EFFECT OF CHLORPROMAZINE ON THE CEREBRAL CIRCULATION

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UDC 615.214.22:547.869.2.
015.4:612.824

Intravenous injection of chlorpromazine in a dose of 2-3 mg/kg lowered the tone of the cerebral vessels and the general arterial pressure. The volume velocity of the cerebral blood flow increased if the arterial pressure remained stabilized or fell only moderately. In severe hypotension induced by chlorpromazine the cerebral blood flow decreased.

KEY WORDS: circulation; cerebral vessels; chlorpromazine.

Chlorpromazine is widely used in diseases of the central nervous system associated with disturbance of the cerebral hemodynamics. Some workers include chlorpromazine as one of a combination of drugs used in the treatment of acute cerebrovascular diseases [4]. These workers regard the decrease in tone of the cerebral vessels that follows intravenous injection of chlorpromazine as a self-regulatory response to the fall in systemic arterial pressure.

The writers have investigated the effect of chlorpromazine on the tone of the cerebral vessels and the volume velocity of the cerebral blood flow when the flow of blood to the brain was stabilized and also when the arterial pressure level was varied.

EXPERIMENTAL METHOD

Experiments were carried out on 19 adult cats anesthetized with chloralose and urethane and artificially ventilated [1]. The volume velocity of the cerebral blood flow was recorded by a flowmeter [2] with the arterial pressure either unstabilized or stabilized. The flowmeteter was connected to the carotid arteries and the appropriate vessels were ligated [5]. To maintain the pressure constant in the carotid arteries, a stabilizer of the regional arterial pressure [3] was used. Resistography [5] was used in a separate series of experiments. In these cases, instead of the flowmeter, the resistograph was connected to the carotid arteries. Blood clotting was prevented by intravenous injection of heparin. The systemic arterial pressure and the perfusion pressure were recorded by mercury manometers. Chlorpromazine (0.25% solution) was injected intravenously in doses of 2-3 mg/kg body weight.

EXPERIMENTAL RESULTS

With the blood pressure in the carotid arteries unstabilized (6 experiments) chlorpromazine infrequently evoked phasic changes in the volume velocity of the blood flow. At first there was a temporary (1-2 min) decrease of the blood flow on the average by 26±3.5% ($P < 0.001$). The blood pressure fell by 47±4.3% ($P < 0.001$). Later (in 2 experiments) the blood flow rose rapidly, so that by the end of the second minute after injection of the chlorpromazine it was 7-10% higher than initially, although the arterial pressure remained low (Fig. 1A). A phase of increase of blood flow also was observed in the other experiments, but it did not reach the initial level. Later in all the experiments the blood flow gradually decreased parallel with the progressive decrease in arterial pressure and it remained low until the end of the experiment (60 min or more).

Department of Pharmacology, Semipalatinsk Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR V. V. Zakusov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 80, No. 10, pp. 72-74, October, 1975. Original article submitted January 10, 1975.

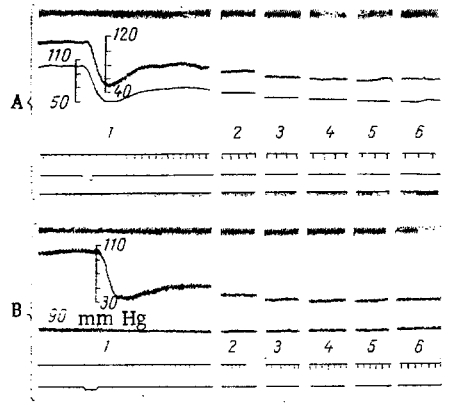

Fig. 1

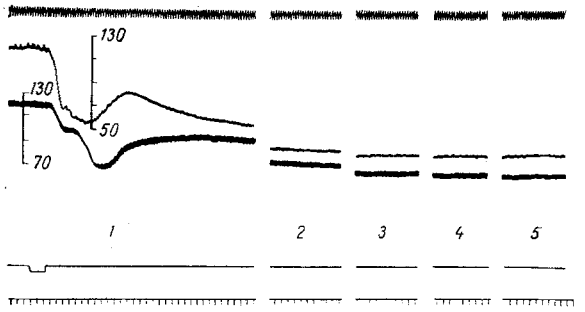

Fig. 2

Fig. 1. Effect of chlorpromazine (2 mg/kg, intravenously) on volume velocity of cerebral blood flow: A) with blood pressure in carotid arteries unstabilized; B) stabilized. From top to bottom: respiration (controlled), systemic arterial pressure, pressure in carotid arteries, volume velocity of blood flow (distance between marks 3 ml), marker of injection of chlorpromazine, time marker (2 sec). 1) At time of injection; 2, 3, 4, 5, 6) 5, 10, 20, 40, and 60 min, respectively, after injection of chlorpromazine.

Fig. 2. Effect of chlorpromazine (3 mg/kg, intravenously) on tone of cerebral vessels. From top to bottom: respiration (controlled), systemic arterial pressure, perfusion pressure, marker of injection of chlorpromazine, time marker (5 sec). 1) At time of injection; 2, 3, 4, 5) 5, 10, 20, and 40 min, respectively, after injection of chlorpromazine.

With the blood pressure in the carotid arteries stabilized (6 experiments) intravenous injection of the same doses of chlorpromazine caused a steady increase in the blood flow. This effect often persisted until the end of the experiments (Fig. 1B).

In 7 experiments the combined resistance of the cerebral vessels was recorded by autoperfusion with the flow rate stabilized. After intravenous injection of chlorpromazine the perfusion pressure in the cerebral vessels fell on the average by $29 \pm 2.5\%$ ($P < 0.001$). The effect appeared immediately after injection of the drug and it often persisted until the end of the experiments (Fig. 2).

Chlorpromazine thus lowers the tone of the cerebral vessels irrespective of the systemic arterial pressure. This is shown by the increase in cerebral blood flow when the perfusion pressure was stabilized, and also by the resistographic experiments. However, when the perfusion pressure was not stabilized the cerebral blood flow could fall in connection with the considerable fall of the systemic arterial pressure.

The mechanism of the vasodilator action of chlorpromazine on the cerebral vessels is not yet known. The resistographic experiments showed that, with a marked increase in the volume of the perfusion system, the response of the perfused vessels to intravenous injection of chlorpromazine was delayed; this indicates a direct effect of the drug on the cerebral vessels or on local mechanisms of regulation of their tone. Further experiments are necessary to solve these problems.

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