Original Article

Comparison of In-Hospital Course of Patients having First Acute Myocardial Infarction with or without Pre-Infarct Angina

Muhammad Arif Nadeem, Tariq Waseem, Syed Mohsin Ali Shah and Abdul Hafeez Khan

Background: Acute myocardial infarction (AMI) is the most common cause of morbidity and mortality and to reduce myocardial infarct size a new technique i.e. ischemic pre-conditioning has evolved. The brief periods of ischemia followed by re-perfusion appear to pre-condition the heart and make it more resistant to a subsequent longer period of ischemia. Pre-conditioning is defined as "a rapid, adaptive response to a brief ischemic insult, which slows the rate of cell death during a subsequent, prolonged period of ischemia."

Material and Methods: A comparative study was conducted to identify the patients of AMI with or without pre-infarction angina, to find out the differences in their in-hospital course and to assess the prognostic value of pre-infarction angina in first episode of AMI during hospital stay.

Results: Twenty-five patients with (Group A) and 25 patients without (Group B) pre-infarction angina were compared for their in-hospital course. Mean age ± SD in Group A was 55 ± 7 years and in Group B 54 ± 8 years. There were 18 (72%) males and 7 (28%) females in Group A, and 17 (68%) males and 8 (32%) females in Group B. As far as the baseline risk factors in two groups were concerned, 5 vs 7 patients had diabetes mellitus, 7 vs 8 had hypertension, 16 (64%) vs 13 (52%) were smokers, 3 vs 4 had obesity, 4 vs 5 had family history of IHD and 5 vs 6 had hyperlipidemia in Group A and Group B respectively. Regarding the intake of anti-anginal medication like calcium channel blockers, beta-blockers and nitrates in the two groups, there were more patients in Groups A as compared to B who were taking them ($p<0.05$). Similarly there were 10 (40%) vs 2 (8%) patients in Groups A and B respectively who were taking aspirin ($p<0.05$). In-hospital complications like cardiogenic shock, CCF, LVF, RVF, recurrent ischemic pain, infarct extension and rhythm abnormalities were more in Group B as compared to Group A ($p<0.05$).

Conclusion: The presence of pre-infarction angina had a favorable effect on in-hospital course after AMI i.e. a lower incidence of in-hospital mortality, a lower incidence of in-hospital complications, development of significantly smaller infarct size.

Keywords: AMI, Pre conditioning, Pre infarct angina, Infarct size

Introduction

In the history of attempts to reduce myocardial infarct size, only few therapies have stood the test of time; one is re-perfusion and the other is pharmacologic therapies such as calcium channel blocking agents, beta adrenergic blocking agents, oxygen radical scavenging agents and neutrophil inhibitors. The newest technique for reducing the size of myocardial infarction is ischemic pre-conditioning.[1] The brief periods of ischemia followed by re-perfusion appear to pre-condition the heart and make it more resistant to a subsequent longer period of ischemia.[2]

Pre-conditioning is defined as "a rapid, adaptive response to a brief ischemic insult, which slows the rate of cell death during a subsequent, prolonged period of ischemia." It has been seen that pre-infarction angina has the potential to pre-condition the heart; one would predict that it would do so only in infarcts that had been re-perfused.[3] Pre-conditioning protects myocardium against a greater subsequent ischemic insult with less threat of infarction.[4] It has been seen that patients with pre-infarction angina may suffer from a less severe infarct than those thought to undergo sudden coronary occlusion without the opportunity for pre-conditioning.[5]

It has also been seen that patients with AMI have a lower in-hospital death rate if they had history of angina within the 48 hours period that precedes infarction.[6] Patients having the history of pre-infarction angina presenting with first AMI has been reported to be associated with lower in-hospital incidence of sustained ventricular arrhythmias, a lower incidence of pump failure, a lower incidence of cardiac mortality, higher ejection fraction, smaller

diastolic volume and a lower incidence of aneurysm formation.[7] There is also a lower incidence of cardiogenic shock and reduction in in-hospital death from acute anterior myocardial infarction in patients having pre-infarct angina, which is contributing factor in development of collateral circulation.[8] It has been seen that previous angina before non-thrombolized AMI is a marker of increased risk of infarct extension, recurrent ischemic pain and mitral regurgitation.[9]

Aims & Objectives

1. To identify the patients of AMI with or without pre-infarction angina.
2. To find out the differences in in-hospital course of patients having AMI with or without pre-infarction angina.
3. To assess the prognostic value of pre-infarction angina in first episode of AMI during hospital stay.

Material and Methods

Inclusion Criteria

Both men and women of any age presenting with first episode of AMI with or without pre-infarction angina were included.

