EFFECT OF ADRENALIN AND NORADRENALIN ON VOLUME VELOCITY OF THE CEREBRAL BLOOD FLOW AND OXYGEN TENSION IN BRAIN TISSUE

M. D. Gaevyi

UDC 615.357.452.015.4 : 612.824

In acute experiments on 36 anesthetized cats using controlled respiration, intravenous injection of adrenalin and noradrenalin (10 μg/kg) increased the volume velocity of the blood flow as the result of a marked increase in the systemic arterial pressure. With the arterial pressure stable or with moderate hypertension, the blood flow in the vessels of the brain was at first reduced, but frequently it later showed a moderate increase. The oxygen tension in the brain tissues was largely dependent on changes in the blood flow.

Information on the effect of adrenalin and noradrenalin on the cerebral blood flow and oxygen tension in the brain tissues is contradictory [5, 7-15]. The reason for the differences of opinion is evidently the fact that adrenomimetics cause marked changes in the general hemodynamics and these, in turn, affect both the cerebral blood flow and the oxygen concentration in the brain. Analysis of data in the literature showed that most investigations were undertaken without the use of methods ruling out the possible effects of arterial pressure on the cerebral hemodynamics.

With these observations in mind it was decided to investigate the action of adrenalin and noradrenalin on the cerebral blood flow and oxygen tension in the brain tissues (pO_2) at different levels of arterial pressure and of blood flow into the brain.

EXPERIMENTAL METHOD

Acute experiments were carried out on 36 anesthetized cats (chloralose-urethane) weighing 2-3 kg under controlled respiration [2]. The volume velocity of the cerebral blood flow was recorded by a flow water [3] connected to the carotid arteries while their extracranial branches were ligated on both sides [6]. The basilar artery or vertebral arteries were ligated to remove the connection between the perfused region and the systemic arterial circulation. To stabilize the pressure in the carotid arteries, a regional pressure stabilizer was connected to the flow meter [4]. In some series of experiments, autoperfusion of the brain vessels was carried out with a constant output pump, thus stabilizing the blood flow into the brain. The oxygen tension in the brain tissue was measured by a polarographic method and recorded with an oxyhemograph [1]. An amalgamated electrode was inserted into the parietal cortex to a depth of 2-3 mm. Adrenalin and noradrenalin were injected intravenously (10 μg/ml) and into the carotid artery (0.3-0.5 μg/kg).

EXPERIMENTAL RESULTS

In experiments without stabilization of the arterial pressure, intravenous injection of adrenalin and noradrenalin caused a significant increase in the volume velocity of the cerebral blood flow of 53±11 and 45±16%, respectively, and an increase in pO_2 in the brain tissues by 22±8 and 39±10.6%, respectively (Table 1). The effect was most marked after 1 min, at the time of a sharp increase in arterial pressure (Figs. 1A and 2A). After 2 min the blood flow usually fell to its initial level or even below it (difference

Department of Pharmacology, Semipalatinsk Medical Institute. (Presented by Academician V. V. Parin.) Translated from Byulleten Éksperimental'noi Biologii i Meditsiny, Vol. 72, No. 9, pp. 57-60, September, 1971. Original article submitted February 12, 1970.

TABLE 1. Effect of Adrenalin and Noradrenalin on Volume Velocity of the Cerebral Blood Flow and Oxygen Tension in the Brain Tissues (pO_2)

Experimental conditions	Dose of preparation (in μg/kg)	Blood flow (in ml/min)		Change in pO_2 (in %)	Measurement of arterial pressure (in mm)	
		initial data	after injection of prep.		initial data	after injection of prep.
Adrenalin						
Stabilized arterial pressure	10	17±2,1	25±2,8 $P<0,05$	+22±8 $P<0,05$	86±2,7	139±3,3 $P<0,05$
Stabilized pressure in carotid arteries	10	18±2,6	9±1,7 $P<0,05$	Not measured		
Stabilized blood flow into the brain	0,3—0,5	18,6±2,4		+8±0,7 $P<0,05$	No significant changes	
Noradrenalin						
Stabilized arterial pressure	10	17±2	24,4±2,3 $P<0,05$	+39±10,6 $P<0,05$	84±2,2	143±3,4 $P<0,05$
Stabilized pressure in carotid arteries	10	18,8±2,4	9,2±1,6 $P<0,05$	Not measured		
Stabilized blood flow into the brain	0,3—0,5	19±1,8		+4+2,3 $P>0,05$	No significant changes	

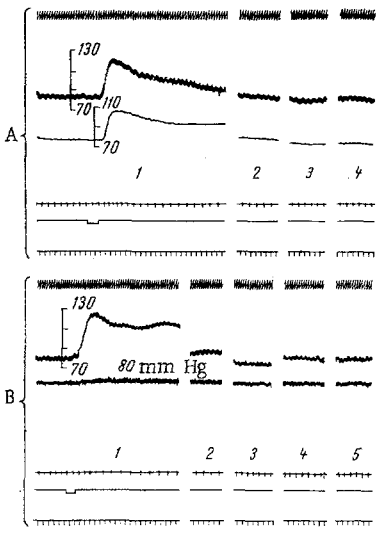

Fig. 1. Effect of adrenalin (10 μg/kg), intravenously) on cerebral blood flow with pressure in carotid arteries not stabilized (A) and stabilized (B). In A: 1) initial data and immediately after injection of adrenalin, 2,3,4) 5, 10, and 20 min, respectively after its injection. In B: 1) initial data and immediately after injection of adrenalin, 2,3,4,5) 4, 6, 10, and 20 min, respectively after its injection. From top to bottom: respiration (controlled), systemic arterial pressure, pressure in carotid arteries, blood flow (interval between marks 2 ml), marker of injection of adrenalin, time marker 5 sec.

