CONTENT OF NICOTINAMIDE COENZYMES IN THE LIVER AND MYOCARDIUM OF RATS POISONED WITH DICHLOROETHANE

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The content of nicotinamide coenzymes in the liver and myocardium was studied in experiments on male rats 24 h after dichloroethane poisoning (0.5 ml/kg by the intragastric route). Parallel with disturbance of the morphological structure of the liver and myocardium and an increase in alanine and asparagine aminotransferase activity in the blood serum, dichloroethane was shown to reduce the concentration of nicotinamide coenzymes and to disturb the ratio between their oxidized and reduced forms in these organs.

KEY WORDS: dichloroethane; nicotinamide coenzymes.

One aspect of the toxic action of dichloroethane, as of other chlorinated hydrocarbons, is damage to the cell mitochondria [1, 8, 11]. Dichloroethane has been shown [4] to disturb oxidative phosphorylation in rat liver mitochondria.

Considering that one of the factors determining the rate and direction of oxidoreductive processes in the cell is the content of nicotinamide coenzymes and the ratio between their oxidized and reduced forms [5, 7], it was decided to study the content of these components of the respiratory chain in the liver and myocardium of rats poisoned with dichloroethane.

EXPERIMENTAL METHOD

Experiments were carried out on 66 male albino rats weighing 180-220 g. Acute poisoning was produced by administration of a single dose of a 20% solution of dichloroethane in sunflower oil (0.5 ml/kg body weight) by the intragastric route.

The rats were decapitated 24 h after poisoning and the content of nicotinamide coenzymes (NAD+ NADP and NAD · H_2 and NADP · H_2) was determined in the liver and myocardium [12]. The total content of the coenzymes was calculated as the sum of the oxidized and reduced forms and their ratio was expressed by the coefficient K.

Activity of alanine (ALT) and asparagine (AST) aminotransferases in blood serum obtained from the rats at decapitation was determined by a unified method [2]. Pieces of the organs were mounted in 10% formalin solution and examined histologically. Sections were stained with hematoxylin and eosin.

EXPERIMENTAL RESULTS AND DISCUSSION

The rats developed a picture of acute poisoning accompanied by typical symptoms [3, 6, 9] 24 h after receiving a single dose of dichloroethane by the intragastric route. Of the 38 rats poisoned, 30 survived. Marked congestion of the parenchymatous organs was observed at autopsy. Histological investigation revealed congestion of the hepatic vessels, including the smallest, with degenerative changes in the hepato-

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TABLE 1. Changes in Content of Nicotinamide Coenzymes in Liver and Myocardium of Rats 24 h after Dichloroethane Poisoning

Organ	Group of animals	No. of rats	Statistical index	Content of coenzymes (μg/g wet weight of tissue)			K
				NAD + NADP	NAD·H_2 + NADP·H_2	sum of oxidized and reduced forms	
Liver	Control	14	$M \pm m$	342±7,0	261±10,0	603±16,6	1,31±0,04
	Experimental (dichloroethane)	16	$M \pm m$	277±15,3	223±12,5	499±17,3	1,24±0,03
			P	<0,01	<0,05	<0,001	>0,1
Myocardium	Control	14	$M \pm m$	362±9,2	213±6,3	575±8,3	1,70±0,07
	Experimental (dichloroethane)	14	$M \pm m$	290±19,2	200±20,5	490±23,6	1,45±0,05
			P	<0,01	>0,1	<0,01	<0,01

cytes of the character of cloudy swelling and fatty degeneration (particularly marked in the central zones of the hepatic lobules). The stromal elements of the myocardium were edematous, the walls of the coronary vessels showed marked plasmoragia, and stasis and recent thrombi were present in the vessels.

ALT activity in the serum was increased from 0.94 ± 0.1 to 2.46 ± 0.28 μmoles pyruvate and AST activity from 0.68 ± 0.08 to 3.28 ± 0.42 μmoles pyruvate ($P < 0.001$). The greater increase in AST activity was probably attributable to the ability of dichloroethane to damage not only the liver but also other parenchymatous organs rich in this enzyme (heart muscle, kidneys). The increased activity of transamination enzymes in the blood serum was evidence of the harmful action of dichloroethane on the cell membranes, with a resultant liberation of these enzymes into the blood stream. Cellular permeability is known to depend directly on the state of metabolism as a whole and of energy metabolism in particular [8, 10].

Injury to the cell membranes could change the content of nicotinamide coenzymes in the tissues and could disturb the ratio between their oxidized and reduced forms. In fact, acute dichloroethane poisoning was accompanied by lowering of the total content of nicotinamide coenzymes in the liver on account of both oxidized and reduced forms; the ratio between oxidized and reduced forms was substantially unchanged. The content of nicotinamide coenzymes in the myocardium fell mainly on account of oxidized forms, with a consequent decrease in the ratio between oxidized and reduced forms (Table 1).

It can be concluded from these results that dichloroethane not only disturbs the morphological structure of the liver and myocardium and increases ALT and AST activity in the blood serum but also induces marked changes in the content of nicotinamide coenzymes in the liver and myocardium. Probably dichloroethane not only disturbs the oxidoreductive conversions of the coenzymes but also depresses their synthesis or stimulates their breakdown.

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