Exclusion Criteria

Patients with evidence of old myocardial infarction and those presenting with chest pain, which later on proved to be non-cardiac in origin. Patients unable to provide a clear clinical history regarding presence or absence of pre-infarction angina were excluded from the study.

Methods

The study was conducted in East Medical Ward (EMW) of Mayo Hospital, Lahore. Patients were admitted through emergency. This was a comparative prospective study of 50 patients having their first presentation with AMI with or without pre-infarction angina. Twenty-five patients with and 25 patients without pre-infarction angina were compared for their in-hospital course. The diagnosis of AMI was established on any two of the three criteria, i.e. history of chest pain suggestive of cardiac origin, an ECG criteria of an abnormal ST-segment elevation of 1mm above iso-electric TP segment measured at J point in two or more than two contiguous leads in the absence of left bundle branch block (LBBB) or ventricular rhythm, and elevated cardiac enzymes. After establishing the diagnosis, all such patients were admitted in CCU and ICU attached with East Medical Ward. A careful history was taken for the presence and absence of pre-infarction angina which was defined as presence of typical chest pain occurring at rest or during exercise and relieved by rest or sublingual nitroglycerine.[7] The patients were grouped into two, group A patients having pre-infarction angina and group B patients without it. These patients were monitored continuously throughout their admission on ECG monitors and their in-hospital course was clinically evaluated on twice daily basis along with full ECG recordings. The variables assessed in all admitted patients were age, gender, presence of coronary risk factors (diabetes mellitus, hypertension, smoking, obesity, family history of IHD, hyperlipidemia, asthma), previous use of anti-anginal medicines, time from onset of pain to presentation to hospital, use of thrombolytic therapy, incidence of in-hospital complications like cardiogenic shock, congestive cardiac failure (CCF), left ventricular failure (LVF), right ventricular failure (RVF), rhythm abnormalities, recurrent ischemia and infarct extension, on echocardiography (left ventricular ejection fraction, aneurysm formation, papillary muscle rupture, ventricular septal defect [VSD] and clot in left ventricle [LV]) and in-hospital mortality.

Regarding above variables following investigations were specifically done:

- A bedside monitor was connected with the patients to monitor ECG continuously for detection of any arrhythmias.
- 12 lead ECG.
- Initial cardiac enzymes.
- X-ray chest P.A. View.
- Echocardiography.

Results

Mean age ± SD in Group A was 55 ± 7 years and in Group B, comprised of 25 patients without history of pre-infarction angina, was 54 ± 8 years ($p>0.05$). There were 18 (72%) males and 7 (28%) females in Group A, and 17 (68%) males and 8 (32%) females in Group B.

As far as the baseline risk factors in two groups were concerned, 5 (20%) vs 7 (28%) patients had diabetes mellitus ($p>0.05$), 7 (28%) vs 8 (32%) had hypertension ($p>0.05$), 16 (64%) vs 13 (52%) were smokers ($p>0.05$), 3 (12%) vs 4 (16%) had obesity ($p>0.05$), 4 (16%) vs 5 (20%) had family history of ischemic heart disease ($p>0.05$) and 5 (20%) vs 6

(24%) patients had hyperlipidemia (p>0.05) in Group A and Group B respectively. No patient in Groups A and B had history of asthma in this study (**Figure 1**). Regarding the intake of anti-anginal medication in the two groups, 14 (56%) vs 4 patients were taking calcium channel blockers (p<0.05), 13 (52%) vs 3 patients were taking beta-blockers (p<0.05) and 10 (40%) vs 2 (8%) patients were taking nitrates (p<0.05) in Groups A and B respectively. Similarly there were 10 (40%) vs 2 (8%) patients in Groups A and B respectively who were taking aspirin (p<0.05) **(Table 1)**.

When time from onset of pain to presentation was observed, the mean ± SD of hours in Group A was 3.6 ± 2.1 vs 1.6 ± 0.6 hours in Group B (p<0.001). The range in Group A was 0.55 to 8.00 hours vs 0.87 to 7.50 hours in Group B **(Table 2)**.

In-hospital complications in the two groups were as follows: 1 in Group A vs 6 patients in Group B (p<0.05) had cardiogenic shock, 1 in Group A vs 6 in Group B (p<0.05) had congestive cardiac failure (CCF), 2 in Group A vs 8 in Group B (p<0.05) had left ventricular failure (LVF) and 1 in Group A vs 2 patients in Group B (p>0.05) had right ventricular failure (RVF) **(Table 3)**.

