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Research Article

Experimental Duodenal Ulcer and Pancreatitis: Correction Possibilities

Lychkova AE[1]*, Terentyev AA[2], Ashrafova TR[3] and Puzikov AM[3]

[1]GBUZ Moscow Clinical Scientific Center Named After A.S. Loginov DZM, Russia

[2]FSAOU HE "Russian National Research Medical University Named After N.I. Pirogov" Ministry of Health of the Russian Federation, Russia

[3]AMG "Estetik", Russia

***Corresponding Author:** Lychkova AE, GBUZ Moscow Clinical Scientific Center Named After A.S. Loginov DZM, Russia.

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Abstract

Introduction: Peptic ulcer disease is a chronic recurrent disease prone to progression and caused by a disorder of the general and local mechanisms of nervous and humoral regulation of the main functions of the gastroduodenal system.

Aim of the Study: The aim is to model two acid-dependent diseases - DC ulcers and pancreatitis (P).

Materials and Methods: The experiments were carried out on 22 Wistar rats with a body weight of 220 - 240g, which are in vivarium conditions with free access to food and water. In gentle conditions, an upper-median laparotomy was performed on an animal fixed on its back, the bulbar section of the DC was removed into the wound and 0.05 ml of 100% glacial acetic acid was applied to the serous membrane using an applicator. The wound was sutured in layers. After 5 days, a relaparotomy was performed under gentle conditions and 0.1 ml of 50% picrylsulfonic acid was injected into the pancreatic duct. After 5 days, the motor function of the fundal and antral sections of the stomach, DC and pancreatic duct was recorded. Next, the animals were divided into 2 groups: the first was a model of DC and P ulcers, the second was correction of DC and P ulcers with serotonin at a dose of 100 mcg/kg.

Results: The motor function of the gastrointestinal tract was recorded 10 days after modeling of DC and P ulcers electromyographically (EMG) in animals of both groups. The amplitude-frequency characteristics of slow waves and spikes, the power of tonic and phase contractions, and propulsive activity were recorded on the EMG curve. The control group consisted of 6 animals of comparable body weight. The statistical analysis was performed using the Mann-Whitney small sample method at $p < 0.05$.

Conclusion: Electromyographic studies in comorbid experimental pathology show the spread from the focus of excitation in the bulbar department of the DC (the area of the ulcer) gradually fading antegrade and retrograde excitation waves. In comorbid pathology, antroduodenal coordination is disrupted, the administration of serotonin gradually restores it. The propulsive activity of the pancreatic duct in comorbid pathology is repeatedly increased, which supports the inflammatory process in the bulbar department of the pancreas and pancreas: the introduction of serotonin reduces the motor function of the pancreatic duct by 3.7 times, that is, it has a cytoprotective effect. Electromyography as a research method can be used to assess the motor function of the stomach, DC and pancreatic duct in comorbid pathology.

Keywords: *Duodenal Ulcer; Pancreatic Duct; Electromyography; Peptic Ulcer Disease*

Introduction

Peptic ulcer disease is a chronic recurrent disease prone to progression and caused by a disorder of the general and local mechanisms of nervous and humoral regulation of the main functions of the gastroduodenal system. The aggressive link of ulceration includes an increase in the mass of lining cells (often hereditary), hyperproduction of gastrin, impaired nervous and humoral regulation of gastric acid production, increased production of pepsinogen and pepsin, impaired gastroduodenal motility (delay or, conversely, acceleration of evacuation from the stomach, contamination of the gastric mucosa with *Helicobacter pylori* (*H. pylori*) microorganisms [1].

Weakening of the protective properties of the mucous membrane of the stomach and duodenum may occur as a result of a decrease in the production and violation of the qualitative composition of gastric mucus, a decrease in the secretion of bicarbonates, a decrease in the regenerative activity of epithelial cells, a deterioration in blood supply to the gastric mucosa, a decrease in the content of prostaglandins in the stomach wall (for example, when taking nonsteroidal anti-inflammatory drugs.

