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EFFECT OF α-TOCOPHEROL ON RESPONSE OF THE ADRENALS TO COLD STRESS

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The protective action of antioxidants during exposure to extremal factors is associated with their ability not only to inhibit lipid peroxidation (LPO) reactions in target organs, but also to inhibit the generalized neuroendocrine response of the body [1, 2]. This last fact suggests that antioxidants may have an antistress action. Meanwhile, the writers have shown that a single dose of ionol or tocopherol can cause a sharp rise of the plasma corticosteroid level [3]. Hence the need for an investigation of these properties of antioxidants.

The aim of this investigation was to study the response of the adrenals in control rats and rats receiving α-tocopherol (AT) kept under exposure to cold.

EXPERIMENTAL METHOD

Experiments were carried out in winter on Wistar rats divided into eight groups (12-14 animals in each group). Control animals and animals receiving AT for 7 days (5% AT acetate in oil, 4 mg daily per rat with the food) were exposed to cold (5°C for 2, 5, and 20 h). The intensity of LPO in the body was judged from the AT concentration in the liver [6] and the content of diene conjugates (DC) in the hepatic lipids. The rate of ascorbate-dependent lipid peroxidation (ADLP) in a 5% liver homogenate was estimated from the accumulation of malonic dialdehyde (MDA) [5]. Meanwhile corticosteroid production by the adrenals of the experimental animals was studied in vitro. Slices of adrenals from four rats were pooled into two parallel samples and incubated for 2 h at 37°C in 4 ml of Krebs–Ringer bicarbonate buffer with 200 mg % glucose, saturated with a mixture of 95% O_2 and 5% CO_2. ACTH was added to one of the parallel samples in a dose of 6 U/g tissue.

Corticosteroids were separated by thin-layer chromatography and determined quantitatively [4].

EXPERIMENTAL RESULTS

As was expected, keeping the rats for 5-20 h in the cold induced stress. Biosynthesis of deoxycorticosterone (DOC) and corticosterone at these times was higher than in the control (Table 1). Elevation of the MDA level and an increase in the rate of ADLP in liver homogenates from these animals could be regarded as a manifestation of this stress. The DC concentration fell (Table 2).

Prolonged administration of AT did not change the character of hormone synthesis. The DC and MDA levels in the liver likewise were unchanged. Meanwhile accumulation of AT was observed in the liver, and this probably was the reason for the steep decline in the rate of ADLP in the liver homogenates (Tables 1 and 2).

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TABLE 1. Steroid Production by Adrenal Slices and Changes in It under the Influence of ACTH in Control Rats and Rats Receiving AT in the Course of Cold Stress (M ± m)

Experimental conditions	Steroid production, μg/100 mg tissue in 1 h						
	−ACTH			+ACTH			
	aldosterone	corti-costerone	DOC	aldosterone	corti-costerone	DOC	
	I	II	III	IV	V	VI	
Control (1)	0,94±0,19	4,19±0,38	1,00±0,22	1,02±0,17	5,64±0,55	1,51±0,32	
Cold:							
2 h (2)	1,59±0,31	4,41±0,37	—	1,74±0,11	6,62±0,67	—	$P_{II-V}<0,05$
5 h (3)	0,92±0,31	7,17±0,79	2,00±0,28	1,04±0,08	7,10±0,58	3,66±0,37	$P_{III-VI}<0,05$
20 h (4)	1,35±0,19	6,18±0,31	1,02±0,21	1,10±0,15	6,92±0,26	1,19±0,17	
AT (5)	0,87±0,11	4,82±0,28	1,05±0,31	1,26±0,25	7,16±0,91	1,41±0,14	
Cold 2 h + AT (6)	1,60±0,45	3,85±0,86	—	2,07±0,40	7,17±0,83	—	$P_{II-V}<0,05$
Cold 5 h + AT (7)	0,70±0,08	6,82±0,33	1,84±0,27	1,05±0,28	10,18±0,69	2,92±0,37	$P_{II-V}<0,05$
Cold 20 h + AT (8)	0,52±0,11	4,97±0,40	1,03±0,33	0,81±0,17	7,30±0,53	0,81±0,20	$P_{III-VI}<0,05$
	$P_{4-8}<0,05$	$P_{1-3}<0,05$	$P_{1-3}<0,05$	$P_{1-2}<0,05$	$P_{3-7}<0,05$	$P_{1-3}<0,05$	
		$P_{1-4}<0,05$				$P_{5-7}<0,05$	
		$P_{5-7}<0,01$					

TABLE 2. Parameters of LPO Activity and AT Concentration in Liver of Control Rats and Rats Receiving AT in the Course of Cold Stress (M ± m)

Experimental conditions	AT, mg/100 g liver	DC, optical density units/mg lipids	MDA, nanomoles/g liver	Rate of ADLP, nanomoles MDA/g liver/min
Control (1)	1,32±0,20	0,56±0,02	27,1±1,8	5,4±0,58
Cold:				
2 h (2)	1,16±0,26	0,50±0,03	23,2±1,1	4,5±0,42
5 h (3)	1,50±0,26	0,47±0,03	69,7±11,0	8,1±0,58
20 h (4)	1,60±0,12	0,38±0,02	34,8±1,2	9,7±0,50
AT (5)	4,24±0,40	0,53±0,03	23,2±1,3	0,6±0,00
Cold 2 h + AT (6)	2,81±0,19	0,44±0,03	27,1±1,8	0,7±0,03
Cold 5 h + AT (7)	1,9±0,16	0,49±0,05	31,1±2,3	0,4±0,01
Cold 20 h + AT (8)	3,3±0,62	0,45±0,05	27,1±1,2	0,4±0,00
	$P_{1-5}<0,001$	$P_{1-3}<0,05$	$P_{1-3}<0,001$	$P_{1-3}<0,01$
	$P_{5-6}<0,001$	$P_{1-4}<0,001$	$P_{1-4}<0,01$	$P_{1-4}<0,001$
	$P_{5-7}<0,001$	$P_{5-6}<0,05$	$P_{5-7}<0,05$	$P_{1-5}<0,001$

AT caused a significant change in the response of the systems of the body to cold. The hormonal response of the experimental animals was shorter in duration (Table 1). After a stay of 20 h in the cold, despite continuing exposure, corticosterone biosynthesis was the same as initially, and aldosterone production was much lower than in the control. This response was not the result of exhaustion of secretion, but the result of a change in extra-adrenal regulatory influences, for in response to ACTH in vitro there was a significant increase in corticosterone production. The increase in amplitude of the response of the experimental animals to ACTH after exposure to cold for 5 h will be noted. This response, like inhibition of cold-activated LPO (Table 2), was probably due to AT. The fall in the AT level in the tissues during the first hours of exposure to cold indicates increased utilization of this compound.

The results are evidence that administration of small doses of α-tocopherol, on the one hand, increases the sensitivity of the adrenals to central influences, but on the other hand, it shortens the duration of increased glucocorticoid secretion. This effect of the antioxidant may lie at the basis of its adaptation-inducing action.

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