TROPHIC EFFECT OF CATECHOLAMINES ON SECRETORY FUNCTION OF EXHAUSTED GASTRIC GLANDS

S. V. Anichkov and L. L. Grechishkin

UDC 612.323.014.32.014.46:615.361.8

According to L. A. Orbeli's theory [6, 7], the sympathetic nervous system is the chief regulator of recovery processes. Its role is especially important when the work of a fatigued organ is concerned [4]. In the modern view the influence of the sympathetic nerves directed toward restoration of building and energy-forming material used up by the organ during work is effected through the liberation of catecholamines. The study of the action of catecholamines of exogenous origin on the function of the stomach when in a state of fatigue as a result of prolonged secretion is therefore of special interest. The work of Ya. P. Sklyarov and co-workers [5, 8] is relevant to this issue; they found that after food stimulation lasting many hours the content of nitrogenous substances and the digestive power of the gastric juice fall sharply, and that administration of adrenalin restores these indices.

In the present investigation the effect of various catecholamines on the secretory function of the gastric glands was studied when the glands were exhausted by prolonged and combined administration of stimulators of secretion (acetylcholine and histamine), and also when the tissue depots of catecholamines had been emptied by administration of reserpine.

EXPERIMENTAL METHOD

Three series of chronic experiments were carried out on 6 dogs weighing 18-21 kg with a gastric fistula. All substances were given by continuous intravenous infusion, carried out by means of a special adapter enabling the infusion to be given at a predetermined speed (1 ml per min) for several hours by ensuring a constant pressure [2]. Pharmacological agents—acetylcholine chloride, histamine hydrochloride, L-adrenalin chloride, L-noradrenalin bitartrate, isoprenaline—were injected through a thin polyethylene catheter introduced into a vein of the forelimb. The dogs were fasted for 18 h before taking part in the experiment. Every 20 min the volume of gastric juice and its acidity (pH) and the concentration of pepsin in the juice (in mg/ml) were determined. The pepsin concentration was determined by Gates' method [9] as modified in the authors' laboratory. Altogether 34 chronic experiments were carried out.

EXPERIMENTAL RESULTS

In a preliminary series of 8 experiments the gastric glands were exhausted by an intravenous infusion of histamine (1 μg/kg body weight/min) together with acetylcholine (15 μg/kg body weight/min) lasting for 7 h. These two stimulators, acting as synergists, activated both the chief and the parietal cells of the gastric mucous membrane causing hypersecretion with the highest possible indices of acidity and of pepsin concentration.

Perfusion began with injection of histamine. At the beginning of its action, histamine causes a temporary increase in pepsin concentration, followed after 1 h by a sharp decrease. Most investigators are of the opinion that this increase in the pepsin concentration in the juice is not the result of active function of the chief cells, but takes place as a result of passive "washing out" of pepsinogen granules from the ducts of the glands, in which they accumulate during a period of relative rest [3, 10]. Eighty minutes after the beginning of the experiment acetylcholine started to be injected together with histamine. The combined action of the two stimulators led to a sharp increase in the volume of secretion (110±16 ml in 20 min) and to an even greater increase in the pepsin concentration in the juice. The mean pepsin concentration was 1.44±0.20 mg/ml and the rate of pepsin production was 140±25 mg over a period of 20 min. This fresh increase in the pepsin concentration is explained by active secretion by the chief cells due to the action of acetylcholine.

Division of Pharmacology, Institute of Experimental Medicine, Academy of Medical Sciences of the USSR, Leningrad. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 64, No. 10, pp. 37-39, October, 1967. Original article submitted October 5, 1966.

The secretion was maintained at this high level in most dogs for 3-4 h, and sometimes for 5-6 h, after which all the indices fell. Pepsin production was the first to fall, and it was followed 20-40 min later by the volume of secretion. On the average the pepsin concentration fell to 0.3±0.1 mg/ml by the 5th or 6th hour of the experiment, although in some experiments it was close to zero. The volume of secretion was 35±10 ml in 20 min. The acidity of the juice remained at the level of pH 1.4-1.5, although the total production of hydrochloric acid by the stomach fell by an amount corresponding to the decrease in the volume of secretion. These changes in gastric glands caused by the excessive load. In some animals (2 of 8) it was impossible to produce a severe degree of exhaustion in an experiment lasting 7 h, thus demonstrating great individual differences in the resistance of the secretory apparatus of the stomach in dogs.

