THE EFFECT OF β-MERCAPTOPROPHYLAMINE ON THE CARDIOVASCULAR SYSTEM AND THE MORPHOLOGICAL COMPOSITION OF PERIPHERAL BLOOD

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V. A. Kozlov*

(Presented by Member of the Academy of Medical Sciences of the USSR N. N. Zhukov-Verezhnikov)
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Radiation pathology comprises a complex of different disorders, the most important of which are disturbances of the cardiovascular system and the development of the hemorrhagic syndrome.

The aim of this work was to study the effect of one of the representatives of the aminothiol group, β-mercaptopropylamine (MPA) which has a pronounced protective action in acute radiation sickness [1-11] on the function of the cardiovascular system, the peripheral blood, and the strength of the blood capillaries.

EXPERIMENTAL METHODS AND RESULTS

Experiments were made on nonirradiated rabbits, guinea pigs, cats, rats, and frogs. The doses of MPA were calculated on the basis of the hydrochloride of the preparation.

To study the action of MPA on the heart of male winter frogs (Rana temporaria) isolated by the method of Straub, the contractions of the heart were recorded on the smoked paper of a kymograph. The MPA was used in dilutions of 1 : 250,000, 1 : 10,000, 1 : 1000, 1 : 500, and 1 : 100.

At a concentration of 1 : 250,000 the preparation increased the amplitude of contractions of the isolated heart with a simultaneous increase in the frequency of the rhythm. Five minutes after the end of perfusion with the MPA solution, heart activity was restored to its initial state. Weakening of the systole was hardly discernible and there was no significant change in the rhythm of heart contractions with 1 : 10,000-1 : 1000 solutions. When the concentration of the preparation was increased to 1 : 500 the amplitude of heart contractions was reduced and the rhythm increased somewhat in frequency. Perfusion of the heart with a 1 : 100 solution resulted in diastolic arrest of the heart.

The action of MPA on respiration and blood pressure was studied in acute trials on 10 rabbits and 7 cats narcotized with urethane. Pressure in the common carotid and respiration were recorded on a kymograph. MPA was injected into the vena femoralis. In all trials the dose of the preparation was 30 mg/kg.

When MPA was injected into rabbits there was a brief and minor fall in arterial pressure of 20-30 mm. When blood pressure was reduced, respiration ceased temporarily, and then the amplitude increased and the rhythm of respiratory movements increased in frequency. Respiration was restored to its initial level after 2-3 min.

After the phase of reduction in blood pressure, the preparation had a marked pressor effect in cats. Arterial pressure increased by 50-60 mm and a return to the initial level was noted after 5 min. The brief initial increase in pressure is not specific, as it is also observed when physiological solution is injected. G. S. Liberman (quoted in [8]) observed a similar reaction to the injection of 100 mg MPA per kg in trials with cats.

Disconnection of the sinocarotid reflexogenic zone in rabbits (lubrication with a 10% phenol solution) did not eliminate the hypotensive effect observed when MPA was injected. The changes in respiration were however less pronounced.

Resection of the vagi in rabbits and cats did not change the hypotensive reaction to injection of MPA but did reduce the pressor effect (Fig. 1). If, on injection of the preparation, the arterial pressure in cats increased by 50-

* Moscow.

