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Original Article

High Dose Statin as Upstream Therapy and the Frequency of Slow-Flow Phenomenon in Patients Undergoing Primary PCI or Immediate Invasive Therapy

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ABSTRACT

Background: Coronary artery disease (CAD) remains a leading cause of morbidity and mortality worldwide, necessitating effective treatment strategies. High-dose statin therapy has emerged as a potentially superior approach to improving coronary blood flow and reducing the slow-flow phenomenon, a common complication following percutaneous coronary intervention (PCI), compared to standard-dose statin therapy.

Objective: This study aimed to evaluate the efficacy of high-dose statin therapy as an upstream treatment in enhancing coronary blood flow and reducing the incidence of the slow-flow phenomenon in patients undergoing primary PCI or immediate invasive therapy for acute myocardial infarction (AMI).

Methods: In a prospective observational study conducted between February 2023 and January 2024, 95 patients with AMI scheduled for primary PCI or urgent treatment were enrolled and divided into two groups: high-dose statin (n=48) and standard-dose statin (n=47). Group A received high-dose atorvastatin before PCI, while Group B was given the standard statin dosage. Baseline characteristics, clinical parameters, coronary angiography findings, and adverse events were recorded. The primary outcome was the incidence of the slow-flow phenomenon, assessed using Thrombolysis in Myocardial Infarction (TIMI) flow grades. Statistical analysis was performed using SPSS version 25.

Results: The high-dose statin group showed a significant reduction in the incidence of the slow-flow phenomenon post-PCI (10.4% in Group A vs. 31.9% in Group B, p=0.014) and improved TIMI flow grades. No significant differences were found in baseline characteristics or clinical parameters between the groups. Adverse events were comparable between both groups.

Conclusion: High-dose statin therapy prior to PCI significantly reduces the slow-flow phenomenon and improves coronary blood flow in patients with AMI, supporting its use as an effective upstream therapy in CAD management. Further large-scale studies are warranted to confirm these findings and explore the long-term benefits of high-dose statin therapy in diverse populations.

Keywords: High-dose statin therapy, Coronary artery disease, Slow-flow phenomenon, Percutaneous coronary intervention, Acute myocardial infarction, TIMI flow grade.

INTRODUCTION

Cardiovascular diseases, particularly acute myocardial infarction (AMI), continue to pose a significant global health challenge, with primary percutaneous coronary intervention (PCI) or urgent invasive therapy being pivotal in the timely restoration of coronary blood flow and minimization of myocardial damage (1). Despite advancements in treatment protocols, the occurrence of the slow-flow phenomenon post-PCI remains a concerning complication, often associated with adverse clinical outcomes (2,3,4). The slow-flow phenomenon, characterized by a delayed or impaired blood flow through the coronary arteries subsequent to successful revascularization, predominantly affects the microcirculation and is associated with increased morbidity and mortality among AMI patients (5). This condition's etiology is multifactorial, involving complex interactions among inflammation, thrombosis, and endothelial dysfunction, which together contribute to the microvascular damage observed (6,7). These challenges underscore the urgency for innovative treatment strategies aimed at addressing this critical aspect of coronary intervention.

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Statins, widely recognized for their lipid-lowering properties, have demonstrated additional benefits, including anti-inflammatory effects, antithrombotic properties, and endothelial protection, which extend beyond their cholesterol-reducing capabilities (8,9). Recent evidence suggests that the preemptive use of high-dose statins prior to PCI in AMI patients may confer superior outcomes, potentially due to these drugs' multifaceted effects on the cardiovascular system (10,11). However, the specific impact of high-dose statins on the prevalence of the slow-flow phenomenon in the context of primary PCI or immediate invasive therapy remains a subject of ongoing investigation (12). This prospective study aims to explore the relationship between the administration of high-dose statin therapy as an upfront treatment and the incidence of the slow-flow phenomenon in individuals undergoing primary PCI or immediate invasive treatment for AMI (13). By delving into the potential protective effects of high-dose statins on coronary microcirculation, this research endeavors to shed light on novel therapeutic approaches that could enhance the treatment paradigm for patients with acute myocardial infarction, thereby contributing to the broader quest for reducing the burden of cardiovascular diseases worldwide.

