EFFECT OF NITROGLYCERIN ON REGULATION OF THE CEREBRAL CIRCULATION

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Investigations by the use of radioisotopes and electromagnetic and resistographic methods showed that nitroglycerine increases the cerebral blood flow and lowers the tone of the intracranial vessels. It also has a marked depriming effect on the central regulation of the cerebral circulation, inhibits cerebrovascular reflexes, and has a protective effect in experimental disturbances of the cerebral circulation of adrenergic nature.

KEY WORDS: nitroglycerine; cerebral blood flow.

Investigations have shown that nitroglycerine increases the cerebral circulation and lowers the tone of the intracranial vessels [1, 7-10]. However, no information could be found in the literature on its effect on the nervous regulation of the intracranial circulation. Nevertheless nitroglycerine has been shown to have a depriming effect on the centers of vasomotor control and to enhance suprasegmental inhibition [2, 3].

It was accordingly decided to investigate the action of nitroglycerine on the cerebral circulation and its nervous control. Research in this direction is also important to shed light on the role of the vasomotor centers in the regulation of cerebrovascular tone.

EXPERIMENTAL METHOD

Experiments were carried out on 39 cats weighing 3-4 kg, anesthetized with urethane (0.5 g/kg) and chloralose (50 mg/kg) and artificially ventilated.

In the experiments of series I the cerebral blood flow was measured with the aid of radioactive xenon-133 on the UAU-100 apparatus. The results were analyzed with the Minsk-22 computer. The cerebral blood flow was determined by successive derivation of indicator function [6].

The state of the cerebral circulation also was judged from the inflow of blood into the cats' brain through the internal maxillary artery, recorded by an electromagnetic blood flowmeter. The EEG from the parietal region, the EEG from lead II, and the blood pressure in the femoral artery were recorded at the same time.

The vascular component of the action of the drug on the cerebral hemodynamics was differentiated by separate bilateral perfusion of the carotid and vertebral arteries [4].

By means of the ABC-1 apparatus the acid–base balance and partial oxygen pressure (pO_2) were determined in samples of arterial blood and cerebrospinal fluid.

EXPERIMENTAL RESULTS AND DISCUSSION

The experiments with radioactive xenon-133 showed that nitroglycerine (0.5 mg/kg) caused a marked increase in the volume velocity of the intracranial blood flow. Similar results were obtained in the experiments to record the inflow of blood into the brain by an electromagnetic flowmeter. Immediately after intravenous injection of nitroglycerine the intracranial circulation was increased by 37 ± 7.1%. The compounds lowered the systemic arterial pressure by 52 ± 2.4% but caused no significant changes in the EEG or ECG (Fig. 1).

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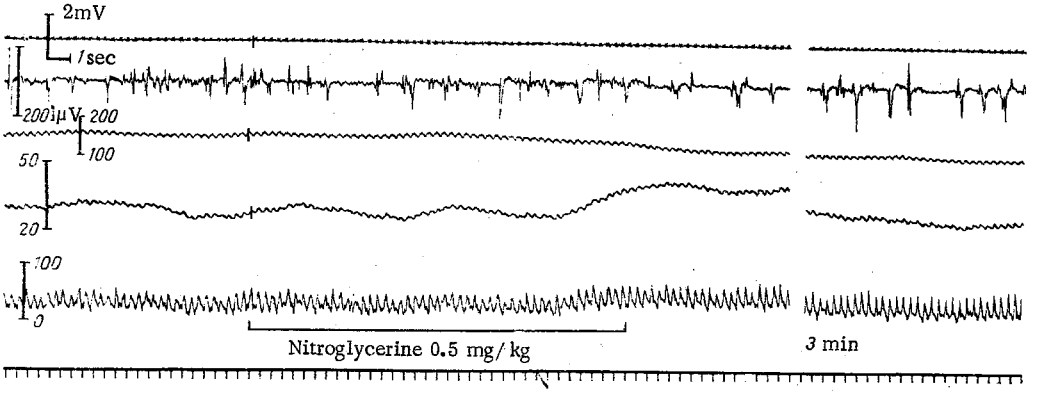

Fig. 1. Change in intracranial blood flow of cat under influence of nitroglycerine (0.5 mg/kg, intravenously). From top to bottom: ECG in lead II, EEG from parietal region, blood pressure (in mm Hg), averaged and phasic blood flow in right internal maxillary artery (in ml/min), marker of injection of drug.

