STUDY OF THE ACTION OF NORADRENALIN ON THE BLOOD FLOW IN THE BRAIN USING KRYPTON-85

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Experiments on dogs have shown that noradrenalin, if injected into the general circulation, does not change the volume of blood flowing per unit time per gram of brain tissue. Despite a statistically significant increase in the resistance of the cerebral arteries, the blood flow remains unchanged because of a simultaneous increase in the mean arterial pressure. Injection of noradrenalin directly into the blood vessels of the brain reduces the cerebral blood flow.

There is as yet no unanimity regarding the character of the effect of noradrenalin on the blood flow in the brain. Investigators using the nitrous oxide method [6, 9] observed a decrease in the cerebral blood flow in response to injection of noradrenalin. Electromagnetic measurements of the volume velocity of the blood flow through the internal carotid artery revealed an appreciable increase [5, 8] or no effect whatever [2] under the influence of noradrenalin. No response to noradrenalin could be discovered in the isolated vessels of the brain [1].

The object of this investigation was to study the effects of noradrenalin on quantitative changes in the cerebral blood flow under the conditions of a relatively normal arterial pressure and stable arterial CO_2 tension.

EXPERIMENTAL METHOD

Experiments were carried out on dogs. A Boyle's apparatus was connected to the input end of a respiratory pump and endotracheal anesthesia was maintained with a mixture of nitrous oxide and oxygen (4 : 1). Scoline was used as the muscle relaxant.

The blood flow in the brain was determined with the aid of Kr^{85} [3, 7].

The mean arterial pressure was recorded on a Mingograph. Noradrenalin was injected intravenously by continuous infusion (12-36 μg/min) in order to obtain a stable increase in the mean arterial pressure.

In some experiments noradrenalin was injected by the intracarotid route in fractional doses.

EXPERIMENT RESULTS

In the control the mean arterial pressure was 137±4.7 mm Hg and the regional cerebral blood flow 0.93±0.02 ml/g/min; the resistance of the cerebral arteries was 1.4±0.019 mm Hg/ml/100 g/min. All values corresponded to a value of pCO_2 = 40 mm Hg [4].

In response to intravenous infusion of noradrenalin (24-36 μg/min), despite a marked increase in mean arterial pressure ($P < 0.001$) the cerebral blood flow remained within normal limits. Meanwhile a marked increase in the resistance of the cerebral arteries was observed ($P < 0.02$).

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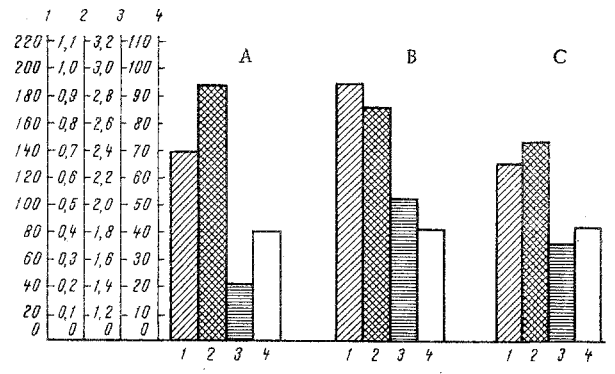

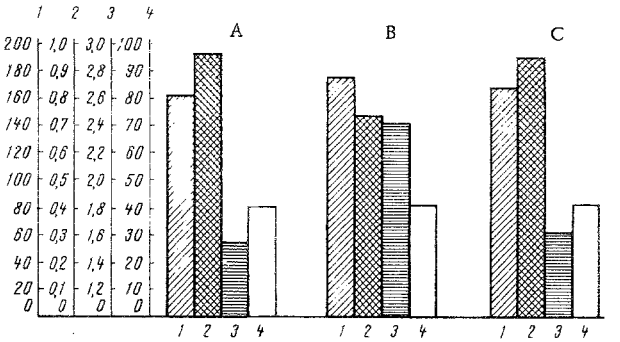

Fig. 2

Fig. 1. Effect of intravenous infusion of noradrenalin on regional cerebral blood flow. 1) Mean arterial pressure (in mm Hg); 2) regional cerebral blood flow (in ml/g/min); 3) resistance of cerebral arteries (in mm Hg/ml/100 g/min); 4) arterial CO_2 tension (in mm Hg); A) background; B) infusion of noradrenalin (24 μg/min); C) period after infusion of noradrenalin.

Fig. 2. Effect of intracarotid injection of noradrenalin on regional cerebral blood flow. A) Background; B) noradrenalin injected directly by the intracarotid route (12 μg); C) control. Remainder of legend as in Fig. 1.

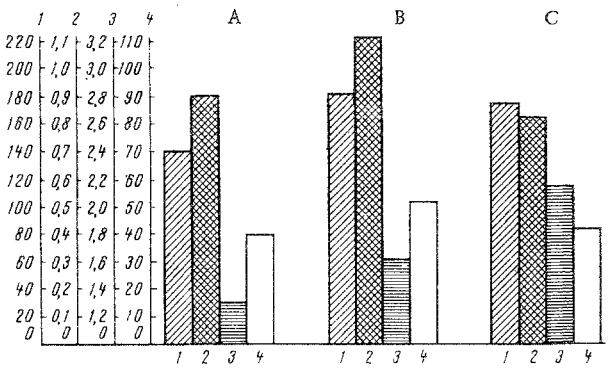

Fig. 3. Effect of noradrenalin on cerebral blood flow depending on fluctuations in arterial CO_2 tension. A) Background; B) infection of noradrenalin (24 μg/min); C) hyperventilation. Remainder of legend as in Fig. 1.

When the infusion stopped, the mean arterial pressure returned to its initial value. Meanwhile an increase in the regional cerebral blood flow was observed, when compared both with the control ($P < 0.001$) and with its value during injection of noradrenalin ($P < 0.05$). Despite cessation of infusion of noradrenalin, the resistance of the vessels remained above its initial value ($P < 0.001$), and this evidently accounted for the decrease in the regional cerebral blood flow (Fig. 1).

The absence of marked changes in the cerebral blood flow in the period of noradrenalin infusion was explained by a simultaneous increase in the mean arterial pressure. Whether this increase in resistance of the cerebral arteries was the result of the direct effect of noradrenalin on the vessel walls or a compensatory response to elevation of the mean arterial pressure could evidently be shown by experiments in which noradrenalin was injected directly into the carotid artery.

Intracarotid injection of noradrenalin (12 μg) was not followed by significant changes in the mean arterial pressure (Fig. 2; $P = 0.25$), although the regional cerebral blood flow was considerably reduced ($P < 0.001$).

Meanwhile a marked increase in the resistance of the cerebral arteries was observed ($P < 0.001$).

In a few experiments a marked increase in the regional blood flow in the brain and a decrease in resistance of the cerebral arteries were observed in response to intravenous infusion of noradrenalin. Synchronous determination of the arterial pCO_2 showed that this was due to an increase in the CO_2 tension in the arterial blood, and restoration of the normal pCO_2 by hyperventilation led to a decrease in the regional cerebral blood flow and to an increase in the resistance of the brain vessels (Fig. 3).

It can be concluded from these results that noradrenalin can act directly on the cerebral blood flow. The marked increase in mean arterial pressure following intravenous infusion of noradrenalin cancels out the effect of this drug. The CO_2 tension in the blood plays an important role in the manifestation of the effect of noradrenalin on the cerebral blood flow.

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