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## ENTERAL TUBE FEEDING IN ACUTE PANCREATITIS AND ITS COMPLICATIONS

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The use of early enteral tube feeding in patients with acute pancreatitis improves the course of the disease, but is dangerous for the development of intestinal complications. The aim of the study was to improve the results of comprehensive treatment of patients with acute pancreatitis by preventing complications of enteral tube feeding. The clinical material is based on the results of treatment of 79 patients with acute pancreatitis who received enteral tube feeding and were divided into a comparison group and the main group (in addition to the tube received an emulsion of simethicone). It was found that the recovery of intestinal absorption (at the peak of exacerbation of the inflammatory process of the pancreas or in the early postoperative period) occurs at  $2.2 \pm 0.3$  days, and membrane digestion – at  $4.1 \pm 0.5$  days from the start of treatment. The use of simethicone emulsion for the prevention of intestinal complications on the background of enteral tube feeding reduced the incidence of intestinal complications in the first two days after treatment by 32.1 % ( $p=0.001$ ), for 3–4 days – by 36.4 % ( $p=0.0004$ ) and 7 days – by 23.3 % ( $p=0.004$ ).

**Key words:** pancreatitis, complications, enteral nutrition, membrane digestion, intestinal absorption, prevention.

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## ЕНТЕРАЛЬНЕ ЗОНДОВЕ ХАРЧУВАННЯ ПРИ ГОСТРОМУ ПАНКРЕАТИТІ ТА ЙОГО УСКЛАДНЕННЯ

Застосування раннього ентерального зондового харчування у хворих з гострим панкреатитом покращує перебіг захворювання, однак небезпечно розвитком кишкових ускладнень. Метою дослідження було покращення результатів комплексного лікування хворих на гострий панкреатит шляхом профілактики ускладнень ентерального зондового харчування. В основу клінічного матеріалу покладені результати лікування 79 хворих з гострим панкреатитом, що отримували ентеральне зондове харчування та були розділені на групу порівняння та основну групу (додатково в зонд отримували емульсію симетикону). Встановлено, що відновлення кишкового всмоктування (на піку загострення запального процесу підшлункової залози або у ранньому післяопераційному періоді) відбувається на  $2,2 \pm 0,3$  добу, а мембранного травлення – на  $4,1 \pm 0,5$  добу від початку лікування. Застосування емульсії симетикону для профілактики кишкових ускладнень на фоні призначення ентерального зондового харчування дозволило зменшити частоту розвитку кишкових ускладнень в перші дві доби від початку лікування на 32,1 % ( $p=0,001$ ), на 3–4 добу – на 36,4 % ( $p=0,0004$ ) та 7 добу – на 23,3 % ( $p=0,004$ ).

**Ключові слова:** панкреатит, ускладнення, ентеральне харчування, мембранне травлення, кишкове всмоктування, профілактика.

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Acute pancreatitis remains an urgent problem of modern medicine, which is associated with a high risk of complications during the course of the disease, mortality in which reaches 5.5 %, and in severe acute pancreatitis – varies between 40–70 % [13]. However, according to the literature, early enteral tube feeding (ETF) in patients with acute pancreatitis significantly improves the course of the disease by reducing the number of complications and reducing mortality [10].

It should be noted that the efficacy of ETF in patients with acute pancreatitis depends on a number of factors (type of enteric mixture (semi-elemental, polymeric), the timing of recovery of motor-evacuatory function of the intestine, intestinal absorption, etc.). Thus, there are many studies according to which ETF should be started as early as possible (24–48 hours after hospitalization) compared with parenteral nutrition [1]. However, compliance with these recommendations is dangerous for the development of intestinal complications of ETF, namely: large residual volumes – 39 %, diarrhea – 14.7 %, bloating – 13.2 %, vomiting – 12.2 %, regurgitation – 5.5 % [8].

Considering diarrhea as a pathological condition in which there are changes in both the form of feces (watery or mushy) and the frequency of defecation (more than 3 times a day, with the volume of stool exceeding 200 ml), there are five pathogenetic variants: secretory, osmotic, exudative, motor and mixed. Diarrhea, which occurs with the use of ETF in patients with acute pancreatitis, is usually of a mixed nature and is due to both impaired intestinal motor function (paresis) and lack of intestinal absorption (the volume of liquid fecal masses is from 500 to 1000 ml per day) [14].

