

Meeting abstract

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Nitrate tolerance-induced deterioration of the ischemic adaptability of the heart

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Introduction

We tested whether postconditioning limited infarct size in rabbits with haemodynamic nitrate tolerance.

Methods

Male rabbits made tolerant to the hypotensive response to 30 µg/kg intravenous nitroglycerin (NG) by a preceding one-week exposure to transdermal NG (0.07 mg/kg/h) were subjected to 35 min coronary occlusion (test ischemia) followed by 3 h of reperfusion with the following additional interventions: no intervention (NI); postconditioning pacing (PPC): five cycles of 5 min periods of rapid ventricular pacing (500 b.p.m.), or postconditioning coronary occlusion (PCO): five cycles of 5 min coronary occlusion with 10 min interpacing/interocclusion intervals, applied after the end of the test ischemia. These protocols were applied in both nitrate-tolerant and non-tolerant animals. Infarct size expressed as a percentage of area at risk (I/R) was determined by triphenyltetrazolium chloride staining, left ventricular cyclic nucleotides were determined by radioimmunoassay from samples out of the area at risk, 75 min after the test ischemia.

Results

In non-tolerant animals both PPC and PCO reduced the I/R compared to the NI group. When animals had been made nitrate-tolerant, the I/R was significantly higher in the NI group compared with non-tolerant animals and the beneficial effect of the PPC or PCO on the I/R disappeared.

Conclusion

We conclude that (i) nitrate tolerance blocks postconditioning induced by either PPC or PCO, (ii) PPC is more effective post-conditioning challenge than PCO, and (iii) nitrate tolerance per se reduces the capability of the heart to tolerate an ischemic insult.