[6] and increased glycogen synthesis in the liver at the expense of nonnitrogenous residues of amino acids [9]. The intensification of transcription and translation processes through the influence of glucocorticoids completes the chain of changes in adaptive synthesis of enzyme proteins [3, 4].

The results described above indicate that during prolonged physical exertion glucocorticoids play an important role in the regulation of enzyme synthesis and in the provision of amino acids prepared (transaminated) specially for this process.

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EFFECT OF SODIUM SUCCINATE ON SOME INDICES OF CARBOHYDRATE METABOLISM OF THE ISCHEMIC MYOCARDIUM

Kh. D. Bairamkulov and V. V. Gatsura

UDC 616.127-005.4-092.9-085.31: 547.461.4]-07:616.127-008.9-074

The effect of sodium succinate on the concentrations of lactic and pyruvic acids and of glucose in blood draining from the ischemic zone was investigated in experiments on dogs in which the coronary artery was ligated. After intracoronary injection of the compound in doses of 2 and 10 mg/kg the lactic acid concentration was lowered in blood flowing from the ischemic zone: In a dose of 10 mg/kg sodium succinate reduced the assimilation of glucose by the ischemic area of myocardium a little. After intravenous injection of sodium succinate in a dose of 100 mg/kg the lactic acid concentration also fell significantly and the utilization of glucose by the ischemic myocardium was inhibited and its concentration in the arterial blood rose considerably. The reduction in the blood lactic acid concentration may have been due to activation of the Krebs' cycle and increased utilization of oxygen in the ischemic region of the myocardium.

KEY WORDS: myocardial ischemia; succinate; carbohydrate metabolism.

During regional hypoxia of the myocardium succinic acid has many advantages as a source of energy because of the greater rapidity of its oxidation and because of the flavin nature of succinate dehydrogenase [2]. Accumulation of reduced forms of NAD is the factor limiting energy formation in the ischemic myocardium.

Department of Pharmacology, Kursk Medical Institute.

(Presented by Academician of the Academy of Medical Sciences of the USSR V. V. Zakusov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 82, No. 12, pp. 1439-1441, December, 1976. Original article submitted May 21, 1976.

TABLE 1. Effect of Sodium Succinate on Some Indices of Carbohydrate Metabolism of Ischemic Myocardium (in % of initial level; M ± m)

Series of experiments	Parameters	Initial data, absolute values	Time after ligation of coronary artery, min		
			5	30	60
Control	LA V	1,98±0,16	+127,7±27,5*	+238,0±36,3*	+261,5±40,4*
	A	2,20±0,12	+2,2±2,2	+25,0±6,6*	+43,1±6,4*
	PA V	0,104±0,006	+20,7±8,8*	+25,3±9,0*	+28,2±10,9*
	A	0,139±0,006	+6,7±5,6	+12,6±6,3	+12,3±7,5
	G V	81,8±1,9	—7,0±2,9*	—16,7±2,9*	—21,0±2,2*
	A	85,1±2,1	+3,6±3,0	+3,3±4,3	+0,8±3,1
	Pe	3,8±1,1	13,9±1,4*	21,9±1,5*	24,4±1,5*
I – sodium succinate, Na 2 mg/kg, by intracoronary injection	LA V	2,07±0,58	+118,2±46,3*	+89,4±29,0*°	+87,7±28,5*°
	A	3,12±0,78	—6,9±9,2	—14,8±10,7°	—22,7±8,8*°
	PA V	0,091±0,007	—0,3±2,4	—3,2±3,5°	+3,6±3,6
	A	0,107±0,005	+3,3±3,3	—8,9±5,2	—1,7±4,6
	G V	83,14±5,1	—9,2±4,1*	—2,7±11,8	—8,9±15,5
	A	84,5±5,1	+6,8±4,5	+20,7±8,5*	+25,4±13,6
	Pe	1,8±1,5	+15,1±4,8*	+17,4±4,7*	+15,8±4,4*
II – sodium succinate, Na 10 mg/kg, by intracoronary injection	LA V	1,86±0,39	+94,3±17,8*	+89,6±28,8*°	+50,1±20,0*
	A	2,72±0,68	—2,1±8,0	—7,1±14,2°	—4,9±12,5°
	PA V	0,098±0,002	+7,4±3,2*°	+13,8±9,9	+14,4±12,3
	A	0,105±0,002	+2,2±4,3	+7,4±9,1	+7,4±10,6
	G V	84,89±4,90	—8,0±3,1	—0,3±10,4	+0,5±11,6
	A	84,82±5,18	+7,7±3,7	+15,5±5,9	+17,4±8,5
	Pe	—0,7±10,14	+12,6±3,0	+15,5±4,7	+17,2±3,8
III – sodium succinate, 100 mg/kg, intravenously	LA V	2,01±0,33	+89,4±22,0*	+90,8±39,7*°	+65,0±26,8*°
	A	2,25±0,37	+13,2±15,4	—6,6±9,0	—6,9±9,1°
	PA V	0,116±0,009	—7,5±3,5°	+4,2±6,7	—3,8±7,5°
	A	0,118±0,005	—2,0±2,99	+5,4±3,2	—0,8±4,5
	G V	71,3±13,3	—6,9±1,9*	+7,4±5,4	+30,5±9,1*°
	A	79,3±8,3	+6,1±3,3	+26,9±8,4*°	+37,0±9,2*°
	Pe	—0,3±4,4	+11.2±3,4*	+15,0±3,3*	3,0±8,7