The use of ETF in patients with acute pancreatitis can cause digestive and dynamic types of intestinal flatulence [4]. The balance between gas-producing and gas-absorbing microorganisms is disturbed and there are signs of flatulence (increased gas formation in the intestinal loops), and the presence

of maldigestion and malabsorption syndromes interferes with normal transport and absorption of gases (digestive type of flatulence) and reflex suppression of intestinal motility.

The liquid intestinal contents, in which various organic substances (proteins, fats, bile acids, mucopolysaccharides, mucus, soap, etc.) are dissolved, are foams with a large number of small bubbles, each of which is surrounded by a layer of viscous mucus. In turn, the mucous foam, which covers a thin layer of the surface of the intestinal mucosa, disrupts parietal digestion and absorption of nutrients [3]. It should be noted that the methods of management of patients with intestinal disorders on the background of acute pancreatitis, arising from the use of ETF, as well as prevention of their development are insufficiently developed. Thus, according to the literature, to reduce the effects of flatulence use loperamide, activated carbon (carbolene), etc. [12]. However, the effectiveness of these drugs is quite low, which requires further scientific research.

**The purpose** of the work was to improve the results of comprehensive treatment of patients with acute pancreatitis by preventing complications of enteral tube feeding.

**Materials and methods.** The clinical material summarized in the paper is based on the results of ETF of 79 patients with acute pancreatitis, who were treated in the clinic of the Department of Surgery No. 2 of Bogomolets national medical university from 2015 to 2020. The study included patients with moderate and severe disease according to the International Association of Pancreatology Classification (Cochin, India, 2011) and Acute Pancreatitis Classification Working Group (2012) [15]. The severity of the course was determined using the scales RANSON (severe course – more than 6 points) and APACHE II (severe course – more than 8 points), so the course of moderate severity was observed in 31 (39.2 %) and severe in 48 (60.8 %) patients. Depending on the features of the chosen treatment tactics (the nature of the ETF), patients are divided into two groups: comparison (standard ETF) – 39 patients, the main (standard ETF+antiflatulants) – 40 patients. Patients were in the age range of 21–50 years, averaging 39.3±1.2 years. There were 47 men (59.5 %), 32 women (40.5 %), patients of the two groups did not differ significantly in age, sex ( $\chi^2=0.207$ ,  $p=0.91$ ) and severity ( $\chi^2=0.16$ ,  $p=0.996$ ). When determining the etiological factors of acute pancreatitis biliary etiology occurred in 23 (29.1 %) patients, alcohol – in 56 (70.9 %) patients.

To determine the timing of the recovery of intestinal absorption and membrane digestion before the start of ETF performed a test with glucose load and a test to diagnose lactase deficiency [5]. In 79 patients before the start of ETF was loaded with lactose and glucose at the rate of 1 g per 1 kg of body weight by introducing disaccharides into the tube for ETF, determined the nature of the glycemic curve on an empty stomach and after loading with lactose for 2 hours after exercise, which was carried out every 12 hours from the moment of hospitalization of the patient to recovery of function of intestines. To determine the effectiveness of the recovery of intestinal absorption and membrane digestion in the main and comparison groups studied the following laboratory parameters: blood hematocrit, total protein, albumins, cholesterol, Na<sup>+</sup> and K<sup>+</sup> plasma, C-reactive protein, plasma osmolarity, urine specific gravity, fecal pH.

In order to prevent the development of diarrhea and flatulence during ETF before its use in patients of the main group in the tube was injected emulsion of simethicone (Espumisan<sup>®</sup> L, Berlin-Chemie AG, Germany), the drug was added to the mixture for enteral nutrition (2 ml (80 mg) or 50 drops 3–5 times per day). The mixture for ETF was administered dropwise using a roller dispenser at a rate of 25 ml per hour in a continuous mode (for 20 hours).

Statistical analysis was performed using Statistica 10 (Serial Number: STA999K347150-W) and MEDCALC<sup>®</sup> (open access Internet resource, <https://www.medcalc.org/calc/>). The normality of data distribution was determined by the Shapiro-Wilk test. Due to the parametric distribution of the analyzed data, the results were presented as means and their standard deviation (M±SD). The difference between the groups was established using Student's t test for independent samples. Differences in the sample distribution were evaluated using the criterion  $\chi^2$  test. Differences between indicators were considered significant at  $p<0.05$ .

