ACTION OF α-METHYL-p-TYROSINE ON DEVELOPMENT OF NEUROGENIC DEGENERATION OF THE GASTRIC WALL AND ITS NORADRENALIN CONTENT

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The effect of α-methyl-p-tyrosine (50 mg/kg) was studied on the development of hemorrhagic erosions in the stomach wall and the noradrenalin content in it during electrical stimulation of immobilized rats. The α-methyl-p-tyrosine significantly increased the number of hemorrhagic erosions of the stomach wall and potentiated the fall in its noradrenalin level arising as a result of electrical stimulation.

KEY WORDS: noradrenalin; neurogenic degeneration of the stomach.

The investigations of Anichkov and co-workers [1, 2] demonstrated the important role of an excessive discharge and subsequent exhaustion of the reserves of the sympathetic mediator noradrenalin in the development of neurogenic degeneration of the stomach, heart, and liver. The question arises whether the degree of lowering of the noradrenalin level significantly influences the depth of development of the degenerative lesions and to what extent the decrease depends on the rate of noradrenalin resynthesis after intensive loss of the mediator through excessive stimulation.

To study this problem the substance α-methyl-p-tyrosine, a known inhibitor of noradrenalin synthesis, was used in the investigation described below.

EXPERIMENTAL METHOD

Experiments were carried out on 44 male albino rats weighing 180-220 g. Neurogenic degeneration of the stomach was induced by electrical stimulation of the immobilized rats for 3 h with square pulses (7-7.5 V, 50 Hz, 10 msec). The animals were decapitated immediately after the end of stimulation, the stomachs were opened along the lesser curvature, and after examination for the presence of destructive lesions of the mucous membrane, they were immersed in liquid oxygen. The severity of the degenerative changes in the stomach wall was assessed from the number of hemorrhagic erosions per animal of each group. After precipitation of the proteins of the gastric tissue homogenate with 5% TCA, catecholamines were adsorbed on alumina. The catecholamines were than eluted with 0.25 N acetic acid. Noradrenalin was determined fluorometrically [3]. Details of the method were described previously [7]. The α-methyl-p-tyrosine (50 mg/kg) was injected intraperitoneally 18 h before the beginnning of electrical stimulation of the rat.

EXPERIMENTAL RESULTS AND DISCUSSION

Electrical stimulation of the immobilized rats for 3 h led to the development of hemorrhagic erosions in the gastric mucous membrane [4, 5]. The mean number of lesions in each rat of this group was 4.8. At the same time, the noradrenalin level in the stomach wall of the animal fell from 0.23 ± 0.03 μg/g in the control to 0.08 ± 0.04 μg/g ($P < 0.002$).

If injected before electrical stimulation of the rats, α-methyl-p-tyrosine appreciably increased the number of lesions in the stomach wall and the degree of lowering of the noradrenalin level in it. Whereas

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in the rats subjected to electrical stimulation, the mean number of lesions was 4.8 ± 0.8; in animals receiving injections of α-methyl-p-tyrosine before stimulation it was increased to 10.3 ± 2 ($P < 0.02$). The noradrenalin concentration in these rats was only 0.04 ± 0.01 μg/g. In rats receiving α-methyl-p-tyrosine without subsequent stimulation the noradrenalin level was close to that in rats receiving stimulation only (0.12 ± 0.03 μg/g).

The aggravating action of α-methyl-p-tyrosine on the development of neurogenic degeneration of the stomach and the fall in its noradrenalin level can evidently be explained by the inhibitory action of the compound on catecholamine synthesis [16, 19-21]. The stage of conversion of tyrosine into dopa, which is catalyzed by tyrosine hydroxylase, is known to limit the rate of the process of synthesis of these amines as a whole [14].

These results agree with those of investigations in which accelerated catecholamine synthesis [11-13, 17] was disturbed by administration of tyrosine hydroxylase inhibitors [10, 13, 15]; which led to a decrease in the catecholamine concentration in the animals.

It is useful to compare these results with those obtained by the use of L-dopa and α-methyl dopa [6-8]. Dopa prevented the development of neurogenic degeneration of the stomach wall and the fall in the noradrenalin level in it; α-methyl dopa had no such action. These findings agree with the observations of Pukhova and Matlina [9] that dopa stimulates noradrenalin synthesis and prevents the decrease in its concentration in the organs of rats during electrical stimulation of the sciatic nerve.

The inhibitory action of α-methyl-p-tyrosine on the development of neurogenic degeneration of the stomach can be compared with the analogous action of reserpine [6] – a substance that disturbs the synthesis and retention of noradrenalin in the vesicles of sympathetic terminals [18].

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