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INCREASING GAP JUNCTION COUPLING WITH ROTIGAPTIDE REDUCES THE INCIDENCE OF VENTRICULAR ARRHYTHMIAS DURING REGIONAL ISCHAEMIA

doi:10.1136/heartjnl-2012-303148a.6

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Gap junction (GJ) coupling plays an important role in determining the electrophysiological properties of intact myocardium. Pharmacologically increasing coupling reduces the incidence of spontaneous and programmed arrhythmias and may have an anti-arrhythmic effect during acute ischaemia.

A pro-arrhythmic model of regional ischaemia was developed in isolated perfused rat hearts (n=6/group (0, 15, 30, 60 min of LAD occlusion)). During ischaemia, all hearts experienced VPB, 60% experienced VT with arrhythmia incidence peaking at 12 min. On reperfusion, hearts undergoing 15 min of ischaemia were significantly pro-arrhythmic (Incidence of VT/VF 83% vs 60 min, 0%, p<0.02).

The 15-min model was used to assess the effects of increasing coupling, with Rotigaptide, on arrhythmia incidence during ischaemia and reperfusion. Hearts (n=9/group) were perfused with either (1) No drug (control), (2) Rotigaptide (50 nM) pre-occlusion, (3) Rotigaptide at occlusion or (4) Rotigaptide at reperfusion.

Pre-treatment with Rotigaptide afforded a significant reduction in arrhythmia score during ischaemia (0.90 ± 0.24 vs control 2.52 ± 0.49 , p<0.05), driven by reducing the incidence of VT (11% vs 66%, p<0.05). Treatment with Rotigaptide at occlusion showed a trend towards a reduction in arrhythmia score but failed to reach significance (1.26 ± 0.23 vs control 2.52 ± 0.49 , p=0.09). During reperfusion, arrhythmia score and incidence of VT/VF were similar across all groups.

In acute ischaemia, increasing GJ coupling, prior to, or, at the time of LAD occlusion reduced the burden of ventricular arrhythmias during ischaemia but did not alter reperfusion arrhythmogenesis. Increasing coupling in the early stage of regional ischaemia afforded the most substantial reduction in ventricular arrhythmias.