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PROGNOSTIC VALUE OF DETERMINATION OF LYMPHOCYTE SUCCINATE DEHYDROGENASE ACTIVITY AND THERAPEUTIC EFFICACY OF SODIUM SUCCINATE DURING RESUSCITATION OF RATS

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The dehydrogenase activity of lymphocytes is known to reflect the enzyme activity and metabolic changes in the internal organs [1, 2, 5, 8]. Clincial and experimental studies in the last few years have shown that low lymphocyte succinate dehydrogenase (SDH) activity is an unfavorable prognostic sign in a number of somatic and infectious diseases [3, 4]. However, the way in which SDH activity of the lymphocytes changes during clincial death and in the postresuscitation period, and whether changes in SDH activity of the lymphocytes are of prognostic value, and finally, whether by using sodium succinate to optimize energy metabolism in terminal states, it is possible to increase the survival rate of animals subjected to clincial death, have not been studied.

EXPERIMENTAL METHOD

Experiments were carried out on anesthetized noninbred male rats weighing 180-210 g kept in the animal house on an ordinary diet. The animals were divided into two groups: one group consisted of animals subjected to clinical death from acute blood loss (58 rats), the other group of animals treated 30 min before clincial death by intraperitoneal injection of sodium succinate in a dose of 20 mg/kg. Clincial death lasting 4 min was induced by acute bleeding from the carotid artery, and compression of the incubation tube for 7 min, and these procedures were followed by resuscitation by the method in [7]. The effect of preliminary injection of sodium succinate was assessed by the time of appearance of cardiac contractions and the corneal reflex, and the duration of survival of the resuscitated rats. In addition, SDH activity of the lymphocytes was estimated by the method in [6] in each experimental animal five times (before blood loss and asphyxia, at the end of clincial death, and 5, 15, and 90 min after resuscitation).

EXPERIMENTAL RESULTS

A fall of SDH activity in the lymphocytes was observed during clincial death, and the worse the outcome of resuscitation, the greater the degree of inhibition of this enzyme. During the first few minutes after resuscitation SDH activity in the lymphocytes increased and exceeded its original level. The group of animals dying in the early postresuscitation period was an exception (Table 1).

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TABLE 1. Dynamics of SDH Activity of Blood Lymphocytes of Animals during Clinical Death and in Early Postresuscitation Period (M ± m)

Duration of survival of rats after resuscitation	Stages of experiment				
	Before clinical death	During clinical death	After resuscitation		
			5 min	15 min	90 min
Under 24 h	15,60±0,12	8,30±0,15*	8,40±1,46	6,10±0,81	5,60±0,65
From 24 to 48 h	15,00±0,52	9,20±0,56*	15,40±0,91*	12,00±0,98*	10,70±0,42
From 48 to 72 h	16,80±0,52	10,00±0,48*	18,70±0,48*	13,60±0,48*	14,00±0,63
From 72 h to 2.5 months	16.30±0,11	11,00±0,27*	18,10±0,37*	13,10±0,24*	14,50±0,20*

Legend. At each time from 7 to 11 animals were used. No significant differences were found between SDH activity in the lymphocytes in the different versions of clinical death, and for that reason the results obtained by microscopy of lymphocytes of rats subjected to clinical death from blood loss and mechanical asphyxia are pooled into groups depending on duration of survival after resuscitation. SDH activity of lymphocytes expressed as number of granules of reaction product per cell. Quantitative data obtained by microscopy of 8250 lymphocytes. *P < 0.05 compare with preceding period.

TABLE 2. Constants of Equation for Time Course of Lymphocyte SDH Activity in First Period After Resuscitation

Duration of survival, days	Constant		Maximum of SDH activity	
	α	$\bar{v}\beta$	Time, min	Amplitude, number of granules per lymphocyte
2	4,67	—0,198	5,04	18,7
3	6,08	—0,276	3,60	19,1
4	3,60	—0,242	4,10	17,3

TABLE 3. Constants for Equation Describing Relationship between Lymphocyte SDH Activity and Duration of Survival of Animals after Resuscitation

Parameter	Constant		Prognostically favorable parameter, number of granules per lymphocyte
	T_0	k	
Lymphocyte SDH activity			
Before clinical death	$16{,}0\cdot10^{-6}$	0,969	17,3
During clinical death	$11{,}4\cdot10^{-3}$	0,498	15,8
Maximum of activity during resuscitation	$48{,}0\cdot10^{-3}$	0,217	27,9

The period of primary activation of SDH, observed 5 min after resuscitation, was followed after 15-90 min by a second moderate fall in activity of the enzyme, which may have been due to some extent to endogenous toxemia, which is known to reach a maximum 30 min after resuscitation [9]. Thus in the early period of resuscitation fluctuating changes in lymphocyte SDH activity were observed, and these changes can be described by an empirical equation of a "control curve":

$$Q = Q_0 + \alpha \cdot t \cdot e^{-\beta t},$$

Where Q_0 is a parameter of SDH activity during clinical death; t the time after resuscitation (in min); and α and β are constants obtained by the method of least squares by using levels of activity 5 and 15 min after resuscitation.

Constants of the empirical equation and the maximum of lymphocyte SDH activity are given in Table 2. Characteristically, with more rapid and intensive activation of SDH a tendency

TABLE 4. Effect of Sodium Succinate on Resuscitation of Animals (% of surviving rats)

Parameter	Experimental conditions		P
	Resuscitation	Sodium succinate + resuscitation	
Appearance of cardiac contractions not later than after 60 sec	28,6	50,0	<0,05
Fibrillation, asystole	16,1	7,2	>0.05
Recovery of corneal reflex:			
10 min	—	25,0	
30 min	25,4	58,0	<0,05
Duration of survival:			
Under 1 h	24,5	6,1	<0,05
Over 2 days	31,5	39,3	>0,05

was noted for the length of survival of the animals after clinical death to increase. This correlation is found particularly clearly when graphs were plotted, but on general grounds it can be postulated that this correlation is nonlinear, and that a certain level exists beyond which the probability of survival falls sharply. It will be evident that a nonlinear relationship exists between lymphocyte SDH activity before death, at the time of death, and during resuscitation (the peak of activity), and the duration of survival, and this relationship can be described by an exponential function (Table 3):

$$T = T_0 \cdot e^{kQ},$$

where T_0 is a constant (in days), denoting the duration of survival in the absence of SDH activity, e is the base of natural logarithms; k a constant attached to Q, and Q the SDH activity of the lymphocytes.

By means of this equation it is possible to calculate what the lymphocyte SDH activity ought to be for the outcome of resuscitation to be more favorable, viz., a duration of survival of 30 days. These optima were found to differ during different periods. It will be noted that such a level is really attainable, although the optimal level during resuscitation was found to differ sharply from the level actually observed (Table 1); moreover, on the basis of other calculations, it ought to have been reached sooner — not later than after 30 sec.

Correction of energy metabolism, of course, is not the only method of optimization of resuscitation, although it deserves further study. The results of resuscitation of rats receiving sodium succinate before clinical death indicate that preliminary administration of this metabolite improved the results of resuscitation somewhat (Table 4).

It can be concluded from this investigation that determination of the level of lymphocyte SDH activity can be used as a prognostic criterion and that preliminary injection of sodium succinate has a definite beneficial effect on the outcome of resuscitation in the early postresuscitation period.

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