Effect of Statin Therapy In Ventricular Arrhythmias In Patient With Acute Anterior Myocardial Infarction

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Keywords:
Atorvastatin, Arrhythmia, Myocardial infarction.

Abstract:

Background: *Though statins are widely used in acute coronary syndrome (ACS), there is a paucity of information on the efficacy of high dose statin therapy in reducing the incidence of ventricular arrhythmias after acute myocardial infarction. Arrhythmias are relatively common in acute myocardial infarction (AMI) anterior, and sometimes progress to cardiac arrest. This study was planned to evaluate the role of high dose atorvastatin therapy in prevention of ventricular arrhythmias after acute anterior myocardial infarction.*

Methods: *This study was conducted in NICVD from December 2010 to October 2011. Total 200 patients with newly diagnosed acute anterior myocardial infarction who received thrombolytic therapy were included in the study. They were divided into two groups. Group I (n=100) was selected for high dose atorvastatin therapy and group II (n=100) was selected for conventional doses of atorvastatin therapy. 24 hours Holter monitoring was performed 48 hours after hospital admission to evaluate arrhythmia.*

Results: *Majority of the patients belonged to age range of 40 to 59 years with a male predominance. Patient characteristics regarding age, sex, drug use, risk factors for ventricular arrhythmia, body mass index, left ventricular ejection fraction were similar in two study groups. There was no electrolyte imbalance or renal impairment in any patient in either group. A significant difference in frequency of ventricular arrhythmias was found between the two groups. Ventricular premature beats were found in 66% patients in group I and 97% patients in group II (p=0.001) whereas non sustained ventricular tachycardia were observed in 0% and 4% in group I and group II respectively.*

Conclusion: *High dose atorvastatin therapy is associated with lower frequency of ventricular arrhythmias after acute anterior myocardial infarction.*

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Introduction:

Coronary heart disease (CHD) is a major cause of mortality globally and this health problem is reaching epidemic in both developed, as well as, in developing countries.[1] Ischaemic heart disease becomes an important health hazard in the third world countries including Bangladesh.[2]

Many patients who survive an acute myocardial infarction remain at risk of recurrent cardiac events and sudden cardiac death.[3] Arrhythmias are the commonest cause of sudden cardiac death (SCD), with ventricular tachycardia (VT) or ventricular fibrillation (VF) implicated in the majority of cases.[4] Ischaemic VF is usually caused by "trigger" such as ventricular premature beat or ventricular tachycardia.[5] Early studies on the use of ambulatory ECG recording (24 hours Holter monitoring) in the risk stratification of patients post acute myocardial infarction (AMI) reported that the detection of ventricular arrhythmias, most often non-sustained ventricular tachycardias (NSVT) or frequent ventricular premature beats (VPB) is predictive of serious arrhythmic events and death.[6]

Statin is the cornerstone in the management of dyslipidaemia.[7] Clinical trials demonstrated that statin therapy is associated with significant reduction in cardiovascular morbidity and mortality.[8] These favorable results are not

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entirely explained by lipid modulation itself. However, recent data suggests that the beneficial effect of statin may extend to mechanism beyond cholesterol reduction and could be related to potential anti-arrhythmic properties of such drugs against ventricular arrhythmia.[9]

This study attempted to evaluate how patients with acute anterior myocardial infarction get benefit from a preventive statin approach by comparing the frequency of ventricular arrhythmias between patients receiving high dose atorvastatin therapy with those receiving conventional doses of atorvastatin

Study Methods:

This Interventional study was conducted in NICVD (National Institute of Cardiovascular Diseases), Dhaka, from December 2010 to October 2011. Informed written consent was taken from every patient or near relatives. A total of 200 patients with newly diagnosed acute anterior myocardial infarction who received thrombolytic therapy were included in this study. Patients with previous treatment with high dose of atorvastatin, patients with electrolyte imbalance, patients with acute heart failure (Killip class II, III, IV), patients with previous myocardial infarction, percutaneous coronary intervention and coronary artery bypass grafting, cardiac arrest, cardiogenic shock after hospital admission, patients on antiarrhythmic drug, patients having cardiomyopathy, congenital heart disease or valvular heart disease, co-morbid conditions (Chronic kidney disease, Liver disease, malignancies), patients unwilling to be included in the study were excluded.

