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EFFECT OF PHENTOLAMINE ON THE CEREBRAL CIRCULATION

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The effect of phentolamine on the volume velocity of the cerebral blood flow, tone of the cerebral vessels, and partial pressure of oxygen in the brain tissue was studied in acute experiments on anesthetized and unanesthetized cats. Intravenous injection of phentolamine led to a prolonged fall of blood pressure and of the tone of the intracranial and, to a lesser degree, the extracranial vessels. The volume velocity of the cerebral blood flow was reduced in animals with marked phentolamine hypotension. If the perfusion pressure was stabilized, the blood flow was increased. Changes in pO_2 in the brain tissue corresponded largely to the blood flow. Preliminary atropinization and denervation of the carotid zones did not alter the effect of phentolamine. Phentolamine reduced or abolished the constrictor action of noradrenalin and phenylephrine on the brain vessels.

KEY WORDS: *circulation; brain vessels; phentolamine.*

Data on the effect of phentolamine on the cerebral circulation are few in number and contradictory in nature [7, 9-11]. Since phentolamine lowers the systemic blood pressure considerably, it is difficult to judge the response of the cerebral vessels to it.

The object of this investigation was to study the action of phentolamine on the vessels of the brain under conditions excluding the effect of general hypotension on the cerebral circulation.

EXPERIMENTAL METHOD

Acute experiments were carried out on 70 cats of both sexes weighing 2-3 kg under general (1 μg/kg urethane, intravenously) or local (0.25% procaine solution) anesthesia in conjunction with muscle relaxants (diplacin* was injected intravenously at the rate of 0.05-0.1 mg/kg per minute). In the overwhelming majority of experiments controlled respiration was used. The effect of phentolamine was judged from the volume velocity of the cerebral blood flow under conditions of an unstabilized and stabilized perfusion pressure, resistographic data, pO_2 in the brain tissue (by a polarographic method), and the velocity of the blood flow (by the hydrogen clearance method) in the parietal cortex [1-4, 6]. Phentolamine was injected intravenously in a dose of 0.5 mg/kg or intraarterially in doses of 0.005-0.1 mg/kg.

*1,3-Di(β-playneciniumethoxy)benzene hydrochloride — Translator.

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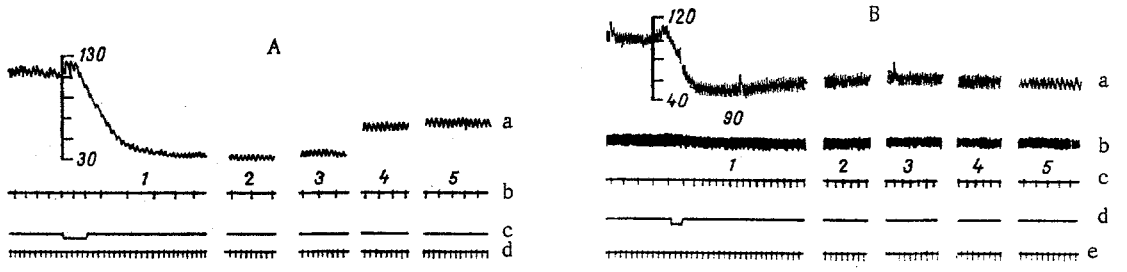

Fig. 1. Effect of phentolamine (0.5 mg/kg, intravenously) on volume velocity of cerebral blood flow with pressure in carotid arteries unstabilized (A) and stabilized (B): a) systemic arterial pressure (in mm Hg); b) volume velocity of cerebral blood flow (distance between markers 3.0 ml); c) marker of injection of phentolamine; d) time marker, 5 sec; e) stabilized pressure in carotid arteries: 1) at time of injection; 2, 3, 4, 5) 5, 10, 30, and 60 min later, respectively.

EXPERIMENTAL RESULTS AND DISCUSSION

With an unstabilized arterial pressure intravenous injection of phentolamine reduced the volume velocity of the cerebral blood flow by 30 ± 4.7% ($P < 0.001$). The effect developed immediately after injection (Fig. 1A); it was most marked in the first minute, and was observed until the end of the experiment (60-90 min). In 5 of the 12 experiments, after a brief decrease in the blood flow, it was accelerated, although in only two experiments was it higher than the initial level, by 18.3 and 10.0% respectively, at the third minute. Later the blood flow again fell gradually. The clear decrease in volume velocity of the cerebral blood flow coincided with a sharp fall in the general arterial pressure. The hypotensive effect was observed immediately; it was most marked in the first minute (a fall of 42.5 ± 2.7%; $P < 0.05$), and it showed a tendency to recover toward the end of the experiment. The value of pO_2 in the brain tissue fell parallel with the blood flow. The greatest decrease in pO_2 (by 30.1 ± 3.8%; $P < 0.01$) was observed in the first minute, and this index remained lower than initially by 12.6 ± 1.2% ($P < 0.001$) until the end of the experiment.