Modeling of gastric and duodenal ulcers is carried out as follows. The serous-muscular membrane of the organ wall is dissected in the form of a circle with a diameter of at least 20 mm. The visible submucosal vessels are stitched along the dissection line with separate nodular sutures. A section of the organ wall is excised between the applied nodular sutures. The formed defect in the wall of the organ is fixed with double-row seams along the circumference to the adjacent organ. The method allows you to create a model of a giant penetrating ulcer of the stomach or duodenum for pathomorphological studies, pharmacological tests and the development of new surgical interventions [2].

Chronic pancreatitis (CP) and peptic ulcer disease are classified as acid-dependent diseases. Cystic-inflammatory transformation (KW) of the duodenum - inflammatory and cystic lesion of its wall with localization in the descending part of the intestine occurs in patients with CP. There are three possible mechanisms for the development of KW:

1. Inflammation of the dorsal part of the head of the pancreas, embedded in the wall of the duodenum, due to a violation of the outflow of secretions through the Santorini duct;
2. Secondary spread of the inflammatory process from the head of the pancreas to the paraduodenal fiber and the wall of the duodenum;
3. Rarely - primary inflammatory cystic lesion of truly heterotopic pancreatic tissue with secondary obstructive pancreatitis. When modeling pancreatitis, bile acid salts are introduced into the common bile duct. Bile acid salts are administered without cannulation of the large papilla of the duodenum. When modeling acute pancreatitis of moderate severity, turnstiles are applied to the common bile duct above and below the confluence of the distal duct of the pancreas. A 50% solution of bile with a pH of 6.0 is injected into the common bile duct at a dose of 0.2 mg/kg, and then the distal duct of the pancreas is bandaged after 15 minutes and the turnstiles are removed. When modeling severe acute pancreatitis, two turnstiles are applied to the common bile duct above the confluence of the distal duct of the pancreas and below the confluence of the proximal duct of the accessory lobe of the pancreas. In this case, a 50% solution of bile with a pH of 6.0 is administered at a dose of 0.2 mg/kg and after 15 minutes both ducts of the rat pancreas are ligated. The method provides an increase in the probability of successful repeatability of the results of reproducing the model of acute pancreatitis of varying severity in rats by taking into account the obstruction of the ductal system of the pancreas of rats and the etiological criterion for the development of acute pancreatitis with the parallel development of CP [3].

An excess of hydrochloric acid entering the duodenum (DC) from the stomach can play a role in the pathogenesis of chronic pancreatitis, this can cause spasm of the Oddi sphincter, dyskinesia of the pancreatic ducts and reflux of hydrochloric acid, bile and DC enzymes into the latter. Premature activation of hydrolytic enzymes of the pancreas occurs. The combination of these pathogenetic mechanisms leads to the development of pancreatitis.

In the experiment, a model of DC ulcer and pancreatitis was previously reproduced in isolation on various models, whereas in the clinic their combination is often observed in one patient.

Aim of the Study

The aim is to model two acid-dependent diseases - DC ulcers and pancreatitis (P).

Materials and Methods

The experiments were carried out on 22 Wistar rats with a body weight of 220 - 240g, which are in vivarium conditions with free access to food and water. In gentle conditions, an upper-median laparotomy was performed on an animal fixed on its back, the bulbar section of the DC was removed into the wound and 0.05 ml of 100% glacial acetic acid was applied to the serous membrane using an applicator. The wound was sutured in layers. After 5 days, a relaparotomy was performed under gentle conditions and 0.1 ml of 50% picrylsulfonic acid was injected into the pancreatic duct. After 5 days, the motor function of the fundal and antral sections of the stomach, DC and pancreatic duct was recorded. Next, the animals were divided into 2 groups: the first was a model of DC and P ulcers, the second was correction of DC and P ulcers with serotonin at a dose of 100 mcg/kg.

The motor function of the gastrointestinal tract was recorded 10 days after modeling of DC and P ulcers electromyographically (EMG) in animals of both groups. The amplitude-frequency characteristics of slow waves and spikes, the power of tonic and phase contractions, and propulsive activity were recorded on the EMG curve. The control group consisted of 6 animals of comparable body weight. Statistical analysis was carried out using the Mann-Whitney small sample method at $p < 0.05$.

