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# EFFECT OF NORADRENALIN ON REACTIVE MYOCARDIAL HYPEREMIA IN DOGS

V. L. Golubykh, A. Yu. Pavlenko, and A. V. Trubetskoi

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Under the influence of noradrenalin (NA) the coronary vessels undergo predominantly vasodilatation in response to an increase in the work of the heart and the intensity of its metabolism [4]. Comparison of responses of the coronary vessles and the oxygen consumption (with administration of NA and isoproterenol) showed that the magnitude of the dilator response lags behind that of the oxygen consumption in response to NA but precedes vasodilatation in response to isoproterenol [6]. Chronic experiments [2, 7] showed that injection of NA, with constant cardiac rhythm, induces a biphasic response of the coronary vessels with transient initial dilatation of the coronary vessels followed by their prolonged constriction. However, the effect of NA on coronary vascular tone in the period of ischemia and reactive hyperemia (RH) remains unclear, although we know that β-adrenergic blockade leads to a reduction of myocardial RH whereas, on the contrary, α-adrenergic blockade increases RH [5].

In the investigation described below the effect of NA on dilatation of the coronary vessels during RH was investigated in more detail.

## EXPERIMENTAL METHOD

Experiments were carried out on 9 dogs, weighing 12 kg on average, under hexobarbital anesthesia with morphine premedication (75 and 5 mg/kg body weight, respectively). Thoracotomy was performed in the 5th intercostal space and the animal was artificially ventilated on the RO-3 apparatus. The pressure in the left ventricle was measured by means of a catheter introduced through its wall into its lumen. To stabilize the blood pressure (BP) a cannula connected to a reservoir was introduced through the brachiocephalic artery into the ascending aorta. The pressure in the arterial system and left ventricle was measured by means of a Hewlett-Packard transducer. The coronary blood flow was measured by means of a Statham SP 2201 electromagnetic flowmeter in the circumflex or descending branch of the left coronary artery (lay-on transducers 2-3 mm in diameter). The coronary blood flow was arrested for 20 sec at the beginning of development of the cardiac response to injection of NA (series I), and also after injection of NA, as soon as the parameters of the cardiodynamics had returned

Institute of Experimental Cardiology, All-Union Cardiologic Scientific Center, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR V. N. Smirnov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 103, No. 3, pp. 264-266, March, 1987. Original article submitted April 22, 1986.

 

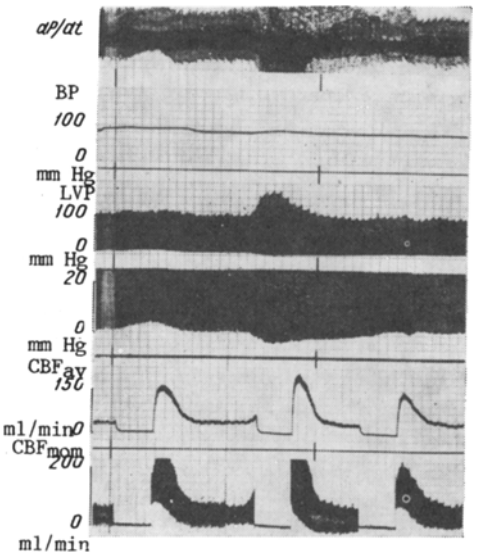


Fig. 1. Effect of injection of NA into left ventricle on magnitude of myocardial RH. On left — control occlusion for 20 sec and RH; on right — RH to occlusion of the same duration in initial and late phases of action of NA; dp/dt) first derivative of LVP; BP) averaged value of pressure in aorta; $CBF_{av}$) averaged value of blood flow in coronary artery; $CBF_{mom}$) momentary value of coronary blood flow. Time marker 1 sec.