With a stabilized perfusion pressure a marked increase in the volume velocity of the cerebral blood flow was observed after administration of phentolamine. The action of the drug began immediately after its injection, it was maximal (72.3 ± 10.1%; $P < 0.001$) in the first minute, and it continued until the end of the experiment (Fig. 1B).

In a series of experiments to determine the velocity of the blood flow in the parietal cortex by the hydrogen clearance method immediately after intraarterial injection of phentolamine (0.01-0.05 mg/kg) it rose on average by 12.1 ± 3.1% ($P < 0.05$), and this was followed by a progressive decline, evidently on account of the fall in blood pressure.

In the resistographic experiments intravenous injection of phentolamine lowered the tone of the intracranial vessels (Fig. 2). The effect appeared immediately after the injection and reached a maximum (by 37.0 ± 2.4%; $P < 0.01$) in the first minute. Later the perfusion pressure had a tendency to recover, but it remained 15.3 ± 5.6% ($P < 0.05$) lower than initially by the end of the experiment.

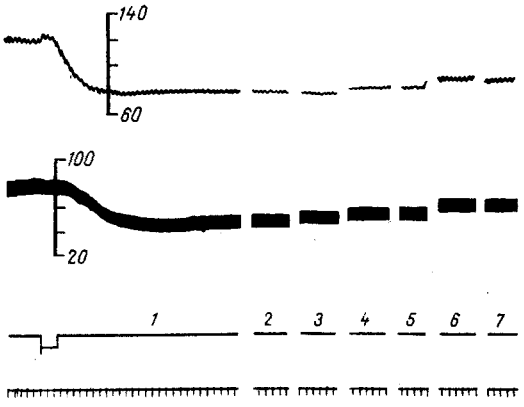

Fig. 2. Effect of phentolamine (0.5 mg/kg, intravenously) on tone of cerebral vessels. From top to bottom: systemic blood pressure; perfusion pressure in cerebral vessels; marker of injection of phentolamine; time marker 5 sec: 1) at time of injection; 2, 3, 4, 5, 6, 7) 3, 5, 10, 30, 60, and 90 min later, respectively.

Comparison of the response of the intracranial and extracranial vessels to injection of phentolamine (0.005 mg/kg, intraarterially) revealed differences in sensitivity to the drug: The tone of the cerebral vessels fell on average by 30.7 ± 6.8% ($P < 0.05$), but the tone of the extracranial vessels fell by 40.4 ± 5.8% ($P < 0.001$). No significant difference in the response of the vessels to phentolamine was found in the anesthetized and unanesthetized animals.

Preliminary atropinization (1 mg/kg) of the animals and denervation of the carotid sinuses caused no appreciable alteration in the effects of phentolamine. Phentolamine considerably reduced or completely abolished the constrictor action of noradrenalin and phenylephrine on the brain vessels and on pO_2 in the brain tissue.

There is information that phentolamine prevents the constrictor response of the brain vessels to sympathetic nerve stimulation [5, 11] and to injection of noradrenalin [8] and abolishes spasm of the brain vessels caused by mechanical or electrical stimulation [10]. It can tentatively be suggested that the dilator effect of phentolamine is due to inhibition of adrenergic vasoconstriction. However, according to Louis [11], blockage of the α-adrenoreceptors does not cause any significant change in the cerebral blood flow; in this worker's opinion, this confirms views expressed by many other investigators on the weak adrenergic control of cerebrovascular tone.

The absence of changes in the cerebral blood flow under conditions of systemic hypotension prevents any conclusions being drawn regarding the specific response of the brain vessels to phentolamine. In these experiments marked phentolamine hypotension could be accompanied by a decrease in the cerebral blood flow, whereas if the perfusion pressure was stabilized, the blood flow was invariably increased. This is evidence of a dilator response of the brain vessels, as the resistographic experiments confirmed. However, the possibility cannot be ruled out that the dilator action of phentolamine on the brain vessels, observed by the present writers and others [9], is due not only to blockade of the α-adrenoreceptors, but also to subsidiary mechanisms [10].

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