

# Reduction of Peri - Procedural Myocardial injury by Loading dose of Atorvastatin during Elective Percutaneous Coronary Intervention

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### Abstract

#### Key Words :

IHD, PCI, Atorvastatin, Myocardial injury

**Background:** The purpose of the study was to find the effect of loading dose of atorvastatin on the reduction of myocardial injury resulting from percutaneous coronary intervention (PCI).

**Methods:** A total 100 consecutive patients were included in this study of which 50 patients were in the group I who were treated with a loading dose of atorvastatin and the rest 50 patients were in the group II who were treated without the loading dose of atorvastatin. The occurrence of myocardial injury was measured by serum cTn-I level in patients undergoing PCI with or without loading dose of atorvastatin.

**Results:** Elevation of cTn-I after PCI reflects peri-procedural myonecrosis and presage adverse outcome. In this study incidence of cTn-I rise following PCI was 86% without atorvastatin pretreatment and 10% with atorvastatin pretreatment. The incidence of myonecrosis is less in atorvastatin pretreated group and the difference was statistically significant.

**Conclusion:** It is concluded that the loading dose of atorvastatin significantly reduce myocardial injury resulting from percutaneous coronary intervention.

(*Cardiovasc. j.* 2015; 8(1): 3-7)

### Introduction:

Coronary heart disease is one of the leading causes of death in the developed world as well as in the developing countries like Bangladesh. A population based study found the prevalence of ischemic heart disease to be 6.5 per thousand in Bangladesh.<sup>1</sup> PCI has become one of the cardinal treatment strategies for coronary artery disease. Technical advances have expanded the capabilities of balloon angioplasty. Despite these advances, the incidence of post procedural cardiac marker elevation has not substantially decreased since the first serial assessment 20 years back. As of now, these post procedural cardiac marker elevations are considered 'peri-procedural myocardial injury' (PMI) with worse long-term outcome.<sup>2</sup>

PMI is synonymous with peri-procedural myocardial infarction in most of the cases. In patients with normal baseline values, elevations of cardiac marker level above 99<sup>th</sup> percentile of

upper reference limit are indicative of peri-procedural myocardial necrosis. By convention, increases of bio-markers greater than 3×99<sup>th</sup> percentile upper reference limit have been designated as defining PCI-related myocardial infarction.<sup>3</sup> Incidence of PMI may vary depending on choice of bio-marker assay, cut-off values and frequencies of blood analyses. In non-selective multi-center series post procedural elevation of creatine kinase Myocardial band (CK-MB) mass and Cardiac Troponin I (cTn-I) above upper reference limit were found in 23±12% and 27±12% of patients respectively.<sup>2</sup>

The overall incidence of post procedure CK-MB elevation was found in different studies were 18.7%, 22.0% and 25.2%.<sup>4-6</sup> In one study periprocedural MI was found about 40%.<sup>7</sup> Different patient-related factors, lesion characteristics and procedure-related factors are considered as putative risk factors for PMI.<sup>2,5</sup>

Different strategies have been proposed and tested to prevent peri-procedural myocardial infarction. Some clinical and experimental data suggest that 3-hydroxy-3-methylglutaryl co-enzyme A (HMG-CoA) reductase inhibitors (statins) may exert anti-thrombotic effects, independent of cholesterol reduction, by affecting the vessel wall as well platelet function. Pre-procedural statin therapy was associated with a lower risk of troponin-I and CK-MB elevation after stent implantation.<sup>2</sup>

Patients who have transient elevation in cardiac markers have higher mortality during extended follow up than those who did not and are independent of other predictors of mortality.<sup>8</sup>

Among troponins, cTn-I is the most specific marker with a significant correlation, concordance and high predictive value for long-term event-free survival. The marker elevation per se may not be the primary cause of death but may be marker indicating greater plaque burden and relatively widespread atherosclerosis. These findings have important implications for daily interventional cardiology practice and highlight the risk associated with the common practice of overlooking or ignoring small infarctions as complication of PCI.<sup>9</sup>

So, this study was undertaken to evaluate the protective effect of loading dose of atorvastatin in the reduction of peri-procedural myocardial injury during elective PCI.