Similarly, 2 in Group A vs 8 (32%) patients in Group B (p<0.05) had recurrent ischemic pain, 1 in Group A vs 6 (24%) in Group B (p<0.05) had infarct extension and 2 in Group A vs 8 (32%) patients in Group B (p<0.05) had rhythm abnormalities **(Table 3)**.

While in-hospital mortality between two groups was analyzed, there was only 1 in-hospital death in Group A vs 6 (24%) in Group B (p<0.05) **(Figure 2)**.

Fig 1 **Baseline Risk Factors Differences (n=50)**

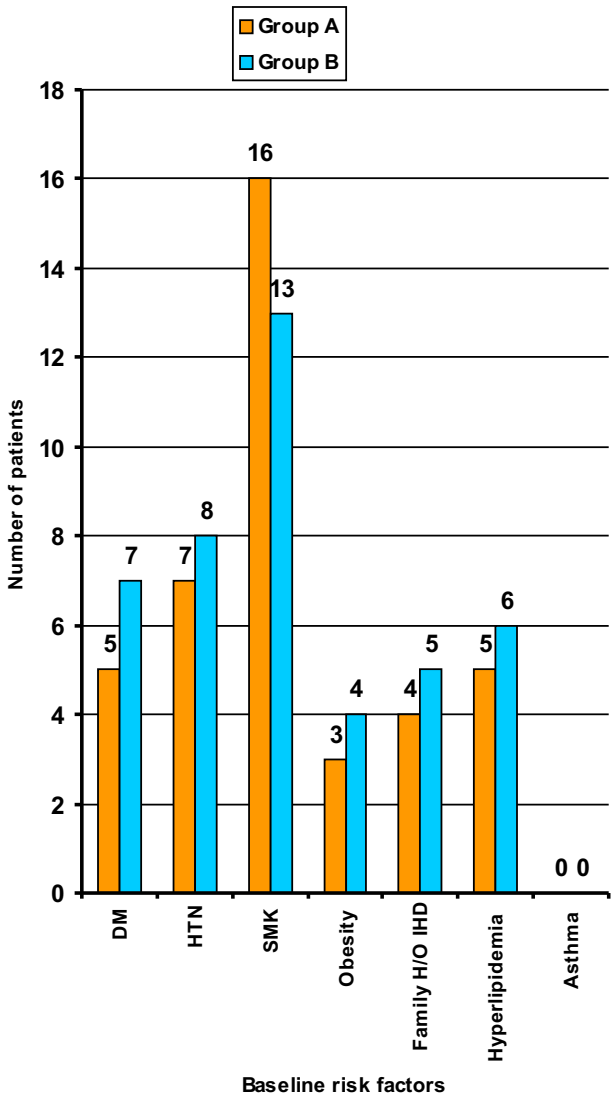


Table-1: Differences in intake of anti-anginal medication.

Anti-anginal Drugs	Group A No. (%)	Group B No.(%)	P Value
Calcium Blockers	14 (56%)	04 (16%)	<0.05
Beta Blockers	13 520%)	03 (12%)	<0.05
Nitrates	10 (40%)	02 (08%)	<0.05
Aspirin	10 (40%)	02 (08%)	<0.05

Table-2: Differences in Time from onset of Pain to Presentation (hours).

	Group A	Group B	P Value
Mean±SD	3.6±2.1	1.6±0.6	<0.001
Range	0.55-8.00	0.87-7.50	<0.05

Table-3: In-Hospital Complications.

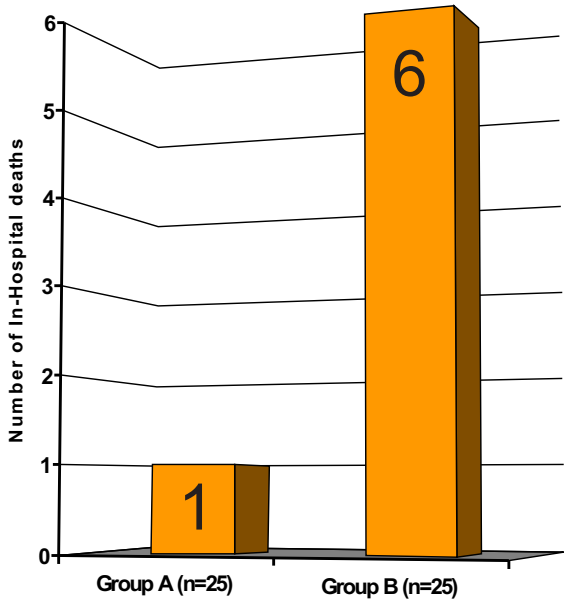
Complications	Group A No. (%)	Group B No.(%)	P Value
Cardiogenic Shock	01	06 (24%)	<0.05
CHF/CCF	01	06 (24%)	<0.05
LVF	02	08 328%)	<0.05
RVF	01	02	>0.05
Recurrent ischemic pain	02	08 (32%)	<0.05
Infarct extension	01	06 (24%)	<0.05
Rrhythm abnormalities	02	08 (32%)	<0.05