Purposive sampling was done. Patients who are considered as group I received 80 mg atorvastatin at admission and daily for 3 days followed by 20 mg/day, those who were considered as group II received 20 mg atorvastatin/day from admission and onward.

24 hours Holter ECG monitoring was done 48 hours after hospital admission. Data were recorded by a recorder of DMS 300-7 containing compact flash card-Sandisk (64 MB). The recorder was driven by single 1.5 volt AA size alkaline battery. It was attached to the seven chest lead positioned according to mentioned colour code. Holter data were analyzed by computerized analysis method using Victor Bravo Inc. (Premium-10) DSM, Nevada, USA system. Artifacts were removed annually. Remaining data were taken as printed output.

Statistical analysis:

Data for each patient was collected in a predesigned data collection form. Data were analyzed and significance of differences was estimated by using Computer based SPSS (Statistical Package for Social Science) program. Results of the study and statistical analysis were presented by tables and figures. Comparison between two groups was done by student's t-test and chi-square test. p value of less than 0.05 was considered as significant.

Results:

Out of 200 patients, majority of the patients of group I and Group II (78.0% and 82.0% respectively) were male. The mean age was found 50.7±11.2 years in group I and 51.4±11.5 years in group II. 58.0% patients group I are over weight followed by normal weight (33.0%) and obese (9.0%). The Group II had a similar distribution of body mass index (BMI) with over weight (51.0%), normal weight (33.0%) and obese (16.0%). The mean BMI of Group I was 26.2±3.1 kg/m^2 and Group II was 26.7±3.9 kg/m^2. Mean systolic blood pressure was 130.7±14.8 mmHg in Group I and 129±15.9 mmHg in Group II. Mean diastolic blood pressure was 86.3±8.1 mmHg in Group I and 84.8±7.8 mmHg in Group II. Pulse was 79.7±6.7 /min and 77.2±11.3/min in Group I and Group II respectively. Mean level of RBS and Serum creatinine between two groups were 10.9±4.9, 10.8±4.4 and 1.2±0.5, 1.4±1.8 respectively. The mean level of serum electrolyte (Na^+) and serum electrolyte (K^+) between two groups were 137.4±19.8, 138.0±13.1 and 4.1±0.4, 4.1±0.5 respectively. Mean left ventricular ejection fraction was 46.1 ± 6.8 in Group I and 45.5 ± 5.2 in Group II.

Table-I

Baseline clinical characteristics of study population (n=200)

Baseline clinical characteristics	Early and high dose statin (n=100)	Conventional statin (n=100)	p value
Age	50.7±11.2	51.4±11.5	0.70
Sex (male/Female)	78%/22%	82%/18%	0.48
BMI (kg/m^2)	26.2±3.1	26.7±3.9	0.34
Smoking habit	76%	80%	0.49
Hypertension	86%	87%	0.83
Diabetes mellitus	54%	49%	0.48
Dyslipidaemia	40%	40%	1.00
Obesity	3%	2%	0.65
Family H/O premature CAD	38%	37%	0.88
Systolic BP (mmHg)	I30.7 ±14.8	129±15.9	0.45
Diastolic BP (mmHg)	86.3±8.1	84.8±7.8	0.18
Pulse (rpm)	79.7±6.7	77.2±11.3	0.06
Random blood sugar (mmol/l)	10.9±4.9	10.8±4.4	0.93
Serum creatinine (mg/dl)	1.2±0.5	1.4±1.8	0.23
Serum electrolyte (Na^+) (meq/l)	137.4±19.8	138.0±13.1	0.79
Serum electrolyte (K^+) (meq/l)	4.1±0.4	4.1±0.5	0.99
LVEF in %	46.1 ± 6.8	45.5 ± 5.2	0.46

Holter monitoring parameters between the two groups shows the difference in incidence of VPB/ Couplet/Triplet/Bigeminy/Trigeminy were statistically significant ($p<0.05$). Only 4 (4%) patient in group II develop NSVT and no patient in group I develop NSVT. However the differences in incidence of SVT and AV block was not statistically significant ($p>0.05$).

