

Application of the ursodeoxycholic acid upon alkaline form of the gastroesophageal reflux disease

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Modern integrated circuits of conservative treatment of gastroesophageal reflux disease (GERD) are focused on eliminating the symptoms caused by acid aggression and endoscopic evidence of disease [!

]. Accordingly, the treatment regimen as used antireflux therapy: proton pump inhibitors, histamine H₂ receptor blockers, antacids, prokinetics [!

]. The main disadvantage of the recommended pharmacological approaches, according to the authors, is their lack of effectiveness due to the impact of a one-sided orientation - only on acid reflux esophagitis, excluding the possibility of having other options pH-oesophageal reflux disease: a mixed alkali and, when observed duodenogastroesophageal reflux (DGR) [!

]. GDR reflyuktat at GDP can be different bile, pancreatic juice, duodenal secret. According to leading experts in the gastroenterology branch, the degree of damage to the lining of the esophagus is more significant with the latest version. This facilitates a direct damaging effect agents such as bile acid (BA) and pancreatic enzymes in the gastro reflyuktant on esophageal mucosa, which leads to the destruction of the protective mucus epithelium damage, activate inflammatory cell damage, ulcer formation erosive changes, in the later stages - to intestinal metaplasia, dysplasia, neoplasia [!

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The purpose of the study. Studies on the effect of ursodeoxycholic acid (UDCA) on the clinical course and the dynamics of laboratory parameters in mixed and alkaline versions of GERD.

Materials and techniques. 117 patients with GERD were examined, 48 were selected with a mixed (pH 4.0 to 6.0), and 4 with GERD alkaline (above pH 6.0) (23 males and 29 females, average age 34.8 ± 7.2). In studies of GERD patients with mixed and alkaline reflux options we have provisionally designated as the alkaline version of the disease. The study was conducted on 52 selected patients. GERD was verified on the basis of specific complaints, medical history, clinical and laboratory data, results of endoscopy. Clinical evaluation of patients with symptoms of GERD was assessed using the scale of Likert. Endoscopic examination of the esophagus was performed by device of «Olympus» company (Japan) according to standard procedure. The study was conducted by transendoscope intragastric pH, topography by using acidogastrometr "AGM-03" ("Source-System", Friazino). The presence of the GDR at the absence of daily pH monitoring and intraesophageal bilimetria were determined by endoscopic pattern and concentration of bile in the gastric juice. Endoscopic criteria of DGR were: dehiscence pyloric reflux of bile from the duodenum into the stomach and the presence of bile in the stomach [!]. Biochemically GDR was evaluated by the concentration of bilirubin in gastric juice by means of a spectrophotometer at wavelength 420 nm [3], by the activity of the enzyme phospholipase A2 [5] LCD spectrum by A. Ivanov technique [4] and the phospholipid fractions according to Cates [6]. The obtained data were processed by the technique of variation statistics.

Patients were treated by following regimen: pantoprazole 40 mg 2 times a day (proton pump inhibitor), itopride hydrochloride 200 mg 3 times a day (prokinetic), UDCA (Ursosan, «PRO MED.CS Praha as», Czech Republic) 250 mg 2 times a day for 4 weeks.

Investigation results. As a result of the study, 52 selected patients had purely "alkaline" variant with a pH above 7.0 was observed with only 9, while in

the remaining 43 patients was recorded mixed version of GERD. Endoscopic examination of 19 patients revealed erosive esophagitis, the rest - only catarrhal changes in the esophageal mucosa. 7 patients were found hiatal hernia. Also at endoscopy 27 (52%) patients had dehiscence pyloric antrum erosion, 41 (78.8%) patients for visible bile reflux.

Evaluating the effectiveness of relief of the main symptoms of GERD before and after the treatment was carried out on a five-point Likert scale system. In our study, rates of dyspeptic symptoms on this scale ranged from 3 to 5 and the end of treatment were 12 points (Table 1)

Table 1

Dynamics of clinical manifestations of GERD patients examined

Signs	The number of points on the Likert scale	
	Before treatment	After treatment
heartburn	3-5	1
belch	2-5	1-2
regurgitation	3-4	2

Note: **Likert scale:**

1. Does not disturb
2. Slightly disturbs (possible to leave without attention)
3. Mildly disturbs (does not influence on day activity and does not disturb at night)
4. Intensively disturbs (day and night)
5. Violently disturbs, interrupts day activity regularly and does not give possibility to sleep at night

Transendoscopic gastric pH-metry before and after treatment showed significant changes in the pH in the antrum of the stomach (Table 2).

Table 2

Indicators of intragastric pH in the stomach of patients with GERD

Patients	Corpus gastricum	Antrum
Before treatment	1,2±0,06	2,6±0,25
After treatment	1,4±0,08	4,7±0,15*

Note: here and further * the difference is significant in comparison with the test groups (< 0,05)

The study of bilirubin in the gastric juice in the dynamics showed a reduction in its level of more than 1.5-fold compared with the level before treatment (Fig. 1). Change of phospholipase activity in the gastric juice during treatment showed marked decrease in activity of the enzyme phospholipase A2 in patients with $38,5 \pm 2,80$ nmol / min / ml of gastric juice to $21,7 \pm 3,40$ nmol / min / ml ($p < 0.01$) (Figure2).

The spectrum in bile LCD TLC showed that there were fatty acids in bile in conjugation with glycine and taurine. At the same time the attention was drawn that patients with a lower content of primary bile acids LCD - $0,24 \pm 0,003$ mg% and a high content of secondary (deoxybile) LCD - $0,34 \pm 0,06$ mg%. After a course of treatment, these figures were $0,16 \pm 0,02$ and $0,13 \pm 0,03$ mg%, respectively.

Investigation of phospholipid range found bile (Table 3) and revealed patients with a high level of toxic pool fraction of lysophosphatidylcholine (LPC), at a much lower content of a pool of fractions of phosphatidylcholines (PC). Against the background of the therapy were significant changes in the measures, and in the content of sphingomyelin fraction (SF), lysophosphatidylcholine (PEA) and other small fractions (cardiolipin, phosphatidylserin, phosphatidic acid) essentially no significant difference wasn't noted.

Table 3

The spectrum of bile phospholipids in patients with GERD

Patients	LPC, g/l	SF, g/l	PC, g/l	PEA, g/l	Other fractions, g/l
Before treatment	$0,31 \pm 0,015$	$0,48 \pm 0,02$	$1,99 \pm 0,11$	$1,35 \pm 0,07$	$0,36 \pm 0,02$
After treatment	$0,12 \pm 0,015^*$	$0,52 \pm 0,015^*$	$3,12 \pm 0,12^*$	$1,10 \pm 0,06$	$0,40 \pm 0,025$

Patients with GERD do not have a significant decline in life quality, parameter estimation which is an integral part of the study in the dynamics of the effectiveness of therapy. Analysis of life quality according to questionnaire patients GSRS in our study during treatment revealed a positive trend on all scales with the greatest severity assessment of reflux syndrome, dyspeptic symptoms and abdominal pain (Fig. 3).

Analysis of life quality by questionnaire GSRS in patients in our study during treatment revealed a positive trend on all scales with the greatest severity assessment of reflux syndrome, dyspeptic symptoms and abdominal pain.

Thus, clinical studies have shown that GERD as aggression factor is not only hydrochloric acid but also LCD patients with concomitant diseases of the hepatobiliary system. In this case, the use of acid suppressive therapy is not only capable of completely arrest the deterioration of the disease. To prevent generating exposure reflyuktanta with mixed composition administration of UDCA promotes more consistent protection of the esophageal mucosa in these embodiments of GERD.