Reperfusion strategy in patients with ST-Segment Elevation Myocardial Infarction (STEMI): Comparative study between primary percutaneous coronary intervention and fibrinolytic therapy

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Reperfusion therapy is the cornerstone in management of STEMI. This study was designed to evaluate both in-hospital and 30 days outcome in patients with STEMI treated with primary percutaneous coronary intervention (PPCI) versus fibrinolysis. This prospective, controlled, study included 140 patients with STEMI who were eligible for reperfusion therapy. In hospital and 30 days major adverse cardiovascular events (MACE) were reported and head to head comparison was done between PPCI versus fibrinolysis. All-cause mortality was reported in 5% of patients (10% versus 0% in fibrinolysis and PPCI respectively, p=0.07), recurrence of ischemic symptoms was reported in 18% of patients (30% versus 7% in fibrinolysis and PPCI respectively, P =0.02), heart failure was evident in 22% of patients (33% versus 10% in fibrinolysis and PPCI respectively, P =0.02). PPCI is safe and effective treatment option for patients with STEMI.

Key words. Reperfusion, STEMI, PPCI, fibrinolysis, ischemia.

INTRODUCTION

The primary goal in the management of acute myocardial infarction (AMI) is to start reperfusion therapy as quickly as possible. The benefits of reperfusion therapy are well documented regardless age, gender and other baseline characteristics. Patients who derive the most benefit are those who are treated early and those at high risk such as patients with anterior myocardial infarction (Vivekananthan et al, 2004). An ongoing challenge for the clinical cardiologist remains the choice of optimal reperfusion therapy for patients with STEMI (McKay R, 2003). Both fibrinolysis and PPCI can restore ante-grade flow in most occluded coronary arteries. Fibrinolysis cannot be given for every patient with STEMI due to presence of contraindications and it can achieve successful reperfusion in 60-64% of patients (Michels and Yusuf, 2003). However, PPCI can achieve successful reperfusion in up to 96% of patients. Meta analysis of 23 randomized trials showed that PPCI results in better short and long term survival (Dalby et al, 2003). PPCI appears to have its greatest mortality benefit in high risk patients. In patients with cardiogenic shock, an absolute 9% reduction in 30 days mortality with coronary revascularization instead of immediate medical stabilization was reported in SHOCK trial (Hochman et al, 1999). In this study, in hospital and 30 days MACE were reported in patients with STEMI treated with either fibrinolysis or PPCI.

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PATIENTS AND METHODS

Study Design

This prospective, controlled, non-randomized study included 140 consecutive patients with STEMI who were eligible for reperfusion. The study was conducted at the Department of Cardiology, Benha University Hospital in the period from May 2013 to August 2015. Key inclusion criteria were patients with STEMI presented within 12 hours from onset of ischemic chest pain with ECG evidence of ST elevation in two contiguous leads with the cut off points: ≥ 0.2 mV in men or ≥ 0.15 mV in women in leads V2-V3 and / or ≥ 0.1 mV in other leads, often with reciprocal ST-segment depression in contra lateral leads. Key exclusion criteria were: patients who had absolute contraindication to fibrinolysis, cardiogenic shock at the time of admission, patients older than 80 years, patients presenting later than 12 hours from the onset of symptoms with no signs of ongoing ischemia.

Study protocol

Eligible patients were classified into 2 groups according to reperfusion strategy:
A. Group I: 60 patients who were treated with fibrinolysis
B. Group II: 80 patients who were treated with PPCI.

Methods

Baseline evaluation

All patients had review of medical history on admission to emergency department including analysis of demographic data (age, sex), risk factors of coronary atherosclerosis, contraindications to fibrinolytic therapy, time from symptom onset, prior CAD, prior PCI or CABG, associated co morbidities. General and cardiac examination was done, 12 leads ECG was performed immediately on admission, 90 minutes post streptokinase, immediately after PPCI, and every 6 h during the first 24 hours, and once daily until discharge, routine laboratory investigations including cardiac biomarkers (Troponin I & CK-MB) were taken.

Coronary angiography and PPCI

Aspirin (300 mg loading, then 75 mg maintenance) and clopidogrel (600 mg loading, then 150 mg/day maintenance for one week, then 75 mg/day for one year) were given on admission and after PPCI. Un-fractionated heparin (UFH) of 10000 units bolus dose was given after sheath insertion. The procedure was done according to the standard technique for coronary angiography and PCI. Trans femoral approach was done in all patients using 6 Fr sheaths. Diagnostic coronary angiography was done to explore non-infarct related artery. XB or Judkin left guide catheters were used for lesions in the left system, while Judkin right catheters for lesions in right coronary artery (RCA). Thrombus aspiration and glycoproteins inhibitors (Eptifibatide or Tirofiban intracoronary bolus followed by intravenous infusion for 12 hours) were used in lesions with heavy thrombus burden and or impaired TIMI flow after the procedure. The operator determined the length and diameter of implanted stents. Sheaths were removed 4 hours post procedure.

