Role of Activation of Cholinergic Influences in Recovery of Electrical Activity of the Stomach and Small Intestine during the Early Postoperative Period in Rats

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The effects of neostigmine and calcium pantothenate on electrical activity of the stomach and small intestine were studied in chronic experiments on rats after laparotomy with implantation of a probe into the jejunum and electrodes into different portions of the gastrointestinal tract. At the early terms after surgery, stimulation of endogenous acetylcholine release intensified electrical activity of the stomach, duodenum, and jejunum. Treatment with neostigmine and calcium pantothenate did not accelerate the recovery of the migrating myoelectrical complex, but promoted the recovery of the general intensity of action potential generation in the stomach and small intestine.

Key Words: *neostigmine; calcium pantothenate; migrating myoelectrical complex; stomach; small intestine*

Suppression of cholinergic activating effects mediated mainly by acetylcholine is a cause of suppressed intestinal motility after operations on the abdominal organs [4,5]. The mechanism of suppression of parasympathetic activity during the early postoperation period includes inhibition of acetylcholine release from stimulatory fibers located in the myoenteral plexus [6]. Anticholinesterase drugs are used for stimulation of intestinal motility via activation of acetylcholine [3,5]. The effect of Neostigmine produces a cholinomimetic effect due to reversible inhibition of cholinesterase and potentiation of the effect of endogenous acetylcholine.

Suppression of cholinergic stimulation after surgery can be also caused by pantothenic acid deficiency [6]. Acetylcholine is synthesized in cholinergic neuron terminals from choline. Free choline in nerve terminal is acetylated by choline acetyltransferase (a cytosol enzyme); acetylcoenzyme A (final product of glycolysis) formed in mitochondria during oxidative decarboxylation of pyruvate serves as the donor of acetyl groups. Calcium pantothenate stimulates the synthesis of acetylcoenzyme A as the only essential component (substrate) in its structure [2]. Exogenous pantothenic acid stimulates the production of endogenous acetylcholine, which leads to stimulation of intestinal smooth muscle cells.

Reports about the stimulatory effect of pantothenic acid on the motor function of the small intestine after interventions on abdominal organs are scanty [6] and we failed to find data on the effect of calcium pantothenate on electrical activity of the stomach and small intestine.

Here we compared the effects of cholinergic drugs (neostigmine and calcium pantothenate) on electrical activity of the stomach and small intestine after surgical interventions on abdominal organs.

MATERIALS AND METHODS

The study was carried out on adult male Wistar rats (n=15) with initial weight of about 400 g. Before

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the experiment the animals received full-value natural ration.

After 18-h food deprivation, median laparotomy was carried out under ketamine narcosis, a probe was implanted into the proximal portion of the jejunum, and needle electrodes [1] were implanted into the antral wall of the stomach and proximal portions of the duodenum and jejunum. After fixation, the probe and electrodes were conducted through soft tissues of the abdominal wall and pelvic area, pulled under the skin on the tail, and brought out 5-6 cm from the tip of the tail [1].

Experiments were carried out during the early postoperative period (days 1-7 postoperation). The animals were divided into 3 groups.

Group 1 rats (controls; n=5) were infused with saline into the jejunum during the first 3 days postoperation; group 2 animals (n=5) received 0.2 mg/kg neostigmine, and group 3 ones (n=5) received 0.75 mg/kg calcium pantothenate. In order to create the same conditions for control and experimental animals, the volume of saline for controls was the same as the volume of drugs injected to experimental rats (0.2 ml).

Basal electrical activity was recorded in rats of all groups for 1 h after overnight fast. This was followed by infusion of the drug through the probe into the intestine; electrical activity was recorded for 2 h. On days 1 and 2, the animals received 8 ml glucose saline solution into the intestine after the end of registration. Starting from day 3 the rats received common fodder. The rats were allowed free access to water over the entire experiment, except the hours of electrical activity recording. After the experiment the animals were sacrificed by LD narcosis.

Electrodes for electrical activity recording were connected to an amplifier with 0.1 mV sensitivity. The registration was carried out in a narrow frequency band (1-100 Hz), the signal was transferred to PC. Analysis of EMG included evaluation of the time parameters of migrating myoelectrical complex (MMC): period and duration of phase III.

The data were statistically processed using Student's paired test, the differences were considered significant at $p<0.05$.

RESULTS

Basal records on day 1 after surgery were characterized by the appearance of chaotic solitary action potentials (AP) and AP packs of low intensity in the stomach, duodenum, and jejunum of all animals. Analysis of EMG recorded over 2 h after infusion of the drugs showed the following results. In the control group, electrical activity of the stomach, duodenum, and jejunum did not change after injection of saline (Fig. 1). In group 2 continuous AP packs appeared on EMG of the stomach, duodenum, and jejunum, while periods of rest were virtually absent. Potent high-amplitude AP were most pronounced during the 2nd hour after neostigmine infusion. In group 3, electrical activity also increased in all studied gastrointestinal compartments.

