Abstract: P6423

Cardioprotective effect of metoprolol in myocardial ischemic/reperfusion injury: the role of total ischemic time.

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Topic(s):
Acute Coronary Syndromes: Pharmacotherapy

Citation:
Background: Metoprolol administration before reperfusion has shown relevant cardioprotective effect in the AMI in preclinical setting. However, the translation to clinical arena has controversial results. The time at drug administration in the context of total duration of ischemia have been pointed as fundamental aspects to be studied. Purpose: evaluate the cardioprotective effect of metoprolol administration regarding to the total time of ischemia, using a swine model of reperfused AMI. Methods: 50 pigs were subjected to 3 temporary protocols of left anterior descending (LAD) coronary artery occlusion followed by reperfusion. 30 pigs undergoing 40 minutes of ischemia (T40) were randomized 2:1 to intravenous placebo or metoprolol administrated 20 minutes after LAD occlusion. 10 pigs undergoing 20 minutes of ischemia 20 (T20) and 10 pig undergoing 60 minutes of ischemia 60 (T60) were randomized 1:1 to intravenous placebo or metoprolol. Before reperfusion a CT study was performed to establish the area at risk (AAR). CMR was performed at 7 and 45 days after AMI. Results: 48 subjects comprised the 7-day CMR follow-up (1 dead in the metoprolol T40, 1 dead in the placebo T40) while 41 subjects comprised the 45-day CMR follow-up (5 deceases in the placebo T40 group, and 2 in the placebo T60 group). AAR was similar among groups (Table 1, Panel B). At 7-day follow-up, IS was higher in the placebo groups as compared to the metoprolol groups, but only reach significant difference in the T40 (29,67% vs. 22,85%, p=0.04, Table 1, Panel A). LVEF measured at 45-day follow-up was higher in the metoprolol groups vs the control groups, but the differences were statistically significance in the T40 (32,76% vs 39,68% p= 0.04, Panel C). Conclusions: Metoprolol administrated early before reperfusion reduced IS and improved medium-term LVEF compared to placebo. But only T40 receiving metoprolol shows significant protection vs placebo. These findings suggest a relevant effect of metoprolol ischemic/reperfusion injury, but depending on the total ischemic time, establishing a potential temporary cardioprotection opportunity window.

<table>
<thead>
<tr>
<th>20 mins. Ischemia (T20)</th>
<th>40 mins. Ischemia (T40)</th>
<th>60 mins. Ischemia (T60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLACEBO</td>
<td>METOPROL</td>
<td>PLACEBO</td>
</tr>
<tr>
<td>P value</td>
<td>PLACEBO</td>
<td>METOPROL</td>
</tr>
<tr>
<td>AAR</td>
<td>32 28,14-37,89</td>
<td>33,41 28,12-38,32</td>
</tr>
<tr>
<td>IS</td>
<td>1,96 0,92-3,61</td>
<td>0 0-0,65</td>
</tr>
<tr>
<td>LVEF</td>
<td>54,36 49,75-58,97</td>
<td>55,34 53,14-60,88</td>
</tr>
</tbody>
</table>

Values are median (interquartile range) Bold indicates statistical significance. AAR= Area at Risk (% of Left ventricular). IS= Infarct Size (% of Left ventricular). LVEF= Left ventricular ejection fraction (%)

P value at 0.05.
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