MATERIAL AND METHODS

This study employed a prospective, observational design to explore the impact of high-dose statin therapy as an upfront treatment on the occurrence of the slow-flow phenomenon in patients undergoing primary percutaneous coronary intervention (PCI) or immediate invasive therapy for acute myocardial infarction (AMI). Conducted between 1st February 2023 and 31st January 2024, the research was a collaborative effort between the Department of Cardiology at MTI Lady Reading Hospital, Peshawar, and the Department of Cardiology at Shifa International Hospital, Islamabad.

A cohort of ninety-five patients diagnosed with AMI and scheduled for primary PCI or urgent treatment were included in the study. Enrollment took place at the Department of Cardiology at MTI Lady Reading Hospital, Peshawar, from September 2022 to October 2023. Informed consent was duly obtained from every participant, affirming their voluntary participation. Participants were systematically divided into two distinct groups based on the statin regimen assigned. Group A comprised patients who were administered high-dose statin medication, specifically Atorvastatin, as an initial intervention prior to undergoing PCI or immediate invasive therapy. Conversely, Group B consisted of patients who received standard-dose statin therapy, in line with prevailing clinical guidelines. The assignment of patients to either group was determined through a process of computer-generated random numbers, ensuring an unbiased distribution across the two treatment modalities.

Comprehensive documentation of participants' baseline demographic characteristics, medical history, and clinical parameters was undertaken. Vital clinical indicators, including blood pressure, heart rate, and laboratory results, were meticulously recorded. The coronary angiography procedure, executed by experienced interventional cardiologists, facilitated the evaluation of coronary flow pre and post PCI, utilizing the Thrombolysis in Myocardial Infarction (TIMI) flow grades as a benchmark for assessing the slow-flow phenomenon.

For the purpose of data analysis, SPSS version 25 was utilized. The study deployed descriptive statistics to encapsulate the demographic and clinical characteristics of the cohort. Categorical variables were analyzed employing the Chi-square test or Fisher's exact test, as deemed appropriate, while continuous variables were examined using the Student's t-test or Mann-Whitney U test. A threshold p-value of less than 0.05 was established as indicative of statistical significance.

Ethical integrity was maintained throughout the study, with approval secured from the respective hospital research review boards. The investigation was conducted in strict accordance with the ethical standards stipulated in the Declaration of Helsinki, along with prevailing norms of Respectable Medical Practice, ensuring the protection of participants' rights and well-being.

RESULTS

In this study, a total of 95 participants were assessed to explore the effects of high-dose versus standard statin therapy in patients undergoing primary PCI or immediate invasive therapy for acute myocardial infarction. The demographic and baseline characteristics of the participants are outlined in Table 1. The distribution of gender across the two groups revealed a higher percentage of males in Group B (Standard Statin) at 80.9% compared to 72.9% in Group A (High-Dose Statin), with females constituting 27.1% and 19.1% of Groups A and B, respectively. The mean age was comparable between the two groups, with Group A having an average age of 62.5 years (SD ± 8.2) and Group B slightly older at 63.1 years (SD ± 7.5). Hypertension was present in 41.7% of participants in Group A and 46.8% in Group B, while the prevalence of diabetes mellitus was 31.3% and 38.3%, respectively. Smoking habits were also noted, with 37.5% of Group A and 42.6% of Group B being smokers.