In another series of 16 experiments, immediately after the appearance of signs of exhaustion of the gastric glands a prolonged (1 h) intravenous infusion of one of the catecholamines was given: adrenalin (3 μg/kg body weight/min), noradrenalin (3 μg/kg/min), or isoprenaline (1.5 μg/kg/min). The volume of secretion gradually began to increase 40-60 min after administration of the catecholamines ended, reaching on the average 40% of the maximal level in the experiment (44±18 ml/20 min); the pepsin concentration in the juice increased at the same time (1.1±0.3 mg/ml), while the pepsin production reached 27% (36±5 mg in 20 min). Injection of the exhausting factors histamine and acetylcholine continued during this period.

The last series of experiments was carried out on two reserpinized dogs. Reserpine was injected intramuscularly in a daily dose of 0.05 mg/kg for 10 days. Spontaneous secretion of gastric juice (5-10 ml in 20 min) with high acidity (pH 1.4) but with a low pepsin concentration (0.4 mg/ml) was observed in the reserpinized dogs. Exhaustion of the gastric glands during the combined action of histamine and acetylcholine developed much quicker in these dogs than after 60-80 min. The maximal level of secretion at the beginning of the experiment was 45% lower than in the intact dogs (60±12 ml juice in 20 min). The concentration and output of pepsin likewise were 50% lower (0.7±0.2 mg/ml).

In this case also, slow infusion of catecholamines in the above doses in the period of low secretion led to an appreciable increase in pepsin concentration in the juice (0.8±0.5 mg/ml), although it was much smaller than in the intact dogs. The volume of secretion was almost unchanged. Evidently, the emptying of the catecholamine depot taking place under the influence of reserpine disturbs the nutrition of the gastric mucous membrane and causes more rapid exhaustion of the gastric glands.

The restorative effect of catecholamines on the function of the gastric glands when fatigued may be regarded as analogous to the Orbeli–Ginetsinskii phenomenon in striped muscle. The results of the present investigation demonstrate that the sympathetic nerves of the gastric mucous membrane play the role of controllers of nutrition of the tissues.

Work undertaken in the authors' laboratory during the last 10 years has established that the sympathetic nervous system participates in the development of experimental degeneration of the gastric mucous membrane [1]. Experimental results have shown that destructive changes in the stomach wall caused by excessive stimulation are reflex in character and develop as a type of neurogenic degeneration, in which the descending arc of the reflex travels along sympathetic nerve fibers. The sympathetic nerves, which usually maintain the normal level of metabolic processes in the mucous membrane, when stimulated to excess cause nutritional disturbances in this membrane, i.e., they cause the development of degeneration.

LITERATURE CITED

1. S. V. Anichkov and I. S. Zavodskaya, The Pharmacotherapy of Peptic Ulcer [in Russian], Leningrad (1965).
2. S. V. Anichkov and L. L. Grechishkin, Farmakol. i Toksikol., No. 5, 587 (1965).
3. B. P. Babkin, The Secretory Mechanism of the Digestive Glands [in Russian], Leningrad (1960), p. 230.
4. A. G. Ginetsinskii, Russk. Fiziol. Zh., 6, Nos. 1-3, 198 (1923).
5. Z. V. Dovgan', The Nervous Mechanism of Excitation of the Gastric Glands [in Russian], Candidate Dissertation, Chernovtsy (1952).
6. L. A. Orbeli, Izvest. Lesgafta Petrograd. Nauchn. Inst., 6, 187 (1923).
7. L. A. Orbeli, Klin. Med. (Moscow), No. 5, 648 (1937).
8. Ya. P. Sklyarov, In the book: Mechanism of Action of Hormones [in Russian], Kiev (1959), p. 237.
9. F. L. Gates, Proc. Soc. Exp. Biol. (New York), 24, 936 (1927-1927).
10. A. Gilman and G. Cowgill, Am. J. Physiol., 97, 124 (1931).