PLASMA AND MYOCARDIAL ALDOSTERONE AND ELECTROLYTE LEVELS IN RATS WITH ACUTE ALCOHOL INTOXICATION AFTER SINGLE TREADMILL EXERCISE

A. R. Antonov, Yu. V. Nacharov, A. S. Sorokin, and G. S. Yakobson

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The modifying effect of ethanol on neuroendocrine regulation and ionic homeostasis in the body has been confirmed by a number of investigations [2, 9]. Meanwhile the results of a study of the trend of these changes have been extremely contradictory. This applies also to the mineralocorticoid function of the adrenals, especially in the late stages after acute alcoholic intoxication. To estimate the functional reserves of a given system physical exercise tests are used [4, 5, 8], but there have been only isolated studies of electrolyte metabolism [3] and parameters of the pituitary-adrenocortical system in the postexercise period [11]. This aspect is even more important for the comprehensive evaluation both of the endocrine-metabolic reactions and of the state of the cardiovascular system in response to the use of exercise tests in the late period after alcoholic excess.

The aim of this investigation was to study the dynamics of ECG parameters and the plasma aldosterone and electrolyte concentrations in response to single treadmill exercise (STE) 14 days after acute alcoholic intoxication, and also the distribution coefficient of Na^+, K^+, Ca^{2+}, and Mg^{2+} between the plasma and myocardium experimentally.

EXPERIMENTAL METHOD

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 the STE test was carried out with free choice of load. The belt moved at a speed of 16 m/min. Samples of blood plasma and myocardium were obtained from the rats before the test and 1, 3, 6, 12, and 24 h thereafter. The plasma aldosterone concentration (PAC) was measured by radioimmunoassay using commercial kits from "CIS" (France). Plasma levels of K^+, Na^+, Ca^{2+}, and Mg^{2+} were determined on a Hitachi-180-80 atomic absorption spectrophotometer. The distribution coefficient of K^+pl/K^+m, Na^+pl/Na^+m, Ca^{2+}pl/Ca^{2+}m, and Mg^{2+}pl/Mg^{2+}m was calculated as the ratios between plasma and myocardial electrolyte concentrations. The EOG was recorded in six standard derivations on a "Kardiolux-300T" electrocardiograph (Yugoslavia), after which the heart rate (HR), and the length of the PQ, QRS, and VQT intervals were measured. The results were subjected to statistical analysis by Student's test using standard programs.

EXPERIMENTAL RESULTS

Table 1 gives data showing that before the STE there was no difference in PAC of the alcoholized (AR) and intact (IR) rats. Later, however, their time course was in opposite directions, and by the end of the recovery period, this parameter was higher in AR than in IR.

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TABLE 1. Dynamics of PAC in Recovery Period after STE in Rats with Acute Alcoholic Intoxication

Stage	AR, mmoles/lite	IR, mmoles/liter
Before STE	1,1±0,1 (2)	1,0±0,15 (10)
Time after STE, h		
1	0,33±0,09 (8)*	1,4±0,16 (6)
3	0,23±0,04 (8)	0,18±0,07 (6)
6	0,3±0,05 (10)	0,4±0,7 (6)
12	1,4±0,3 (7)	1,1±0,3 (6)
24	1,3±0,2 (10)*	0,3±0,2 (6)

TABLE 2. Dynamics of Ratios K^+pl/K^+m, Na^+pl/Na^+m, $Ca^{2+}pl/Ca^{2+}m$, and $Mg^{2+}pl/Mg^{2+}m$ in Recovery Period after STE in Rats with Acute Alcoholic Intoxication (relative units)

Stage of investigation	AR				IR			
	K^+pl/K^+m	Na^+pl/Na^+m	$Ca^{2+}pl/Ca^{2+}m$	$Mg^{2+}pl/Mg^{2+}m$	K^+pl/K^+m	Na^+pl/Na^+m	$Ca^{2+}pl/Ca^{2+}m$	$Mg^{2+}pl/Mg^{2+}m$
Before STE	0,14±0,002* (9)	7,0±0,07* (9)	6,7±0,4* (9)	0,19±0,04 (9)	0,13±0,001 (10)	8,7±0,05 (10)	12,1±0,1 (10)	0,15±0,002 (10)
Time after STE, h								
1	0,14±0,004* (8)	3,2±0,2* (8)	7,5±0,8* (8)	0,12±0,01* (8)	0,17±0,003 (6)	6,5±0,03 (6)	21,0±0,5 (6)	0,16±0,01 (6)
3	0,16±0,004 (8)	3,2±0,1* (8)	8,3±0,7 (8)	0,17±0,01 (8)	0,16±0,006 (6)	5,6±0,2 (6)	8,1±0,1 (6)	0,18±0,01 (6)
6	0,16±0,005 (10)	3,2±0,1* (10)	3,1±0,4* (10)	0,21±0,008 (10)	0,17±0,007 (6)	7,4±0,4 (6)	13,1±0,9 (6)	0,16±0,008 (6)
12	0,16±0,008 (7)	3,3±0,2* (7)	4,2±0,2* (7)	0,24±0,01* (7)	0,17±0,001 (6)	7,7±0,4 (6)	10,0±0,6 (6)	0,15±0,02 (6)
24	0,14±0,03 (6)	3,6±0,2* (6)	2,4±0,5* (6)	0,23±0,008 (6)	0,18±0,006 (6)	8,1±0,3 (6)	12,6±0,1 (6)	0,18±0,01