Fibrinolytic therapy

Streptokinase 1.5 million units over 1 hour. Patients were closely monitored during infusion. Success of reperfusion was measured after 90 minutes from the start of streptokinase by ECG and clinicaly. Failure of reperfusion was defined as less than 50% resolution of ST segment elevation, 90 minutes after start of steptokinase and or persistance of chest pain.

Echocardiography

Transthoracic echo was done at baseline, 30 days, using General Electric System Vivid-3 machine with (2.5-5) MHZ probe. Two dimensional echo, M-Mode, Doppler and Simpson’s methods were performed to obtain measurements of LV volumes, ejection fraction, and segmental wall motion abnormality.

Study end points

1- Primary end point: 30 days composite end point of all-cause mortality, re-infarction (acute MI that occurs within 28 days of admission MI), re-ischemia (chest pain and or ECG changes), heart failure, and cerebrovascular stroke.

2- Secondary end point: 30 days LVEF

Statistical analysis

Data are presented as mean ± SD for continuous data and as number (%) for categorical data. Between groups comparison was done using student t-test for continuous data and Chi-square test for qualitative data. Level of evidence was detected to be significant at P value <0.05. The collected data were tabulated and analyzed using SPSS version 19 software.

RESULTS

A. Study Population

The mean age was 54±10 years (56± 7 y versus 55± 8 y in group I and II respectively, P =0.12), Between groups
Table 1. Baseline characteristics of study population

<table>
<thead>
<tr>
<th>Variable</th>
<th>All patients&lt;br&gt;n = 140</th>
<th>Group I&lt;br&gt;Fibrinolysis&lt;br&gt;n = 60</th>
<th>Group II&lt;br&gt;PPCI&lt;br&gt;n = 80</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years Mean ± SD</td>
<td>54±10</td>
<td>56±7</td>
<td>55±8</td>
<td>0.12</td>
</tr>
<tr>
<td>Male Sex n (%)</td>
<td>126 (90%)</td>
<td>52 (87%)</td>
<td>74 (93%)</td>
<td>0.39</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>14 (10%)</td>
<td>6 (10%)</td>
<td>8 (10%)</td>
<td>1</td>
</tr>
<tr>
<td>DM</td>
<td>54 (39%)</td>
<td>22 (37%)</td>
<td>32 (40%)</td>
<td>0.79</td>
</tr>
<tr>
<td>Hypertension</td>
<td>52 (37 %)</td>
<td>26 (43%)</td>
<td>26 (33%)</td>
<td>0.43</td>
</tr>
<tr>
<td>Smoking</td>
<td>110 (78 %)</td>
<td>46 (77%)</td>
<td>64 (80%)</td>
<td>0.57</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>74 (53%)</td>
<td>24 (40%)</td>
<td>50 (63%)</td>
<td>0.07</td>
</tr>
<tr>
<td>Prior angina</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>---</td>
</tr>
<tr>
<td>Prior PCI/CABG</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Prior AMI/CHF</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
</tbody>
</table>

PPCI = Primary percutaneous coronary intervention, DM=Diabetes Mellitus, CABG= Coronary artery bypass grafting, AMI = acute myocardial infarction, CHF= congestive heart failure

comparison showed no statistical significant differences in baseline characteristics. Table 1

B. Time from symptoms onset to admission

23% of patients were presented within the first 3 hours (23% versus 23% in group I and II respectively, P =1). 53% of patients were presented between 3 and 6 hours (57% versus 50% in group I and II respectively, P =0.19), 24% of patients were presented after 6 hours (20% versus 27% in group I and II respectively, P =0.15).

C. Target segment of STEMI according to ECG

Anterior STEMI was the most common type of infarction; 57% of patients (57% versus 57% in group I and II respectively, P =1), inferior infarction was reported in 17% of patients (24 % versus 10% in group I and II respectively, P =0.15 ), 13% of patients had antero-lateral STEMI (13% versus 13% in group I and II respectively, P =1), infero-lateral infarction was reported in 8% of patients (3% versus 13% in group I and II respectively, P =0.14), 5 % of patients had inferior, right and posterior infarction (3 %versus 7% in group I and II respectively, P = 0.19)

D. Door to balloon time (D2B) in PPCI group

The mean D2B time was 70±10 minutes. D2B time within 60 minutes was reported in 57% of patients, while 37% of patients had time between 60-90 minutes and 6% of patients had door to balloon time more than 90 minutes. Figure 1.

E. PPCI data

The culprit artery was LAD in 70% of patients, while RCA in 17% of cases, and LCX in 13% of patients. 42% of patients had single vessel disease, 2 vessel disease was evident in 35% of patients, while 3 vessels disease was reported in 23 % of patients. Floppy wire was used in all patients. Pre dilatation was done in 60% of cases either due to shortage of aspiration devices or presence of critical lesion after thrombus aspiration, or failure of aspiration catheter to restore patency. Intracoronary glycoprotein inhibitors were used in 40% of cases, followed by intravenous infusion for an average 12 hours. Manual aspiration devices were used in 30% of patients, large thrombus burden or impaired TIMI flow was the main indications. Implantation of BMS was performed in 100% of all patients. 80% had 1 stent while 20% had 2 stents. The mean stent diameter was 3±0.3mm while the mean stent length was 21±5mm. The mean inflation pressure was 14±1 ATM. Post dilatation was done in 40% of patients due to residual stenosis inside the stents. Pre PCI TIMI 0 flow was detected in 57% of patients, TIMI I in 40% while TIMI II in 3% of patients. TIMI flow at the end of PCI was III in 87% of patients and II in 13% of
patients. Distal embolization occurred in 3% of patients, 7% of patients had no reflow which was treated with repeated intracoronary injection of adrenaline and GPI.