Table-4: Echocardiographic Data

Echocardiography	Group A	Group B	P Value
EF% (Mean±SD)	55±7.8	44±7.9	<0.001
Aneurysm n(%)	03	13 (52%)	<0.05
Papillary muscle repture n (%)	02	01	>0.05
VSD n (%)	01	05	>0.05
Clot in LV n (%)	04	05	>0.1

CHF/CCF: Congestive Heart/Cardiac Failure LVF: Left Ventricular Failure RVF: Right Ventricular Failure
EF: Ejection Fraction VSD: Ventricular Septal Defect LV: Left Ventricle

Fig 2 **Difference in In-Hospital mortality between two groups (p<0.05)**



Discussion

Pre-infarction angina before an episode of AMI has a favorable prognostic impact on in-hospital course due to the effect of ischemic pre-conditioning, which is now a powerful and reproducible method of delaying cell necrosis. The clinical observation of pre-conditioning would have important therapeutic implications because once its mechanism is elucidated, it may form the basis for new therapies in cardiovascular medicine.[1]

In this study, out of total 50 patients, equal number of 25 patients was compared having history of pre-infarction angina with an equal number without any history of pre-infarction angina before the first episode of AMI. There were no significant differences between the two groups in respect of age, gender and baseline risk factors. This finding is comparable with previous studies.[6-7] There was a statistically significant difference ($p<0.05$) between the two groups regarding the intake of anti-anginal medication before the first AMI. The patients with pre-infarction angina were on anti-anginal medication (calcium channel blockers, beta blockers, nitrates and aspirin), which was comparable with the study done by Kloner et al.[6]

The time from onset of chest pain to hospital

presentation in patients with angina was longer as compared to patients without angina. This delay may indicate that possibly patients experiencing chest pain become accustomed to have chest pain, so it may take him or her longer to come to the hospital with the onset of the chest pain of myocardial infarction. This was also more or less equal to same study mentioned above.[6]

When in-hospital complications were compared, there was statistically significant difference between patients of two groups, as far as cardiogenic shock in 1 (4%) vs 6 (24%) patients, CCF in 1 (4%) vs 6 (24%) and LVF in 2 (8%) vs 8 (32%) patients were concerned. The patients with a previous history of angina were less likely to develop cardiogenic shock, CCF and LVF as compared to patients without previous history of angina. This was more or less equal to the previous studies.[8,10] There was no statistically significant difference between those patients who developed RVF having pre-infarct angina versus without it. It was probably because of the small number of patients who develop RVF in this study.

There was statistically significant difference in patients with previous history of angina versus without angina who developed recurrent ischemic pain, 8 (32%) vs 2 (8%), infarct extension, 6 (24%) vs 1 (4%) and rhythm abnormalities, 2 (8%) vs 8 (32%) patients. The patients with pre-infarction angina were more likely to develop recurrent ischemic pain ($p<0.05$) and infarct extension ($p<0.05$) as also shown by previous studies because of the fact that patients with pre-infarction angina have more severe multi-vessel coronary artery disease.[6-7,9,11-12] The rhythm abnormalities were seen in less number of patients who had previous history of angina before infarction as compared to patients who had no pre-infarct angina ($p<0.05$). Thirty two percent patients in Group B having no previous history of angina developed more malignant arrhythmias like ventricular fibrillation and sustained ventricular tachycardias comparable more or less with previous studies.[7-8]

The limitation of infarct size was seen in those patients who had history of pre-infarct angina as compared to those who had no pre-infarct angina. There was statistically significant difference ($p<0.05$) between patients having pre-infarction angina versus no pre-infarction angina regarding in-hospital mortality. Only 1 (4%) patient having pre-infarction angina died as compared to 6 (24%)patients with no pre-infarction angina. This was comparable more or less with previous studies.[6-7]

All these findings suggest that pre-infarction angina has a protective effect against myocardial damage after abrupt coronary occlusion. The presence of pre-infarction angina is associated with a lower incidence of in-hospital complications and mortality. Multivariate analyses reveal that the absence of pre-infarction angina is an independent predictor of in-hospital cardiac mortality. The potential mechanisms of cardioprotection by previous angina are still debatable. However, some authors observed that patients who experienced angina for more than 1 week before coronary occlusion have greater number of collateral development.[8,13] The presence of collateral vessels could not be examined and studied in this study due to poor compliance of patients and non- availability of 24 hours angiography facility in this set up.

