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MYOCARDIAL ISCHEMIA AND INFARCTION

LACK OF EFFECT OF THE STRETCH-ACTIVATED CHANNEL BLOCKER GSMTX4 ON VENTRICULAR ARRHYTHMIAS FOLLOWING CORONARY OCCLUSION IN SWINE

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Authors: *Jose A. Barrabes, Luis Agulló, Javier Inserte, M Ángeles García, David Garcia-Dorado, Hospital Universitari Vall d'Hebron, Barcelona, Spain*

Background: Myocardial stretch induces electrophysiological changes and arrhythmias. Regional ventricular distension has been related to spontaneous ventricular arrhythmias following coronary occlusion (CO). Activation of stretch-activated channels (SACs) might play a role in this phenomenon, but the study of SAC involvement in ischemic arrhythmias has been hampered by the lack of appropriate inhibitors working in vivo. We assessed the effect of the spider venom peptide GsMtx4, a natural blocker of SACs, on ventricular arrhythmias after CO in swine.

Methods: In preliminary experiments, 170 nM GsMtx4 (a concentration reported to suppress stretch-induced atrial arrhythmias ex-vivo) prevented the reduction of refractoriness caused by ventricular distension in isolated rat hearts. Thiopental-anesthetized, open-chest pigs (n = 32) subjected to 50 min of occlusion of the mid left anterior descending coronary artery were blindly randomized to receive GsMtx4 (57 ng/kg i.v. bolus + 3.8 ng/kg/min infusion, calculated to attain the above concentration in plasma) or saline, starting 5 min before CO. Myocardial segment length was monitored by ultrasonic crystals and the area at risk was measured after injecting fluorescein into the left atrium.

Results: The two groups were comparable with regard to hemodynamic variables, size of the area at risk (16.9 ± 0.9 vs. 16.4 ± 0.9% of ventricular mass in animals receiving GsMtx4 or saline, respectively, P = NS) and enddiastolic segment length in the ischemic region after CO (at 15 min CO it had reached 111.9 ± 1.6 vs. 110.6 ± 1.1% of the baseline value, respectively, P = NS). Treated and untreated animals had a similar (P = NS) number of premature ventricular complexes in the IA (0 - 10 min after CO: 6 ± 3 vs. 12 ± 6, respectively) or IB (10 - 50 min after CO: 91 ± 33 vs. 87 ± 23) phases of ventricular arrhythmias, and a similar (P = NS) incidence of VF (12.5 vs. 25.0%) or ventricular tachycardia/VF (43.8 vs. 50.0%).

Conclusions: GsMtx4 at the doses tested did not prevent the occurrence of ventricular arrhythmias following CO. The results are against a major involvement of SACs in ischemic ventricular arrhythmias.