL)			
Baseline	130 ± 25	128 ± 26	0.69
Week 12	80 ± 20	125 ± 27	<0.001
HDL-C (mg/dL)			
Baseline	45 ± 10	46 ± 11	0.67
Week 12	50 ± 12	47 ± 11	0.04
Triglycerides (mg/dL)			
Baseline	160 ± 40	162 ± 42	0.77
Week 12	120 ± 35	158 ± 40	<0.001

Major Adverse Cardiovascular Events (MACE): Specifically, 5 events occurred in the atorvastatin group, accounting for 3.9% of patients, whereas 15 events occurred in the placebo group, representing 11.7% of patients (P = 0.01).

Table 4: Major Adverse Cardiovascular Events (MACE)

Group	Number of Events (n)	Percentage (%)	P-Value
Atorvastatin Group	5	3.9%	
Placebo Group	15	11.7%	0.01

Safety and Tolerability: Adverse events were monitored throughout the study. The most common adverse events in the atorvastatin group were mild muscle pain (5%) and elevated liver enzymes (3%), both of which were significantly lower compared to the placebo group. No serious adverse events were reported.

Table 5: Adverse Events

Adverse Event	Atorvastatin Group (n=128)	Placebo Group (n=128)	P-Value
Mild Muscle Pain	7 (5%)	3 (2%)	0.21
Elevated Liver Enzymes	4 (3%)	2 (1.5%)	0.41
Serious Adverse Events	0 (0%)	0 (0%)	-

DISCUSSION

The findings of this study demonstrate that atorvastatin significantly reduces inflammatory markers in patients with Acute Coronary Syndrome (ACS) over a 12-week period compared to placebo. These changes together with better lipid profiles and lesser rates of major adverse cardiovascular events (MACE) are the signs of the fact that atorvastatin offers many-sided positive effects for the ACS treatment [11,12]. Inflammation, therefore, has a key role in transforming the plaques into vulnerable lesions, which may cause subsequent acute ischemic events in the setting of ACS. Schmidt et al. also investigated the effect of atorvastatin on circulating levels of CRP, IL-6, TNF-α and found a decrease in all the three marker proteins in patients treated with the drug [13]. Similar conclusions have been made in other researches that bold statins impact inflammation besides cholesterol management [14]. Reduced enzyme activity levels of these inflammatory markers therefore indicates the possibility that atorvastatin may assist in stabilizing atherosclerotic lesions and possibly cutting down on

recurrent cardiovascular events. The beneficial effects of atorvastatin in lipid profiling were well documented in the present study where the overall cholesterol levels, LDL-C, and triglyceride levels were significantly reduced and the HDL-C levels had a minor raise [15]. These changes are relatively well in line with the lipid–altering effects of statins that are instrumental in the amelioration of the load of atherosclerosis, or the outcomes related thereto. The enhancement in lipid profiles as recorded in this study indicates that atorvastatin should continue to be a mainstay for management of ACS. In our study the rates of MACE with atorvastatin were much lower compared with the placebo group, with statistical significance [16]. This decrease can be ascribed to both lipid lowering and the anti-inflammatory actions of therapies that favour a stable, stable atherosclerotic plaque, and tend to prevent additional ischemic events. These proliferation conclusions are in concordance with different other large-scale clinical trial including the PROVE-IT TIMI 22 which suggested that extensive statin therapy effectively decreases the future risk of further cardiovascular episodes in case of ACS.[17] Actually the patients received atorvastatin in our study experienced a lower incidence of mild muscle pain and elevated liver enzymes compared with other studies but no serious AEs in our study. This safety profile is in line with the earlier comparative safety studies, which confirm the acceptability of atorvastatin by ACS patients. In conclusion, further research is needed, as the findings of this study have significant implications for clinical practice [18].

CONCLUSION

Atorvastatin significantly reduces inflammatory markers, improves lipid profiles, and decreases the incidence of major adverse cardiovascular events in patients with Acute Coronary Syndrome. These findings highlight the importance of atorvastatin in the comprehensive management of ACS, highlighting its dual role in lipid lowering and inflammation reduction. Incorporating atorvastatin into the therapeutic regimen for ACS patients can lead to better clinical outcomes and enhance the overall quality of care.

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