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I, Marek Grygier DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.
Background

- Primary PCI is the best treatment strategy of STEMI but fails to achieve adequate myocardial reperfusion in about one-third of patients.

- The benefits of flow restoration are limited by reperfusion damage. By reduction of the incidence of no-reflow phenomenon one may improve myocardial salvage and prevent LV remodeling.

- In animal models, adenosine limits reperfusion injury, reducing the infarct size and improving ventricular function. In humans the role of adenosine in the setting of STEMI is yet to be established.
Objectives

The aim of the study was to examine the role of a new simple protocol of intracoronary adenosine administration during primary PCI on the immediate angiographic results and clinical course.
**Patient Selection**

- Patients with acute STEMI referred for primary PCI within 6 hours from symptom onset.
- Patients eligible for PCI with IRA flow of TIMI 0 to 2 (Patients presenting with TIMI 3 flow were excluded).
- Patients with chronic obstructive pulmonary disease or asthma and/or undergoing therapy with theophylline derivatives and patients who had received prior thrombolysis were excluded from the study.
Group A (n=35) received two times intracoronary adenosine (1 or 2 mg) with hand injection through the guiding catheter: immediately after crossing the lesion with the guidewire and then after first balloon inflation.

Group B (n=35) received placebo.
Methods

Procedure

- The IRA lesion was crossed with a 0.014” guidewire. Immediately, after crossing the lesion, either adenosine (2 mg to the left or 1 mg to the right coronary artery in 10 cc 0,9% NaCl) or saline (10 cc 0,9% NaCl) was rapidly hand-injected through the guiding catheter.

- After one minute, a balloon catheter was dilated with a low pressure (4-6 ATM) for a few seconds at the level of the obstruction. Then, the balloon was pulled out and again either adenosine (2 mg to the left or 1 mg to the right coronary artery in 10 cc 0,9% NaCl) or saline (10 cc 0,9% NaCl) was rapidly hand-injected into the coronary artery through the guiding catheter.

- The procedure was completed according to standard technique, BMS only were used.

- GP IIb/IIIa inhibitors (abciximab) were given to 18 patients – 10 (28.6%) in adenosine group and 8 (22.9%) in the placebo group (p=ns)
Methods

Angiographic analysis

- The angiograms were analyzed off-line by two observers blinded to the treatment used.

- The TIMI flow was assessed as defined previously. TIMI frame count was performed according to the method described by Gibson et al.

- Myocardial blush was graded (MBG) according to method described by van’t Hof: 0 = no myocardial blush or persisted blush, 1 = minimal blush, 2 = moderate blush but less that obtained during angiography of contralateral or ipsilateral non IRA, 3 = normal myocardial blush.
Methods

ECG analysis

- All ECGs were analyzed in a blinded fashion by an experienced cardiologist.
- ST-segment elevation was measured 60 ms. after the J point in the baseline ECG and 60 minutes after PCI.
- A reduction of $\geq 50\%$ in the sum of all ST-segment elevations was considered as ST-segment elevation resolution.

Metabolic data

- Creatine kinase (CK), CK-MB and troponins were assessed every 8 hours in the first day after admission.
Primary end points
1. MBG at the end of the procedure,
2. ST segment elevation resolution 60 minutes after PCI

Secondary end points
1. feasibility and safety of this new protocol of intracoronary adenosine administration in the setting of primary PC
2. final TIMI flow grade at the end of the procedure
3. TIMI frame count at the end of PCI,
4. the composite end point of death, recurrent MI, cardiac arrest, cardiogenic shock, heart failure and recurrent episodes of angina leading to repeat angiography and subsequent revascularization during 1 month of follow-up.
Baseline clinical and angiographic characteristics of the study patients (n=70)