**Results of the study and their discussion.** Surgical interventions, including minimally invasive, under general and local anesthesia were performed in 61 (77.2 %) patients, in 18 (22.8 %) patients only conservative therapy was used. From the moment of admission to the hospital, all patients received comprehensive treatment in accordance with generally accepted principles: analgesia, installation of a nasogastric tube, intravenous restoration of fluid and electrolyte losses. In order to reduce HCl secretion and prevent stress ulcers, patients received H<sub>2</sub>-histamine receptor blockers or proton pump inhibitors. Nonsteroidal anti-inflammatory drugs and/or narcotic analgesics were prescribed to treat the pain syndrome. In case of confirmation of severe acute pancreatitis, comprehensive treatment of patients was carried out in the intensive care unit.

The average blood glucose level in 79 (100 %) patients before disaccharide loading was  $3.82 \pm 0.8$  mmol/l. In 30 patients (37.98 %) on the second day from the beginning of treatment there was a recovery of intestinal absorption and membrane digestion, which manifested itself in 10 minutes after glucose and lactose loading, an increase in blood glucose to  $5.35 \pm 0.4$  mmol/l, and after two hours the glycemic curve returned to the initial level- $3.9 \pm 0.5$  mmol/l.

In 40 patients (50.63 %) on the second day from the beginning of treatment there was a violation of membrane digestion, namely there was an increase in blood glucose levels in 10 minutes after enteral administration to  $5.4 \pm 0.4$  mmol/l, which indicated recovery of intestinal absorption, however, after loading with lactose at the same time, blood glucose levels rose to  $4.2 \pm 0.4$  mmol/l and returned to baseline within two hours.

The glycemic curve in 9 (11.4 %) patients after loading with lactose and glucose in violation of both intestinal absorption and membrane digestion was an isoline, a significant difference between blood glucose after loading with glucose and lactose was not registered ( $3.9 \pm 0.4$  mmol/l and  $3.8 \pm 0.5$  mmol/l, respectively) ( $p > 0.05$ ).

The distribution of patients depending on the timing of recovery of intestinal absorption and membrane digestion are shown in table 1.

Table 1

**Distribution of patients depending on the timing of recovery of intestinal absorption and membrane digestion**

Date	Number of patients			
	Recovery of intestinal absorption		Recovery of membrane digestion	
	The absolute number	%	The absolute number	%
First	-	-	-	-
Second	47	59.49	9	11.39
Third	28	35.4	51	64.56
Fourth	4	5.11	19	24.05
<b>Total</b>	79	100	79	100

As can be seen from the table, the most frequent recovery of intestinal absorption was registered at  $2.2 \pm 0.3$  days from the start of treatment, and membrane digestion-at  $4.1 \pm 0.5$  days. Prolonged recovery of intestinal digestion relative to intestinal absorption is associated with the accumulation in the intestine of large amounts of gas, liquid content due to paresis, which on the background of enteral tube feeding causes the development of osmotic diarrhea.

Therefore, in 42 (53.2 %) patients, in addition to the use of glucose loading test and lactase deficiency test, the onset of intestinal absorption was determined by using a 3 % solution of potassium iodide. The peculiarity of the method is the determination of the terms of recovery of intestinal absorption by recording the excretion of potassium iodide with saliva in 10 minutes after its enteral tube administration (20 ml of 3 % solution). The transparent secretion taken in a test tube, in case of recovery of intestinal absorption changes the color to blue at addition to it the indicator – starch (2 ml of 10 % of solution). This is an indication for the appointment of ETF. The sensitivity of the technique was 87.36 %, specificity – 81.5 %.

The study also analyzed and investigated a significant difference in laboratory parameters of recovery of intestinal absorption and membrane digestion in patients with acute pancreatitis on the background of ETF (table 2).

