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THE INHIBITORY EFFECT OF REMOTE ISCHAEMIC CONDITIONING ON A CELLULAR MODEL OF CARDIAC HYPERTROPHY

doi:10.1136/heartjnl-2012-303148a.13

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Remote ischaemic conditioning (RIC) protects against ischaemia-reperfusion injury, but it is unclear whether it could also attenuate adverse cardiac remodelling post-MI. We hypothesised that RIC

generates a blood born signal capable of reducing the hypertrophic response by modulating gene expression associated with remodelling.

Superfusate was collected from ischaemic conditioned Langendorff perfused rat hearts (RIC-superfusate). Blood was taken from healthy volunteers after three cycles of upper arm conditioning (RIC-serum). The RIC-superfusate/serum was applied to H9c2 cardiomyoblasts in culture treated with endothelin-1 (ET-1) to stimulate hypertrophy. Immunofluorescence was used to determine cell area. Expression of four genes associated with cardiac remodelling: BNP, α-actin, βMHC and ms^{-1} were determined using qRT-PCR. Response was compared to saline/unconditioned serum.

ET-1 (100 ng/ml) caused a significant degree of cellular hypertrophy after 48 h: 22.8±1.1 vs 16.4±0.7 mm^2 in untreated cells (n=300 p<0.01). Pre-treatment with RIC-superfusate/RIC-serum significantly reduced ET-1 induced hypertrophy from 19.8±0.8 to 14.7±0.6mm^2 and 23.6±1.5 to 16.1±1.1mm^2 respectively (n=300 p<0.01). RIC-superfusate caused a significant decrease in ET-1 induced expression of α-actin (fold-change 8.0±0.4 to 1.7±0.1, n=4 p<0.01), βMHC (6.5±0.5 to 2.5±0.3, n=4 p<0.01), BNP (1.3±0.3 to 0.4±0.2, n=4 p<0.05) and ms^{-1} (31.6±2.7 to 13.0±1.4, n=4 p<0.01) after 48 h. RIC-serum significantly reduced ET-1 induced expression of βMHC (7.7±1.0 to 3.9±0.5, n=4 p<0.05) and ms^{-1} (15.4±2.7 to 7.0±0.7, n=4 p<0.05) after 48 h.

Our data supports the hypothesis that RIC initiated humoral signalling may attenuate the deleterious process of cardiac remodelling. The findings identify a new therapeutic approach that may be beneficial in reducing adverse ventricular hypertrophy post-MI.