EFFECT OF NORADRENALIN ON THE COLLATERAL CORONARY CIRCULATION

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A. V. Sapozhkov

Department of Pharmacology (Head, Docent V. V. Gatsura), Kemerovo Medical Institute
(Presented by Active Member AMN SSSR V. A. Sanotskii)
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Reports have recently been published indicating that noradrenalin and phenylephrine may have a favorable effect on the outcome of the collapse caused by myocardial infarction [1, 2, 5]. In connection with the promising results of the clinical application of sympathomimetic amines in coronary disease, the study of their action on the collateral circulation in the heart muscle is of undoubted interest [3, 4]. The object of the present investigation was to study this action of noradrenalin.

EXPERIMENTAL METHOD

Experiments were conducted on dogs weighing from 7 to 20 kg, anesthetized with morphine (5 mg/kg subcutaneously) and hexobarbital (50 mg/kg intraperitoneally).

The descending branch of the left coronary artery was dissected and ligated in its middle third, and a cannula was inserted into the peripheral end of the artery. The retrograde blood flow in the descending branch of the left coronary artery was recorded by means of a photoelectric drop counter, giving an automatic record of the number of drops of blood flowing from the artery on the drum of a kymograph, and the total outflow during different time intervals was determined. The blood flowing from the artery was mixed with heparin solution and reinjected into the femoral vein.

The action of noradrenalin was investigated in doses of 0.5 and 4 μg/kg. Fifteen experiments were carried out in which the action of noradrenalin was investigated in a dose of 0.5 μg/kg, and 12 experiments in which a dose of 4 μg/kg was studied.

EXPERIMENTAL RESULTS

In a dose of 0.5 μg/kg, noradrenalin caused a transient increase in the retrograde coronary flow, a rise of arterial pressure, and a slowing of the heart rate (Fig. 1). The maximal increase in the retrograde flow was observed in all 15 experiments during the first 2 min (1st min $-16.0 \pm 2.9\%$, $P < 0.001$; 2nd min $-9.0 \pm 3.4\%$, $P < 0.02$). In 9 of the experiments the increased retrograde flow lasted for 7 min after the injection of noradrenalin. In all the experiments the changes in the retrograde flow developed against the background of the pressor action of noradrenalin, which also was most marked during the first 2 min (1st min $-22.0 \pm 2.4\%$, $P < 0.001$; 2nd min $-5.7 \pm 2.3\%$, $P < 0.05$). In all the experiments, however, during the 4 min after the injection the normal arterial pressure was restored, whereas the retrograde flow remained increased. This fact indicates that after the administration of small doses of noradrenalin, an increase may take place in the collateral blood flow without any significant changes in the arterial pressure.

A very slight slowing of the heart rate in the first 2 min after the injection of noradrenalin was observed in only 7 of 15 experiments.

In a dose of 4 μg/kg, in all 12 experiments noradrenalin caused a sharp increase in the retrograde flow during the first 2 min after injection of the drug (1st min $-33.3 \pm 5.9\%$, $P < 0.001$; 2nd min $-23.2 \pm 6.1\%$, $P < 0.01$). In 8 experiments, after the retrograde blood flow returned to the control level, a very slight further fall in its value was observed (Fig. 2). In 2 experiments the level of the retrograde blood flow remained elevated until the end of the in-

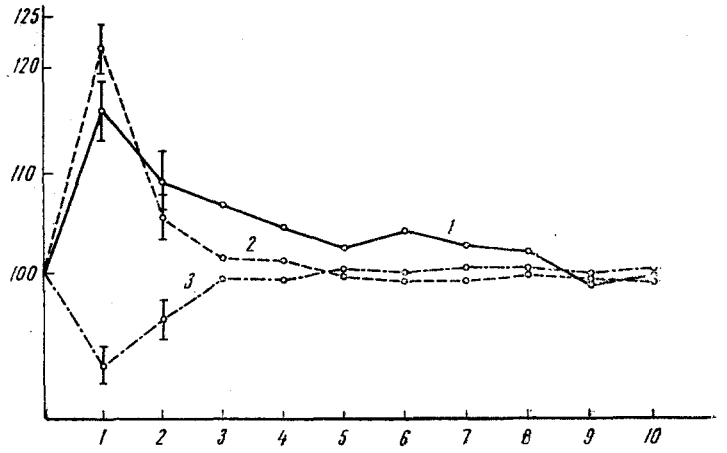

Fig. 1. Effect of noradrenalin in a dose of 0.5 μg/kg on the retrograde coronary flow in the descending branch of the left coronary artery, on the general arterial pressure, and on the heart rate. Along the axis of ordinates—changes in the retrograde coronary flow (1), in arterial pressure (2), and in the heart rate (3) (as % of initial values); along the axis of abscissas—time (in min).

vestigation, and in 2 other experiments the retrograde flow returned to its original level 2 min after the injection of noradrenalin.

The changes in the arterial pressure after injection of noradrenalin in a dose of 4 μg/kg took the form of a sharp depressor reaction, arising during the first 2 min after the injection (1st min—43.8±4.8%, $P<0.001$; 2nd min—10.3±4.0%, $P<0.05$). Thereafter, the arterial pressure returned to normal, with a tendency towards a slight fall. In 2 of the 12 experiments it became stabilized after the maximal rise at the initial level. A slowing of the heart rate was also observed for 2 min after the injection of noradrenalin (1st min—11.2±4.3%, $P<0.05$; 2nd min—7.2±2.9%, $P<0.05$).

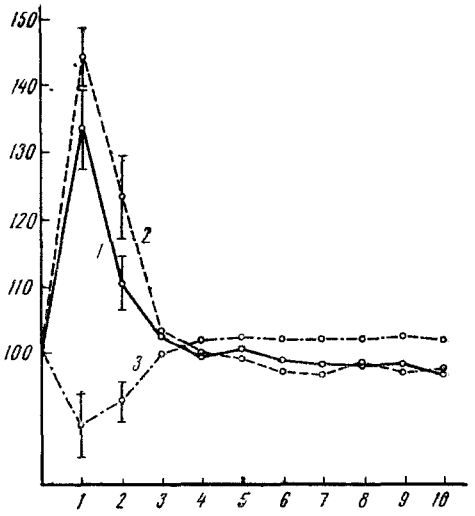

Fig. 2. Effect of noradrenalin in a dose of 4 μg/kg on the retrograde coronary flow in the descending branch of the left coronary artery, the general arterial pressure, and the heart rate. Legend as in Fig. 1.

Analysis of the effect of noradrenalin on the collateral circulation in the myocardium shows that the changes in the level of the retrograde blood flow during the first 2 min after injection of the drug were due to its pressor action on the general arterial pressure. The differences observed between the action of small (0.5 μg/kg) and large (4 μg/kg) doses of noradrenalin on the retrograde flow into the coronary artery requires further study.

SUMMARY

A study was made of the action of noradrenalin (in doses of 0.5 μg/kg and 4 μg/kg) on collateral coronary circulation of dogs. Administration of 4 μg/kg caused a brief increase in the retrograde coronary flow in direct proportion to its pressor effect. Low doses of noradrenalin induced stable increase in the retrograde blood flow in the descending branch of the left coronary artery against the background of the normalized general blood pressure.

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