Multiple pre-conditioning stimuli attenuate protection against the infarct size in rabbits

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The aim of the study was to determine if the repeated periods of 5 min ischemia and 10 min reperfusion (5 iso/10 rep) are protective against the infarct size in a collateral deficient model. Methods: Forty-one rabbits were divided into 7 groups. Group (Gp) A (n = 5) was subjected to one cycle of 5 iso/10 rep, GpB (n = 5) was subjected to two 5 iso/10 rep, GpC (n = 7) to four 5 iso/10 rep, GpD (n = 7) to six 5 iso/10 rep, GpE (n = 7) to eight 5 iso/10 rep while GpF (n = 5) served as control. After the last ischemia and reperfusion all the Gps (except GpF) were subjected to 45 min regional ischemia and 2 hours reperfusion. The elapsed time from the first preconditioning stimulus to the final 45 min ischemic insult was 15, 30, 60, 90 and 120 mins, respectively for the Gps A, B, C, D and E. Infarct size (I) and risk zones (R) were delineated with the aid of tetrazolium staining and fluorescent particles. I/R ratio was expressed in percent (% I/R).

<table>
<thead>
<tr>
<th>Groups</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>G</th>
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<tr>
<td>%/IR</td>
<td>2.2 ± 2.6*</td>
<td>19.5 ± 4.1*</td>
<td>23.3 ± 3.4*</td>
<td>41.8 ± 6.9*</td>
<td>47.1 ± 7.6*</td>
<td>NS</td>
<td>NS</td>
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<tr>
<td>*p &lt; 0.001 vs. A, B, C, T2 &lt; 0.05 vs G</td>
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Conclusion: These results indicate that protection against infarct size diminishes after multiple and repetitive preconditioning stimuli in rabbits.

Reperfusion damage is mediated by a stable long-lasting cardiac metabolite which is probably not a protein

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We have previously reported that after global ischemia (IS) of an isolated heart cardiodepressant agents are released during reperfusion (R) which induced a pronounced but reversible decrease in contractility. In a serially perfused non ischemic second heart (H2) (double heart model), this effect was not attributable to changes in pH or concentration of electrolytes of the coronary effluent and the metabolites do probably not derive from coronary endothelium. In order to further characterize the chemical structure of these mediators we investigated whether storage of the coronary effluent for several hours or days, heating to 56°C for 30 minutes or protease treatment influence the negative inotropic effect.

Two isolated guinea pig hearts were perfused separately at constant flow (10 ml/min) with a modified Krebs-Henseleit solution oxygenated with 95% O2 and 5% CO2. This was followed by serial perfusion without (group 1, n = 5) and with (group 2, n = 5) preceding IS (10 min) of the first heart (H1). In group 1 no significant changes of the left ventricular contractile parameters of H2 were observed during serial perfusion. In group 2, after a global 10-min IS of H1 left ventricular (LV) systolic pressure of H2 (basal 76.3 ± 3.5 mmHg, SEM) immediately decreased by 16%, +LVdP/dtmax (1491.9 ± 112.4 mmHg/s by 22%, -LVdP/dtmax (2613.1 ± 56.8 mmHg/s) by 30% when R was started. Coronary perfusion pressure (77.1 ± 3.4 cmH20) decreased by 26%. These parameters returned to baseline within 10 min. Heart rate did not change significantly. The cardiodepressant effect of the coronary effluent was not destroyed by protease treatment (chymotrypsine 0.005 U) or by heating the coronary effluent to 56°C for 30 min. Coronary effluent kept at room temperature for 24 hours before delivery to H2 also retained its activity.

These data suggest the release of a stable, long-lasting cardiodepressant agent from myocardial tissue after global IS during R. The resistance against protease treatment and heating suggests that the mediator is not a protein.

Production of interleukin-6 triggers an enhanced acute phase response after percutaneous coronary angioplasty in patients with unstable angina

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IL-6 is the major inducer of the acute phase proteins production, we have measured IL-6 and CRP levels in 23 UA pts, undergoing single-vessel PTCA. Venous blood samples were taken immediately before PTCA and 6, 24, 48, 72 h after the end of the procedure. Results (median and range): Before PTCA, elevated levels of CRP (>3 mg/l) were observed in 23/32 pts (73%, G1) and normal levels in 9/23 pts (26%, G2). Detectable levels of IL-6 (undetectable in normals) were found in 13/23 (57%) G1 pts, but in none G2 pts. After PTCA, in G1 pts CRP levels increased from 2.5 (0.4–147) mg/l to 48 h and then returned to the baseline value by 48 h (2.5 (0.4–47) mg/l; p = 0.97 vs baseline). Conversely, CRP levels remained elevated at 48 h and decreased to baseline at 72 h, consistently with the plasma half life of CRP compared to that of IL-6. No changes in CRP and IL-6 levels were observed in G2 pts. There was a significant correlation between the peak values of IL-6 and CRP (r = 0.53, p = 0.01). The figure shows the median values of IL-6 (levels in CRP (squares), in G1 pts. Conclusion: UA pts with elevated levels of CRP exhibit an enhanced production of IL-6 early after PTCA, followed by a large increase of CRP. In turn, IL-6 production may be triggered by powerful pro-inflammatory stimuli contained in the plaque core or may reflect a lower threshold for IL-6 synthesis in this subset of UA pts.