Title: CORONARY DILATORS INCREASING O_2 DEMAND AND MYOCARDIAL ISCHEMIA

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Introduction. In recent years, the important role of coronary arterial spasm in the pathogenesis of acute myocardial infarction has received significant support from investigations performed in patients with the use of coronary arteriography.[1] The new data obtained with this method drew attention to the old problem of administering antispasmodics to patients with coronary heart disease. In the last three decades, therapy has centered on attempts to increase coronary blood flow without increasing oxygen consumption, that is 'benign' vasolidatation as opposed to that associated with an enhanced myocardial oxygen demand and characterized as 'malignant' vasodilatation.[2] In the present study, two classical antispasmodics increasing myocardial oxygen demand - papaverine and aminophylline - were re-evaluated in animal experiments with different models of acute coronary insufficiency.

Methods. The experiments were performed on open-chest cats anesthetized with pentobarbital (30 mg/kg, i.v.). The following two models of acute myocardial ischemia were used. 1) Ligation of coronary artery (LAD). Outflow from the coronary sinus was measured with a flowmeter, oxygen saturation with an oximeter, and myocardial oxygen consumption was calculated. Myocardial oxygen tension in normal and ischemic areas were determined polarographically.[3] Epicardial ST-segment mapping was performed.[4] 2) Perfusion of coronary artery at stabilized insufficient level. The inflow into the LAD was maintained by a pump providing constant flow. The perfusion volume was gradually decreased to the point of evident ST-segment elevation after which the same level was maintained throughout the experiment. Papaverine and aminophylline were injected i.v. in the first model (1-2 and 3-7 mg/kg, respectively), and intracoronary (i.c.) in the second model (0.1-0.3 mg and 0.5-1.0 mg, respectively).

Results. When the coronary artery was ligated, i.v. papaverine and aminophylline caused a significant increase in coronary sinus outflow (CSO) and myocardial oxygen consumption (MVO_2). MVO_2 was increased from 0.83 ± 0.07 to 1.24 ± 0.12 ml/min ($P < 0.001$) when papaverine was injected and from 0.78 ± 0.07 to 1.11 ± 0.10 ml/min, ($P < 0.001$) when aminophylline was injected. The increase in CSO was accompanied by an improved ECG pattern. The sum of the ST-segment elevations from all epicardial electrode positions was reduced from 40 ± 5 to 20 ± 4mV, ($P < 0.001$) with papaverine and from 43 ± 4 to 30 ± 6mV, ($P < 0.05$) with aminophylline. Oxygen tension in the ischemic area was increased by papaverine to a greater extent than by aminophylline. Under conditions of stabilized insufficient perfusion, papaverine and aminophylline aggravated the ischemic ECG pattern.

Discussion. In the ligation series, when the drugs were injected i.v., they could increase collateral blood flow. Under conditions of perfusion of the coronary artery at a stabilized insufficient level combined with i.c. injection of the drugs, the possibility for increase in blood supply to the ischemic area was highly improbable. Thus, despite the increase in MVO_2 reflecting elevation of oxygen demand, papaverine and aminophylline improved the signs of myocardial ischemia (myocardial oxygen tension and ECG pattern) as long as there was a possibility of an increase in blood supply to the affected zone. When this was not possible, the symptoms were actually aggravated. The results suggest that there is no basis for dividing coronary dilators into 'benign' and 'malignant' according to their ability to increase myocardial oxygen requirements. A coronary dilator enhancing oxygen demand may prove beneficial even following complete coronary artery occlusion.

References.

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