In vivo evidence that carbenoxolone attenuates the delayed antiarrhythmic effect of cardiac pacing

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Introduction: We have previously reported that rapid cardiac pacing preserves the function of gap junction channels (GJ) during ischaemia and reperfusion, 24h later. This result has suggested a role for these channels in the delayed antiarrhythmic protection.

Purpose: The present study was designed to provide further evidence to this relationship using carbenoxolone (CBX), a pharmacological inhibitor of GJs.

Methods: Under light anaesthesia (pentobarbitone 30 mg.kg-1) 22 dogs were paced through the right ventricle (4x5 min, 240 beats.min-1), and 24 hours later subjected to a 30 min occlusion of the left anterior descending coronary artery (LAD). In 12 out of these paced dogs CBX, in concentrations of 50 (n=7) and 100 µM (n=5), was given in intracoronary infusion 20 minutes before and throughout the occlusion period. Another group of dogs (n=10) that were instrumented but not paced, served as controls. We assessed the severity of ischaemia and arrhythmias (VPBs, VT episodes, incidence of VT and VF), as well as the relative changes in tissue electrical impedance.

Results: Compared with controls, cardiac pacing significantly reduced the severity of arrhythmias (VPBs: 294 ± 78 vs. 64 ± 26; VT: 7.4 ± 2.2 vs 1.1 ± 0.6; VF: 13% vs 11%) and decreased GJ electrical uncoupling. Administration of CBX enhanced the closure of GJs and resulted in dose dependent increase both in the arrhythmia (CBX50: VPB: 82 ± 10, VT:15 ± 1.0, VF 57%; CBX100: VPB: 307 ± 131, VT: 7.4 ± 5.7, VF 40%) and ischaemia severity.

Conclusion: These results support the hypothesis that GJ channels play a significant role in the delayed antiarrhythmic effect of rapid cardiac pacing.