### Methods:

All patients admitted in the Department of Cardiology of NICVD, Dhaka fulfilling the criteria of inclusion was considered. History and clinical examination were carried out and recorded in pre designed structured proforma. Baseline investigations blood tests for angiogram were carried out for each of the patients.

Troponin I value was measured by Immulite 1000 Troponin I. (SIEMENS Medical Solutions Diagnostics, Los Angeles, CA, USA) on the day before the procedure and 24 hours after the procedure. Patients who had cTn-I  $\geq 1$  ng/ml was designated as having periprocedural myocardial injury and cTn-I  $\geq 3$  ng/ml was designated as having PCI related myocardial infarction.

12 lead resting ECG was done before sending the patient to cath lab, during the procedure, 01 hour after the procedure, next morning after the procedure. Coronary angiogram were evaluated

for i) Stenosed vessels, number and degree of stenosis (expressed as percentage of occlusion, 0-100%), ii) Number of stenosed vessels was expressed as single/double/triple vessel diseases depending upon number of epicardial vessels to have significant stenosis and iii) Type of lesions expressed as Type I, II, III and IV according to ACC/AHA classification of lesion.

Patients were divided in two groups: The group I- treated with a loading dose of 80mg atorvastatin and group II- treated without a loading dose of 80mg atorvastatin. Data were noted- Length and diameter of stent, balloon and stent inflation pressure and total inflation time. Periprocedural events like side branch occlusion, coronary vasospasm, coronary dissection were noted.

Following the procedure, the patient was brought routinely to CCU for at least 24 hours where their hospital course and lab parameters were monitored. Patients were evaluated clinically and investigated for following complications: Persistent angina, new ischemic episode, non Q-wave MI, congestive cardiac failure, cardiac arrhythmia

### Results:

This non-randomized controlled clinical trial was carried out in a total 100 consecutive patients were included in this study of which 50 patients were in the group I who were treated with a loading dose of 80mg atorvastatin and the rest 50 patients were in the group II who were treated without the loading dose of atorvastatin. The purpose of the study was to find the effect of loading dose of atorvastatin on the reduction of myocardial injury and infarction resulting from PCI and also to determine the beneficial effects of atorvastatin on peri-procedural outcome in PCI. The findings of the study obtained from data analysis are presented below.

**Table-I**

*Distribution of Risk factors by groups (n=100).*

Risk factors	Groups		p value*
	Group-I (n=50)	Group-II (n=50)	
Smoking	33 (66.0)	35 (70.0)	0.668
Hypertension	26 (52.0)	32 (64.0)	0.224
Diabetes mellitus	14 (28.0)	22 (44.0)	0.096
Dyslipidemia	10 (20.0)	8 (16.0)	0.603
Family H/O premature CAD	14 (28.0)	10 (20.0)	0.349

\*Chi-square test was done to measure the level of significance.

Table I shows the distribution of risk factors by groups. There was no significant difference between the groups.

**Table-II**  
*Medication used prior to PCI between groups (n=100).*

Drug history	Groups		p value*
	Group-I (n=50)	Group-II (n=50)	
Aspirin	50 (100.0)	50 (100.0)	
Clopidogrel	46 (92.0)	43 (86.0)	0.338
Statin	47 (94.0)	43 (86.0)	0.182
Beta-blocker	48 (96.0)	44 (88.0)	0.269
ACE inhibitors	34 (68.0)	33 (66.0)	0.832

\*Chi-square test was done to measure the level of significance.

Table II shows the drugs taken by the study population before the procedure. Most of the patients took aspirin, clopidogrel, statin (usual 10 mg daily), beta-blocker and ACE inhibitors. There was no significant difference between the groups.

**Table-III**  
*Comparison of TIMI flow between groups before and after stenting (n=100).*

TIMI flow	Groups		p value*
	Group-I (n=50)	Group-II (n=50)	
Pre PCI			
• TIMI-I	8 (16.0)	6 (12.0)	0.467*
• TIMI-II	35 (70.0)	35 (70.0)	
• TIMI-III	7 (14.0)	9 (18.0)	
Post PCI			
• TIMI-II	1 (2.0)	2 (4.0)	0.999**
• TIMI-III	49 (98.0)	48 (96.0)	

\*Chi-square test was done to measure the level of significance.

