**Infarct-size reduction induced by ischaemic postconditioning is dependent on $\beta_2$-adrenoceptor activation in the Langendorff perfused rat heart**

Peter Penson, William Ford, Emma Kidd, Kenneth Broadley

*Pharmacology Division, Welsh School of Pharmacy, Cardiff, United Kingdom*

Ischaemic postconditioning (POST) is a cardioprotective phenomenon which reduces infarct size after ischaemia and reperfusion. The protection is achieved by stuttering reperfusion i.e. cycling brief periods of ischaemia and reperfusion at the end of a longer period of ischaemia (Zhao *et al.*, 2003). The protective mechanism of POST is not fully understood. We investigated the possibility that release of endogenous catecholamine and subsequent activation of β-adrenoceptors (β-ADR) was involved.

Male Sprague-Dawley rats 300-450g were anesthetised with an intraperitoneal injection of pentobarbitone sodium (54mg/rat). Heparin (10 IU/rat) was also given by the same route. Hearts were excised and Langendorff perfused at constant pressure (60 mmHg) with oxygenated ($95\%O_2/5\%CO_2$) Krebs-Henseleit buffer + insulin (100 $mU.ml^{-1}$). Hearts were immersed in perfusate and temperature was maintained at 37˚C. A 5-0 suture was passed behind the left main coronary artery allowing the induction of reversible regional ischaemia. After 20 min. stabilisation, all hearts were subjected to 35 min of ischaemia followed by 120 min reperfusion. POST was achieved by 3 cycles of 30 sec reperfusion and 30 sec reocclusion at the end of the ischaemic period. Experiments were repeated in the presence of the β-ADR antagonists, timolol 1μM (non-selective) and ICI-118551 10 nM ($\beta_2$ selective) present in the buffer for the final 10 min. of ischaemia and the first 10 min. of reperfusion. The ischaemic area at risk was determined by reocclusion and Evans blue staining. Infarct size was determined by triphenyltetrazolium chloride staining and was expressed as a percentage of the area at risk. Statistical analysis was performed by one-way ANOVA and Tukey's *post-hoc* test. Mean values ±SEM are reported in the text.

In control tissues infarct size was 35.3 ± 6.2 % (n=7) of the area at risk. POST significantly ($P<0.05$) reduced this to 11.0 ± 2.9% (n=7). When POST was bracketed by timolol, infarct size (67.2 ± 9.6%, n=5) was significantly larger than control. Timolol alone had no effect on infarct size (n=4). POST protection was abolished by ICI-118551. Infarct size was significantly ($P<0.05$) increased by ICI-118551 alone (76.8 ± 6.7%, n=7) and when combined with postconditioning (79.7 ± 5.3, n=4).

We have demonstrated that β-ADR activation is necessary for POST protection and that a $\beta_2$-ADR adrenoceptor antagonist applied at reperfusion, not only prevents POST protection, but increases infarct size in non-POST hearts. These results suggest that activation of $\beta_2$ adrenoceptors at reperfusion limits infarct size and are potentially relevant in the clinic when non-selective β-ADR antagonists are used.

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