TABLE 1. Changes in Central Hemodynamics and Postocclusion RH in Initial Phase of Action of NA

| Parameter | Before occlusion | | Peak of RH | |
|---|---|---|---|---|
| | control | NA | control | NA |
| CBF, ml/min | $56 \pm 5$ | $68 \pm 16$ | $180 \pm 20$ | $231 \pm 21$ |
| | $p < 0,01$ | | $p < 0,001$ | |
| BP, mm Hg | $88 \pm 3$ | $92 \pm 3$ | $86 \pm 2$ | $90 \pm 3$ |
| | n/s | | n/s | |
| LVP, mm Hg | $89 \pm 6$ | $109 \pm 4$ | $95 \pm 3$ | $109 \pm 4$ |
| | $p < 0,01$ | | $p < 0,01$ | |
| HR, beats/min | $163 \pm 10$ | $161 \pm 9$ | $16 \pm 8$ | $165 \pm 8$ |
| | n/s | | n/s | |
| CVR, relative units | $1,8 \pm 0,2$ | $1,7 \pm 0,2$ | $0,57 \pm 0,05$ | $0,49 \pm 0,05$ |
| | n/s | | $p < 0,01$ | |

Legend. Here and in Table 2: CBF) coronary blood flow, BP) arterial pressure, HR) heart rate, CVR) coronary vascular resistance, n/s) not significant.

to their initial level (series II). NA was injected into the left ventricle in a single dose of 0.5 mg. The resistance of the coronary vessels was calculated as the ratio of the mean blood flow and the pressure in the original state and at the peak of RH. The results were subjected to statistical analysis by Student's t test.

## EXPERIMENTAL RESULTS

Injection of NA led to an increase in left ventricular pressure (LVP), and the first derivative of LVP with respect to time, both before and during occlusion of the coronary vessels. Arrest of the blood flow in the coronary artery without injection of NA led to a decrease in the first derivative of LVP (especially of the relaxation phase) and an increase in the end-diastolic pressure (Fig. 1). The peak of RH in these cases amounted to 233 ± 21% of the initial blood flow. As the data in Table 1 show, not only was the blood flow increased at the peak of RH, but the resistance of the coronary vessles also was significantly reduced compared with the control (series I).

TABLE 2. Changes in Central Hemodynamics and Postocclusion RH in Period of Action of NA when Parameters of Cardiodynamics Returned to Control Level

| Parameter | Before occlusion | | Peak of RH | |
|---|---|---|---|---|
| | control | NA | control | NA |
| CBF, ml/min | 58±11 | 58±9 | 169±32 | 146±29 |
| | n/s | | $p<0,05$ | |
| BP, mm Hg | 87±5 | 86±5 | 85±5 | 85±5 |
| | n/s | | n/s | |
| LVP, mm Hg | 98±6 | 101±9 | 97±5 | 101±5 |
| | n/s | | n/s | |
| HR, beats/min | 168±13 | 168±14 | 166±11 | 164±8 |
| | n/s | | n/s | |
| CVR, relative units | 1,97±0,4 | 1,95±0,3 | 0,6±0,08 | 0,68±0,09 |
| | n/s | | $p<0,05$ | |

In the second series the peak of RH was determined when the parameters of the cardiodynamics did not differ significantly from the control level (Table 2). The action of NA during this period on the peak of RH was expressed as a fall of the latter below the control level. Compared with initially, for instance, the blood flow was increased by the action of NA by 155 ± 8%, compared with 209 ± 23% in the control. The decrease in resistance at this stage of the action of NA was less than in the control (62 ± 3 and 63 ± 3%, respectively).

The results showed that NA has a biphasic action at the peak of RH. The first, initial phase of action of NA can be linked with predominance of the $\beta_1$-adrenergic action on the myocardium, which is confirmed by activation of the contractile activity of the heart, and as the result of its metabolism. The initial phase of increase of the coronary blood flow was abolished in experiments in [7] by $\beta_1$-adrenergic blockade. In the later phase of action of NA in the present experiments, on the other hand, limitation of the postocclusion dilatation was observed. In the experiments mentioned above [2, 7] limitation of the blood flow during the action of NA was delayed and was linked with α-adrenergic constriction. According to Ross [4], the α-adrenergic mechanism limits metabolic vasodilatation of the coronary vessels, leading to reduction of the myocardial oxygen demand.

The peak of RH thus cannot be considered as an absolute indicator of maximal dilatation of the coronary vessels. This conclusion is in agreement with previous data obtained during stimulation of sympathetic nerves [1]. NA has a phasic action on the peak of RH. The first phase is due to activation of the myocardial β-adrenoreceptors, the second phase to a constrictor effect of α-adrenergic nature, which is delayed.

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