ANALYSIS OF THE MECHANISM OF THE THERAPEUTIC ACTION OF HYPERBARIC OXYGEN IN POISONING BY ORGANOPHOSPHORUS COMPOUNDS

N. V. Savateev, V. D. Tonkopii, L. M. Brestkina, and A. E. Gromov

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Experiments on rabbits showed that acute poisoning with paraoxan leads to the development of hypoxia with a rapid fall in the oxygen tension in the muscles and venous blood and a shift of the acid-base balance toward uncompensated metabolic acidosis. Administration of oxygen under a pressure of 3 atm for 2-4 h considerably prolonged the survival of the poisoned animals. Hyperbaric oxygen caused the oxygen tension in the muscles and venous blood to rise but without restoring the disturbed acid-base balance to normal.

In acute poisoning with organophosphorus compounds hypoxia develops [1, 5, 7]. The use of artificial respiration or inhalation of an oxygen–air mixture under these conditions abolishes the arterial hypoxemia but has no effect on the oxygen lack in the tissues and venous blood [5, 6].

The writers showed previously that administration of oxygen under a pressure of 3 atm to rats with acute dipteryx poisoning alleviated the course of the poisoning and increased the survival rate of the animals.

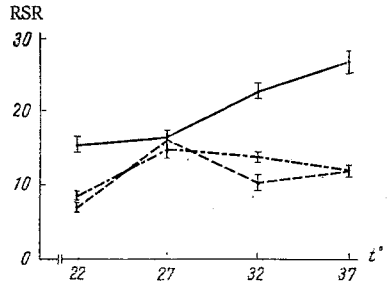

Fig. 1. Changes in pO_2 in muscle of a rabbit poisoned with paraoxan (1), of an intact rabbit exposed to hyperbaric oxygen (2), and of a poisoned rabbit exposed to hyperbaric oxygen (3). Abscissa, time (in min); ordinate, pO_2 (in relative units).

The object of this investigation was to study the mechanism of the therapeutic action of oxygen under pressure in hypoxia caused in animals by acute poisoning with paraoxan.

EXPERIMENTAL METHOD

Experiments were carried out on 32 rabbits. Paraoxan was injected intramuscularly in doses of 0.25 and 0.5 mg/kg.

The partial oxygen pressure (pO_2) in a muscle of the hind limb was recorded by means of a solid platinum electrodes; the anode was a Ag–AgCl plate fixed to the animal's ear. The parameters were recorded on a type OH 101/1 Hungarian polygraph. The value of pO_2 was determined in relative units, taking pO_2 in the muscle of an unpoisoned animal as 100. To determine pO_2 in the venous blood a model ABC-1 micro-Astrup apparatus was used with a closed Clark's electrode. The acid-base balance was investigated by means of the same apparatus. The values of the partial CO_2 pressure (pCO_2), the base excess/deficit (BED), standard bicarbonate (SB), and buffer base (BB) were calculated from the Siggaard-Andersen monogram.

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TABLE 1. Changes in Acid-Base Balance and pO_2 in Venous Blood of Rabbits after Poisoning with Paraoxan in Dose of 0.25 mg/kg

State of animals	pO_2 (in mm Hg)	pH	BED	BB	SB	pCO_2 (in mm Hg)
		meq/liter				
Normal	30±2,5	7,4±0,22	2,12±0,88	53,2±4,2	23,6±2,5	35,8±4,4
Agony	3,6±0,95	6,91±0,03	25,4±2,04	23,64±1,5	8,4±0,4	49,4±3,2

TABLE 2. Changes in pH and pO_2 in Venous Blood of Rabbits after Poisoning with Paraoxan in Dose of 0.25 mg/kg and Exposure to Hyperbaric Oxygen (3 atm)

Index	Normal	Poisoned animals (in h)		
		½	1½	3
pH	7,37±0,002	6,72±0,08	6,77±0,09	6,89±0,08
PO_2	28,6±1,96	13,6±1,16	19,2±1,65	17,6±1,12

Note. Rest of indices of acid-base balance not calculated because of very low pH values.

The animals were placed in a 100-liter pressure chamber immediately after receiving the poison,and they remained there in an atmosphere of oxygen under a pressure of 3 atm for 2-4 h. To remove the excess of carbon dioxide the chamber was constantly ventilated with pure oxygen. The value of pO_2 in the muscle was recorded before poisoning and continuously thereafter until death of the animals in the control, and in the experimental animals throughout their stay in the chamber.

Blood for analysis was taken from the femoral vein, for venous blood reflects better than arterial the composition of the intercellular fluid and the level of oxidation in the tissues [2, 8]. Blood samples from animals exposed to the effects of oxygen compression were taken 30, 90, and 180 min after they were taken out.

EXPERIMENTAL RESULTS

The rabbits of the control group developed convulsions 6-7 min after receiving the injection of paraoxan in a dose of 0.5 mg/kg, and death occurred on the average 15 min after the injection. The period of survival of the animals placed in the pressure chamber was increased to 1.5-2 h ($P < 0.01$). Convulsions occurred at the same times as in the control animals and they lasted 30 min, after which the animals fell into a coma. All the animals died a few minutes after their removal from the pressure chamber.

In a dose of 0.25 mg/kg paraoxan caused death of the animals on the average after 28 min. The use of hyperbaric oxygen prolonged the survival of the rabbits from 3 h to 1.5 days.

In the control rabbits poisoned with paraoxan pO_2 in the muscle fell very quickly, especially during convulsions (Fig. 1). In the intact animals exposed to oxygen at a pressure of 3 atm the value of pO_2 in the muscle was increased by 5-6 times. When the poisoned animals were placed in the pressure chamber an increase in pO_2 in the muscle was observed only during the first 3-4 min, i.e., when no signs of poisoning were present. During convulsions the character of the fall in pO_2 in the muscle was the same as in the control animals. However, the pO_2 level never fell to zero, but reached 15-20% of its initial value.

In the rabbits poisoned with paraoxan in a dose of 0.25 mg/kg the pO_2 level in the venous blood at the beginning of coma was lowered by 10 times (Table 1). During exposure to hyperbaric oxygen pO_2 in the venous blood fell by only half of its normal value (Table 2).

Acute poisoning of the animals with paraoxan thus led to the development of severe hypoxia. The low oxygen partial pressure in the muscle and in the venous blood was evidence of the predominance of a circulatory type of hypoxia, which developed as the result of slowing of the blood flow and disturbance of the permeability of the vessel wall [6]. The use of hyperbaric oxygen under these conditions prevented pO_2 in the muscle and in the venous blood from falling to the critical level. However, the severity of the disturbances in paraoxan poisoning was evidently so great that essentially no compensation of the hypoxia occurred.

Severe acidosis (Table 2), mixed (metabolic and respiratory) in character, was found in the venous blood of the control and experimental animals. The increase in the partial CO_2 pressure during paraoxan poisoning was due to the inadequate pulmonary ventilation, which developed as a result of bronchospasm and severe inhibition of the respiratory center [3]. Such marked changes in the acid-base balance were evidently connected with the appearance of an excess of nonvolatile acids, which accumulate in marked hypoxia, in the blood stream [11].

An organism can live only within a very narrow range of fluctuations of pH, not more than ± 0.3 [8, 9]. Despite the fact that in the poisoned animals exposed to hyperbaric oxygen the changes in pH were considerably larger, the period of their survival was significantly prolonged. This is understandable, for hyperbaric oxygen sharply increases the amount of dissolved oxygen in the blood plasma. However, in severe circulatory hypoxia this did not lead to restoration of the normal acid-base balance and it did not alter the outcome of the poisoning.

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