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ACTH-DEPENDENT CORTICOSTERONE SECRETION INHIBITED BY THE ANTIOXIDANT INDOL

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UDC 612.453.018.064:612.433.451].063:
615.272.4.014.425

KEY WORDS: ionol, ACTH, emotional-painful stress

It was shown previously that preliminary administration of the antioxidant ionol (dibunol) significantly limited the rise of the blood cholesterol level in animals with emotional-painful stress [4]. However, the mechanism of this stress-limiting effect is not yet clear. In particular, it is not known whether the antioxidant influences so important a stage of the stress reaction as the ACTH-dependent response of corticosterone formation and secretion by the adrenals.

The aim of this investigation was to study this problem by assessing the effect of ionol on the response of the adrenals to triple injections of ACTH and also to emotional-painful stress.

EXPERIMENTAL METHOD

Experiments (five series) were carried out on male Wistar rats weighing 200-220 g. ACTH (corticotrophin, from Kaunas Endocrin Preparations Factory) was injected subcutaneously in a dose of 2 units/100 g body weight 3 times in the course of 6 h, at intervals of 2 h. This order of administration of ACTH approximately simulated 6-hourly exposure to stress. Stress was produced in the form of an anxiety neurosis by the method of Desiderato and co-workers [6].

Ionol was injected intraperitoneally in a dose of 60 mg/kg before the first injection of ACTH or before the beginning of exposure to emotional-painful stress, daily for 4 days. The plasma and adrenal corticosterone levels were determined by the method of Botvin'ev [1]; extraction with methylene chloride was followed by chromatography on columns with silica-gel [3].

EXPERIMENTAL RESULTS

The results are evidence that the plasma corticosterone level in the control was 5.7 μg%, which corresponds according to data in the literature to the state of physiological rest [7]. The corticosterone concentration in the adrenals 1 h after the last of the three injections of ACTH was doubled, whereas its concentration in the blood plasma was trebled. Preliminary injection of ionol significantly (almost by half) reduced the increase in corticosterone concentration in the adrenals, and at the same time, almost completely prevented the rise of its concentration in the blood plasma.

Similar results were obtained during stress: 2 h after the end of exposure to stress the corticosterone concentration in the adrenals was doubled, and in the blood plasma it was trebled compared with the control. Preliminary administration of ionol led the increase

Research Institute of General Pathology and Pathological Physiology, Academy of Medical Sciences of the USSR, Moscow. Central Research Laboratory, Irkutsk Medical Institute. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 107, No. 1, pp. 42-43, January, 1989. Original article submitted February 25, 1987.

 0007-4888/89/0001-0048$12.50

in corticosterone concentration in the adrenals to be reduced by two-thirds, and at the same time, the rise of the plasma corticosterone concentration was not significant.

The facts described above indicate that injection of ionol prevented corticosterone accumulation in the adrenals and an increase in its concentration in the blood, which are usually observed after injection of ACTH. Ionol has a similar effect on the corticosterone concentration in the adrenals and blood plasma in emotional-painful stress. It can be concluded from these data that ionol limits the ACTH-dependent accumulation and secretion of corticosterone by the adrenal in stress, and thereby prevent realization of the pituitary-adrenal component of the stress reaction. The cellular mechanisms of this effect of the adrenal level require further study. In the context of this account, two facts are important.

1. The effect of ionol demonstrated by this investigation at the adrenal level does not rule out the possibility that this antioxidant limits the stress reaction at the central level, for it has now been proved that ionol can inhibit excitation of cortical neurons arising under the influence of epileptogens [2].

2. Ionol, like other antioxidants, has an adrenolytic action at the level of the effector organs; it prevents the toxic action of catecholamines on cardiomyocytes contracting in culture [5].

It is thus a reasonable hypothesis that the stress-limiting action of ionol and of other antioxidants is effected, first, at the adrenal level, second, at the level of the brain centers determining the stress reaction, and third, at the level of the effector organs.

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