Results and Discussion

Modeling of DC and P ulcers led to changes in EMG indicators (Table 1).

Organ	The frequency of slow waves	Amplitude of slow waves	The power of tonic contractions	Frequency of adhesions	The amplitude of the adhesions	Power of phase reductions	Propulsive activity
The Fundal Part of the Stomach	8,3+0,13	0,1+0,02	0,83+0,004	2,0+0,1	0,1+0,015	0,2+0,011	4,15+0,5
Antrum of the stomach	8,0+0,2	0,11+0,004	0,88+0,003	2,0+0,17	0,1+0,02	0,1+0,014	4,4+0.5
Control	4,0+0,2	0,1+0,03	0,4+0,02	1,0+0,06	0,1+0,003	0,1+0,007	4,0+0,18

Table 1: *Gastric electromyogram indicators for duodenal ulcer and pancreatitis.*

From the table 1 it follows that the propulsive activity of the fundal part of the stomach exceeds that in the control by 3.7% (p 0.06), whereas the propulsive activity of the antral part of the stomach exceeds that in the control by 10% (p 0.05). That is, gradually attenuating antegrade and retrograde waves of excitation spread from the focus of excitation in the bulbar department of the DC (the area of the ulcer).

The results of the study of duodenal EMG in the combined modeling of DC and P ulcers are shown in table 2.

Organ	The frequency of slow waves	Amplitude of slow waves	The power of tonic contractions	Frequency of adhesions	The amplitude of the adhesions	Power of phase reductions	Propulsive activity
The duodenum	9,0+0,13	0,1+0,011	0,9+0,003	1,0+0,14	0,02+0,0015	0,02+0,003	45+0,5
Control	22,0 +1,3	0,1+0,004	2,2+0,003	1,0+0,17	0,1+0,02	0,1+0,013	22,0+0,8

Table 2: *Indicators of duodenal EMG in combined pathology.*

From the table 2 it follows that the propulsive activity of DC in combined pathology exceeds that in the control by 113.6% (p 0.001), and the propulsive activity increases mainly due to relaxation of the circular muscle layer, as evidenced by an 80% decrease in the power of phase contractions. The antro-duodenal coordination is 1:0.1 (normally 1:4). The data obtained indicate that the phenomenon of circulation of increased excitability occurs in the area of formation of an ulcerative defect - the so-called "re-entry" phenomenon.

The results of the study of the motor function of the pancreatic duct are shown in table 3.

Organ	The frequency of slow waves	Amplitude of slow waves	The power of tonic con-tractions	Frequency of adhesions	The amplitude of the adhesions	Power of phase reductions	Propulsive activity
Pancreatic duct	8,3+0,9	0,18+0,014	1,494+0,008	1,0+0,14	0,02+0,0015	0,02+0,003	74,4+2,5
Control	8,0+0,3	0,1+0,004	0,8+0,003	1,0+0,17	0,1+0,02	0,1+0,013	8 ,0+0,6

Table 3: *Indicators of motor function of the pancreatic duct in combined pathology.*

Table 3 shows that the power of tonic contractions in comorbid experimental pathology was increased by 32.1% (p 0.05), the power of phase contractions was reduced by 80% (p 0.05), and the propulsive activity was increased by 8.3 times (p 0.001). That is, a decrease in the power of phase contractions leads to a decrease in the tone of the circular muscle layer of the pancreatic duct against the background of an increase in the tone of the longitudinal muscle layer (the power of tonic contractions), which generally leads to an acceleration of the passage of pancreatic juice into the DC and supports the inflammatory process in the duodenum and in the pancreas (in the latter case, due to possible retrograde spread excitations in the smooth muscle cells of the ducts).

The administration of serotonin to animals of the second group led to a change in the indicators of motor function of the studied organs in comorbid pathology. Gastric electromyogram indicators for duodenal ulcer and pancreatitis under the conditions of serotonin administration (Table 4).

