EXPERIMENTAL STUDY OF THE SOVIET ANESTHETIC AGENT INHALAN (METHOXYFLUORANE)

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Experiments on dogs, cats, and rabbits showed that the Soviet general anesthetic inhalan, which is identical with the Western product pentrane (methoxyfluorane), can provide safe and easily controlled anesthesia with minimal depression of the vital functions.

Because of its noninflammable and nonexplosive properties, because of its marked anesthetic and analgesic effects, the low risk of overdosage, and the stability of the hemodynamics during anesthesia, methoxyfluorane has gained wide popularity [1-5].

In 1967, at the writers' suggestion, E. K. Tsirul' synthesized a compound identical with methoxyfluorane which is now produced in the Soviet Union under the name inhalan. Inhalan (2,2-dichloro-1,1-difluoro-ethylmethyl ester) is a colorless liquid with a pleasant fruity odor. Its specific gravity is 1.4, boiling point 104°C, and vapor pressure 25 mm Hg at 20°C. When mixed with air and oxygen it is noninflammable and nonexplosive. The compound is chemically stable and it is compatible with soda-lime.

The object of this investigation was to study experimental anesthesia using inhalan.

EXPERIMENTAL METHOD

In 40 acute experiments on dogs, rabbits, and cats, the clinical manifestations of inhalan anesthesia were studied. The EEG (fronto-occipital lead), ECG (lead II), and intra-aortic pressure were recorded on a polygraph. The dogs were anesthetized by the endotracheal method using the UNA-1 anesthetic apparatus, while cats and rabbits were anesthetized by means of a special inhaler. The cardiac output was determined by the thermodilution method with graphic recording of the dilution curve on the Mingograph-81 apparatus. The concentration of inhalan in the arterial blood was determined by infrared spectrometry on a type UR-10 spectrograph.

EXPERIMENTAL RESULTS

Inhalan produced anesthesia of any desired depth in experiments on the various species of animals. The period of habituation of the animal to the odor of the compound usually passed smoothly if the concentration of the anesthetic agent was gradually increased. The stage of excitation was short in duration. In the surgical stage of anesthesia the pupils were narrow and did not react to light, breathing was regular and deep, and the arterial pressure was 15-20 mm below its initial value. The animals tolerated the anesthesia well in this stage for as long as 4-5 h. With deepening of the anesthesia, respiration was gradually and slowly depressed. During artificial ventilation of the lungs, the most convenient and valuable criterion of overdosage was the gradual fall of arterial pressure. Dilatation of the pupils was observed only in the late stages of overdosage of the anesthetic.

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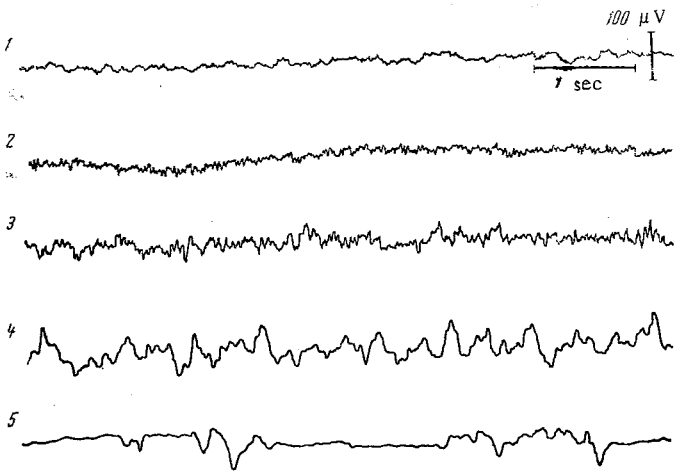

Fig. 1. Effect of methoxyfluorane (inhalan) on the dog EEG: 1) initial EEG; 2) EEG associated with methoxyfluorane concentration in the arterial blood of 6 mg %; 3) EEG with concentration 16 mg %; 4) EEG with concentration 27 mg %; 5) EEG with methoxyfluorane concentration in arterial blood 38 mg %.

