Effect of Stimulation of Cholinergic Muscarinic Receptors on Norepinephrine Accumulation in Esophageal and Gastric Mucosa in Rats

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An hour and half after injection of norepinephrine its concentration in the mucosa of the lesser curvature of the stomach increases and in the greater curvature decreases. Stimulation of muscarinic receptors with pilocarpine leads to a marked rise of norepinephrine concentration in the esophageal mucosa and in the mucosa of the lesser curvature. It is supposed that stimulation of muscarinic receptors of the gastrointestinal tract after injection of exogenous norepinephrine induces accumulation of this transmitter in structures with abundant cholinergic innervation. Selective norepinephrine accumulation in the mucosa of the esophagus and lesser gastric curvature is apparently due to its high permeability for norepinephrine contained in saliva.

Key Words: *catecholamines; esophageal mucosa; stomach*

Stimulation of exocrine gastrointestinal glands is accompanied by enhanced release of various growth factors (epithelial, nerve, etc.) [3,4,6,7]. This process depends on activity of sympathetic nervous system [7,8,10]. However, the possibility of accumulation of norepinephrine (NE) in esophageal and gastric mucosa induced by high plasma concentration of this transmitter against the background or without pilocarpine-induced stimulation of muscarinic receptors remains unclear.

MATERIALS AND METHODS

Experiments were carried out on 58 random-bred male rats weighing 250±50 g divided into 3 groups: intact rats, rats injected with 40 μg/kg NE followed by stimulation of gastrointestinal muscarinic receptors with pilocarpine (1 mg/kg), and rats injected with NE (40-100 μg/kg).

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The animals were deprived of food 24 h before the experiment to synchronize the function of exocrine gastrointestinal glands and had free access to water. The rats were narcotized with Nembutal (40 mg/kg) 20 min after NE injection. Forty-five minutes later the animals received pilocarpine (1 mg/kg), and secretory cycle was stimulated for 40 min. The contents of NE and epinephrine (E) in blood (0.5 ml) and mucosa specimens (10 mg) from the esophagus and the lesser and greater curvatures of the stomach were measured by high-performance liquid chromatography with electrochemical detection [1]. The data were processed statistically using the Student's *t* test.

RESULTS

In control animals the concentration of NE in mucosa specimens far surpassed its plasma content. Plasma and tissue concentrations of E were much lower than those of NE (Table 1). Intraperitoneal injection of NE changed NE and E concentrations in the mucosa but not in the plasma: the content of NE increased

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TABLE 1. Content of Norepinephrine (NE) and Epinephrine in the Mucosa of Esophagus, Greater and Lesser Curvatures of the Stomach, and Blood of Rats Injected with NE (*M±m*)

Tissue	Norepinephrine		Epinephrine	
	control	injection of NE	control	injection of NE
Mucosa from, ng/g:				
esophagus	335±49.4 (8)	239±30.7 (9)	52.6±9.7 (9)	39.7±9 (9)
lesser gastric curvature	233±47.5 (8)	361±38.9 (9)*	48.4±10.7 (8)	39.9±9 (9)
greater gastric curvature	357.3±41.9 (8)	235±18.8 (10)**	85.8±20 (8)	46.2±8.5 (9)*
Blood plasma, ng/ml	3.2±0.78 (8)	3.8±0.76 (10)	0.33±0.05 (8)	1.1±0.26 (9)**

Note. Here and in Table 1, *$p<0.05$, **$p<0.01$, ***$p<0.001$ compared with the control. Number of experiments is shown in parentheses.

TABLE 2. Content of Norepinephrine (NE) and Epinephrine in the Mucosa of Esophagus, Greater and Lesser Curvatures of the Stomach, Blood, and Gastric Juice of Rats Injected with NE against the Background of Pilocarpine Stimulation (*M±m*)

Tissue	Norepinephrine		Epinephrine	
	control	injection of NE	control	injection of NE
Mucosa from, ng/g:				
esophagus	431±86.7 (8)	685.2±106.3 (11)*	85±11.2 (8)	34.2±7.2 (9)***
lesser gastric curvature	302±50 (8)	666.5±76.5 (11)***	105±18.3 (7)	68±11.9 (10)
greater gastric curvature	376±60 (8)	418.7±67.8 (10)	70±9.3 (8)	56.5±13.9 (11)
Blood plasma, ng/ml	3.7±0.42 (9)	3.31±0.59 (13)	0.59±0.08 (8)	0.4±0.07 (10)
Gastric juice, ng/ml	11.9±1.96 (8)	11.3±11.9 (9)	2.62±0.51 (7)	2.38±0.29 (9)

in mucosa from the lesser curvature and decreased in the greater curvature, while in esophageal mucosa and in the plasma NE concentration remained unchanged. The content of E rose only in the plasma, while in other tissues it was unchanged.

Thus, parenteral injection of NE affected plasma concentration of E and to a lesser extent NE concentrations in the mucosa of the lesser and greater gastric curvatures. Stimulation of muscarinic receptors with pilocarpine modulates NE content in parallel with stimulation of secretory activity. Under these conditions, injection of NE markedly increased the concentration of this transmitter in the mucosa of the esophagus and lesser gastric curvature (Table 2), while in the greater curvature, gastric juice, and plasma it remained unchanged. The concentration of E decreased only in the esophageal mucosa and in the plasma, while in gastric juice it did not differ from the control (Table 2).

These findings suggest that stimulation of muscarinic receptors in animals preinjected with NE induced primary accumulation of this transmitter in the mucosa of the esophagus and lesser gastric curvature, i.e., structures with abundant cholinergic innervation.

It can be concluded that injection of NE in the absence of stimulation of muscarinic receptors results in a rise of plasma concentration of E as soon as 1.5 h postinjection, the content of NE being unchanged. Stimulation of muscarinic receptors activates secretory function of salivary and other exocrine gastrointestinal glands. Selective accumulation of NE in the esophageal mucosa and mucosa of the lesser curvature may be due to their high permeability for NE contained in the saliva.

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