CHOLINERGIC MECHANISM REGULATING PROTEIN AND NUCLEIC ACID METABOLISM IN THE GASTRIC MUCOSA

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Injection of neostigmine increased the protein content in the gastric mucosa of dogs during chronic experiments. In response to excitation of the gastric glands by sham feeding an increase in the RNA content and ribonuclease activity was observed. Excitation of the cholinergic regulatory mechanism thus leads to an increase in the protein and RNA content in the gastric mucosa. Blocking the cholinergic regulatory mechanism by atropine reduces the protein and nucleic acid content in both the resting and the secreting gastric mucosa.

The cholinergic regulatory mechanism plays an important role in the secretory function of the gastric glands [2, 5, 7, 9, 11, 14, 18]. Protein synthesis [1, 4, 7] is directly related to the pepsin content in the gastric mucosa [15]. The regulation of tissue metabolism in the stomach by the nervous system has received little study [14].

The role of the cholinergic mechanism regulating protein and nucleic acid metabolism in the gastric mucosa was studied in the resting state and during secretion.

EXPERIMENTAL METHOD

Acute and chronic experiments were carried out on dogs with a gastric fistula and also on gastroesophagotomized animals. The gastric mucosa was studied under chronic experimental conditions by Sklyarov's biopsy method [16]. The protein content was determined by the diffuse salting-out method [6], nucleic acids by the method of Tsanev and Markov [17], and ribonuclease (RNase) by the method of Fierst and Stocks [19] with the gastric glands in a resting state and during secretion. The gastric glands were stimulated by sham feeding the animal for 3 min and by subcutaneous injection of 0.5 ml of a 0.01% solution of histamine. The cholinergic regulatory mechanism was excited by injecting acetylcholine (AC, 0.75 mg/kg) into the animal 5 min after an injection of 0.05 mg/kg neostigmine to destroy the cholinesterase (CE), and also by measured sham feeding of the animal under chronic experimental conditions. The cholinergic regulatory mechanism was blocked by subcutaneous injection of 0.05 mg/kg atropine.

EXPERIMENTAL RESULTS AND DISCUSSION

In the acute experiments the RNA and DNA content in the gastric mucosa was increased after administration of AC and neostigmine. During the first hour this increase was very small, by the end of the 3rd hour the nucleic acid content was increased by 1.5-2 times. In the chronic experiments the same dose of AC induced restless movements and salivation in the animal. These facts suggest that the dose of AC was close to toxic.

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Only neostigmine, which not only inhibits cholinesterase but also facilitates interaction between AC and the cholinergic receptor [8], was used in the next series of experiments. Injection of neostigmine caused a significant increase in the protein content, from 3.34 ± 0.10% to 3.64 ± 0.15% (per gram wet weight of tissue) in the course of 1-1.5 h ($P < 0.05$).

As a result of excitation of the vagus nerves in the sham-feeding experiments the RNA content in the mucosa rose significantly – at the height of secretion from 5.3 ± 0.7 to 6.4 ± 0.5 mg/g wet weight of tissue. Besides the increase in the RNA content the RNase activity also was increased from 26.3 ± 4.0 to 50.8 ± 11.9 μg P_i/mg N, indicating an increased intensity of RNA synthesis in this period. At the height of secretion of gastric juice during the period of maximal hydrochloric acid and pepsin production in the mucous membrane, considerable changes in tissue metabolism aimed at providing for the secretory function are known to take place. At the end of secretion the RNA content in the mucosa falls, returning to or close to its initial level after 30-60 min [15]. As a result of these experiments it can thus be concluded that excitation of the cholinergic regulatory mechanism of the gastric glands induces an increase in the protein and nucleic acid content in the gastric mucosa. These findings are in agreement with those obtained by Guberniev and Il'ina [3], who studied the salivary gland, pancreas, and liver, in which they found an increase in nucleic acid synthesis in connection with increased secretory activity of the digestive glands.

After blocking the cholinergic regulatory mechanism of the secretory process by atropine the protein content in the mucosa fell both with the gastric glands in a resting state (from 2.33 ± 0.28 to 2.15 ± 0.27%) and during histamine secretion (to 1.99 ± 0.49%), although this decrease was not significant. The decrease in the nucleic acid content (RNA from 5.3 ± 0.7 to 4.4 ± 0.7 mg, DNA from 3.4 ± 0.8 to 2.0 ± 0.55 mg) under the influence of atropine in the nonsecreting mucosa likewise was not significant. Together with a decrease in the RNA content under the influence of atropine, the RNase activity was considerably increased (from 26.3 ± 4.0 to 80.4 ± 23.6 μg P_i/mg N; $P > 0.02$), indicating predominance of RNA breakdown in the nonsecreting gastric mucosa. Injection of atropine after sham feeding led to a significant decrease in the RNA level (from 6.4 ± 0.5 to 4.7 ± 0.67 mg), whereas the decrease in the DNA content was not significant. RNase activity was unchanged (50.8 ± 11.9 and 50.9 ± 9.7 μg P_i/mg N).

Sham feeding after injection of atropine did not cause any increase in the RNA content or RNase activity in the mucosa.

It can thus be concluded from these experiments that blocking the cholinergic regulatory mechanism reduces the protein and nucleic acid content in both the secreting and the nonsecreting gastric mucosa.

The cholinergic mechanism regulating the activity of the gastric glands evidently plays an important role in the protein and nucleic acid metabolism in the gastric mucosa.

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