THE EFFECT OF THE ADRENAL GLANDS ON ENZYMATIC ACTIVITY OF BLOOD AND TISSUES DURING RESUSCITATION

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With dying and clinical death profound disruption occurs in the metabolism of the organism [3, 12, 13]. Normalization of metabolic processes is favored by resuscitation [2, 18]. The positive therapeutic action of corticosteroids on reanimation is conditioned by this [7, 8, 11]. The effect of the adrenals on enzymes of blood and tissue during acute blood loss and resuscitation has not been sufficiently clarified in the literature [9], although it is known that it is the enzymatic portion of metabolism which is the most important object of neuro-hormonal regulation [6, 16].

This investigation studies the influence of the functional state of the adrenals on changes in the aldolase and glutathione content of the blood, heart and liver during resuscitation.

TABLE 1. Aldolase Activity in Blood of Cats, Resuscitated after Clinical Death Caused by Partial Blood Loss

Group of animals	No. of animals	Initial data	Resuscitation after recovery of spontaneous respiration	
			After 7 min	After 80 min
		M±m		
Intact	20	12,7±2,3	19,7±2,6 P<0,02	25,1±2,5 P<0,001
Adrenalectomized	12	14,6±3,4	14,1±2,3 P>0,05	15,9±2,6 P>0,05
Animals with autotransplanted adrenal glands	12	7,5±1,4	8,0±2,7 P>0,05	13,3±2,2 P<0,05

METHODS

Seventy cats were used in the experiment: in 44 a lethal blood loss was induced, after which they were resuscitated; 26 served as controls. Resuscitation was performed according to the complex method devised by V. A. Negovskii et al. [12]. The adrenals were removed simultaneously under operative conditions with barbamyl anesthesia (100-120 mg/kg). Adrenalectomized animals were used in the experiment 4 days post operation. During the first 3 days they were supported with cortisone (10 mg/kg/day) and salt solution.

Autotransplantation of adrenals was performed immediately after their removal. The adrenals were placed under the capsule of the upper pole of the kidney [24]. Over the first 3 days the animals received supportive doses of cortisone and salt solution. The experiments started 2 weeks after autotransplantation.

Aldolase activity of blood and tissues homogenized in physiological solution, was determined by the method of Tovarnitskii and Valuiskaya [14]; glutathione content by the method of Woodward and Frei as modified by Chulkova [15]. The index of blood glutathione was calculated with regard to the hematocrit [1].

RESULTS

Aldolase. During resuscitation in intact animals an increase in the activity of the glycolytic enzyme aldolase is noted in the blood (Table 1). A true increase in the aldolase activity of the plasma is detected immediately after resumption of spontaneous respiration. At the end of the first hour of the recovery period the aldolase content is almost twice the initial value ($P < 0.001$). In adrenalectomized animals the aldolase activity of the plasma does not change. Small doses of cortisone appear sufficient to support blood aldolase activity in adrenalectomized animals under ordinary conditions, but cannot support the necessary concentration of the enzyme in the plasma during the

the post-hypoxic period. Neither is a significant increase in plasma aldolase activity observed during resuscitation in animals with autotransplanted adrenals. After resuscitation from clinical death the plasma aldolase activity in animals with autotransplanted adrenals actually increased in comparison to the initial value ($P < 0.05$). But even after such an increase it was not higher than the level of aldolase activity observed in intact animals before phlebotomy. (see Table 1). The results of experiments on cats corresponds to data obtained earlier on experiments with dogs [8] which indicated the regulating influence of adrenal cortical hormones on plasma glycolytic enzyme activity during resuscitation.

It had been established that after adrenalectomy the activity of different enzymes in muscle and in liver decreased and that this decrease could be delayed by addition of cortisone and prednisone [22, 23, 25]. It is possible that this takes place as well in our experiments on adrenalectomized animals which have received supportive doses of cortisone, and in experiments with autotransplantation of adrenals. In these animals the aldolase activity of the myocardium and liver was the same as in animals with intact adrenals (Table 2).

Within an hour after resuscitation the tissue aldolase activity in adrenalectomized cats and in cats with autotransplanted glands had not changed significantly from the level in animals with intact adrenal glands.

Differences in enzyme content of the tissues appeared when data were compared obtained from control animals and from animals which had undergone clinical death. In animals with intact adrenals a true decrease in aldolase content was observed in the liver after resuscitation.

It is important that the drop in liver aldolase activity in intact animals develops parallel to an increase in blood aldolase activity. In this way the aldolase content in the myocardium does not actually changes, which may be expected on the basis of published data concerning the increase in aldolase levels in the blood flowing out from the heart during hypoxia [19]. The absence of changes in aldolase content of the myocardium and liver during resuscitation in animals with extirpated or autotransplanted adrenals correlates well with the absence of changes in blood aldolase activity in such animals.