Organ	The frequency of slow waves	Amplitude of slow waves	The power of tonic contractions	Frequency of adhesions	The amplitude of the adhesions	Power of phase reductions	Propulsive activity
The Fundal Part of the Stomach	7,0+0,93	0,12+0,003	0,84+0,006	2,0+0,1	0,1+0,015	0,2+0,011	4,2+0,5
Antrum of the stomach	6,7+0,3	0,1+0,004	0,67+0,003	1,8+0,17	0,1+0,02	0,18+0,014	3,7+0.5
Control	4,0+0,2	0,1+0,03	0,4+0,02	1,0+0,06	0,1+0,003	0,1+0,007	4,0+0,18

Table 4: *Gastric electromyogram indicators for duodenal ulcer and pancreatitis under the action of serotonin.*

From the table 4 it follows that the administration of serotonin increases the propulsive activity of the fundal part of the stomach by 1.4% ($p > 0.1$), reduces the propulsive activity of the antrum by 15.9% ($p < 0.05$), that is, it reduces the excitability of smooth muscle cells of the antrum of the stomach. The results of the study of EMG of DC with combined modeling of ulcers of DC and P under the action of serotonin are shown in table 5.

Organ	The frequency of slow waves	Amplitude of slow waves	The power of tonic contractions	Frequency of adhesions	The amplitude of the adhesions	Power of phase reductions	Propulsive activity
The duodenum	11,1+0,43	0,16+0,012	1,776+0,003	1,2+0,14	0,03+0,0011	0,02+0,003	49,0+3,5
Control	22,0+1,3	0,1+0,004	2,2+0,003	1,0+0,17	0,1+0,02	0,1+0,013	22 ,0+0,8

Table 5: *Indicators of duodenal EMG in combined pathology under the action of serotonin.*

Table 5 shows that under the action of serotonin, the power of tonic contractions of the longitudinal muscles decreased by 11.8% ($p < 0.05$), the power of phase contractions decreased by 79.9% ($p < 0.05$), propulsive activity increased by 122.7% ($p < 0.001$). The antro-duodenal coordination was 1:2.23. Thus, the administration of serotonin optimized the coordination function of the antroduodenal complex.

The results of the study of the motor function of the pancreatic duct in comorbid pathology under the action of serotonin are shown in table 6.

Organ	The frequency of slow waves	Amplitude of slow waves	The power of tonic contractions	Frequency of adhesions	The amplitude of the adhesions	Power of phase reductions	Propulsive activity
Pancreatic duct	6,3+0,7	0,15+0,012	0,825+0,006	1,2+0,13	0,03+0,0015	0,036+0,002	22,9+2,5
Control	8,0+0,3	0,1+0,004	0,8+0,003	1,0+0,17	0,1+0,02	0,1+0,013	8,0+0,6

Table 6: *Indicators of motor function of the pancreatic duct in combined pathology.*

Table 6 shows that the power of tonic contractions in comorbid experimental pathology with the introduction of serotonin was increased by 9.1% ($p < 0.05$), the power of phase contractions was increased by 80% ($p < 0.05$), propulsive activity was increased only 2.25 times (a decrease of 3.7 times compared with the model, $p < 0.001$). That is, despite the uneven increase in the power of tonic and phase contractions, the tone of the circular muscle layer of the pancreatic duct mainly increases, which generally leads to a decrease in the passage of pancreatic juice in the DC under the action of serotonin in conditions of comorbid pathology and to a lesser extent supports the inflammatory process in the duodenum and in the pancreas.

Thus, the administration of serotonin reduces the propulsive activity of the smooth muscles of the pancreatic duct in comorbid pathology compared with the model, which inhibits the development of the inflammatory process in the DC and pancreas.

Conclusion

1. Electromyographic in comorbid experimental pathology, the spread from the focus of excitation in the bulbar department of the DC (the area of the ulcer) is shown gradually fading antegrade and retrograde excitation waves.

2. In comorbid pathology, antroduodenal coordination is disrupted, the administration of serotonin gradually restores it.
3. The propulsive activity of the pancreatic duct in comorbid pathology is repeatedly increased, which supports the inflammatory process in the bulbar department of the pancreas and pancreas: the introduction of serotonin reduces the motor function of the pancreatic duct by 3.7 times, that is, it has a cytoprotective effect.
4. Electromyography as a research method can be used to assess the motor function of the stomach, DC and pancreatic duct in comorbid pathology.

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