The other potential mechanism of beneficial effects of previous angina on in-hospital outcome is the use of anti-anginal medication.[6] This finding was observed in this study as well. Another mechanism of better in-hospital outcome in patients with preceding angina before AMI is ischemic pre-conditioning. This phenomenon is observed by many experimental models.[1-4] This was also observed in this study. Yet another interesting mechanism is the difference in intrinsic thrombolytic systems in patients with pre-infarction angina. Re-perfusion is achieved more rapidly in patients with pre-infarction angina history.[14] This observation was not studied in this study because of the economic factors and non-availability of more advanced bio-chemical laboratory facility in this set up.

Conclusion

The presence of pre-infarction angina has a favorable effect on in-hospital course after AMI i.e. a lower incidence of in-hospital mortality, a lower incidence of in-hospital complications and development of significantly smaller infarct size.

Department of Medicine
Services Institute of Medical Sciences, Lahore.
theesculapio@hotmail.com
www.sims.edu.pk/esculapio.html

References

1- Kloner RA, Yellon D. Does Ischemic preconditioning occur in patients? J Am Coll Cardiol 1994; 24:1133-42.

2- Murry CE, Jennings RB, Reimer KA. What is ischemic pre conditioning? *In:* Przyklenk K, Kloner RA, Yellon DM (eds). Ischemic preconditioning: The Concept of Endogenous Cardioprotection. Norwell, MA: Kluwer Academic, 1994: 3-17.

3- Ovize M, Kloner RA, Hale SL, Przyklenk K. Coronary cyclic flow variations "precondition" ischemic myocardium. Circulation 1992; 85: 779-89.

4- Opie LH. Mechanisms of cardiac contraction and relaxation. *In:* Branwald E (Ed.). Heart disease. A Textbook of Cardiovascular Medicine 5th edition. Pennsylvania, W.B. Saunders Co., 1997: 387-388.

5- Ottani F, Galvani M, Ferrini D, Sorbello F, Limonetti P, Pantoli D et al. Prodromal angina limits infarct size, a role of ischemic preconditioning. Circulation 1995; 91: 291-7.

6- Kloner RA, Shook T, Przyklenk K, Davis VG, Junio L, Methews RV et al. Previous angina alters in hospital outcome in TIMI-4, a clinical correlate to pre conditionaing? Circulation 1995; 92: 1064-5.

7- Anzai T, Yoshikawa T, Asakura Y, Abe S, Akaishi M, Mitamura H et al. Pre-infarction angina a major predictor of left ventricular function and long term prognosis after a first Q-wave myocardial infarction. J Am Coll Cardiol 1995; 26: 319-327.

8- Perez-Castellano N, Garcia EJ, Abeytua M, Soriano J, Serrano JA, Elizaga J et al. Influence of collateral circulation on in-hospital death from anterior acute myocardial infarction. J Am Coll Cardiol 1998; 31: 512-518.

9- Kloner RA, Muller J, Davis V. Effects of previous angina pectoris in patients with first acute myocardial infarction not receiving thrombolytics. Am J Cardiol 1995; 75: 615-617?

10- Ruocco NA, Bergelson BA, Jacobs AK, Frederick MM, Fascon DP, Ryan TJ. Invasive versus conservative strategy after thrombolytic therapy for acute myocardial infarction in patients with antecedent angina. A report from thrombolysis in myocardial infarction phase II (TIMI II). J Am Coll Cardiol 1992; 20:1445-51.

11- Cupples LA, Gagnon DR, Wong ND, Ostfeld AM, Kannel WB. Pre-existing cardiovascular conditions and long term prognosis after initial myocardial infarction. The Framingham Study. Am Heart J 1993; 125:863-72.

12- Barbash GI, White HD, Modan M, VandeWerf F. Antecedent angina pectoris worse outcome after myocardial infarction in patients receiving thrombolytic therapy experience gleaned from the International Tissue Plasminogen Activator/ Streptokinase Mortality Trial. J Am Coll Cardiol 1992; 20:36-41.

13- Hirai T, Fujita M, Yamanishi K, Ohno A, Miwa K, Sasayama S. Significance of pre-infarction angina for preservation of left ventricular function in acute myocardial infarction. Am Heart J 1992; 124:19-23.

14- Andreotti F, Pasceri V, Hackett DR, Davies GJ, Haider AW, Maseri A. Preinfarction angina as a predictor of more rapid coronary thrombolysis in patients with acute myocardial infarction. N Engl J Med 1996; 334:7-12.