Mechanism of Synergism between Sympathetic and Parasympathetic Autonomic Nervous Systems in the Regulation of Motility of the Stomach and Sphincter of Oddi

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The mechanisms of stimulatory effect of the sympathetic trunk on gastric motor activity and vagal inhibitory effect on electromotor activity of the sphincter of Oddi were studied. Gastric contractions were augmented by preganglionic serotoninergic fibers related synaptically to serotoninergic neurons, while inhibition of electromotor activity of the sphincter of Oddi was elicited by activation of α- and β-adrenoceptors.

Key Words: *stomach, sphincter of Oddi; activity; regulation; rabbits; dogs*

The sympathetic and parasympathetic systems can either stimulate or inhibit motor activity of the gastrointestinal tract (GIT). Intensive and low frequency stimulation (1-5 Hz) of the sympathetic trunk (ST) usually produces excitatory effects. These excitatory effects were neither abolished by atropine (0.1-1.0 mg/kg) nor prevented by bilateral vagotomy. Hexamethonium (5-100 mg/kg) or guanethidine (3.3-20.0 mg/kg) did not abolish these effects, but transformed them into excitatory ones [2]. These excitatory effects result from activation of fine afferent fibers via the axon reflex. Sympathetic potentiation of GIT motility could also be mediated via α-adrenoceptors. Smooth muscle membrane contains α_1-adrenoceptors mediating excitation and contraction of smooth muscles, α_2-adrenoceptors inhibiting smooth muscles of GIT [1], and P1- and P2-excitatory and inhibitory purinoreceptors [1,4]. Previous studies demonstrated histamine release from postganglionic sympathetic fibers and excitation of serotonergic fibers and neurons of the submucous plexus in the colon, which in 30% cases was promoted by the contacts between serotonergic fibers and intramural nitrergic fibers [3]. Generally, the data on the mechanisms of sympathetic potentiation of GIT contraction are contradictory.

Little is known on the mechanisms of reflex influences from the stomach and duodenum on the biliary excretion system, in particular, on the sphincter of common bile duct (sphincter of Oddi). Transection of splanchnic nerves decreases the tone of this sphincter. However, neither elimination of preganglionic neural fibers caused by transection of splanchnic nerves, nor postganglionic sympathectomy made by extirpation of solar plexus nodes prevented the duodenum-sphincter reflex, although it was markedly weakened under these conditions.

The study of neural regulation of the sphincter of Oddi is important in view of the wide use of vagotomy in clinical practice. It is known that parasympathetic denervation increases the rate and amplitude of phasic contractions of the sphincter of Oddi. The researchers noted the possibility of inhibiting electromotor activity of the sphincter of Oddi by vagal stimulation. There is no consensus on the effects of parasympathetic nerve on the motility of biliary excretion ducts.

Here we studied the mechanisms of inhibition of electromotor activity of the sphincter of Oddi during

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vagus nerve stimulation and activation of stomach motility during ST stimulation.

MATERIALS AND METHODS

Experiments were carried out on 24 dogs and 15 rabbits. In the study of the mechanisms of potentiation of gastric motility induced by ST stimulation, the pressure was recorded by the balloon method using a sensitive EMT-35 electrical transducer (0-30 mm Hg). ST was stimulated in the thorax with an ESL-2 electrical stimulator. The pulses (duration 1.5 msec, amplitude 1-15 V, repetition rate 1-20 Hz, and train duration 30 sec) were applied via a bipolar fork electrode 0.5 mm in diameter. To minimize parasympathetic influences, ST was stimulated in the thorax, where it has no cholinergic fibers. In addition, some experiments were carried out after cervical vagotomy and degeneration of vagal fibers, possible vagosympathetic anastomoses included.

Gastric motility was assessed by the intragastric pressure.

In the study of the inhibitory mechanisms of electromotor activity of the sphincter of Oddi caused by vagal stimulation we used bipolar needle platinum electrodes (diameter 0.3 mm, length 0.5 mm, and interelectrode distance 1.5 mm). Fast summational potentials were recorded in mV, their frequency was expressed as the number of fast potentials per 100 slow waves of basic electrical rhythm (BER).

The degree of myorelaxation was evaluated by the decrease in the amplitude of summational potentials and the amplitude of slow component of action potential. Myorelaxation of the sphincter of Oddi was observed during weak stimulation (0.5-5.0 V, 5 Hz, 2 msec) of the peripheral end of the vagus nerve.

The results were analyzed statistically using Student's *t* test.

RESULTS

Control experiments showed that stimulation of ST could not only inhibit, but also stimulate stomach contraction. This stimulatory effect was stable during repeated stimulation at 3-10-min intervals. The stimulatory effect developed more frequently (73% cases) than the inhibitory one (11% cases). In other cases neither stimulatory, nor inhibitory effects were observed. Inhibition and the absence of responses were observed more frequently during weak stimulation (0.5-5.0 V).

The control stimulations also showed that weak baseline peristaltic activity or its absence at low initial intragastric pressure (6-12 mm Hg) promoted the development of the excitatory effect.

Active peristalsis promoted the appearance of rarely observed inhibitory effect. Weak peristalsis (or its absence) promoted the development of a stimulatory phenomenon in response to ST stimulation in 14 of 19 dogs. Activation of gastric motility manifested in the appearance of single tonic contractions after stimulation series applied for 30-60 sec.

