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PLASMA ALDOSTERONE AND ELECTROLYTE LEVELS IN THE MYOCARDIUM OF RATS WITH ACUTE ALCOHOL INTOXICATION AFTER A SINGLE PHYSICAL LOADING TEST (SPLT)

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KEY WORDS: acute alcohol intoxication; single physical loading test; mineralocorticoid function of the adrenals

The modifying effect of ethanol on neuroendocrine regulation and on ionic homeostasis in vivo is confirmed by many investigations [2, 9]. Meanwhile information on the trend of these changes is extremely contradictory. This applies also to the mineralocorticoid function of the adrenals, especially in the late period after acute alcohol intoxication. To assess the functional reserves of these systems physical loading tests have been used [4, 5, 8], but there have been only solitary studies of electrolyte metabolism [3] and the aldosterone concentration in the recovery period [11]. This aspect, nevertheless, is particularly important for a comprehensive analysis both of endocrine-metabolic reactions and of the state of the cardiovascular system in response to loading tests in the late period after alcoholic excess.

The aim of this investigation was to study the time course of the plasma aldosterone and electrolyte concentrations in response to SPLT 14 days after acute alcohol intoxication, and also the coefficient of distribution of Na^+, K^+, Ca^{2+}, and Mg^{2+} between the plasma and myocardium, and the ECG parameters under experimental conditions.

EXPERIMENTAL METHOD

Experiments were carried out on male Wistar rats weighing 180-210 g, receiving 40° ethanol intraperitoneally in a dose of LD_{25}. Intact rats (IR) served as the control. On the 14th day an SPLT was carried out, involving running on a treadmill with free choice of load. The speed of movement of the treadmill was 16 m/min. Blood plasma and myocardium were sampled before and 1, 3, 6, 12, and 24 h after SPLT. The plasma aldosterone concentration (PAC) was measured by radioimmunoassay using commercial kits from the firm "Sorin" (France). Concentrations of K^+, Na^+, Ca^{2+}, and Mg^{2+} in blood plasma and myocardium were determined on a Hitachi 180-80 atomic absorption spectrophotometer. The coefficient of distribution K^+pl/K^+m, Na^+pl/Na^+m, $Ca^{2+}pl/Ca^{2+}m$, and $Mg^{2+}pl/Mg^{2+}m$ represented the ratios of plasma and myocardial concentrations of the electrolytes. The ECG was recorded in six standard leads on a "Kardiolux-300T" electrocardiograph (Yugoslavia), after which HR and the durations of the PQ, QRS, and QT intervals were measured. The results were subjected to analysis by standard statistical programs, using Student's test.

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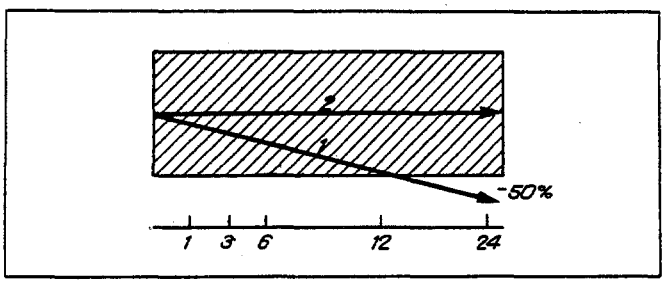

Fig. 1. Time course of PAC in IR (1) and AR (2) after SPLT. Shaded region represents control with confidence limits. Abscissa, time after SPLT.