Clinical parameters at baseline, detailed in Table 2, include measurements such as systolic and diastolic blood pressure, heart rate, LDL cholesterol levels, and hemoglobin. The systolic blood pressure showed a slight difference between the two groups, with Group A recording 125 mmHg (SD ± 10) and Group B at 128 mmHg (SD ± 12), yielding a non-significant p-value of 0.23. Diastolic blood

pressure, heart rate, LDL cholesterol, and hemoglobin levels also did not show significant differences between the groups, with p-values ranging from 0.12 to 0.45, suggesting comparable baseline clinical parameters.

Coronary angiography findings, as presented in Table 3, highlight the impact of statin therapy on the TIMI flow grade before and after PCI. The pre-PCI TIMI flow grades 0/1/2 were observed in 20.8% of Group A compared to 38.3% of Group B, with a statistically significant p-value of 0.047. This suggests a lower incidence of impaired flow in the high-dose statin group before intervention. Post-PCI findings were more notable, with only 10.4% of Group A versus 31.9% of Group B showing TIMI grades 0/1/2, significantly favoring the high-dose statin therapy with a p-value of 0.014. The occurrence of the slow-flow phenomenon, described in Table 4, further supports the potential benefits of high-dose statin therapy, where only 8.3% of Group A experienced this phenomenon compared to 25.5% of Group B, with a significant p-value of 0.032.

Table 1: Participants' Baseline Characteristics (N=95)

Characteristics	Group A (High-Dose Statin) n=48	Group B (Standard Statin) n=47
Gender		
Male	35 (72.9%)	38 (80.9%)
Female	13 (27.1%)	9 (19.1%)
Age Mean ± SD	62.5 ± 8.2	63.1 ± 7.5
Hypertension	20 (41.7%)	22 (46.8%)
Diabetes Mellitus	15 (31.3%)	18 (38.3%)
Smoking	18 (37.5%)	20 (42.6%)

Table 2: Clinical Parameters at Baseline (N=95)

Parameter	Group A (High-Dose Statin) n=48	Group B (Standard Statin) n=47	p-value
Systolic BP (mmHg)	125 ± 10	128 ± 12	0.23
Diastolic BP (mmHg)	75 ± 8	78 ± 9	0.17
Heart Rate (bpm)	80 ± 5	82 ± 6	0.31
LDL Cholesterol (mg/dL)	110 ± 15	112 ± 14	0.45
Hemoglobin (g/dL)	13.5 ± 1.2	13.8 ± 1.1	0.12

Table 3: Coronary Angiography Findings (N=95)

TIMI Flow Grade	Group A (High-Dose Statin) n=48	Group B (Standard Statin) n=47	p-value
Pre-PCI TIMI 0/1/2	10 (20.8%)	18 (38.3%)	0.047
Pre-PCI TIMI 3	38 (79.2%)	29 (61.7%)	
Post-PCI TIMI 0/1/2	5 (10.4%)	15 (31.9%)	0.014
Post-PCI TIMI 3	43 (89.6%)	32 (68.1%)	

Table 4: Occurrence of Slow-Flow Phenomenon (N=95)

Slow-Flow Phenomenon	Group A (High-Dose Statin) n=48	Group B (Standard Statin) n=47	p-value
Yes	4 (8.3%)	12 (25.5%)	0.032
No	44 (91.7%)	35 (74.5%)	

Table 5: Adverse Events

Adverse Event	Group A (High-Dose Statin) n=48	Group B (Standard Statin) n=47	Total (n=95)
Major Bleeding	2 (4.2%)	3 (6.4%)	5 (5.3%)
Reinfarction	1 (2.1%)	2 (4.3%)	3 (3.2%)
Mortality	0 (0%)	1 (2.1%)	1 (1.1%)

Adverse events were monitored throughout the study period, with findings aggregated in Table 5. The incidence of major bleeding events was slightly lower in Group A at 4.2% compared to 6.4% in Group B. Reinfarction rates were 2.1% for Group A and 4.3% for Group B. Mortality was reported only in Group B at 2.1%. These adverse event rates underscore the relative safety and potential benefits of high-dose statin therapy in this clinical setting.

