EFFECT OF DOPA AND α-METHYLDOPA ON DEVELOPMENT OF NEUROGENIC DEGENERATION OF THE STOMACH WALL AND ON THE CATECHOLAMINE CONCENTRATION THEREIN

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Immobilization and electrical stimulation of the skin with square pulses (5-7 V, 50 Hz, 10 msec), for 3 h produced ulceration of the stomach wall in male albino rats. Intraperitoneal injection of dopa (300 mg/kg) 1 h before the beginning of stimulation reduced by 3.5 times the number of ulcers in the stomach wall and, at the same time, prevented the decrease in catecholamine concentration in the stomach wall. Unlike dopa, α-methyldopa did not prevent the development of gastric ulcers or the decrease in catecholamine concentration in the stomach wall.

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For several years the problem of neurogenic degeneration arising in organs (stomach, heart, and liver) after subjection of animals to stimulation of excessive strength has been studied at the Department of Pharmacology, Institute of Experimental Medicine, Academy of Medical Sciences of the USSR. Analysis of the development of neurogenic degeneration of the stomach has revealed the important role of the sympathetic nervous system [1, 5, 6, 10] and of catecholamine [2, 7-9, 11] in its development.

To continue the analysis of the role of endogenous catecholamines in the development of neurogenic degeneration, in the present investigation dopa (dihydroxyphenylalanine) and α-methyldopa were used. Dopa was used as a precursor of noradrenalin [16], and α-methyldopa as a compound leading to the formation of the pseudomediator α-methylnoradrenalin [13, 15].

EXPERIMENTAL METHOD

Experiments were carried out on 97 male rats weighing 160-210 g. Ulceration of the stomach wall was produced by stimulation of the immobilized rats for 3 h [4] with square pulses (5-7 V, 50 Hz, 10 msec). The rats were deprived of food for the 24 h before stimulation, but were allowed free access to water. One hour before the beginning of electrical stimulation the rats received an intraperitoneal injection of dopa or α-methyldopa in a dose of 300 mg/kg. Immediately after the end of stimulation the animals were decapitated, and after the number of gastric ulcers had been counted, they were immersed in liquid oxygen.

After preparation of a homogenate of the stomach tissue, proteins were precipitated with 5% TCA. Catecholamines were adsorbed on Al_2O_3, and after washing with bidistilled water 3 times, they were eluted with 0.25 N acetic acid solution by a noncolumn method [12]. Noradrenalin and adrenalin were determined fluorometrically by the method of Euler and Floding [14], in Govyrin's modification [3] using a fluorometer of Govyrin's design [3]. A fluorescence activation spectrum with a maximum in the region of 365 mμ was used, and the fluorescence spectrum itself had a maximum at 510 mμ. Noradrenalin was purified from adrenalin on the basis of differences in the ability of these amines to be oxidized by $K_3Fe(CH)_6$ in media with different pH values. Oxidation was carried out at pH 6.5 and 3.0, the pH value being varied by addition

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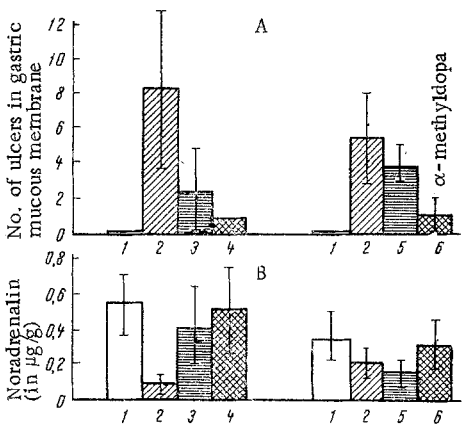

Fig. 1. Number of ulcers in gastric mucous membrane (A) and concentration of noradrenalin in stomach wall (B; in μg/g moist tissue) after electrical stimulation of rats for 3 h. 1) Control; 2) electrical stimulation; 3) electrical stimulation + dopa; 4) dopa; 5) electrical stimulation + α-methyldopa; 6) α-methyldopa.

of 1 M acetate buffer to the eluate. At pH 6.5, oxidation of noradrenalin and adrenalin takes place to an equal degree, while at pH 3.0, mainly adrenalin is oxidized [3, 14].

EXPERIMENTAL RESULTS AND DISCUSSION

Electrical stimulation of the immobilized rats led to the development of hemorrhagic erosions of the gastric mucous membrane. The number of ulcers per animal varied from 6.6 to 8.4 (Fig. 1A). Destruction of the stomach wall was accompanied by a sharp decrease in its concentration of noradrenalin (Fig. 1B) and also of adrenalin.

Injection of dopa into the immobilized rats before electrical stimulation prevented the decrease in noradrenalin and adrenalin concentrations in the stomach wall. This effect can be explained by the ability of dopa, as a precursor or noradrenalin, to promote the biosynthesis of catecholamines and to prevent their exhaustion in the tissues under the influence of liberation of sympathetic mediator from the nerve endings.

The experiments also showed that dopa reduced by 3.5 times the number of ulcers in the stomach wall (Fig. 1).

The question naturally arises of a connection between these two phenomena. Probably the protective action of dopa described above is the result of preservation of the tissue reserves of catecholamines, without which a normal course of tissue metabolic processes is impossible.

This suggestion is supported by the results of experiments with α-methyldopa, a substance close to dopa in its chemical structure, but differing from it in its pharmacological action.

Unlike dopa, α-methyldopa did not prevent either ulceration of the stomach wall or the decrease in the concentrations of noradrenalin and adrenalin in the stomach wall of the rats subjected to immobilization and electrical stimulation (Fig. 1).

Injection of dopa or of α-methyldopa into intact rats did not produce significant changes in the concentrations of noradrenalin and adrenalin in the stomach wall.

The results obtained indicate participation of the sympathetic nervous system in the development of neurogenic degeneration of the stomach and the important role of exhaustion of the catecholamine reserves in this process, as a result of their excessive liberation during excessive stimulation.

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