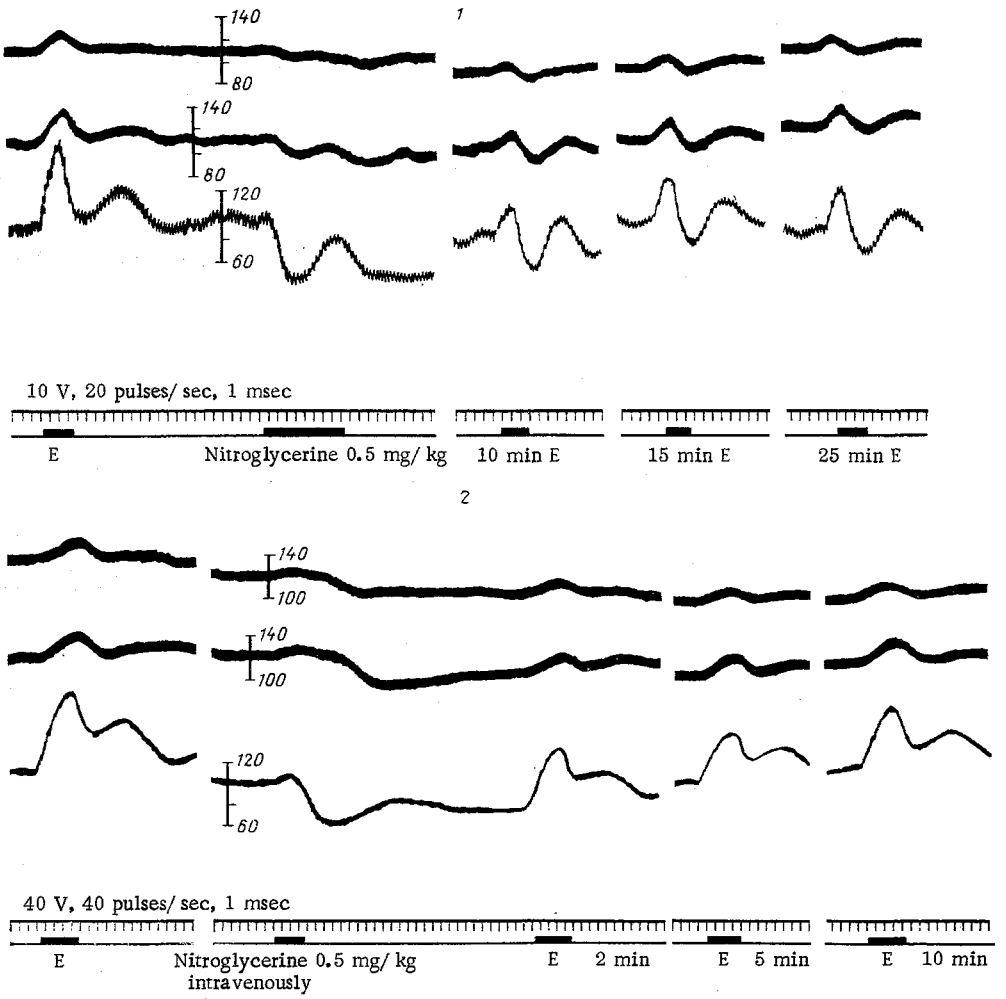

Fig. 2. Effect of nitroglycerine on reflex constrictor responses evoked from low-threshold (1) and high-threshold (2) afferent fibers of tibial nerve. From top to bottom: perfusion pressure in internal maxillary arteries, resistogram of vertebral arteries, blood pressure (in mm Hg), time marker 5 sec, marker of stimulation (E) and injection of drug.

The resistographic experiments (perfusion of the blood vessels with a constant blood volume) showed that the compound in a dose of 0.5 mg/kg reduces the hydraulic resistance in the system of the carotid arteries by 17 ± 2.2% and in the system of the vertebral arteries by 22 ± 2.5%.

In samples of arterial blood taken before injection of nitroglycerine and also 1, 10, and 30 min thereafter, no changes were found in pH, pCO_2, pO_2, or the percentage of oxyhemoglobin. Nitroglycerine has no significant effects on the hydrogen ion concentration, pCO_2, or pO_2 in the cerebrospinal fluid.

To study the effect of nitroglycerine on nervous regulation of the cerebral circulation, its action on reflex constrictor reactions of the intracranial vessels to electrical stimulation of afferent fibers of the tibial nerve (10-40 V, 20-40 pulses/sec, 1 msec) was studied. Experiments showed that nitroglycerine had an inhibitory effect on reflex constrictor responses of the cerebral vessels. The intensity of the depriming effect of the preparation was found to be inversely proportional to the amplitude of stimulation of the afferent fibers of the somatic nerves. When the strength of the stimulus was 10 V, nitroglycerine considerably inhibited vasomotor reflex responses (Fig. 2, 1). With a higher strength of stimulation (40 V) the depriming effect of the compounds was weaker (Fig. 2, 2). The results agree fully with the observations of Bendikov [2] and Kaverina and Bendikov [3], who found that nitroglycerine has its strongest effect on reflex discharges from Aδ fibers arising in response to a lower amplitude of stimulation. Meanwhile the compound had only a weak effect on the ability of the CNS to summate impulses from afferent high-threshold fibers of the C group [2, 3].

The effect of nitroglycerine (0.5 mg/kg, intravenously) also was studied in experimental disturbances of the cerebral circulation of neurogenic (adrenergic) nature, produced by potassium chloride [5]. If nitroglycerine was injected 3-5 min before potassium chloride, considerable weakening of the spasms of the cerebral vessels and of the pressor response of the arterial pressure was observed. Nitroglycerine also lowered the tone of the cerebral vessels and the arterial pressure when raised as the result of the action of potassium chloride on the CNS.

This investigation thus showed that nitroglycerine considerably increases the volume velocity of the intracranial blood flow and lowers the resistance in the arterial systems of the brain. The absence of change in the indices of the acid-base balance in the cerebrospinal fluid under the influence of nitroglycerine rules out the possibility that the action of the compounds on the intracranial hemodynamics is mediated through the pH of the cerebrospinal fluid. Nitroglycerine also has a marked action on the nervous control of the cerebral circulation. It inhibits reflex responses of the cerebral vessels and has a protective action in experimental disturbances of the cerebral circulation of adrenergic nature. The great sensitivity of cerebrovascular reflexes from low-threshold afferent fibers to nitroglycerine is evidence that the compound affects the central regulation of the cerebral circulation. This conclusion can be drawn from data showing that nitroglycerine has a depriming action on the centers of vasomotor control and enhances suprasegmental reticulospinal inhibition [2, 3]. The results now obtained also point to a role of the sympathetic vasomotor senses in the regulation of intracranial vascular tone.

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