Table-II

Comparison of Holter monitoring parameters between study groups (n=200).

Parameters	Group I (n= 100)		Group II (n =100)		P value
	Number	%	Number	%	
Ventricular premature beat (VPB)	66	66.0	97	97.0	0.001
Couplet	3	3.0	12	12.0	0.01
Triplet	1	1.0	10	10.0	0.005
Bigeminy	4	4.0	15	15.0	0.007
Trigeminy	1	1.0	8	8.0	0.01
Non-sustained ventricular tachycardia (NSVT)	0	0.0	4	4.0	
SVT	2	2.0	4	4.0	0.41
AV block	6	6.0	5	5.0	0.75

The number of VPB was 107±66.0 in Group I and 310131 in Group II. Analysis found statistically significant (p=0.001). Figure 2 shows that number of episodes of NSVT was 0 in Group I and 13±4 in Group II.

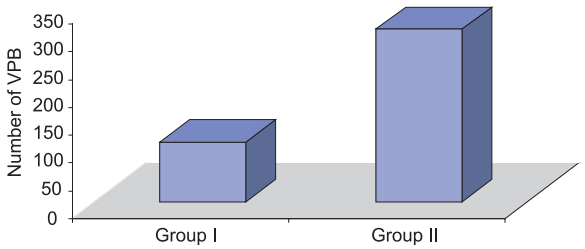

Fig.-1: *Numbers of ventricular premature beats (VPB) between study groups (n= 200)*

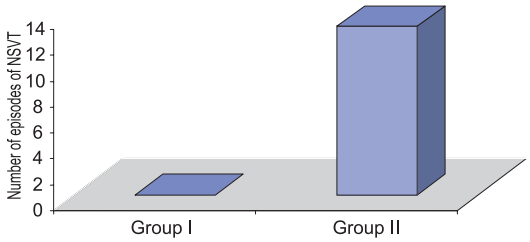

Fig.-2: *Numbers of episodes of non sustained ventricular tachycardia (NSVT) between study groups (n= 200)*

Discussion:

Significant proportion of the patients who die after acute coronary syndrome, die suddenly because of severe arrhythmia.[10] Standard anti arrhythmic drugs fails to reduce, or even increases the incidence of sudden cardiac death due to severe side effects and potentially lethal proarrhythmia.[11] Statin are safe drugs with no proarrhythmic effect and can become a low risk preventive agent for ventricular arrhythmia.[12]

The mean age of the patients was 50.7±11.2 years in group I and 51.2±11.5 years in Group II. The age of most of the patients in both groups ranged from 40 to 59 years (65% in group I and 67% in group II), 24 (24%) patients in group I and 23 (23%) patients in group II were of 40 years or younger, 11 (11%) patients in group I and 10 (10%) patients in group II were older than 60 years. Although the mean age in group II is higher than that in group I, the difference was not statistically significant. These findings correlate with those of other studies.[13-15]

There was male predominance in both group I (78.0%) and group II (82.0%). Only 22 (22%) patients in group I and 18 (18%) patients in group II were females. In the previous studies [13,14] found 89% and 98% of their study subjects being male.

Majority of patients in group I (58.0%) and group II (51.0%) were over weight, 33.0% patients in group I and II had body mass index within normal limits and 9.0% of patients in group I and 16.0 % patients in group II were obese. The mean BMI of group I patients was 26.2±3.1 kg/m^2 and group II was 26.7±3.9 kg/m^2. The differences in BMI in both groups were not statistically significant. These findings correlate with those of other study[15] where overweight and obesity were 60% and 7% respectively.

Analysis of risk factors for coronary artery disease showed that 76% patients in group I and 80% patients in group II were smoker, 86% patients in group I and 87% patients in group II were hypertensive, 54% patients in group I and 49% patients in group II had diabetes mellitus, 40% patients in group I and group II had dyslipidaemia. Similar patterns of risk factors were found by others. [14,16,17]

All the patients in both groups at admission were in sinus rhythm. The mean heart rate was 79.7±6.7 per min in group I and 77.2±11.3 per min in group II (p=0.45). The mean systolic blood pressure and diastolic blood pressure in group I was I30.7 ±14.8 mmHg and 86.3±8.1 mmHg respectively, whereas in group II 129±15.9 mm of Hg and 84.8±7.8 mmHg. There was no statistically significant difference between the two groups of patients. Similar finding was observed by other study with acute anterior myocardial infarction.[18]

Left ventricular ejection fraction in group I was 46.1±6.8% and in group II it was 45.5±5.2%. The difference was statistically not significant (p=0.46). Similar values of ejection fraction were found by other study [18] where they found (40-49) % in acute anterior myocardial infarction.