\*\*Fisher's Exact test was done to measure the level of significance.

Table III shows the comparison of TIMI flow between groups. There was no statistically significant difference in TIMI flow prior to PCI and TIMI flow after PCI.

**Table-IV**  
*Distribution of ECG findings by groups before and after PCI (n=100).*

ECG findings	Groups		p value*
	Group-I (n=50)	Group-II (n=50)	
Pre angioplasty			
• Normal	10 (20.0)	7 (14.0)	0.529
• Ischemic	9 (18.0)	13 (26.0)	
• Infarction	31 (62.0)	30 (60.0)	
Just after procedure			
• No change	49 (98.0)	47 (94.0)	0.309
• Ischemia	1 (2.0)	3 (6.0)	
Change during the Procedure			
• No change	30 (60.0)	23 (46.0)	0.161
• ST change	6 (12.0)	9 (18.0)	0.401
• T wave change	3 (6.0)	4 (8.0)	0.500
• Sinus tachycardia <sup>2</sup>	4 (4.0)	3 (6.0)	0.500
• Sinus bradycardia <sup>2</sup>	4 (4.0)	2 (4.0)	0.691
• PVC	7 (14.0)	8 (16.0)	0.779
• VT	0 (0.0)	1 (2.0)	0.500

\*Chi-square test was done to measure the level of significance.

Table IV shows the distribution of ECG findings by groups. Ischemic change of ECG just after procedure is in 1 (2.0%) and 3 (6.0%) cases in group I and II respectively and ST changes during procedure was in 6 (12.0%) and 9 (18.0%) cases in group I and II respectively. There was no statistically significant difference in ECG changes.

**Table-V**  
*Distribution of procedural characteristics by groups (n=100).*

Procedural characteristics	Groups		p value*
	Group-I (n=50)	Group-II (n=50)	
Diameter of stent (mm)	3.31 ± 2.15	3.04 ± 0.33	0.394
Length of stent (mm)	20.16 ± 7.21	19.22 ± 4.60	0.439
Balloon Inflation pressure (ATM)	9.2 ± 1.7	9.5 ± 1.2	0.458
Stent inflation pressure (ATM)	13.78 ± 1.61	13.36 ± 1.69	0.206
Total inflation time (sec)	28.1 ± 4.8	29.0 ± 3.5	0.276

\*t test was done to measure the level of significance. Data was expressed as Mean ± SD.

Table V shows the distribution of procedural characteristics by groups. The mean diameter of stent, the mean length of stent, average balloon inflation pressure, mean total inflation time and the stent inflation pressure of stent were almost same in both group-I and group-II.

**Table-VI**  
*Distribution of procedural complications by groups (n=100).*

Complications	Groups		p value*
	Group-I (n=50)	Group-II (n=50)	
Procedural complications			
Coronary spasm	3 (6.0)	4 (8.0)	0.999
Side branch occlusion	1 (2.0)	4 (8.0)	0.362
Coronary dissection	1 (2.0)	2 (4.0)	0.999
In-hospital complications			
Persistent angina	1 (2.0)	5 (10.0)	0.204
Cardiac arrhythmia	1 (2.0)	2 (4.0)	0.999
Myocardial infarction (MI)	1 (2.0)	4 (8.0)	0.362

\*Fisher's Exact test was done to measure the level of significance.

Table VI shows the distribution of complications by groups. In Procedural complications like coronary spasm, side branch occlusion, coronary dissection and In-hospital complications like persistent angina, cardiac arrhythmia, myocardial infarction in both the groups were same.

**Table-VII**  
*Comparison of Troponin-I level between groups (n=100).*

Troponin-I level	Groups		p value*
	Group-I (n=50)	Group-II (n=50)	
24 hours after PCI			
<1ng/ml	45 (90.0%)	7 (14.0%)	0.005**
≥1ng/ml	5 (10.0%)	43 (86.0%)	
Total	50	50	
Mean ± SD	1.3 ± 0.5	1.8 ± 1.2	0.005*

\*\*Chi-square test was done to measure level of significance.  
\*t test was done to measure the level of significance.

