

ROLE OF SEROTONIN IN THE MECHANISM OF THE CYTOPROTECTIVE ACTION
OF DEXTRAN ON THE STOMACH

S. N. Fedchenko and D. A. Maslakov

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Hydrocortisone is known to have an enhanced ulcerogenic action on the stomach in thyrotoxicosis [2]. There are solitary reports in the literature [3, 4] of a connection between serotonin release and destructive lesions of the stomach. It was accordingly deemed interesting to study whether serotonin participates in ulcer development when the hormonal balance is disturbed. To test this hypothesis, the effect of injections of dextran together with hormones on serotonin metabolism was studied.

EXPERIMENTAL METHOD

Experiments were carried out on 80 male rats weighing 180-200 g. Hydrocortisone was injected intramuscularly in doses of 12.5 mg/kg (series I) and 25 mg/kg (series II) for 10 days into the animals in which marked experimental hyperthyroidism had been produced by administration of thyroxine, 2.5 mg/kg, for 10 days. In the experiments of series III and IV the animals received these same preparations by a similar scheme but, in addition, they were given dextran intravenously in doses of 10 ml/kg body weight for four injections with intervals of 3 days; two injections were preceded by injection of hydrocortisone [2]. Animals of the control group received injections of equal volumes of physiological saline at the corresponding times.

Serotonin-producing cells (Ec cells) were identified electron-microscopically, by Falk's fluorescence-histochemical method, and by impregnation by Masson's method [1]. Ec cells were counted in an area of 1 mm² of a longitudinal section through the mucous membrane. The serotonin content in the gastric mucosa was determined biochemically by the method in [7].

EXPERIMENTAL RESULTS

It will be clear from Fig. 1 that the number of gastric ulcers in hyperthyroid rats receiving hydrocortisone in doses of 12.5 and 25 mg/kg together with dextran was reduced to 35 and 45%, respectively, compared with 58 and 71% in animals of series I and II. Injection of dextran into animals with hyperthyroidism led to a sharp decrease in the number of detectable Ec cells and a decrease in the granulation index. Ultrastructural analysis showed that most Ec cells were degranulated, which corresponds to lowering of the serotonin level in the mucosa of the antral portion of the stomach in the rats of series I and II (Table 1).

The study of sections impregnated by Masson's method showed that only one-third of Ec cells in the stomach of rats in series III and IV were degranulated (compared with two-thirds in series I and II). Ultrastructural analysis of the stomach of rats in the experiments of series III and IV showed that most Ec cells were in the phase of deposition of secretory granules. However, under these circumstances the predominant feature was blocking of extrusion of the secretion, and this suggests that the endocrine cells mentioned above were in a state of depressed metabolic activity.

The results of the biochemical tests confirmed the histochemical and ultrastructural data. The serotonin level in the mucosa of the antral portion of the stomach of the hyperthyroided animals, treated with dextran and hydrocortisone in doses of 12.5 and 25 mg/kg, was raised to 91 and 76%, respectively, compared with 61 and 21% in the animals receiving hormones but without dextran (Table 1).

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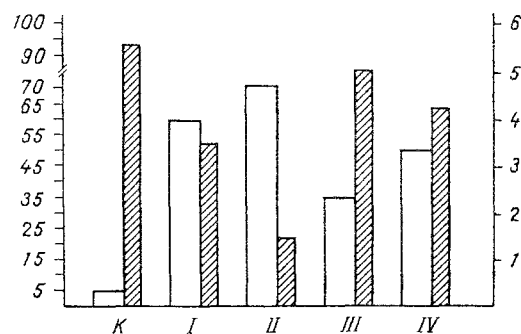


Fig. 1. Serotonin content in mucosa of antral portion of stomach and frequency of gastric ulcer formation. Abscissa, different series of experimental animals; unshaded columns — % of gastric ulcers; shaded columns — serotonin content. Ordinate: on left — frequency of gastric ulcers (in %), right — serotonin content in mucosa of antral part of stomach (in $\mu\text{g}/\text{mg}$ tissue). K) Control.

TABLE 1. Serotonin Content (in $\mu\text{g}/\text{g}$ tissue) in Gastric Mucosa of Rats after Injection of Hormones

| Experimental conditions | Mucous membrane | | | |
|--|------------------------------------|----------------|------------------------------------|--------------------|
| | fundal portion $\bar{x} \pm Sx$ | <i>p</i> | antral portion $\bar{x} \pm Sx$ | <i>p</i> |
| Intact (n= 24) | 1,60±0,13 | | 5,6±0,12 | |
| Thyroxine + hydrocortisone, 12,5 mg/kg (n= 16) | 1,85±0,12 | >0,1* | 3,39±1,14 | <0,05* |
| Thyroxine + hydrocortisone, 25 mg/kg (n= 14) | 1,71±0,28 | >0,5* | 1,36±1,18 | <0,001* |
| Thyroxine + hydrocortisone, 12,5 mg/kg + dextran (n= 14) | 1,50±0,13 | >0,5* >0,1† | 5,09±0,63 | >0,5* <0,001† |
| Thyroxine + hydrocortisone, 25 mg/kg + dextran (n= 12) | 1,70±0,14 | >0,5* >0,5† | 4,25±0,47 | <0,001* <0,001† |

*Differences compared with intact animals significant.

†Differences compared with control (animals receiving hormones alone, without dextran) significant.

The higher serotonin content in the gastric mucosa of animals receiving injections of the hormones together with dextran and the fall in percentage of ulcers produced suggest that these features may be connected or, in other words, that inhibition of serotonin release from the depots can be interpreted as a favorable factor preventing the development of destructive lesions of the gastric mucosa.

The hypothesis that blocking of serotonin extrusion from Ec cells plays a beneficial role is confirmed by investigations [5, 8] which demonstrated a connection between the fall in the serotonin level in the gastric mucosa and the frequency of gastric ulcers.

Considering data in the literature on the inhibitory effect of serotonin on HCl secretion and the stimulation of secretion of alkaline components of the mucus, it can be postulated that the increase in the number of detectable Ec cells and elevation of the serotonin level in the gastric mucosa of hyperthyroid rats, receiving injections of hydrocortisone together with dextran, is compensatory and adaptive in nature.

Intravenous injection of dextran with hydrocortisone, against the background of experimental hyperthyroidism, thus reduces the percentage of lesions in the gastric mucosa by restricting serotonin release.

It is evident that an adequate concentration of serotonin in the stomach and, according to recent data [6], of melatonin also, is responsible for maintaining its structural integrity, and it increases the resistance of the gastric mucosa to the ulcerogenic action of glucocorticoids.

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EFFECT OF ACETYLCHOLINE ON LYSOSOMAL FUNCTION IN THE LIVER AND KIDNEYS OF RATS WITH SEVERE MECHANICAL TRAUMA

L. N. Kobylanskii

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An important role in the pathogenesis of severe trauma, caused by crushing of soft tissues, is played by changes in the cholinergic system expressed primarily as general depression of its physiological activity and a disturbance of acetylcholine metabolism [1, 2]. As a clinical transmitter of nervous excitation in M- and N-cholinergic structures, acetylcholine affects the functional state of organs and tissues by regulating active transport of materials through cell membranes [10, 11]. Acetylcholine accumulation in synapses enhances the readiness of the organism for seizure activity and lowers its resistance to traumatic factors, whereas stimulation of acetylcholinesterase activity or exogenous preparations of this enzyme increase the resistance of animals to trauma [3, 4]. Consequently, direct correlation between the state of function of the cholinergic system and the resistance of the organism to traumatic factors can be postulated.

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