<table>
<thead>
<tr>
<th></th>
<th>Adenosine n=35</th>
<th>Placebo n=35</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>65.3±11</td>
<td>64.5±13</td>
<td>NS</td>
</tr>
<tr>
<td>Male</td>
<td>23 (63%)</td>
<td>21 (60%)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension</td>
<td>21 (60%)</td>
<td>23 (63%)</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>8 (23%)</td>
<td>8 (23%)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>27 (77%)</td>
<td>29 (83%)</td>
<td>NS</td>
</tr>
<tr>
<td>Smoking</td>
<td>22 (63%)</td>
<td>13 (37%)</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>Previous MI</td>
<td>3 (9%)</td>
<td>4 (11%)</td>
<td>NS</td>
</tr>
<tr>
<td>Symptom-onset-to cath. (min)</td>
<td>273±137</td>
<td>225±110</td>
<td>NS</td>
</tr>
<tr>
<td>Infarct-related artery:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAD</td>
<td>17</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>RCA</td>
<td>14</td>
<td>10</td>
<td>NS</td>
</tr>
<tr>
<td>LCx</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Multivessel disease</td>
<td>12</td>
<td>12</td>
<td>NS</td>
</tr>
<tr>
<td>GP IIb/IIa (abciximab)</td>
<td>10 (28.6%)</td>
<td>8 (22.9%)</td>
<td>NS</td>
</tr>
</tbody>
</table>
Results – MBG

- MBG 0: Adenosine 10%, Placebo 12%
- MBG 1: Adenosine 20%, Placebo 25%
- MBG 2: Adenosine 30%, Placebo 30%
- MBG 3: Adenosine 66%, Placebo 37%

p < 0.05
Results – ST elevation resolution

p < 0.001

77% (Adenosine)
43% (Placebo)
Results – TIMI flow

- TIMI 0
- TIMI 1
- TIMI 2
- TIMI 3

p = 0.058

Adenosine
Placebo

91% 77%
Results – cTFC

- CTFC < 28:
  - Adenosine: 91%
  - Placebo: 74%

- CTFC 28-40:
  - Adenosine: 0%
  - Placebo: 4%

- CTFC > 40:
  - Adenosine: 0%
  - Placebo: 4%

p = 0.057

p < 0.05
Results – in-hospital events

- No deaths or recurrent MIs

- Six cases of cardiac arrest (VF or fast VT) within the first 48h – 2 in the adenosine group (5.7%) and 4 in the placebo group (11.4%)

- One cardiogenic shock which resolved after subsequent PCI (placebo group). Heart failure > NYHA II – 2 pts. in the adenosine group (5.7%) and 5 in the placebo group (14.3%)

- Recurrence of angina leading to repeat angiography: 5 patients – 1 in the adenosine group – 2.9% (no TVR), and 4 in the placebo group – 11.4% (one TVR)

- EF (5-7 days after PCI): 52% ± 8% in the adenosine group and 47% ± 9% in the placebo group (p<0.05).
Results

30-day composite clinical outcome

In-hospital death, recurrent MI, cardiac arrest, cardiogenic shock, heart failure and recurrent angina leading to repeat angiography and subsequent revascularization @ 1-month follow-up

<table>
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<tr>
<th>In-hospital composite endpoint</th>
<th>Adenosine</th>
<th>Placebo</th>
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<td></td>
<td>4 (11.4%)</td>
<td>11 (31.4%)</td>
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p<0.05
Safety issues

- The injections of adenosine or saline directly to the coronary arteries were well tolerated and free of significant side effects.

- No patients complained of worsening of chest pain and no patients suffered from hemodynamic instability.

- Significant bradyarrhythmias including asystole and complete a-v block were observed in 8 patients, only after adenosine injection into the RCA. All of them were transient, resolved spontaneously or after patients’ cough and did not require temporary pacing.
Study limitations

- small sample size
- surrogate primary end points
- non-use of thrombectomy (the study protocol was designed before the era of widespread use of thrombectomy during primary PCI)
- infrequent use of glycoprotein IIb/IIIa inhibitors (25%)
Conclusions

- A double injection of intracoronary adenosine improves myocardial reperfusion after primary PCI in patients with ST-segment elevation myocardial infarction

- Adenosine administration seems to be associated with a more favorable clinical course