Overall, the study's findings suggest that high-dose statin therapy prior to PCI or immediate invasive therapy for AMI could be associated with improved coronary flow and a reduced incidence of the slow-flow phenomenon, without a significant increase in adverse events. The numerical data and statistical analyses presented across the tables underscore the potential therapeutic benefits of high-dose statin therapy in enhancing patient outcomes in the context of acute myocardial infarction management.

DISCUSSION

The outcomes of this study underscore the efficacy of high-dose statin therapy in significantly enhancing coronary blood flow and mitigating the occurrence of the slow-flow phenomenon among patients with coronary artery disease (CAD), in comparison to standard-dose statin therapy. These results are in concordance with prior investigations that have highlighted the utility of high-dose statin treatment in reducing cardiovascular events and ameliorating outcomes for individuals afflicted with CAD. Notably, the study conducted by Cannon et al. (14) in 2005 illustrated that a higher dosage of atorvastatin (80 mg) markedly reduced serious cardiovascular events, such as mortality, myocardial infarction, and stroke, as opposed to a conventional dosage of atorvastatin (10 mg). This finding aligns with our observation of a diminished incidence of adverse events within the cohort administered high-dose statins.

In a similar vein, LaRosa et al. (15) in 2007 demonstrated that high-dose simvastatin (80 mg) was more efficacious in lowering LDL cholesterol levels and in curtailing the risk of severe cardiovascular events than moderate doses (20-40 mg), findings which resonate with our study's demonstration of improved coronary blood flow and a reduced incidence of the slow-flow phenomenon in the high-dose statin group. Furthermore, a meta-analysis by the Cholesterol Treatment Trialists' (CTT) Collaboration (16) in 2011, which involved over 170,000 patients with CAD, found that high-dose statin therapy led to a 16% reduction in major cardiovascular events and a 12% decrease in all-cause mortality compared to standard-dose statin therapy, furnishing additional evidence supporting the advantages of high-dose statin therapy in this population (17-19).

Despite these encouraging findings, it is essential to recognize the limitations of our study that may affect the generalizability of the results. The relatively modest sample size and the study's confinement to a single site might impinge upon the diversity of the study population and, by extension, the broad applicability of the findings. This highlights the necessity for further expansive, multi-center studies to corroborate our results and to assess the efficacy of high-dose statin therapy across a more heterogeneous patient cohort. Additionally, while our study indicates a clear benefit of high-dose statin therapy in enhancing coronary blood flow and reducing the incidence of the slow-flow phenomenon, determining the optimal dosage of statin medication remains contingent upon individual patient characteristics and risk factors, advocating for a tailored therapeutic approach.

This research contributes to the burgeoning evidence suggesting that high-dose statin therapy can provide superior outcomes in the management of CAD by augmenting coronary blood flow and diminishing the slow-flow phenomenon, compared to standard-dose statin therapy. These findings bolster the potential of high-dose statin therapy as a salutary intervention for patients with CAD. Nonetheless, additional research is requisite to delineate the optimal dosage and to elucidate the long-term impacts of high-dose statin therapy in this specific patient demographic, ensuring that treatment modalities are both efficacious and customized to the unique needs of individuals with coronary artery disease (20).

CONCLUSION

This study elucidates the significant benefits of high-dose statin therapy in enhancing coronary blood flow and reducing the slow-flow phenomenon in patients with coronary artery disease, highlighting a potential paradigm shift in the management of CAD. The findings suggest that integrating high-dose statin therapy into standard treatment protocols could substantially improve patient outcomes, underscoring the necessity for healthcare professionals to consider more aggressive lipid-lowering strategies in the treatment of CAD. As the global burden of cardiovascular diseases continues to escalate, adopting evidence-based interventions like high-dose statin therapy offers a promising avenue to mitigate cardiovascular risks, thereby improving the longevity and quality of life for individuals with CAD, and ultimately making strides toward advancing public health outcomes.

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