These experiments thus showed that the sensitivity of mice irradiated with microwaves to general anesthetics is evidently changed, and this must be taken into account in the practice of anesthesiology when patients who have been or are being exposed to the action of microwaves are anesthetized.

LITERATURE CITED

1. V. M. Koldaev, Byull. Éksp. Biol. Med., No. 3, 285 (1976).
2. P. F. Rokitskii, Biological Statistics [in Russian], Minsk (1973).

EFFECT OF ORNID ON REGULATION OF THE CEREBRAL CIRCULATION

R. S. Mirzoyan

UDC 615.217.24.015.4:612.824

An investigation by radioisotope, electromagnetic, and resistographic methods showed that Ornid reduces the cerebral blood flow. At the same time it completely inhibits constrictor reactions of the cerebral vessels to stimulation of sympathetic and somatic nerves. Ornid also has a protective action against experimental disturbances of the cerebral circulation of adrenergic nature.

KEY WORDS: Ornid; cerebral blood flow; regulation of the cerebral circulation.

To elucidate the role of the sympathico-adrenal system in the control of the cerebral circulation [1, 6-8] it is interesting to study the effect of the sympatholytic Ornid (orthobromobenzyl-N-ethyl-N,N-dimethylammonium bromide) on the cerebral circulation and its nervous control. No information on the cerebrovascular effects of Ornid could be found in the literature.

EXPERIMENTAL METHOD

Experiments were carried out on 33 cats anesthetized with urethane and chloralose and artificially ventilated.

In the experiments of series I the cerebral blood flow was determined by means of ^{133}Xe on the UAU-100 apparatus. The results were subjected to mathematical analysis on the Minsk-22 computer. The cerebral blood flow was determined by successive derivation of indicator functions [2, 5]. The state of the cerebral circulation also was judged from the inflow of blood into the brain through the internal maxillary artery, recorded by means of an electromagnetic blood flowmeter. The EEG was recorded simultaneously in the parietal region and the EEG in lead II; the blood pressure was measured in the femoral artery.

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 [3]. The acid–base balance and the partial oxygen pressure in samples of arterial blood and CSF were determined by the ABC-1 apparatus.

EXPERIMENTAL RESULTS

Ornid was given in a dose of 10 mg/kg, at which its sympatholytic properties are clearly manifested. Experiments in which the volume velocity of the cerebral blood flow was recorded with the aid of ^{133}Xe showed that, after intravenous injection of Ornid in the above dose, the blood supply to the brain was reduced. Consistent results were obtained in experiments with electromagnetic recording of the inflow of blood into the brain through the carotid artery. Under the influence of Ornid, the intracranial blood flow was reduced on average by 38 ± 5.2%. This effect of Ornid came on immediately after its administration (Fig. 1). Restoration of

---

Laboratory of Pharmacology of the Nervous System, Institute of Pharmacology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR V. V. Zakusov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 87, No. 5, pp. 427-429, May, 1979. Original article submitted May 12, 1978.

 0007-4888/79/8705-0440$07.50

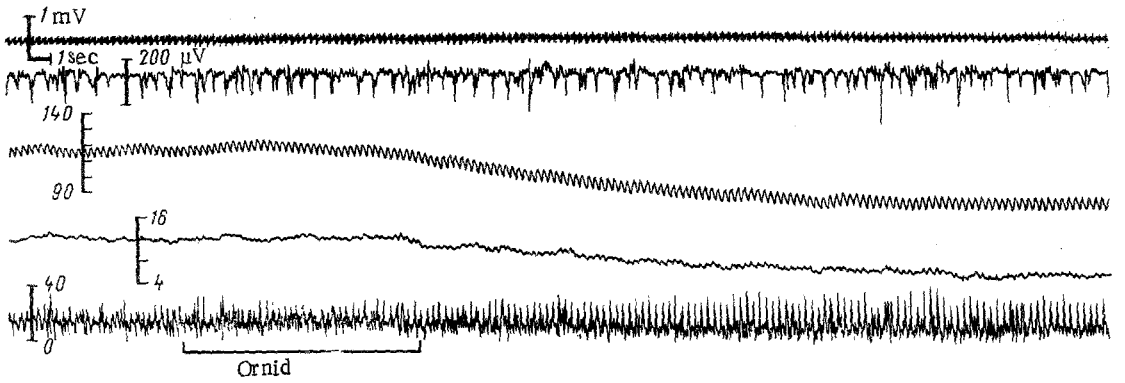

Fig. 1. Changes in cerebral blood flow under the influence of Ornid (10 mg/kg, intravenously). From top to bottom: ECG in lead II, EEG from parietal region, arterial pulse pressure (in mm Hg), and averaged and phasic blood flow in carotid artery (in ml/min).