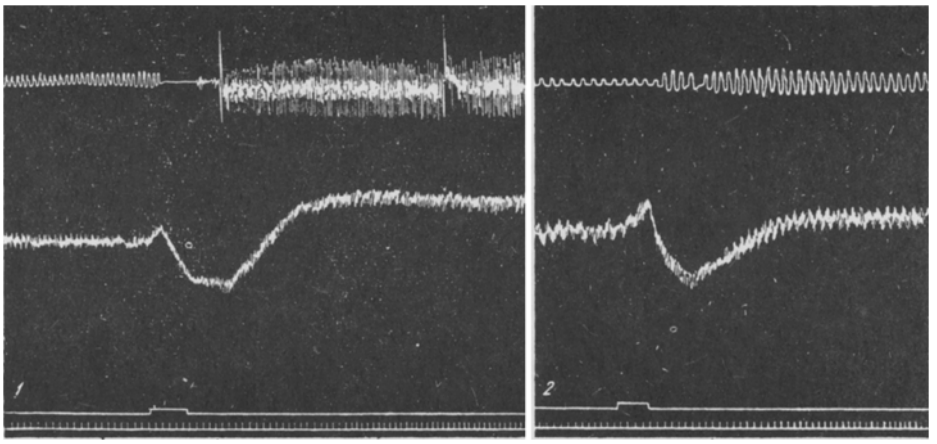

Fig. 1. Effect of intravenous injection of 30 mg MPA per kg on respiration and blood pressure after bilateral vagotomy (cat weighing 2.8 kg). 1) MPA; 2) MPA after vagotomy.

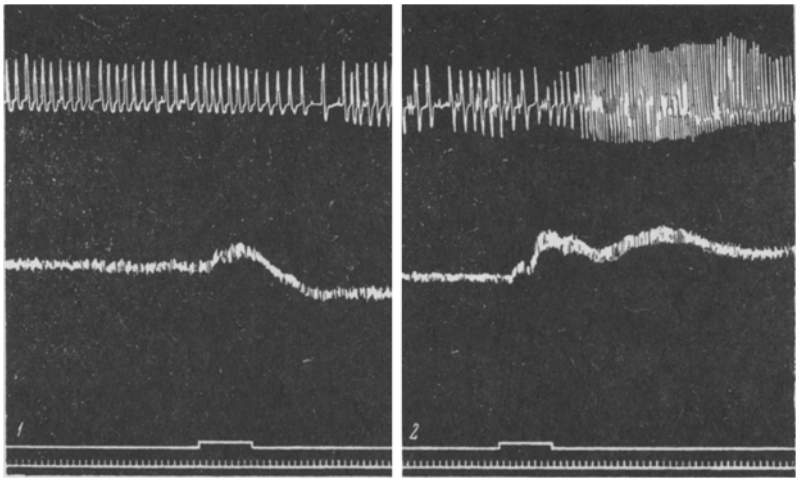

Fig. 2. Effect of intravenous injection with MPA at a rate of 30 mg/kg on respiration and blood pressure of an animal narcotized with atropine (cat weighing 2,4 kg). 1) MPA; 2) MPA after preliminary inspection of atropine (5 mg/kg).

60 mm, after resection of both vagi it rose by only 10-15 mm. Moreover, vagotomy clearly reduced the stimulation of respiration caused by the preparation.

Following blocking of the interoceptors of the vessels in cats by Novocain at a rate of 10 mg/kg there was a monophasic reaction of the arterial pressure to injection of MPA. A hypotensive reaction was observed similar to that in preserved innervation, although the fall in blood pressure was sometimes less. Increases in blood pressure after its initial fall were not noted in these experimental conditions.

Preliminary administration of atropine to the animals completely prevented the hypotensive reaction to MPA; in cats given atropine there was only an increase in blood pressure accompanied by marked stimulation of respiration (Fig. 2).

In a study of the effects of MPA on blood, changes in the morphological composition of the blood (estimation of leukocyte, erythrocyte and thrombocyte counts), the percentage content of hemoglobin, the erythrocyte sedimentation rate,and the coagulation time of blood were considered.

The studies were on guinea pigs of both sexes by standard methods. Blood coagulation rate was estimated on a paraffined slide by the time of cessation of movement of the drop. The trials were in summertime at a room air

temperature of 21 ± 1°. The MPA was given by intravenous injection at a rate of 100 mg/kg. Blood was studied 1, 2½, 4, 6, and 24 h after injection.