Thus, in most cases ST stimulation in dogs produced not inhibitory, but stimulatory effect on gastric motility.

Participation of catecholamines in activation of gastric contractions induced by ST stimulation was examined on 19 animals (several tests were performed on each dog). To this end, presynaptic sympatholytic ornid (bretylium tosilate) was used. Ornid blocking the release of catecholamines from nerve terminals did not abolish the "sympathetic" stimulatory effect and even promoted the development of this effect under conditions, in which it was not observed before ornid treatment. Ornid transformed the inhibitory effects induced by ST stimulation in intact animals into stimulatory ones, and the latter were observed more frequently (in 18 of 19 experiments, *i.e.* in 95% cases, while in control experiments the stimulatory responses were observed in 73% cases). The stimulatory effect was stable during repeated ST stimulation irrespective of the presence or absence of baseline peristalsis. The stimulatory effect was potentiated by ornid. While ST stimulation in intact dogs increased intragastric pressure (measured during tonic contraction of the stomach) from 8.4±1.4 to 17.6±3.4 mm Hg (by 129%, $p<0.02$), similar stimulation in ornid-treated dogs increased intragastric pressure from 9.2±2.0 to 28.4±4.6 mm Hg (by 209%, $p<0.01$). In the latter case, pressure increment was 2 times greater.

Experiments with ornid showed that gastric contraction induced by ST stimulation developed without participation of catecholamines, because suppression of catecholamine release did not prevent, but even promoted the excitatory effect.

Participation of pre- and postganglionic fibers in the development of gastric stimulatory effect was tested in animals receiving ganglioblockers benzohexonium and arfonad (combined or individual application) against the background of ornid. Blockade of nicotinic cholinergic receptors in autonomic ganglia in ornid-treated dogs did not prevent, and in some cases even promoted the development of stimulatory phenomenon. Thoracic stimulation of ST in dogs treated with ornid and benzohexonium (or its analogs) produced the same tonic contraction of the stomach, as was observed in ornid-treated dogs before injection of ganglioblockers. In these experiments, the intragastric pressure increased from 9.0±1.7 to 27.7±3.9 mm Hg (by 208%, $p<0.001$).

Taking these data into consideration, we hypothesized that gastric contraction is triggered by postganglionic nerve fibers, because the stimulatory effects was not eliminated by ganglioblockers. However, it can not be excluded that serotonergic fibers, which are known to be present in GIT, mediate this effect. It is known that serotonin stimulates gastric motility.

Possible involvement of serotonergic fibers in the development of the examined effect was tested in 12 experiments on dogs treated with S3 serotonin receptor blocker (morphine or promedol, n=6) or with S1 and S2 serotonin receptor blocker diprasinum (n=6). The stimulatory effect resistant to ganglioblockers benzohexonium or arfonad was prevented by S3 serotonin receptors blocker (morphine or promedol).

In special series of experiments we used diprasinum (5 mg/kg), a blocker of muscle S1 and S2 serotonin receptors. This agent completely abolished the excitatory effect of ST stimulation. The following stronger stimulation of ST under the action of ornid, benzohexonium, and diprasinum or after combined administration of ornid and diprasinum induced no stomach contraction, which corroborated the hypothesis on availability of serotoninergic fibers in ST, which stimulate GIT motility.

Thus, it is established that serotoninergic fibers produce synergic effects with the vagus nerve on GIT contraction.

The vagal mechanisms involved in the regulation of the sphincter of Oddi functions were studied on 15 rabbits. It was found that stimulation of the peripheral end of the vagus nerve with electrical pulses of middle amplitude (5-20 V, 5 Hz, 2 msec) usually triggered electrical excitation of sphincter muscles, which manifested in an increase in the amplitude of slow waves from 0.88±0.16 to 1.18±0.17 mV (by 32%, p<0.05) and the amplitude of fast summational potentials from 0.73±0.14 to 0.89±0.13 mV (23%, p<0.01). At the same time, the frequency of fast potentials increased by 27% (from 0.66±0.1 to 0.84± 0.15 per 100 slow waves, p<0.05), while frequency of slow waves remained practically unchanged (21.7±2.4 and 22.4±2.2 min, 3%, p>0.5), respectively.

In 40% cases, weak stimulation of the vagus nerve (0.5-5.0 V, 5 Hz, 2 msec) inhibited electrical activity of the sphincter of Oddi (35 of 90 tests). This was accompanied by a decrease in slow wave amplitude in all series from 0.73±0.12 to 0.52±0.13 mV (by 27%, p<0.01), while the frequency of slow wave decreased from 19.3±1.2 to 18.5±1.1 per min (by 5%), and the frequency of fast potentials decreased insignificantly from 0.79±0.08 to 0.67±0.13 per 100 slow waves (by 14%).

The inhibition was prevented by ganglioblocker benzohexonium and combined action of propranolol and dihydroergotoxin (n=18).

A conclusion was made on the synergism between the sympathetic and parasympathetic system in the regulation of gastric activity. Similar to sympathetic system, the vagus nerve can inhibit electromotor activity of the sphincter of Oddi, while serotonergic fibers in ST can stimulate gastric motility similarly to the parasympathetic vagus nerve.

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