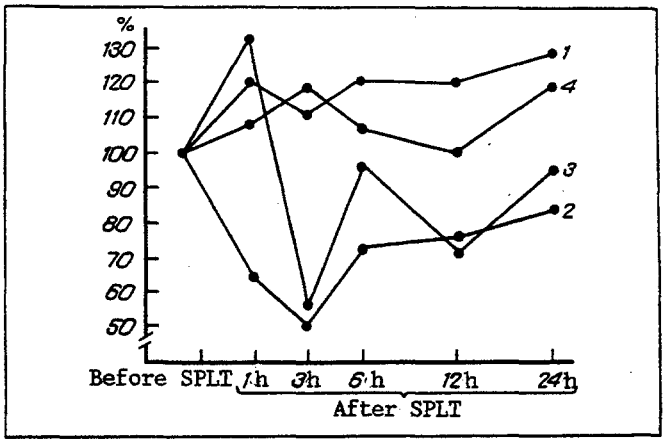

Fig. 2. Time course of coefficient of distribution K^+pl/K^+m (I), Na^+pl/Na^+m (II), $Ca^{2+}pl/Ca^{2+}m$ (III), and $Mg^{2+}pl/Mg^{2+}m$ (IV) in IR after SPLT. Value for intact rats before SPLT taken as 100%.

EXPERIMENTAL RESULTS

Results showing that after SPLT there was no difference in PAC of rats receiving alcohol (AR) and IR (1.1 ± 0.1 nmole/liter and 1.0 ± 0.15 nmole/liter respectively). Later, however, the time course was opposite in the two cases, and toward the end of the recovery period, the level in AR exceeded that in IR (1.3 ± 0.2 nmole/liter and 0.3 ± 0.2 nmole/liter respectively).

Before SPLT the coefficient K^+pl/K^+m and $Mg^{2+}pl/Mg^{2+}m$ was increased, whereas Na^+pl/Na^+m and $Ca^{2+}pl/Ca^{2+}m$ was reduced. The coefficient K^+pl/K^+m was reduced in AR after 1 h, whereas Na^+pl/Na^+m was reduced throughout the period of the investigation; $Ca^{2+}pl/Ca^{2+}m$ was reduced from 6 h until 24 h, and $Mg^{2+}pl/Mg^{2+}m$ after 1 h, but later it exceeded the value of this ratio in IR (Figs. 2 and 3).

Analysis of the ECG parameters (Table 1) shows that HR in AR before SPLT was higher than in IR, and that the PQ and QT intervals also were increased. In the period after SPLT the ECG parameters were virtually identical in the two groups, with the exception of lengthening of QRS in AR after 6 h. Nevertheless, tolerance to physical exercise, determined by the length of time spent running on the treadmill, was lower for AR than for IR (7.0 ± 1.1 min and 14 ± 1.2 min respectively).

In order to interpret the results we set out from the fact that SPLT is a form of stress, the intensity and duration of which in our experiments were determined by the animals themselves. From this standpoint the time course of PAC in IR is natural and regular: a decrease toward the 24th hour was due to predominance of the glucocorticoid component of the stress reaction [6, 7]. Meanwhile in AR, the opposite trend of PAC could hardly have been determined by the background effect of ethanol, since the basal concentrations before SPLT were the same in the two groups. In our view this is due to the functional insufficiency of the myocardium, working under a greater load, as is shown by the high HR, compared

TABLE 1. Time Course of Heart Rate (HR) and PQ, QRS, and QT Intervals in Rats with Acute Alcohol Intoxication after SPLT. Corresponding Parameters for Intact Animals are Given in Parentheses ($x \pm S_x$)

Stage of investigation	HR, beats/min	PQ, sec	QRS, sec	QT, sec
Before SPLT	436±15*	0,42±0,01	0,02±0,001	0,9±0,02
	(371±12)	(0,40±0,001)	(0,02±0,001)	(0,89±0,01)
After SPLT, h				
1	430±16	0,43±0,02	0,02±0,0001	0,94±0,03
	(382±29)	(0,45±0,03)	(0,02±0,0001)	(0,88±0,04)
3	445±16	0,4±0,001	0,02±0,0001	0,96±0,02
	(436±26)	(0,45±0,03)	(0,02±0,0001)	(0,88±0,04)
6	456±10	0,4±0,001	0,026±0,001*	0,96±0,01*
	(429±29)	(0,4±0,02)	(0,02±0,0001)	(0,88±0,04)
12	458±14	0,4±0,01	0,02±0,0001	0,94±0,04
	(460±20)	(0,4±0,002)	(0,02±0,0001)	(0,95±0,02)
24	451±12	0,36±0,07	0,02±0,0001	0,98±0,04
	(460±20)	(0,4±0,02)	(0,02±0,0001)	(0,88±0,04)

Legend. *$p < 0.05$) Differences between groups significant.

