COMPARISON OF FREQUENCIES OF PERI-PROCEDURAL NON-Q-WAVE MYOCARDIAL INFARCTION BETWEEN PATIENTS WHO RECEIVED AND NOT RECEIVED HIGH DOSE ATORVASTATIN BEFORE PERCUTANEOUS CORONARY INTERVENTION

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ABSTRACT

Background: Periprocedural myocardial infarction has been a matter of concern for cardiac interventionists and role of high dose statins is being widely studied now a days. **Objective:** To compare the frequency of peri-procedural non-Q-wave myocardial infarction between patients who received and not received high dose atorvastatin before percutaneous coronary intervention (PCI). **Material and methods:-** This randomized controlled study was carried out from 1st February, to 31st August, 2010 at Ch. Pervaiz Elahi Institute of Cardiology, Multan. A total of 222 patients with unstable angina on chronic statin therapy undergoing PCI were randomized to atorvastatin high dose bolus group I (80 mg,12 hours before intervention, n=111) or group II no atorvastatin (n=111). **Results:** Mean age in group I, was 53 years and in group II, was 55 years. It was noted that majority were female (88%) in group I, whereas Male (92%) in group II. 33% in group I and 37% in group II were diabetics. Similarly hypertension, smoking prevalence was comparable in both groups. Periprocedural MI occurred in 6 (5.4%) patients in group-I and 17 (15.3%) patients in group-II. **Conclusion:** It is concluded from the study that preloading with high dose (80 mg) atorvastatin bolus before PCI reduces peri-procedural MI in patients on chronic statin therapy undergoing PCI.

Key Words:- Periprocedural myocardial infarction, High dose atorvastatin, PCI

INTRODUCTION

Elevation of cardiac biomarkers has been shown to occur in 5-40% of cases after otherwise successful PCI.[1] Even mild myocardial damage with elevation of cardiac troponin T (TnT) or creatine kinase myocardial isozyme (CK-MB) is associated with increased risk of subsequent cardiac events and several strategies have been proposed to address this issue.[2,3] Hydroxyl-3 methygutaryl coenzyme A reductase inhinitors (statins) reportedly reduce myocardial injury during PCI and subsequent cardiovascular events.[4] With the current wide use of drug eluting stents to provide full coverage of coronary lesions, longer stents are neccssary to prevent restenosis and thus more myocardial injury may occur during PCI with stenting.[5,6] In the context of the current applications of statin therapy in a variety of clinical syndromes, the atrovastain for reduction of myocardial damage during angioplasty (ARMYDA) trial demonstrated a significant reduction of peri-procedural myocardial infarction (MI) after a short term pretreatment with atorvastatin in statin-naive patients with chronic stable angina undergoing PCI. In this trial pretreatment with atorvastatin 40 mg/day for 7 days, significantly reduces periprocedural M1 in elective coronary intervention.[7]

The objective of present study was to compare the frequency of periprocedural non-Q-wave myocardial infarction between patients who received and not received high dose atorvastatin before percutancous coronary intervention.

MATERIAL AND METHODS

This randomized controlled study was carried out from 1st February to 31st August 2010 at Ch.Pervaiz Elahi Institute of Cardiology, Multan. A total of 222 patients with unstable agina on chronic statin therapy undergoing PCI were randomized to group I atorvastatin high dose bolus (80 mg 12 hours before intervention, n=111) or no atorvastatin group II (n=111). Peri procedural non Q wave MI was diagnosed by ST changes along with more than three times elevation above normal of cadiac biomarker Trop T, during or after PCI. Risk factors like, DM, hypertension, smoking were noted in all the patients. The data was entered & analyzed in SPSS version 15.

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RESULTS

Distribution of study variables and risk factors are shown in table-I. Mean age of periprocedural MI cases in group I was 53 years and in group II, 55 years. It was noted that majority were female (88%) in group I, whereas male (92%) in group II. 33% in group I and 37% in group II were diabetics. Similarly hypertension, smoking prevalence was comparable in both groups as in table III. Periprocedural MI occurred in 6 (5.4%) patients in group-I and 17 (15.3%) patients in group-II (P=0.015) shown in table-II. Distribution of risk-factors among MI patients in both groups, is shown in table III.

Table I: Study variables in both groups (N=222)

Variable	Group-I (n=111)	Group-II (n=111)
Male	14(12.6%)	92(82.9%)
Female	97(87.9%)	19(17.1%)
Diabetes	37(33.3%)	41(36.9%)
Hypertension	42(37.8%)	42(37.3%)
Smoking	35(31.5%)	34(30.6%)
1 vessel stent	92(82.9%)	91(82.0%)
2 vessel stent	16(14.4%)	18(16.2%)
3 vessel stent	03(02.7%)	02(01.8%)

Table-II: Peri-procedural MI in study population (N=222)

Atorvastatin 80mg	Peri-procedural MI		Total
	No.	Yes	
Not given	94 (84.6%)	17 (15.3%)	111 (100%)
Given	105 (94.5%)	06 (5.4%)	111 (100%)

(P=0.015)

Table III: Risk factors distribution among patients of peri-procedural MI in both groups

Variable	Group I (n=6)	Group-II (n=17)
Mean age	53.66 years	55.88 years
Male	05(83%)	14(82%)
Diabetes	01(16.7%)	02(11.7%)
Hypertension	02(33.3%)	06(35.3%)
Smoking	03(50.0%)	09((52.9%)
1 vessel stent	03(50.0%)	09(52.9%)
2 vessel stent	03(50.0%)	07(41.2%)
3 vessel stent	0(0%)	01(05.9%)

DISCUSSION

Our trial showed that a single high dose atorvastatin bolus before PCI in unstable angina patients significantly reduced peri-procedural MI after PCR. In present study, patients were already on atorvastatin and bolus of 80 mg was given 12 hours before PCI. It was a randomized trial and all the patients were undergoing elective PCI procedures.