Table VII shows the distribution of Troponin-I level by groups. Troponin-I level 24 hours after PCI in less than 1 is found in 45 (90.0%) cases and 7 (14.0%) cases in group I and group II respectively. Troponin-I level 24 hours after PCI in more than or equal to 1 is found in 5 (10.0%) cases and 43 (86.0%) cases in group I and group II respectively. The mean ± SD is found in 1.3 ± 0.5 and 1.8 ± 1.2 in group I and II

respectively. So, mean cardiac Troponin-I level after stenting was significantly lower in group-I than that in the group-II patients (p=0.005).

### Discussion:

In this study, the incidences of myonecrosis in patients undergoing elective PCI with or without pretreatment with atorvastatin were evaluated. Procedural and in hospital complications were also observed.

The distribution of study population according to age, sex and risk factors by groups is recorded in this study. No statistically significant difference was found between the two groups. The results were similar in some other studies.<sup>6</sup>

There was no statistically significant difference in TIMI flow and ECG changes both before and after PCI prior to PCI and TIMI flow after PCI. The results were similar in some other studies.<sup>10</sup>

In Procedural complications like coronary spasm, side branch occlusion, coronary dissection and in-hospital complications like persistent angina, cardiac arrhythmia, myocardial infarction in both the groups were same. Similar pattern of post procedural complications were found in some studies.<sup>6,11</sup> Coronary vasospasm was the most frequently encountered procedural complications.<sup>5</sup> Side branch occlusion was the commonest procedural complication followed by coronary dissection and spasm found in another study.<sup>7</sup>

There were no significant differences found in this study regarding stent parameters, stent length and stent diameter between both groups.

The commonest ECG changes apart from premature ventricular complexes noted during the procedure was ST and T wave changes. Out of 100 patients, 6 (12%) in group-1 and 9 (18%) in group-II had ST segment changes during balloon inflation. T wave changes were noted about 6% and 8% in group I and group II respectively. The ST and T changes persisted in 4 patients (8%) after the procedure. Other ECG changes were sinus tachycardia and sinus bradycardia. The ECG changes both before and after PCI showed no statistically significant differences between group-I and group-II.<sup>10</sup>

No patient needed to undergo repeat PCI or emergency CABG. There was also no significant



difference noted regarding hospital stay and in hospital complications between two groups of patients.

The mean base line Troponin I (ng/ml) is  $0.24 \pm 0.12$  and  $0.21 \pm 0.03$  in group I and II respectively ( $p=0.088$ ). Troponin-I level by groups is recorded before and after PCI in this study. Troponin-I level 24 hours after PCI in less than 1ng/ml is found more in group I (90.0%) than group II (14.0%). Whereas Troponin-I level after PCI in more than or equal to 1 is found more in group II (86.0%) than group I (10.0%). The mean  $\pm$  SD is found in  $1.30 \pm 0.50$  and  $1.80 \pm 1.20$  in group I and II respectively. So, mean cardiac Troponin-I level after stenting was significantly lower in group-I than that in the group-II patients ( $p=0.005$ ). Significant benefit of statin pre-therapy on periprocedural elevation of Troponin-I was also demonstrated in many studies.<sup>11-14</sup>

In this study incidence of cTn-I rise following PCI was 86% without atorvastatin pretreatment and 10% with atorvastatin pretreatment. So the incidence of myonecrosis is less in atorvastatin pretreated group and the difference was statistically significant.

In the present study, the mean value of cTn-I rise at 24 hours following PCI was  $1.3 \pm 0.5$  ng/ml and  $1.8 \pm 1.2$  ng/ml in group I and group II respectively. This finding was statistically significant ( $p < 0.005$ ). Significant difference was also found in some studies in regard to cTn-I level.<sup>15</sup>

### Conclusion:

From this study it is concluded that by measuring serum cardiac troponin I in patients undergoing PCI with pre medication with loading dose of atorvastatin is helpful in reducing post procedural myocardial injury and infarction. So, pre-procedural loading dose of atorvastatin medication reduces the myocardial injury and infarction.

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### Conflict of Interest - None.

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