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EFFECTS OF DILTIAZEM ON ELECTRICAL ALTERNANS OF ST SEGMENT AND VENTRICULAR ARRHYTHMIA INDUCED BY ACUTE CORONARY OCCLUSION

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Effects of diltiazem (DZ) on electrical alternans of ST segment (STEA) and ventricular arrhythmia (VA) during coronary occlusion and reperfusion were examined in anesthetized open chest dogs. Standard II ECG, unipolar surface ECG, His bundle electrogram, bipolar surface electrograms and bipolar monophasic action potentials (MAP) both inside (IZ) and outside (NZ) boundaries of the ischemic zone, and blood pressure were simultaneously recorded. Right atrial appendage was paced at a rate of 180/min. Dogs were divided into two groups. Group A (n=16) included dogs with administration of DZ (0.02 mg/kg/min). Group B (n=29) included dogs without DZ. In addition, in other 5 dogs, regional myocardial blood flow (RMBF) were measured in both ischemic center zone and border zone using H_2 clearance method.

Results: In group A, compared with group B, (1) the incidence of VA, particularly VT and VF, significantly decreased during occlusion. (2) the degree of STEA, MAP alternans and conduction delay were significantly attenuated. (3) RMBF in both zones significantly increased before occlusion, but the decrease in RMBF during occlusion did not improve. (4) there were no significant difference in blood pressure during occlusion between both groups. Our results suggest that the mechanism for the decrease in the incidence of VA, degree of STEA and MA alternans by DZ is not due to the improvement of RMBF and the decrease in pressure rate product, but may be due to the reduction of transmembrane Ca flux into ischemic myocardium.

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EFFECTS OF ALPHA- AND BETA-BLOCKING AGENTS ON ISCHEMIA- AND REPERFUSION-INDUCED ARRHYTHMIAS -STUDIES IN THE CONSCIOUS RAT-

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Most studies on ischemia- and reperfusion-induced arrhythmias have been performed either in the isolated heart preparations or in anesthetized animals. Since the use of anesthetics and denervation can influence the severity of arrhythmias, we have developed a conscious rat preparation, in which coronary artery occlusion and also reperfusion can be achieved, and occluded zone size can be measured. Using this new preparation, we have assessed the effects of an alpha-blocking agent, prazosin and a beta-blocking agent, atenolol on ischemia- and reperfusion-induced arrhythmias. Atenolol (1mg/kg body wt, given i.v. 10 min prior to LAD occlusion, n=12) decreased heart rate and significantly reduced the incidence of ventricular fibrillation from 63% (15/24) to 17% (2/12) ($p < 0.05$). In contrast, prazosin (0.1 or 1mg/kg body wt, given i.v. 10 min prior to occlusion, n=12) significantly increased heart rate. It did not alter the incidence of VF, but dramatically increased mortality from 13% (3/24) to 100% ($p <$

0.001) and 87% ($p < 0.001$) during 30 min of ischemia, respectively. The high mortality with prazosin was associated with a high incidence of bradyarrhythmias. Atenolol also significantly reduced the incidence of reperfusion induced VF following 5 min of coronary occlusion from 100% (15/15) to 58% (7/12) ($p < 0.05$). All groups possessed occluded zone of similar size. Thus, in the conscious rat, atenolol affords some protection against ischemia- and reperfusion-induced VF, whilst at the doses studied, prazosin exacerbates arrhythmias and resultant mortality.

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EFFECTS OF PREEXISTING CORONARY STENOSIS ON VENTRICULAR ARRHYTHMIAS AND ST SEGMENT ELEVATION INDUCED BY ACUTE CORONARY OCCLUSION

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After release of 1st 5 min occlusion of left anterior descending coronary artery, 33 dogs were separated into two groups. Group A included 16 dogs with 4 hrs stenosis before 2nd 10 min occlusion. Group B included 17 dogs with 4 hrs no-stenosis before it. Based on the mean value (12.1 ml/min/100g) of regional myocardial blood flow (RMBF) in ischemic center zone (IZ) during 1st occ., dogs with less than 12.1 of RMBF were selected for the analysis in both groups because those were postulated to have poor collateral flow like in human being.

Results: During 1st occ., there were no differences in RMBF in IZ, conduction delay (CD), ST segment elevation in IZ between group A' (n=11) and group B' (n=10).

During 2nd occ., compared with group B', results in group A' were as follows:

- (1) RMBF in IZ was significantly increased (11.6 ± 1.9 vs 5.7 ± 0.7 ml/min/100g, $p < 0.05$, M±SE).
- (2) CD and ST segment elevation were significantly reduced (18.4 ± 5.6 vs 57.6 ± 17.0 ms, $p < 0.05$ and 5.3 ± 2.5 vs 16.1 ± 4.5 mV, $p < 0.05$, M±SE).
- (3) Incidence of occurrence of ventricular arrhythmias (VA) was significantly reduced.

Our results suggest that reduction of CD, ST segment elevation and incidence of VA during 2nd occ. in group A' was due to the increase in collateral flow stimulated by the preexisting coronary stenosis.

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THE EFFECT OF CORONARY REOCCLUSION ON REPERFUSION ARRHYTHMIA IN CONSCIOUS DOGS

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The effect of coronary reocclusion on reperfusion arrhythmia was evaluated in 31 mongrel dogs. After induction of anesthesia and left thoracotomy, the snare-type polyethylene occluder was placed around the left circumflex coronary artery. Seven days after operation coronary occlusion was produced by the occluder in the awake state, and reperfusion was carried out 1 hour after coronary occlusion. ECG was recorded continuously at slow speed and standard