SHORT COMMUNICATION

EFFECT OF GLUCAGON ON THE PERFUSED RAT HIND-QUARTER VESSELS AND ON PERFUSED CORONARY ARTERIES OF RABBIT

J. SINGH, S. BALA, A.H. KAUR AND K.N. GARG

Department of Pharmacology,
Medical College, Rohtak-124 001 (Haryana)

Summary: In rat hind-quarter perfusion experiments, glucagon (1 μg) produced a significant vasodilatation. On the other hand, in experiments with isolated perfused rabbit heart, glucagon (1 μg) caused coronary vasoconstriction irrespective of whether noradrenaline was added to perfusion fluid or not. Glucagon had no effect on rate or force of contraction of heart.

Key words: glucagon dilatation perfused coronary artery

INTRODUCTION

Effect of glucagon on a variety of vascular beds has been reported. Kock *et al.* (6) demonstrated an increase in blood flow in ascending aorta, coronary artery and renal artery with glucagon (10 $\mu g/kg$) in dogs. No significant change in flow was recorded in the splenic artery whereas the flow in the femoral and carotid artery decreased. Glick (2) reported the dilation of femoral bed following glucagon administration in the perfused hind-limb vessels of dogs. Henneman and Shoemaker (4) studied blood flow in canine hind limbs and found a decrease due to glucagon. In perfusion experiments Merrill *et al.* (8) reported a vasodilatory effect of glucagon on superior mesentric vascular bed of dog. Following glucagon, Kapoor *et al.* (5) reported constriction of perfused artery of rabbit ear, but vasodilation if noradrenaline was added to the perfusion fluid. The present study was undertaken to study the effect of glucagon on perfused rat hind-quarter and coronary arteries of rabbit.

MATERIAL AND METHODS

I. *Rat hind-quarter perfusion:* Method of Sollman and Hanzlick (10) as modified by Gambhir *et al.* (1) was used. Essentially, the method involves a record of the degree of relative negative pressure created in the air inlet system obtained with a sensitive tambour. The degree of relative vacuum depends on the rate of perfusion. The higher the perfusion

rate, the greater the vacuum. The number of bubbles coming out from the Marriot tube corresponds to the vertical shifts of the recording lever. The only air inlet was a hypodermic needle (No. 26) in the pressure tube. A light straw recording lever, which could magnify the diaphragm 15-30 times, was attached to the tambour. The apparatus could record a change of 1 *ml/min* flow by a 4 mm vertical shift of the lever. As the perfusion starts the lever shifts downward till it is stabilized to give a horizontal baseline corresponding to initial flow rate. Responses to constrictor drugs were recorded by an upward shift and those to dilator drugs by a downward shift.

In rats (150-250 *gm*) anaesthetized with pentobarbitone (30 *mg/kg*), the lower abdominal aorta was cannulated. A mass ligature was tied around the cannulated site and upper half of the animal was cut off. The cannula in the aorta was connected to a reservoir containing Ringer-Locke solution (NaCl 9 g, KCl, 4.2 g, $CaCl_2$ 2.4 g, glucose 2.0 g and $NaHCO_3$ 0.5 g/L of water) kept at a height of 30-50 cm. The perfusion fluid was oxygenated before experiment and the pH was maintained at 8.

II. *Perfused heart of rabbit:* The coronary arteries of rabbit were perfused as described by Langendorff and Pfluger (7). The perfusion fluid was Ringer-Locke which was continuously oxygenated.

RESULTS

In rat hind-quarter perfusion experiments, glucagon (1 μg) given in the inflow tube of perfusion system, caused vasodilatation in all the 5 animals. The volume of outflow of perfusion fluid before and after drug was 4.74 ± 0.05 *ml*/4 min and 7.10 ± 0.03 *ml*/4 min respectively. The rise in volume was significant ($P < 0.01$).

Injection of glucagon (1 μg) in 6 experiments on rabbit coronary arteries, caused a reduction in the coronary outflow within 30 sec from control value of 6.58 ± 0.57 *ml*/min to 4.76 ± 1.56 *ml/min*. This effect was significant ($P < 0.05$). Larger doses, 2 μg and 4 μg, in 7 and 5 experiments respectively, did not have any significant effect on the volume of perfusate. In 8 experiments where noradrenaline (0.1 $\mu g/ml$) was added to the reservoir fluid, the injection of all the 3 doses of glucagon (1,2 and 4 μg) caused reduction in coronary outflow. It was observed that glucagon had no effect on the force of contraction and heart rate in both series of experiments (perfusion with usual Ringer-Locke solution as well as with Ringer-Locke solution containing nor-adrenaline), while noradrenaline (1 μg) produced a marked reduction in cornary outflow with significant increase in heart rate and contractility of perfused rabbit heart.

DISCUSSION

In the present study glucagon was a potent vasoactive substance being effective in dose of 1 μg. The vasodilator effect seen in rat experiments is in agreement with the reported effect on vascular beds of dog and man (6,9,11) and may be due to direct action on vascular smooth muscles (6,8,9). The present results do not characterize the mechanism underlying the vasodilator action.

A vasoconstrictor response followed injection of glucagon in perfused rabbit coronary vascular bed; vasoconstrictor response also has been reported by Kapoor *et al. (5)* using rabbit isolated ear arteries. In contrast, Goldschlager *et al.* (3) observed an increase in coronary outflow in dogs and suggested a direct vasodilator action of glucagon. A vasoconstrictor response to glucagon was still observed when the rabbit heart was perfused with fluid containing noradrenaline. However, Kapoor *et al.* (5) demonstrated a vasodilator response to glucagon in perfused rabbit ear arteries with Ringer contaning (0.1 $\mu g/ml$) noradrenaline. The vasoconstrictor effect of glucagon was not accompanied by any significant effect on heart rate and force of contraction, while noradrenaline alone produced a marked reduction in coronary outflow with significant increase in heart rate and contractility. In view of these results vasoconstrictor action of glucagon is apparently not mediated through a release of noradrenaline from the nerve endings as suggested by Kapoor *et al.* (5).

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