Consequently, the engagement or the weakening of the corticosteroid mechanism infringes upon the hypoxic mechanism of mobilizing aldolase in the blood as an enzyme of anaerobic glycolysis. It may be proposed that the phenomenon observed has a definite pathogenetic importance in resuscitation.

Glutathione. Removal or autotransplantation of the adrenals have differing effects on tissue concentration of glutathione. In animals with autotransplanted adrenals the level of glutathione in the myocardium and liver is the same as in intact animals.

In the adrenalectomized cat the liver glutathione activity appeared greater (346 ± 25 against 239 ± 22 mg% in intact animals; $P < 0.001$). One might think that this depended on the giving of supportive doses of cortisone to the animals in the postoperative period. But an increase in glutathione activity in tissues after extirpation of the adrenals was detected in animals even without replacement corticosteroid therapy [5].

TABLE 2. Aldolase Activity in Tissue of Cats (TVE per g Fresh Tissue)

Group of animals	Heart muscle			Liver		
	Control	After 1 h post resuscitation	P	Control	After 1 h post resuscitation	P
	M±m			M±m		
Intact	1 743±112	1 520±45	>0,05	2 099±99	1 781±107	<0,05
Adrenalectomized	1 926±90	1 648±141	>0,05	2 129±103	1 881±104	>0,05
Animals with autotransplanted adrenal glands	1 633±246	1 653±126	>0,05	2 072±132	1 752±153	>0,05

Recovery from clinical death did not produce any essential change in tissue glutathione levels. Attention is brought to the fact that in animals with intact and with autotransplanted adrenals in the period of resuscitation after clinical death there is a tendency toward increase in liver glutathione content (239 ± 22 and 266 ± 26 mg% in the intact, 205 ± 26 and 229 ± 18 mg% in autotransplanted) and in adrenalectomized animals a tendency toward decrease in the level (346 ± 25 and 225 ± 35 mg%). As a result, after resuscitation differences in glutathione content disappear as observed between animals with intact and with extirpated adrenals (266 ± 26 and 322 ± 36 mg%: $P > 0.05$).

Other results are obtained with measurement of the glutathione levels in the blood (Table 3). The index of glutathione activity increases in the period of acute blood loss and remains elevated ($P < 0.01$) during the first hour of resuscitation.

As the data obtained are calculated with allowance for changes in the erythrocyte concentration, the elevation of the glutathione index may be regarded as an increase in the blood glutathione activity. The lack of correlation between indices of glutathione in blood and in tissue attests to the fact that the elevated blood glutathione level during resuscitation does not depend on its content in myocardium and liver.

The increase in blood glutathione activity during oxygen starvation is considered to be a metabolic reaction which permits hypoxia to be overcome [1, 6].

According to present concepts, glutathione has an essential role in the processes of intermediary metabolism. Data is available to show the capacity of glutathione to affect different steps in carbohydrate metabolism [19, 21].

The functional state of the adrenal glands have an important effect on this reaction.

Extirpation of the adrenals, even with subsequent addition of supportive doses of cortisone, eliminates the increase in glutathione activity upon dying and resuscitation.

The increase in glutathione content in the blood was present in sufficient degree ($P < 0.05$) in animals with autotransplanted adrenals; this to a certain degree preserved [10, 21] the mineralocorticoid function of the adrenal glands. It may be suggested that strengthening the glutathione activity in these conditions is connected with anabolic action of mineralocorticoids on the amino acid glutathione, which contains SH-groups.

The results obtained attest to the close dependence of the course of enzymic adaptive reactions on the functional state of the adrenal cortex. This presents the perspective for studying the possible stimulating action of corticosteroid preparations on enzymatic-chemical transformations during resuscitation.

TABLE 3. Glutathione Activity of Blood in Cats Resuscitated after Clinical Death Caused by Acute Blood Loss

Group of animals	No. of animals	Initial data	Dying (terminal pause)	Resuscitation after recovery of spontaneous respiration (M ± m)	
				After 7 min	After 80 min
		$M \pm m$			
Intact	20	3,2±0,32	4,3+0,28 $P<0,01$	3,8±0,22 $P<0,01$	3,7±0,18 $P<0,01$
Adrenalectomized	12	4,1±0,6	4,0 0,22 $P>0,05$	4,1±0,45 $P>0,05$	3,5±0,58 $P>0,05$
Animals with autotransplanted adrenal glands	12	4,0±0,32	4,6±0,24 $P<0,05$	3,7±0,23 $P<0,05$	4,7±0,28 $P<0,05$

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