The results showed no significant change in the leukocyte, erythrocyte, and thrombocyte counts, Hb content, and erythrocyte sedimentation rate after injection with MPA. However, blood coagulation which before injection with MPA occurred after 170 ± 3.1 sec, was considerably accelerated after injection. One hour after injection with MPA the blood coagulation time was 140 ± 5.7 sec, after 2½ h it was 103 ± 4.4, after 4 h 136 ± 4.9, and after 6 h 81 ± 11.3 sec.

The effect of MPA on capillary strength was studied in trials with male rats. Capillary strength was determined by the following method. The experimental animals were injected intraperitoneally with MPA at a rate of 300 mg/kg. After 15 min the abdominal cavity was opened up under ether narcosis and for 3 min the upper mesenteric vein was constricted with metal clamps. After 15, 45, 60, 120, and 180 min the number of petechiae in the whole mesentery was calculated. Capillary strength was evaluated by the number of hemorrhages formed. The control animals were not injected with MPA.

It was found that after only 15 min after injection with MPA the number of petechiae in rats given the preparation was almost 1½ times less than in controls. The number of hemorrhages was lowest after 45 min. The increase in capillary strength was noted during the first hour after injection with MPA; at later stages no significant difference between experimental and control animals was noted.

The results of the trials on the isolated heart of frogs showed that in low concentrations (1 : 250,000) the preparation increased the amplitude of contractions of the isolated heart and in high concentrations (1 : 500) reduced it with simultaneous increase in frequency of the rhythm and diluted 1 : 100 arrested the heart in the diastole.

The action of MPA on the cardiovascular system and respiration of rabbits was shown by a short-term fall in blood pressure and stimulation of respiration.

The character of change in arterial pressure of cats was biphasic, at first a reduction, then an increase.

The depressor action of the preparation was apparently due to stimulation of the M-choline-reactive systems, as with preliminary administration of atropine there was as a rule no hypotensive reaction caused by injection with MPA. The degree of reduction in blood pressure is also reduced following blocking of the interoceptors of the circulatory vessels by Novocain.

The pressor effect observed in the trials with cats after the phase of reduction in blood pressure weakened, intersecting the vagi, or completely removed the blocking of the interoceptors of the vessels with Novocain. It may be assumed that a role in the pressor reaction is played by stimulation by the preparation of the N-choline-reactive systems of the vascular reflexogenic zones and related formations.

From the differences in results obtained in trials with cats, in which there are chemoreceptors in the aortal region, and with rabbits in which there are no chemoreceptors in that region, it may be concluded that the changes in arterial pressure are associated mainly with stimulation of chemoreceptors of the karyoaortal region.

The stimulation of respiration may be explained by reflexes with the carotid-glomeruli, the choline-reactive systems of which are selectively stimulated by this preparation. The lower stimulatory action of MPA on respiration after disconnection of the sinocarotid reflexogenic region and in vagotomized animals supports this hypothesis.

In granting an important role to the reflector mechanisms in the reaction of arterial pressure and respiration to the injection with MPA, we do not rule out a direct influence of the preparation on the vasomotor and respiratory centers.

In our view, the capacity of MPA to increase blood coagulability and to reduce the permeability of the walls of the circulatory vessels deserve attention. This action of MPA is directly related to one of the most severe manifestations of radiation sickness, the development of the hemorrhagic syndrome.

SUMMARY

Beta-mercaptoprophylamine (MPA) in small concentrations causes an increase in the amplitude of contractions of an isolated heart, and in large concentrations – a decrease with a simultaneously rising rhythm frequency; in a 1 : 100 dilution it causes stoppage of the heart in the diastole.

The effect of MPA on the cardiovascular system and respiration in rabbits was manifested by a brief lessening of the blood pressure and stimulation of respiration. Cats were found to have a biphasic character of an arterial pressure change: at first a decrease and then an increase.

The depressor effect of the preparation is offset by preliminary atropinization. The pressor effect was lessened by serving the vagus nerves.

MPA does not produce a substantial influence on the morphological composition of the peripheral blood, hemoglobin level and, ESR but accelerates clotting of the blood and increases the strength of capillaries.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of the first issue of this year.