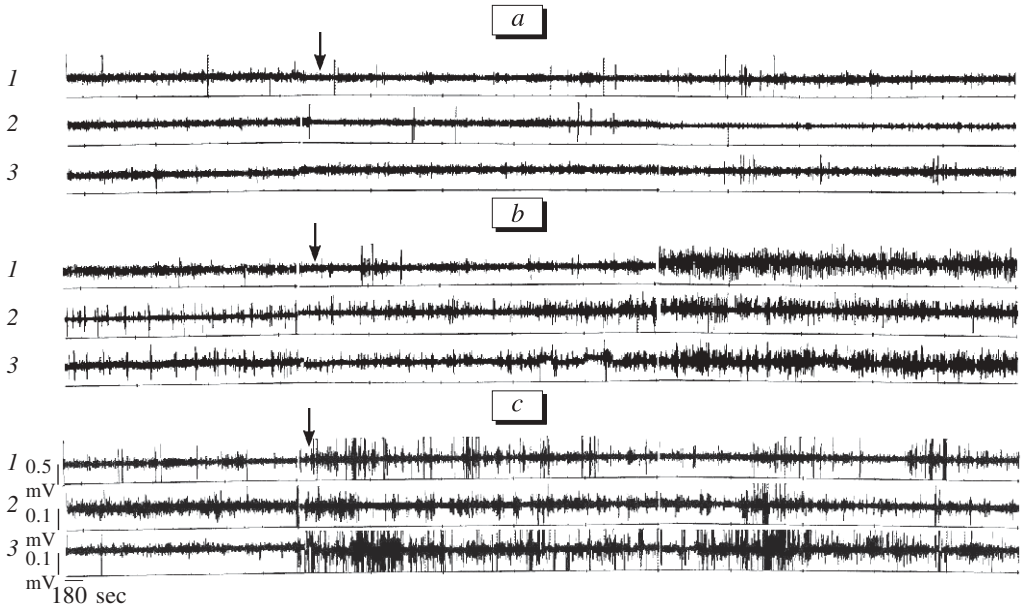

Fig. 1. Electrical activity of the stomach (*1*), duodenum (*2*), and jejunum (*3*) after infusion (arrow) of saline (*a*), neostigmine (*b*), and sodium pantothenate (*c*) on day 1 after the intervention.

Synchronous AP spikes in the stomach, duodenum, and jejunum and potent prolonged AP packs were recorded. Summary intensity of AP after neostigmine treatment was higher than after treatment with calcium pantothenate.

In groups 2 and 3, non-propagating synchronous AP were paralleled by high-amplitude AP, propagating with high speed from the stomach to the jejunum, due to which the mean summary intensity of AP increased significantly. The propagating pattern activity period was equal to 10±2 sec. The amplitude of AP 2-3-fold surpassed the normal maximum AP amplitude. The rate of AP propagation from the duodenum to the jejunum was 0.8-1.0 cm/sec. The period equal to 10 sec is characteristic of basal electric rhythm of the stomach. Hence, the stomach seems to modulate electrical activity of the proximal portions of the small intestine.

In the control group, normal MMC propagating from the stomach to the jejunum was recorded only by day 7 and was 650±50 sec, with phase III duration of 210±60 sec.

The dynamics of recovery of electrical activity was similar in two experimental groups. On day 3 after surgery, basal EMG of the stomach showed pronounced AP packs of different intensity, incessantly following each other. EMG of the duodenum and jejunum showed long synchronous MMC phases III (330±30 sec) with short rest periods (150±50 sec). MMC was absent. These data indicate the presence of virtually permanent contractions of all studied compartments and the absence of coordination of contractile activity between them. By day 4, the intensity of spike activity of the stomach, duodenum, and jejunum corresponded to normal, but no MMC was detected. Periods of rest and activity alternated chaotically. By day 5, the EMG of the duodenum and jejunum exhibited phases III of normal duration. MMC propagating from the stomach to the jejunum was restored only on day 7 after surgery.

Electrical activity of the stomach and small intestine was stimulated by cholinergic drugs stimulating acetylcholine release.

Neostigmine blocking acetylcholinesterase significantly increases the intensity of AP generation in the stomach and small intestine, because under conditions of cholinesterase inhibition one pulse provokes several contractions, the strength and duration of these contractions increased (without anticholinesterase treatment one nerve pulse induces one contraction) [2].

Calcium pantothenate, in addition to compensation for the pantothenic acid deficiency and stimulation of endogenous acetylcholine production, delivers Ca^{2+} ions for biosynthetic processes. All this leads to stimulation of smooth-muscle cells of the stomach and small intestine.

By their effects on electrical activity of the stomach and small intestine during the early postoperative period, neostigmine and calcium pantothenate differed only by the intensity of induced stimulation (more intense after neostigmine), while the patterns of motility and terms of its recovery were the same. The appearance of giant migrating AP propagating from the stomach to the jejunum after infusion of neostigmine and calcium pantothenate is worthy to note. Treatment with neostigmine and calcium pantothenate did not shorten the total duration of MMC recovery in comparison with control animals, but led to earlier recovery of total intensity of AP generation in the stomach and small intestine.

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