not significant), despite the fact that the arterial pressure still remained higher than initially at this time. The value of pO_2 in the brain tissues fell to its initial level after 5-9 min, and later it frequently fell even further (difference not statistically significant). A close connection can be postulated between the observed changes in arterial pressure, in the cerebral blood flow, and in pO_2 in the brain tissues.

In the experiments of series II, in which the pressure in the carotid arteries are stabilized, the changes in the blood flow were found to be dependent on the arterial pressure. Under these conditions intravenous injections of the same doses of adrenalin and noradrenalin reduced the cerebral blood flow by 52±6 and 51±1%, respectively. The effect was most marked after 1-2 min (Figs. 1B and 2B) and lasted for

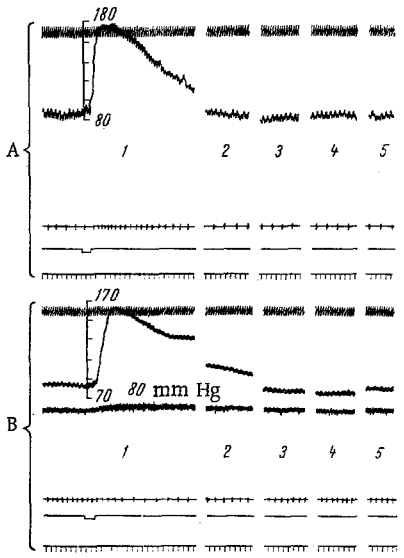

Fig. 2. Effect of noradrenalin (10 μg/kg, intravenously) on cerebral blood flow with pressure in carotid arteries not stabilized (A) and stabilized (B). Legend as in Fig. 1.

7-9 min, after which the blood flow was sometimes slightly increased. This biphasic type of reaction was more characteristic of adrenalin.

To explain this relationship between the changes in pO_2 in the brain tissues and the magnitude of the blood flow, experiments of series III were carried out in which the blood vessels of the brain were autoperfused with a constant output pump. In these experiments the adrenalin and noradrenalin were injected into the carotid artery in small doses (0.3-0.5 μg/kg) sufficient to evoke characteristic responses of the perfused vessels but not to cause significant changes in the general hemodynamics. Under these conditions adrenalin at first caused a small (by 8±0.7%) increase in pO_2, after which it frequently fell below its initial level. For noradrenalin, the change in pO_2 in the brain tissue were not statistically significant.

The results of these experiments thus confirm those obtained by other workers who found a passive increase in the cerebral blood flow after intravenous injection of adrenalin and noradrenalin. This in no way implies that catecholamines do not evoke active responses of the cerebral vessels, as many workers consider. If the arterial pressure is stabilized or moderabely increased, adrenalin and noradrenalin reduce the cerebral blood flow, evidence of an active vasoconstrictor response which, if severe hypertension is present, cannot oppose the considerably increased intravascular pressure, so that the blood flow rises passively. The value of pO_2 in the brain tissue rises correspondingly. Some changes in pO_2 in the brain can evidently take place through the direct effect of the catecholamines on the tissue respiration.

LITERATURE CITED

1. A. I. Beketov and D. I. Sapegin, Lab. Delo, No. 4, 243 (1966).
2. M. D. Gaevyi, Byull. Éksperim. Biol. i Med., No. 8, 121 (1966).
3. M. D. Gaevyi, Fiziol. Zh. SSSR, 53, No. 3, 417 (1967).
4. M. D. Gaevyi, Fiziol. Zh. SSSR, 55, No. 7, 891 (1969).
5. I. V. Golubeva, Effect of Adrenergic Substances on the Blood Oxygen Saturation and Oxygen Tension in the Tissues. Candidate's Dissertation, Simferopol' (1967).
6. N. M. Ryzhova, Fiziol. Zh. SSSR, 52, No. 9, 1079 (1966).
7. A. D. Snezhko, Biofizika, 1, No. 6, 585 (1956).
8. A. E. Troshina, Farmakol. i Toksikol., No. 3, 250 (1960).
9. I. D. Éntina and V. A. Yakovlev, Biokhimiya, No. 6, 567 (1951).
10. H. D. Green and A. B. Denison, Circulat. Res., 4, 565 (1956).
11. J. G. Greenfield and G. T. Tindall, J. Clin. Invest., 44, 1672 (1968).
12. J. Handa, J. C. Meuer, and K. Yoshida, J. Pharmacol. Exp. Ther., 152, 251 (1966).
13. B. D. King, L. Sokoloff, and R. L. Wechsler, J. Clin. Invest., 31, 273 (1952).
14. G. Laborit, C. Baron, and H. Laborit, Agressologie, 6, 721 (1965).
15. L. Sokoloff, Pharmacol. Rev., 11, 1 (1959).