Several randomized trials have shown that statins have beneficial effects on the incidence of long term cardiovascular events in subjects with hypercholesterolemia disease and in patients who underwent coronary intervention. The first randomized trial to demonstrate, pretreatment with atorvastatin compared with placebo was ARMYDA trial. Atorvastatin significantly reduced release of all markers of myocardial damage after coronary intervention, including myoglobin and patients were started on atorvastatin therapy 7 days before coronary intervention regardless of the cholesterol levels. That study used a fixed dose of statin for a short time (atorvastatin 40 mg/d for 1 week) in a randomized fashion.

The ARMYDA-ACS trial was another randomized trial showing that short term pretreatment with atorvastatin reduced the incidence of cardiac events in patients with acute coronary syndromes undergoing early PCI, this benefit is essentially driven by a significant reduction of periprocedural MI.[8] The ARMYDA study group has designed the ARMYDA-ACS trial to assess whether an acute loading with high dose atorvastatin (80 mg atorvastatin 12 hours before and a further 40 mg just before PCI improves clinical outcome in patients with acute coronary syndromes (unstable angina or non-ST segment elevation MI) treated with PCI.[8]

In present study, atorvastatin bolus was given in patients already on statin therapy this was similar to the use of atorvastatin in ARMYDA-Recapture trial.[9] In ARMYDA-Recapture trial two boluses of atorvastatin were used (80 mg atorvastatin given 12 hour before and a further 40 mg dose just before PCI), but in our study we tested the effect of only single (not two boluses) 80 mg dose of atorvastatin given 12 hours before PCI. This was identical to the use of atorvastatin bolus in the recent novel approaches for preventing or limiting events-II (NAPLES-II) trial, which also used a single 80 mg atorvastatin bolus before PCI as was in ARMYDA-Recapture study. ARMYDA trial included patients of stable angina whereas ARMYDA-ACS and ARMYDA-Recapture trial included patients of unstable angina and NSTEMI. In our study we conducted trial in patients of unstable angina.

In the ARMYDA trial, periprocedural MI by creatine kinase MB determination was detected after

coronary intervention in 5% of patients in the statin group and in 18% of those in the placebo group. ARMYDA-ACS trial showed a significant reduction in the incidence of periprocedural MI (5% vs15%), according to these data, 10 patients should be treated with atorvastatin to avoid 1 case of periorocedural MI. ARMYDA-Recapture showed lower incidence of postprocedural creatine kinase-myocardial band and elevation greater than the upper limit of normal in the atorvastatin arm versus placebo (13% vs 24%).[7,8,9] Possible mechanisms of atorvastatin cardioprotection have been investigated in the ARMYDA-ACS study, demonstrating that procedural protection in the atorvastatin arm was paralleled by reduction of PCI induced endothelial activation,[10] as expressed by intercellular cell adhesion molecule-1 and E-selectin levels at 24 hours after intervention. Other explanations include atorvastatin induced early increase of endothelial progenitor cells differentiation and subsequent augmentation of circulating endothelial progenitors cells, with attendant mechanism of action,[11] this is in accordance with animal studies[12] that have shown a reduction of infarct size when an acute statin load is given before ischemia or before reperfusion interestingly, whereas in the animal model this cardio protection may wane with time, it can be restored with an acute high dose atorvastatin given immediately before ischemia/reperfusion,[13] this phenomenon may have potential clinical relevance. Thus the primary benefit derived from atorvastatin reload in our trial appears to be again due to the atorvastatin bolus effect to regain the effects which have waned off with time. Although the pathophysiological explanation for atorvastatin loading benefit in statin naive patients could be lack of statin mediated plaque stabilizing effect in ACS patients "breakthrough" plaque instability with increased or "resistant" plaque inflammation likely explains the relative benefit of atorvastatin reload. The rapid anti-inflammatory, antithrombotic effects of atorvastatin have been described.[14,15] It is likely that ACS patients have increased plaque inflammatory cell density (macrophages and T lymphocytes) with consequent greater local production of inflammatory lymphocytes, as well as suppression of anti-inflammatory mediators (nitric oxide synthase). Thus, although it is conceivable that patients on chronic statin therapy would already have some degree of myocardial protection during PCI, the presence of breakthrough plaque inflammation in the ACS cohort requires the acute suppression afforded by atorvastatin reload (similar to the observation made in the original ARMYDA-ACS) study. Furthermore a dose dependent platelet inhibitory/anti-inflammatory effect of atorvastatin may have been operative.[15,16] In vivo platelet activation and plasma chemokine levels have been demonstrated to be reduced more effectively by higher atorvastatin doses through low density lipoprotein independent mechanisms.[17] As thrombosis and inflammation are intrinsically linked in the pathogenesis of periprocedural myoncecrosis in the setting of PCI, especially in ACS patients, this concept may support the utilization of high dose, intensive atorvastatin load in our study. Our trial is in line with other trials most notably ARMYDA series, NAPLES to support the use of high dose atorvastatin bolus before PCI in patients of unstable angina.

CONCLUSION

It is concluded from the study that preloading with high dose 80 mg atorvastatin bolus before PCI reduces peri-procedural MI in patients on chronic statin therapy undergoing PCI.

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