Holter analysis showed that only 2% of patients in group I and 4% of patients in group II develop

supra-ventricular tachycardia and 6% of patients in group I and 5% of patients in group II develop atrio-ventricular block, both are statistically insignificant (p>0.05).

Ventricular premature beats occurred in 66 (66%) patients in group I i.e. who received high dose atorvastatin therapy, and 97 (97%) patients in group II i.e. who did not received high dose atorvastatin therapy; the differences were statistically significant (p=0.001). Among the ventricular premature beats, couplet occurred in 3% of patients in group I and 12% of patients in group II (p =0.01), triplet in 1% of patient in group I and 10% of patient in group II (p =0.005), bigeminy in 4% of patient in group I and 15% of patient in group II (p =0.007) and trigeminy occurred in 1% of patient in group I and 8% of patient in group II (p =0.01).

Non-sustained ventricular tachycardia occurred in 4% of patients in group II and no patient in group I develop non-sustained ventricular tachycardia. Total number of ventricular premature beat between Group I and Group II was 107±66.0 and 310±131 (p=0.001) and number of episodes of NSVT was 123 in Group II. He et al [19] published a study on 586 consecutive patients with acute coronary syndrome. They were randomly divided into two groups, with early and intensive atorvastatin (n=285) or conventional doses of atorvastatin (n=294). It was observed that frequency of ventricular premature beats were 562±87 in early and intensively treated patients and 1568±121 in patients with conventional doses of atorvastatin and episodes of non sustained ventricular tachycardia were 78±31 in patients with early and intensive statin therapy and 132±36 in patients with conventional doses of atorvastatin, and suggests that early and intensive statin therapy is more efficacious than conventional doses, during early hospitalization for ACS. Michell et al [20] assess the probability of VT/VF recurrence in patients with atherosclerotic heart disease (ASHD), who did not receive lipid-lowering drug therapy (n = 279) with that in patients who received early and consistent lipid-lowering therapy (n = 83). They conclude that in patients with ASHD, lipid-lowering therapy is associated with reduction in the probability of VT/VF, suggesting that part of the benefit of lipid-lowering therapy may be due to an antiarrhythmic effect. Kayikcioglu et al [21]demonstrated that patients presenting with acute myocardial infarction and thrombolytic therapy, early use of statin reduces the incidence of in-hospital ventricular arrhythmia.

Statin are known to prevent progression or even promote regression of atherosclerotic plaques.[22] Furthermore, the anti inflammatory and anti proliferative effects of statin are well established.[23] Additionally statin may have beneficial effect on the coronary arterial tone by regulating the nitric oxide mediated endothelial function through a statin induced increase in the endothelial nitric oxide (NO) production and bioavailability. [24] Moreover, statin may contribute significantly to the plaque stabilization in high risk atherosclerotic lesions by modifying their lipid content.[11]

These effects improve myocardial perfusion, ameliorate myocardial ischaemia reperfusion injury during an ACS and reduce the risk of plaque rupture, thereby preventing the ischaemia induced electrophysiological effects that predispose to ventricular arrhythmia.[7] Statin also improve autonomic neural control and increase electrical stability of myocardium.[25]

The present study shows that, ventricular arrhythmia occurs frequently after acute anterior myocardial infarction. Early and high dose atorvastatin therapy significantly reduces the frequency of ventricular arrhythmia than with conventional doses of atorvastatin therapy after acute anterior myocardial infarction.

Conclusion:

Early and high dose atorvastatin therapy significantly reduces the frequency of ventricular arrhythmia, which indicates that this therapy can be an effective treatment modality for reducing the frequency of ventricular arrhythmia in patients with acute anterior myocardial infarction in early period.

Conflict of Interest - None.

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