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 ischaemia and 10 min reperfusion (5 iso/10 rep) are protective against the infarct size in a collateral deficient coronary 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 final ischaemia all the Gps (except GpF) were subjected to 45 min regional ischaemia and 2 hours reperfusion. The elapsed time from the first preconditioning stimulus to the final 45 min ischaemic 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).

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 ischaemia (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 ischaemic 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 mins 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 (1261.3 ± 56.8 mmHg/s) by 30% when R was started. Coronary perfusion pressure (77.1 ± 3.4 cmH2O) 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 (chymotrypsin 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 suggest 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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C-reactive protein (CRP) levels are predictors of prognosis in unstable angina (UA) and increase further after coronary angioplasty (PTCA). As interleukin-6 (IL-6) is the major inducer of the acute phase proteins production, we have measured IL-6 and CRP levels in 32 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 9/32 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, IL-6 levels increased in 11 pts, with median peak value of 21 (4.4–174) mg/l 24 h after the end of the procedure (p < 0.001 vs baseline). This increase was preceded by a significant increase of IL-6 at 6 h from 2 (0–22) pg/ml to 6.2 (0–300) pg/ml, p = 0.002. IL-6 remained high at 24 h [8 (3–149) pg/ml; p = 0.32 vs 0], and then returned to the baseline value by 48 h [2.5 (0–47) pg/ml; 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 (black bars) and 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.

C-Reactive protein co-localizes in human hearts during acute myocardial infarction

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Plasma levels of C-reactive protein (CRP) correlate with clinical outcome in patients with myocardial ischemia and infarction. We hypothesized that these correlations might reflect active participation of CRP in the local inflammatory response ensuing in the jeopardized myocardium, since upon binding to a ligand CRP is able to activate the classical pathway of complement. In addition, complement activation may subsequently contribute to the expression of tissue and cell death. The aim of this study was to establish whether coronary angioplasty (PTCA) or stent implantation (SI) have the potential to increase serum levels of CRP, and whether the latter affects the short and long term prognosis. Ninety-nine patients (pts) with acute coronary syndromes increased serum levels of C-reactive protein (CRP) are associated to a worse short-term outcome. The aim of this study was to establish whether coronary angioplasty (PTCA) or stent implantation (SI) have the potential to increase serum levels of CRP and whether the latter affects the short and long term prognosis. Ninety-nine pts (mean age 58 ± 7 years, 88 men) with stable angina and obstructive coronary atherosclerosis were randomised to PTCA (49 pts) or SI (50 pts). There were no significant differences among the two groups with respect to baseline clinical characteristics (gender, previous myocardial infarctions, risk factors and therapy) and to angiographic characteristics before the procedures. Serum CRP levels were measured, by nephelometry, 24 hours before and 6 hours, 1, 2, 3 and 4 days after the procedure. All pts were then followed-up for 6 months. Serum levels of CRP were obtained also at 3 and 6 months. Serum levels of CRP (mg/l) were as follows (mean ± SD values):