Legend. LA) Lactic acid (in mM); PA) pyruvic acid (in mM); G) glucose (in mg %); Pe) percentage exception of glucose; V) blood samples from cardiac vein; A) blood samples from aorta; * and °) statistically significant changes in parameters within series and compared with control ($P < 0.05$).

In the initial period of hypoxia, activity of the flavoprotein fragment of the electron transport chain may still remain intact. From this point of view the partial functioning of the Krebs' cycle with the utilization of succinate can be regarded as a compensatory mechanism for the maintenance of energy formation.

Because of the absence of information on the effect of succinic acid on the myocardial energy metabolism in the zone of ischemia, it was decided to investigate this aspect of its pharmacological activity.

EXPERIMENTAL METHOD

Experiments were carried out on 30 adult mongrel dogs anesthetized with pentobarbital (40 mg/kg, intraperitoneally). The animals were artificially ventilated, thoracotomy was performed, and branches of the lateral vein of the heart were cannulated [3]. In this way it was possible to obtain samples of blood flowing directly from the zone of ischemia. After collection of blood from the aorta and the lateral vein of the heart in the initial state, the descending branch of the left coronary artery was ligated. Sodium succinate was injected by the intracoronary route 5-7 min after ligation over a period of 15 min in doses of 2 mg/kg (series I, 10 experiments) and 10 mg/kg (series II, 10 experiments) and also intravenously in a dose of 100 mg/kg (series III, 10 experiments). Blood was tested 10, 15, 30, and 60 min after ligation of the coronary artery. The concentrations of lactic and pyruvic acids and also of glucose (by the orthotoluidine method) were determined in the blood. The results of these observations were compared with those of a control series of 24 experiments on dogs [1].

EXPERIMENTAL RESULTS AND DISCUSSION

The dynamics of the indices of energy metabolism during acute ischemia of the myocardium and changes in the indices produced by sodium succinate are shown in Table 1.

The most significant fact in the action of sodium succinate when injected by the intracoronary and intravenous routes was a statistically significant decrease in the lactic acid concentration in the blood flowing from the zone of ischemia. It is interesting to note that this effect was independent of the dose of succinate, indicating that the capacity for oxidation of this substrate in the myocardium has a limiting effect. A tendency toward a decrease in the lactate concentration also was observed in blood samples from the aorta. Changes in the pyruvate level under the influence of sodium succinate were slight both in venous and in arterial blood, and they did not differ significantly from the control. The effect of sodium succinate on the glucose concentration in blood draining from the ischemic zone showed no change exceeding the limits of variation of this parameter under acute ischemic conditions, although after intracoronary injection of the large dose (10 mg/kg) a tendency was observed for the glucose concentration to be higher than in the control series.

It must, however, be pointed out that in experiments with intracoronary injection of sodium succinate the glucose concentration in the arterial blood was only a little higher than in the control, whereas after intravenous injection these differences were statistically significant.

Under these conditions the index of glucose extraction after intracoronary injection was close to its values in the control series, and only after intravenous injection of succinate in a dose of 100 mg/kg was some tendency observed for it to decrease. The decrease in the glucose extraction index in this last case, accompanied by favorable changes in the functional indices and by lowering of the lactacidemia is indirect evidence of the beneficial effect of succinate on the energy metabolism of the ischemic myocardium.

The disturbance of electron transport to the final stages of the respiratory chain in myocardial ischemia [4] and the accumulation of reduced pyridine nucleotides in the cytoplasm [5] are the initial stage of disorganization of the myocardial bioenergetics. Inhibition of the utilization of pyruvic acid in the Krebs' cycle observed under these circumstances leads to the accumulation of lactate [6], a concentration of which serves as a quantitative indicator of the degree of myocardial hypoxia [8].

The lowering of the lactic acid concentration in blood flowing from the ischemic zone under the influence of sodium succinate and the positive dynamics of functional indices such as the volume velocity of the collateral coronary blood flow and the left-ventricular pressure are evidence that in this period there is a definite oxidative potential of FAD and the possibility of formation of high-energy bonds.

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