

Abstract

Clonidine Augments Cardiomyocyte Apoptosis Caused by In Vivo Ischaemia and Reperfusion

Mohammed Yasin MB BCh, Michelle C. McDonald PhD, Ahila Sivarajah PhD, Julius E. Kieswich BSc, Mohammed M. Yaqoob MD FRCP, Charles J. Hinds FRCA, Christoph Thiemermann, MD PhD FMedSci

Objective: Clonidine protects against cerebral ischaemia-reperfusion (I-R) injury. We investigated if clonidine pre-treatment could also protect against acute myocardial I-R injury. **Methods:** Cardiomyocytes isolated from within the area at risk of rat hearts subjected to regional myocardial ischaemia (25 min) and reperfusion (2 h) were analysed by flowcytometry to detect apoptosis, necrosis and mitochondrial inner membrane potential ($\Delta\psi_m$). **Results:** Surprisingly, pre-treatment with clonidine (90 $\mu\text{g}/\text{kg}$, i.v.) augmented cardiomyocyte apoptosis [$22.6 \pm 2.7\%$ (vehicle control) and $41.8 \pm 1.4\%$, $P < 0.001$]. These pro-apoptotic effects of clonidine were abolished by the mixed α_2 /imidazoline₁-receptor antagonist efaroxan ($26 \pm 2\%$), but not by the selective α_2 -receptor antagonist yohimbine ($46 \pm 3\%$). Cardiomyocyte apoptosis was significantly reduced by ischaemia preconditioning (IPC, $10.4 \pm 2\%$, $P < 0.001$) and pre-treatment with morphine ($10.6 \pm 2\%$, $P < 0.001$). Interestingly, pre-treatment with clonidine ameliorated the cardioprotection afforded by IPC, but not that by morphine. Pre-treatment with clonidine also augmented $\Delta\psi_m$ [$132.7 \pm 7\text{ mV}$ (vehicle control) and $198 \pm 16\text{ mV}$, $P < 0.001$]. **Conclusion:** Pre-treatment of rats with clonidine significantly increased the degree of cardiomyocyte apoptosis caused by acute I-R. This may be due to a higher $\Delta\psi_m$ value, caused by clonidine, during acute I-R.