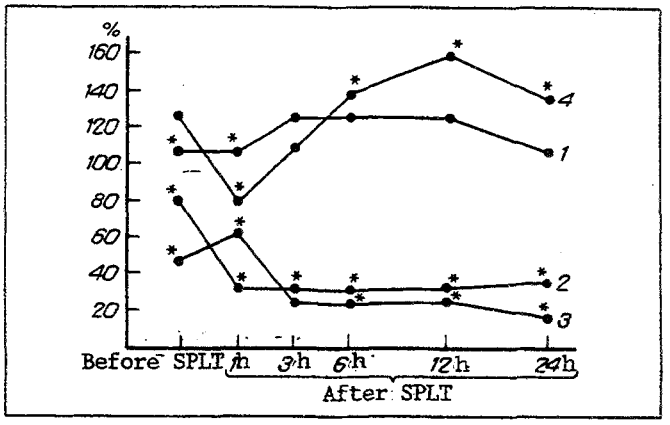

Fig. 3. Time course of coefficient of distribution K^+pl/K^+m (I), Na^+pl/Na^+m (II), $Ca^{2+}pl/Ca^{2+}m$ (III), and $Mg^{2+}pl/Mg^{2+}m$ (IV) in AR after SPLT. Value for intact rats before SPLT taken as 100%. *) Significance of differences from IR group after SPLT ($p < 0.05$).

with IR, even in the late period (14 days) after alcoholic excess. It is logical to suggest that the renin-angiotensinaldosterone system (RAAS), recognized as ensuring volume homeostasis during stress, is included as an extracardiac component of adaptation to changes in the systemic and regional hemodynamics [1, 4].

Acute alcohol intoxication induces changes in the ionic balance between the plasma and myocardium, which persist for a long time and are manifested as overloading of the myocardium with Na^+ and Ca^{2+}. These changes are evidently due equally to the membranotropic action of ethanol [14] and to depression of the ion transport systems [10, 15]. Drzhevetskaya and Belyaev [3] describe evidence of marked hypocalcemia which, they consider, depends on the intensity and duration of the physical exercise. From this point of view SPLT in our experiments is a test of relatively mild intensity.

SPLT in AR leads to aggravation of existing disturbances of electrolyte metabolism, and to even greater overloading of the myocardium with Na^+ and Ca^{2+}, which may perhaps lead to destructive changes in the cardiomyocytes [12, 13] and be manifested as a change in their conducting and contractile properties. Functional insufficiency of the myocardium in AR is evidently the result of a combination of these disturbances. The possibility cannot be ruled out that in the initial stage the electrolyte imbalance is due to some degree to changes in RAAS under the influence of acute alcoholization, but in the late periods the inadequate response of the plasma aldosterone to SPLT in AR is determined, most probably, by the hemodynamic component of myocardial insufficiency, in whose pathogenesis an essential role is played by changes in ionic heterogeneity, although a destabilizing effect of alcohol on this system would seem to be just as likely.

In our view it is an interesting fact that free choice of physical exercise, without causing any marked disturbances of conduction and the contractile function of the heart, at the same time enables the state of the regulatory mechanisms responsible for adaptation to SPLT to be evaluated.

Thus acute alcohol intoxication creates an unfavorable electrolytic background in the blood plasma and myocardium of rats which persists into the late period after ethanol administration. The SPLT reveals the inadequate response of PAC in rats with alcohol intoxication, which can be interpreted as the inclusion of an extracardiac component of compensation of the myocardial functional insufficiency, that is largely due to a change in the K^+, Na^+, Ca^{2+}, and Mg^{2+} balance. Tolerance of AR to physical exercise is lower than in the control, but the free choice of load would seem to be the most physiological situation with which to assess the state of the parameters studied.

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