Amitriptyline improves left ventricular recovery in rat hearts subjected to cardiac ischaemic-reperfusion injury

S.M. Lee, D.A. Saint and M. Hutchinson, Medical School South Building, Frome Road, The University of Adelaide, SA 5005, Australia.

Introduction: Myocardial ischaemic-reperfusion injury remains the number one cause of mortality throughout the developed world. Acute bouts of ischaemia, preceding a longer bout of ischaemia, protects the heart, a phenomenon called preconditioning. To date there is no clinically approved pharmacological preconditioning agent. Amitriptyline, a tricyclic antidepressant with anti-inflammatory properties, was examined in ischemic-reperfused heart with or without ischemic preconditioning.

Methods: Sprague Dawley (300-400g) hearts were examined using the Langendorff technique. Ischemic-preconditioned (IPC) hearts underwent three 5 min bouts of ischaemia and reperfusion followed by 30 min of ischaemia (LTI) and 40 min of reperfusion. Non-preconditioned (NPC) hearts followed the same protocol but without ischaemic-preconditioning. Amitriptyline (10 µmol/l) was administered during the 5 min periods of reperfusion during ischemic-preconditioning (IPA) while the non-preconditioned group was treated with amitriptyline (10 µmol/l) for 30 min before LTI (NPA). Cardiac performance was measured as left ventricular developed pressure (LVDP). Upon completion left ventricles were removed and frozen in liquid nitrogen. p38 phosphorylation and the nuclear chromatin protein HMGB1 were quantified using western blots.

Results: IPC hearts had higher LVDP recovery (82.8 ± 14.9%, n=6) compared to NPC hearts (26.5 ± 10.5%, n=6) (P<0.05). While amitriptyline did not block the preconditioning effect in IPA hearts (69.9 ± 6.16%, n=6) (P>0.05), NPA hearts were protected (90.3 ± 10.0%, n=6) (P<0.05). No interaction was observed for HMGB1 and p38 phosphorylation regardless of whether the heart was preconditioned or treated with amitriptyline (P>0.05). However a Sobel mediator test suggests p38 phosphorylation is indirectly involved in amitriptyline mediated cardioprotection (P>0.05).

Conclusion: Amitriptyline protects against ischaemic-reperfusion injury which may be partially mediated through p38 phosphorylation.