F. In hospital outcome

No mortality in either group, no reported cases of reinfarction, stroke or recurrent ischemia during the hospital stay. 17% of patients had major bleeding (30% versus 3% in group I and II respectively, P =0.006 ), 22% of patients had minor bleeding (40% versus 3% in group I and II respectively, P =0.001 ), 30% of patients had ventricular arrhythmias (40% versus 20% in group I and II respectively, P =0.09 ). 10% of patients needed emergency intervention (20% versus 0% in group I and II respectively, P =0.01 ). Failure of fibrinolysis was the cause of emergency intervention (Rescue PCI) due to persistent chest pain and or less than 50% regression of ST segment elevation in the lead with maximum elevation 90 min after fibrinolysis start, 8% of patients developed heart failure (13% versus 3% in group I and II respectively, P =0.16).

G. Thirty days outcome

The primary end point was reported in 73% versus 17% in group I and II respectively (p=0.001). Mortality was reported in 5% of patients (10% versus 0% in group I and II respectively, p =0.07), recurrence of ischemic symptoms was reported in 18% of patients (30% versus 7% in group I and II respectively, P =0.02). These patients were admitted with unstable angina. However, all of them responded to optimization of medical treatment without the need for urgent revascularization. Heart failure was evident in 22% of patients (33% versus 10% in group I and II respectively, P =0.02), no reported cases of re-infarction or cerebrovascular stroke in both group.

H. Thirty days LVEF

Baseline LVEF was 47±10% in fibrinolysis group versus 48±8% in PPCI patients, p=0.15. At 30 days, no significant changes were reported in either group (47±7% vs 51±11% in group I and II respectively, P=0.2)

DISCUSSION

The present study showed better outcome in PPCI versus fibrinolysis regarding 30 days heart failure and recurrence of ischemic symptoms. We reported predominance of anterior STEMI in 57% of patients (57% versus 57% in group I and II respectively, P =1). Di Mario et al, 2004 reported 55% incidence of anterior infarction, Moreover, in the study derived by Qarawani et al., 2007, anterior infarction was evident in 51% of patients. However, Varani et al., 2008 in their study, only 45% of patients had anterior infarction. In our study, the mean
D2B time was 70±10 minutes. Currently, it is estimated that almost 90% of patients presenting to a hospital with PCI capability and without a clinical reason for delay have a door to balloon time ≤ 90 minutes (Nestler et al, 2009). Nallamuthu et al., 2004 reported that mortality benefit associated with PPCI was lost if the PCI-related delay exceeded 60 min. Combined analysis of the NRMI-2 -3 and -4 showed that this accepted PCI-related delay was much longer, i.e. 114 min and varied considerably depending on various factors like symptoms duration, age and infarction location(Pinto et al, 2006). Glycoprotein inhibitors were used in 40% of cases, while manual aspiration devices were used in 30% of patients, large thrombus burden or impaired TIMI flow were the main indications. Guidelines for 2013 indicate that aspiration devices and GPIIb/IIIa inhibitor are considered as class IIa.

We reported higher rates of major bleeding in the fibrinolytic group. (30% versus 3% in group I and II respectively, P =0.006), 22% of patients had minor bleeding (40% versus 3% in group I and II respectively, P =0.001). These rates were concordant to the results of Zwolle and colleagues, who reported that the incidence of major bleeding within 48 hours after PPCI was low 1.6% and the incidence of minor bleeding was 5.6%. Ten percent of patients needed urgent intervention (20% versus 0% in group I and II respectively, P =0.01). In the STREAM study by Armstrong et al, 2013, emergency angiography was required in 36.3% of patients in the fibrinolysis group. Regarding 30 days outcome, heart failure was evident in 22% of patients (33% versus 10% in group I and II respectively, P =0.02). The better outcome of PPCI group in our study as compared to fibrinolytic group, especially regarding heart failure is in agreement with several trials (DANAMI-2, STAT, STOPAMI-1, and STOPAMI-2) that have demonstrated a better outcome with PPCI compared to fibrinolysis in left ventricular function(Andersen et al, 2003). Unstable angina requiring rehospitalization was reported in 18% of patients (30% versus 7% in group I and II respectively, P =0.02), all-cause mortality occurred in 5% of patients (10% versus 0% in group I and II respectively, p =0.07).The results of this study were concordant with the results of almost all prior trials (Yahya et al., 2013). There was a trend to lower mortality in PPCI patients but due to small sample size this may not reach statistically significant difference like prior studies.

CONCLUSION

Primary PCI induced better short term outcome compared to fibrinolytic therapy in patients with STEMI.

Study limitations

1. Small sample size

2. Lack of randomization

3. Short follow up

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