Legend. Here and in Table 2, number of experimental animals shown between parentheses; *$p < 0.05$.

Before STE, in rats with acute alcohol intoxication (AAI) the ratios K^+pl/K^+m and $Mg^{2+}pl/Mg^{2+}m$ were increased, whereas Na^+pl/Na^+m and $Ca^{2+}pl/Ca^{2+}m$ were reduced. The distribution coefficient K^+pl/K^+m in AR was depressed after 1 h, and Na^+pl/Na^+m throughout the period of testing; $Ca^{2+}pl/Ca^{2+}m$ was reduced from 6 h until 24 h, and $Mg^{2+}pl/Mg^{2+}m$ after 1 h, but thereafter it was higher than the corresponding parameter in IR (Table 2).

Analysis of the ECG parameters showed that HR of AR before STE was higher than in IR, and the PQ and QT intervals also were increased. In the period after STE the ECG parameters were virtually identical in both groups, except lengthening of QRS in AR after 6 h. Nevertheless, physical exercise tolerance, determined as the running time on the treadmill, was lower in AR than in IR (7.0 ± 1.1 and 14.0 ± 1.2 min respectively).

When interpreting the results we assumed that STE is a form of stress, the intensity and duration of which in our experiments were determined by the animals themselves. From this standpoint the dynamics of PAC in IR was natural and regular: a fall after 24 h 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 alcoholic background, for the basal concentrations were equal in the two groups before STE. In our view, this was due to functional insufficiency of the myocardium, working under a heavier load, as shown by the higher HR compared with IR even in the late period (14 days) after alcoholic excess. It is logical to suggest that the pituitary-adrenocortical system, which has the function during stress of maintaining volume homeostasis, functions as an extracardiac component of adaptation to changes in the systemic and regional hemodynamics [1, 4].

Acute alcoholic intoxication causes changes in the ionic balance between plasma and myocardium, which persist for a long time and are manifested as raised blood calcium and magnesium levels and overloading of the myocardium with Na^+ and Ca^{2+}. These changes are evidently due equally to the membranotropic action of ethanol [14] and depression of the ion transport systems [10, 15]. Drzhevetskaya et al. [3] report marked hypocalcemia, which

they consider to depend on the severity and duration of the physical exercise From this point of view STE in our experiments was relatively mild in its intensity.

STE led to aggravation of existing disturbances of electrolyte metabolism in AR: even greater loading of the myocardium with Na^+ and Ca^{2+}, leading to destructive changes in the cardiomyocytes [12, 13] and manifested as a change in their conducting and contractile properties. Functional insufficiency of the myocardium in AR was evidently the result of a combination of these disturbances. The possibility cannot be ruled out that in the initial stage the electrolyte imbalance was due to some degree to changes in the PAS under the influence of acute alcoholization, but in the later stages, the inappropriate response of the plasma aldosterone to STE in AR was most probably due to the hemodynamic component of myocardial insufficiency, an essential role in the pathogenesis of which is played by changes in ionic heterogeneity, although a destabilizing effect of alcohol on this system seems equally likely.

In our view it is an interesting fact that free choice of physical exercise, while not causing any significant disturbances of the conductivity and contractility of the heart, at the same time enables a state of the regulatory mechanisms responsible for adaptation to STE to be evaluated.

Thus acute alcoholic intoxication creates an unfavorable electrolyte background in the blood plasma and myocardium of rats, which persists into the late stages after administration of ethanol. By means of the STE test, an inadequate response of PAC can be detected in AR, and can be interpreted as activation of the extracardiac component of myocardial functional insufficiency, itself largely due to a change in K^+, Na^+, Ca^{2+}, and Mg^{2+} balance. Tolerance of AR to physical exercise is lower in AR than in the control, and the free choice of load would seem to be the most physiological situation for assessment of these parameters.

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