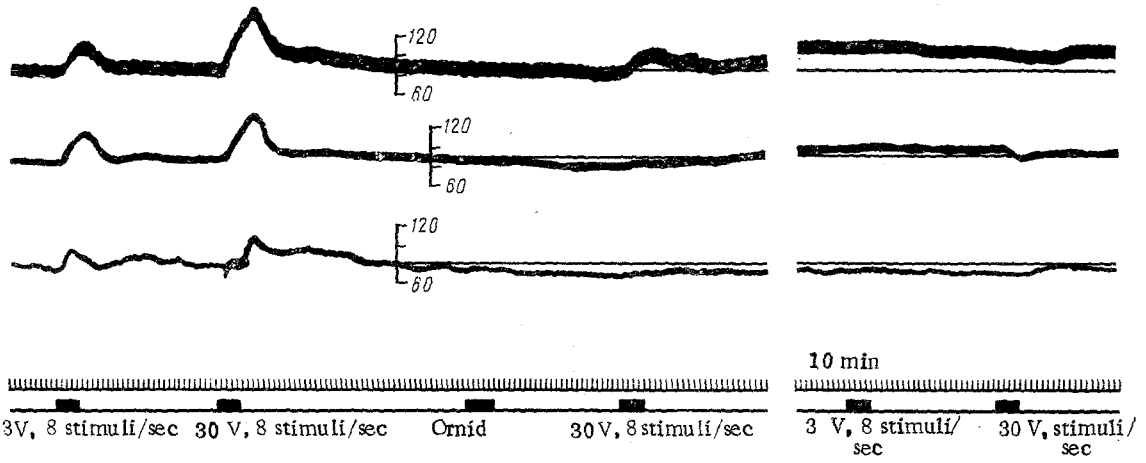

Fig. 2. Effect of Ornid (10 mg/kg, intravenously) on changes in resistance of cerebral vessels induced by electrical stimulation of cervical sympathetic trunks below stellate ganglia. From top to bottom: perfusion pressure in internal maxillary arteries, and in vertebral arteries, arterial pressure, time marker (5 sec), and marker of stimulation and injection of Ornid.

the original level of the cerebral circulation was not observed at any time during the experiment (for 60-120 min). In most experiments Ornid, after transient hypotension, caused the blood pressure to rise considerably. The initial level of the systemic arterial pressure was restored 60-80 min after administration of the drug. In some experiments the hypertensive response was almost completely absent, and the arterial pressure fell gradually under the influence of Ornid.

To detect differences in the action of Ornid on the arterial system a special series of experiments was carried out by the method of separate bilateral perfusion of the carotid and vertebral arteries. These experiments showed that after intravenous injection Ornid caused a transient decrease in tone of the cerebral vessels in the arterial systems studied. This was followed 2-3 min after injection of the drug by an increase in the resistance of the intracranial arteries to the blood flow. At the same time the systemic arterial pressure was increased. Restoration of the original level of cerebrovascular tone and arterial pressure was observed 20-50 min after injection of Ornid.

Ornid has no effect on the acid–base balance in the arterial blood and CSF. No changes were found in pH, pCO_2, pO_2, of the percentage of oxyhemoglobin in the arterial blood 3 and 30 min after intravenous injection of Ornid in a dose of 10 mg/kg. After administration of Ornid no changes likewise were found in pH, pCO_2 and pO_2 in samples of CSF taken at the same time intervals.

To study the effect of Ornid on nervous regulation of the cerebral circulation, its action was studied on constrictor responses of the cerebral vessels to stimulation of sympathetic nerves (3-30 V, 2-8 stimuli/sec, 1 msec) and afferent fibers of somatic nerves (10-40 V, 20-40 stimuli/sec, 1 msec). These experiments showed that Ornid completely blocks the decrease in the inflow of blood into the brain and the increase in tone of the intracranial vessels observed during stimulation of the cervical sympathetic nerves (Fig. 2). The inhibitory effect developed in the course of the first few minutes after injection of the drug and lasted until the end of the experiments (180-200 min). In a dose of 10 mg/kg, Ornid also completely blocked reflex responses of the cerebral vessels in the territory of the carotid arteries and in the vertebral arterial system induced by electrical stimulation of somatic afferent fibers. Meanwhile reflex responses of the arterial pressure were inhibited. This effect was observed 5-10 min after injection of Ornid against a background of raised cerebrovascular tone and hypertension. Restoration of the cerebrovascular reflexes and the pressure response of the arterial pressure was not observed at any time during the experiment (120-180 min).

The action of Ornid also was investigated in experimental cerebrovascular disorders caused by intraventricular injection of KCl [4]. When injected intravenously in a dose of 10 mg/kg 20-40 min before KCl, Ornid weakened spasms of the cerebral vessels caused by the action of KCl on the CNS. Ornid also possesses a therapeutic property: It reduced cerebrovascular tone and the arterial pressure, raised as the result of intraventricular injection of KCl.

Ornid thus reduces the volume velocity of the cerebral blood flow and increases the resistance of the intracranial vessels. The vasoconstrictor effect of Ornid is evidently due to its ability not only to block adrenergic influences, but also to liberate noradrenalin. Ornid also has a marked effect on nervous regulation of the cerebral circulation. It inhibits constrictor reaction of the cerebral vessels to stimulation of sympathetic and somatic nerves and also has a protective effect against experimental disturbances of the cerebral circulation of adrenergic nature. The absence of any changes in the acid—base balance in the CSF after administration of Ornid rules out any possibility that the action of Ornid on the cerebral circulation is effected indirectly through the pH of the CSF.

LITERATURE CITED

1. N. K. Bogolepov, Cerebral Crises and Stroke [in Russian], Moscow (1971).
2. A. P. Meier, K. D. Kalantarov, V. A. Volkov, et al., Med. Radiol., No. 10, 21 (1973).
3. R. S. Mirzoyan, Fiziol. Zh. SSSR, No. 6, 966 (1973).
4. R. S. Mirzoyan, Byull. Éksp. Biol. Med., No. 11, 50 (1975).
5. R. S. Mirzoyan, A. V. Runov, Yu. M. Varentsov, et al., Byull. Éksp. Biol. Med., No. 2, 48 (1975).
6. L. Edvinsson and E. T. MacKenzie, Pharmacol. Rev., 28, 275 (1976).
7. D. H. Ingvar and N. A. Lassen (Editors), Acta Neurol. Scand., Suppl. 64, 56 (1977).
8. N. A. Lassen, Circ. Res., 34, 749 (1974).