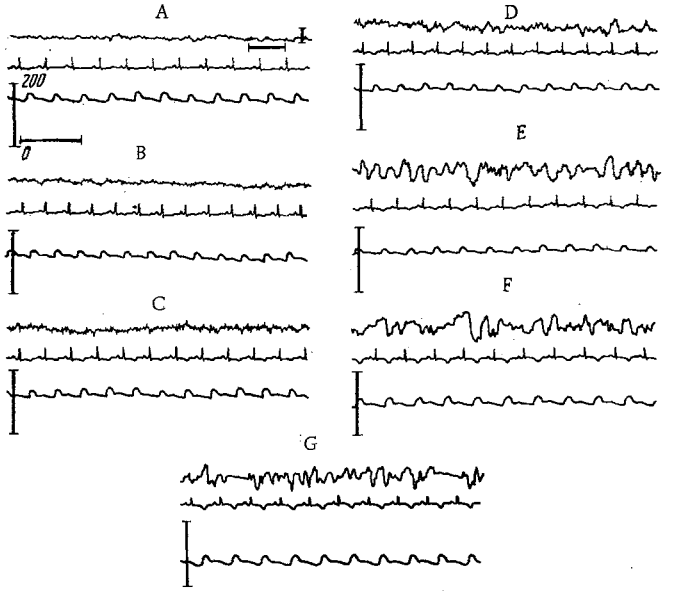

Fig. 2. Effect of methoxyfluorane on EEG, ECG, and intra-aortic pressure of a dog. A) From top to bottom: initial EEG, ECG, intra-aortic pressure; B) 10 min after beginning of anesthesia; C) in surgical stage of anesthesia; D) 30 min; E) 50 min; F) 60 min after beginning of anesthesia; G) EEG, ECG, and intra-aortic pressure 80 min after beginning of anesthesia with vaporizer completely open.

In 30 experiments the EEG was recorded. The initial EEG of the dogs consisted of waves with a frequency of 20-27/sec and amplitude 15-20 μV (Fig. 1). The amplitude of the waves increased to 20-30 μV 4-5 min after the beginning of anesthesia, with no significant change in their frequency. The concentration of anesthetic in the arterial blood was then 4-6 mg %. On further saturation of the animal with the compound a gradual increase in amplitude of the EEG waves to 40-60 μg and a simultaneous decrease in their frequency to 16-18/sec were observed. This period of anesthesia corresponded to the surgical stage. The

blood inhalan concentration was then 10-16 mg %. When the concentration of the compound in the arterial blood was 20-30 mg % the frequency of the EEG waves fell to 4-6/sec and their amplitude increased further to 90-110 μV. When the inhalan concentration reached 35-45 mg % periods of isoelectric "silence" appeared on the EEG, and these gradually increased in duration and were converted into complete depression. These changes were reversible in character and disappeared when the animal came around from the anesthetic.

In ten experiments the intra-aortic pressure was recorded (Fig. 2). In the surgical stage of anesthesia the pressure fell by 15-25 mm. As the depth of anesthesia increased, the pressure gradually fell. In five experiments on dogs the cardiac output was measured by the thermodilution method. In the surgical stage of anesthesia the decrease in cardiac output did not exceed 20% of the original level. As the anesthesia deepened a further decrease in the cardiac output was observed. No irregularity of the cardiac rhythm developed during inhalan anesthesia. Only with an overdosage of the anesthetic in dogs was the positive T wave transformed regularly into negative. The absence of such changes in the experiments on cats and rabbits, and also in man, suggests that these changes in the ECG are a specific feature of the action of inhalan on the dog's heart.

Inhalan is compatible with all muscle relaxants in common use (tubocurarine, diplacin, succinylcholine derivatives). On simultaneous administration of inhalan and tubocurarine to rabbits, the effect of the latter as regards its duration was increased by 50-100% compared with a combination of ether and tubocurarine. In view of the fact that the anesthetic agent contains halogen atoms in its molecule, its combined administration with adrenergic stimulants was investigated. Adrenalin and noradrenalin in doses of 0.01 and 0.002 mg/kg, given by intravenous and intra-arterial injection during deep inhalan anesthesia, caused serious disturbances of the cardiac rhythm in dogs: ventricular tachycardia and ventricular fibrillation. Injection of ephedrine and phenylephrine, producing a persistent elevation of the arterial pressure, was not accompanied by the onset of arrhythmia.

In experiments on animals inhalan (methoxyfluorane) thus provides safe and controllable anesthesia with minimal depression of the vital functions in the surgical stage of anesthesia.

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