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POSTINTOXICATION HYPOTHERMIA AND FREE-RADICAL LIPID OXIDATION IN THE BRAIN AND HEART OF RATS POISONED WITH ORGANOPHOSPHORUS CHOLINESTERASE INHIBITORS

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UDC 616.831+616.12]-008.939.15-39-02:615.217.32]-092.9

KEY WORDS: intoxication; carbophos (malathion), armin, hypothermia, lipid peroxidation.

The aim of this investigation was to study the role of lipid peroxidation (LPO) in the realization of the toxic effects of organophosphorus compounds (OPC).

EXPERIMENTAL METHOD

Experiments were carried out on rats poisoned experimentally with two cholinesterase inhibitors: carbophos (malathion, M) and armin (A), The toxic compounds were given to experimental Wistar rats weighing initially 200-220 g, in a dose of LD_{50} (260 and 1 mg/kg respectively), Healthy animals constituted the control group. The animals were under observation for 30 days after poisoning. Biochemical tests were carried out on the cerebral hemispheres and myocardium Lipids were extracted from homogenates of rat organs during the period from 2 to 30 days after poisoning [4]. Conjugated dienes (CD) were determined spectrophotometrically [5]. Schiff's bases (SB) were determined by a spectrofluorometric method [6]. The temperature in the rats' esophagus was measured by a TPÉM-I electrothermometer. The results were subjected to statistical analysis by Student's t test.

EXPERIMENTAL RESULTS

The experimental results show activation of LPO in the rats' organs in the postintoxication period of poisoning by M and A. This is confirmed by an increase in the content of CD and SB in the cerebral hemispheres and myocardium (Tables 1 and 2). Maximal accumulation of CD in the brain of rats poisoned by M was observed 2, 14, and 21 days after poisoning. At the same time, the maximal increase in CD and SB levels in the brain and myocardium of the rats after poisoning with A was observed after 14 days (Table 2).

Malathion caused hypothermia, as shown by lowering of the esophageal temperature of the poisoned rats. Potentiation of the hypothermic reaction was noted after 14 and 21 days of the experiment (Table 1).

Thus the times of maximal accumulation of CD and SB in the organs of the poisoned rats and the severity of the hypothermic reaction coincided. Armin also evokes a hypothermic reaction, as shown by lowering of the esophageal temperature of the poisoned rats. The maximal fall of temperature was observed after 14 days of the postintoxication period (Table 2). Thus on a model of armin, just as with the action of M, a similar agreement was observed

Bashkir State Medical Institute, Ufa. (Presented by Academician of the Academy of Medical Sciences V. A. Negovskii.) Translated from Byulleten' Éksperimental'nol Biologii i Meditsiny, Vol. 113, No. 5, pp. 493-494, May, 1992. Original article submitted March 12, 1991.

 0007-4888/92/0005-0664$12.50

TABLE 1. Content of LPO Products in Brain and Heart and Changes in Esophageal Temperature of Rats Poisoned with Malathion (M ± m)

Test objects (parameters)	Days of experiment							
	1	2	6	14	16	21	25	30
	Conjugated dienes (D_{232})							
Cerebral hemisphere	0,32±0,02*	0,47±0,04*	0,28±0,02*	0,59±0,06*	0,36±0,02*	0,52±0,04*	0,28±0,02*	0,20±0,01
Myocardium	0,81±0,08*	1,10±0,10*	0,52±0,04*	1,41±0,1*	0,70±0,07*	1,06±0,07*	0,51±0,05*	0,34±0,02
	Schiff's bases (F)							
Cerebral hemisphere	0,19±0,02	0,25±0,02*	0,40±0,01*	0,34±0,02*	0,30±0,03*	0,40±0,02*	0,24±0,02*	0,20±0,02
Myocardium	0,41±0,02	0,51±0,07	1,22±0,22*	1,04±0,66*	0,61±0,06*	1,10±0,14*	0,47±0,07	0,37±0,03
	Esophageal temperature (X/X_0)							
Myocardium	0,99±0,01	0,99±0,01	0,97±0,01	0,96±0,01*	0,99±0,01	0,96±0,01*	0,99±0,01	0,99±0,01

Legend. Here and in Table 2, asterisk indicates data for which $p < 0.05$ compared with intact rats; D_{232} denotes extinction at maximum of absorption of CD (232 nm), F denotes intensity of fluorescence (relative units); X_0 = 36.8 ± 0.03°C

TABLE 2. Content of LPO Products in Brain and Heart and Changes in Esophageal Temperature of Rats Poisoned with Armin (M ± m)

Test objects (parameters)	Days of experiment							
	1	2	7	14	18	21	25	29
	Conjugated dienes (D_{232})							
Cerebral hemisphere	0,20±0,01	0,24±0,04	0,22±0,03	0,45±0,05*	0,26±0,05	0,23±0,03	0,19±0,01	0,18±0,01
Myocardium	0,40±0,02	0,42±0,03	0,44±0,03	0,74±0,08*	0,51±0,06*	0,41±0,02	0,38±0,01	0,38±0,01
	Schiff's bases (F)							
Cerebral hemisphere	0,17±0,02	0,19±0,02	0,22±0,03	0,42±0,04*	0,29±0,03*	0,21±0,03	0,20±0,02	0,19±0,02
Myocardium	0,39±0,04	0,40±0,04	0,43±0,03	0,71±0,04*	0,52±0,05	0,44±0,03	0,40±0,04	0,40±0,04
	Esophageal temperature (X/X_0)							
Myocardium	0,98±0,01	0,99±0,01	0,98±0,01	0,95±0,01*	0,98±0,01	0,98±0,01	0,99±0,01	1,00±0,01

between the severity of hypothermia and the increase in concentration of LPO products. We know that OPC affects metabolism of brain phospholipids through hypothermia. Since the immediate cause of the hypothermia is hypoxia – the leading pathogenetic mechanism [1] of poisoning, it was concluded that the effect of OPC on phospholipid metabolism is nonspecific in character, and is mediated through hypothermia [2]. A comprehensive study of the effect of OPC on lipid metabolism in the whole brain, brain stem, and cerebral cortex revealed a decrease in the concentration of polar lipids, including phospholipids [3]. The essential fact is that this decrease was observed in the case when a whole complex of disturbances was clearly apparent here, and connected with excitation of the cholinergic mediator mechanism (convulsions etc.), i.e., in the toxicogenic phase of poisoning. It can be concluded from the results of these investigations that OPC may have a modifying action on the lipids of the brain and heart through hypothermia in the postintoxication period, by activation of free-radical mechanisms of their oxidation.

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