

# EFFECT OF ETHIMIZOLE ON THE CONTENT OF TRACE ELEMENTS AND METALLOPROTEINS IN FETAL ASPHYXIA

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Changes in the concentrations of iron, copper, and zinc in the blood and brain tissue, and in the ceruloplasmin and carbonic anhydrase activity, and the iron saturation of the blood serum transferrin were found in asphyxiated rabbit fetuses. Administration of ethimizole reversed the pathochemical changes in asphyxia and increased the life span of the fetuses.

Asphyxia still remains a leading cause of prenatal and postnatal mortality [5, 11]. In some clinics ethimizole has been used with success for resuscitating infants asphyxiated at birth [6, 15].

The object of this investigation was to study the effect of ethimizole (imidazolecarboxylic acid ethylamide, a Soviet analeptic) on the tissue and blood levels of trace elements and metalloproteins, the metabolism of which undergoes substantial changes in asphyxia [7, 8].

## EXPERIMENTAL METHOD

On the 29th day of pregnancy the female rabbit was placed in a constant-temperature bath. Laparotomy was performed under local anesthesia and the fetuses removed from the uterus. Fetal asphyxia was induced by ligation of the cord [14]. Ten fetuses acted as the control and asphyxia was produced in 11 fetuses. An injection of 0.3% ethimizole solution in a dose of 0.3 mg/kg body weight was given into the umbilical vessels of the 10 unasphyxiated fetuses. Finally, the same doses of ethimizole were given to 10 asphyxiated fetuses.

TABLE 1. Concentration (in mg %) of Iron, Copper, and Zinc in Blood and Brain Tissues of Rabbit Fetuses ( $M \pm m$ )

Test object	Trace element	Control	Asphyxia	Administra. of ethimizole	
				to intact fetuses	to asphyxiated fetuses
Blood	Iron	62,60±2,25	22,8±2,07	44,06±2,03	39,1±2,02
	P	—	<0,001	<0,001	<0,001
	Copper	0,14±0,04	0,17±0,004	0,19±0,01	0,15±0,02
	P	—	<0,5	<0,5	<0,5
	Zinc	5,23±0,14	0,43±0,01	0,47±0,05	0,52±0,01
	P	—	0,001	0,001	0,001
Brain	Iron	2,07±0,14	3,07±0,04	3,20±0,02	2,50±0,04
	P	—	<0,01	<0,01	<0,01
	Copper	0,27±0,02	0,38±0,01	0,27±0,01	0,34±0,02
	P	—	<0,001	<0,5	<0,001
	Zinc	1,03±0,06	1,98±0,02	1,87±0,03	2,27±0,03
	P	—	<0,01	<0,01	<0,001

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TABLE 2. Activity (in conventional units) of Metalloproteins in Blood Serum of Rabbit Fetuses ( $M \pm m$ )

Investigated characteristic	Control	Asphyxia	Administra. of ethimizole	
			to intact fetuses	to asphyxiated fetuses
Iron saturation of transferrin	$0,19 \pm 0,02$	$0,12 \pm 0,03$	$0,20 \pm 0,03$	$0,17 \pm 0,01$
$P$	—	$<0,001$	$<0,5$	$<0,5$
Ceruloplasmin	$10,1 \pm 0,04$	$8,0 \pm 0,32$	$8,3 \pm 0,40$	$7,7 \pm 0,2$
$P$	—	$<0,01$	$<0,01$	$<0,001$
Carbonic anhydrase	$1,04 \pm 0,03$	$1,36 \pm 0,04$	$1,41 \pm 0,05$	$0,79 \pm 0,06$
$P$	—	$<0,01$	$<0,01$	$<0,001$

The concentrations of iron, copper, and zinc, the ceruloplasmin activity, the iron saturation of the blood serum transferrin [1-3], and the carbonic anhydrase activity [12] were determined. The numerical results were subjected to statistical analysis [10].

## EXPERIMENTAL RESULTS AND DISCUSSION

It will be clear from the results in Table 1 that in asphyxia the serum iron concentration was reduced whereas that in the brain was increased. Injection of ethimizole into intact animals also was followed by a decrease in the iron concentration in the blood and an increase in its concentration in the brain tissue. Meanwhile, if ethimizole was injected into asphyxiated fetuses the iron concentration in the blood was lowered and in the brain increased by a smaller amount than in asphyxiated animals not receiving ethimizole.

The copper concentration in the blood was virtually unchanged in asphyxia and after injection of ethimizole. The copper concentration in the brain tissue was increased in asphyxia. With a combination of ethimizole and asphyxia the degree of this increase was reduced.

The zinc concentration in the blood was considerably reduced in asphyxia. After administration of ethimizole, whether in the absence or in the presence of asphyxia, this decrease was less marked. The zinc concentration in the brain was increased in asphyxia and after injection of ethimizole.

As the results given in Table 2 show, the iron saturation of the blood serum transferrin was reduced in the fetuses with asphyxia, but in asphyxiated fetuses receiving ethimizole it was indistinguishable from the control.

The ceruloplasmin activity was reduced in asphyxia and ethimizole did not affect the degree of this decrease. The carbonic anhydrase activity was increased in asphyxia, whereas the simultaneous injection of ethimizole prevented this change.

Changes in the activity of the metalloprotein enzymes of the blood in severe hypoxia are regarded as a manifestation of increased "working capacity" of an existing enzyme or increased synthesis of new molecules of the enzyme with corresponding changes in the concentrations of the trace elements required for its formation [13]. The movement of trace elements from the blood into the tissues may also have been aided by increased permeability of the blood-tissue barrier in asphyxia [9].

The fact that ethimizole helps to restore the normal concentrations of trace elements and activity of the metalloenzymes in the fetus with asphyxia must, in the writer's opinion, be regarded as beneficial, for the life span of fetuses in asphyxia was increased by  $5 \pm 0.4$  min by administration of ethimizole ( $P < 0.001$ ).

Since the changes in enzyme activity and trace element concentration in organs after injury take place before cell destruction [4, 12] determination of the corresponding changes must play an important role in the explanation of the genesis of asphyxia and determination of the effectiveness of its treatment, including by ethimizole administration.

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