Table 2

**Laboratory indicators of recovery of intestinal absorption and membrane digestion**

Index	Comparison group	Main group	p
Hematocrit of blood, %	$54.2 \pm 0.2$	$46 \pm 0.3$	<0.001
Total protein, g/l	$72.4 \pm 0.4$	$75 \pm 0.3$	0.091
Albumins, %	$49 \pm 0.2$	$57 \pm 0.1$	<0.001
Cholesterol, mmol/l	$3.1 \pm 0.2$	$4.2 \pm 0.2$	0.002
Na+ plasma, mmol/l	$140 \pm 0.4$	$146 \pm 0.3$	<0.001
K+ plasma, mmol/l	$4.3 \pm 0.1$	$4.2 \pm 0.2$	0.66
C-reactive protein, mg/l	$6.0 \pm 0.1$	$4.0 \pm 0.1$	<0.001
Plasma osmolarity, mosmol/l	$325 \pm 3.0$	$305 \pm 2.0$	<0.001
Urine specific gravity	$1.028 \pm 0.003$	$1.022 \pm 0.003$	<0.001
Fecal pH	$5.0 \pm 0.2$	$6.2 \pm 0.1$	<0.001

As can be seen from table 2, the use of antifatulants allowed to normalize the levels of laboratory parameters, the increase of which is a marker of recovery of membrane digestion (hematocrit, albumins, cholesterol, blood plasma osmolarity, C-reactive plasma protein, urine specific gravity and fecal pH) with a statistically significant difference  $p < 0.05$ ). Plasma sodium levels are significantly different in both groups, but are within normal limits. Plasma total protein and potassium levels are normal in both groups and their differences are not statistically significant.

The main clinical symptoms, which were evaluated in the early period in order to detect digestive disorders on the background of the use of ETF were: pain on palpation in the projection of the small and large intestine, rumbling in the abdomen, dyspepsia, diarrhea. Thus, in the main group in the first two days after treatment, these complications occurred in 20 (50 %) patients, in the comparison group in 32 (82.1 %) patients; 3–4 days from the beginning of treatment – in 8 (20 %) patients of the main group and in 22 (56.4 %) patients of the comparison group; 7 days from the beginning of treatment – in 3 (7.5 %) patients of the main group and in 12 (30.8 %) patients of the comparison group. Thus, the use of simethicone on the background of the use of ETF allowed to reduce pain, dyspepsia and diarrhea, that is to normalize intestinal function, and thus significantly improve the results of treatment of this category of patients in the first two days after treatment by 32.1 % ( $p = 0.001$ ), for 3–4 days – by 36.4 % ( $p = 0.0004$ ) and 7 days – by 23.3 % ( $p = 0.004$ ). Also, the reduction of pain in the main group of patients allowed to reduce the use of analgesics (narcotic and non-narcotic) on average by half.

According to the literature, early ETF helps to stabilize the integrity of the intestinal mucosa, reduces the number of complications and reduces mortality in acute pancreatitis [2]. However, the timing of the start of the ETF remains controversial [6]. It is also known that lactase deficiency (hydrolytic enzyme of the small intestine, which breaks down the disaccharide lactose (milk sugar) into glucose and galactose) leads to incomplete breakdown of milk sugar, in turn, undigested lactose is exposed to the corresponding enzymes of the microbial flora of the large intestine, which causes osmotic diarrhea (excretion of watery foamy feces, which has an acidic reaction) and severe gas formation in the colon (flatulence) [11].

It was found that the criterion for the appointment of ETF is the presence of normal intestinal absorption function. In conditions of intestinal paresis, which accompanies acute pancreatitis, especially after surgery on the pancreas, it is important to register the timing of the recovery of intestinal absorption with the help of screening diagnostic methods. It should be noted that according to the literature in the case of impaired carbohydrate tolerance and severe intestinal paresis when using test with glucose load and test for the diagnosis of lactase deficiency in 8 % of cases may develop diagnostic errors, which causes the development of complications from the digestive tract with the use of ETF in 15 % of patients [7]. Therefore, we have developed a method for determining intestinal absorption by studying the excretion of potassium iodide in saliva after its introduction through an enteric tube. The sensitivity of the method is 87.36 %, specificity – 81.5 %. The proposed method of determining the time of onset of enteral nutrition using the indicator method is a simple, non-invasive test that allows you to start ETF in time and avoid the development of its complications.

Also in order to reduce the frequency of intestinal complications during ETF, a method of their prevention by adding an antifatulent simethicone to the mixture is proposed. Simethicone refers to defoamers (antifatulants), the action of which is to release gases from the mucous bubbles. This causes coalescence – the fusion of gas bubbles and the destruction of the foam, as a result of which the free gas is able to be absorbed through the mucous membrane or evacuated together with the intestinal contents. The action of this group of drugs is based on changes in the physicochemical properties of the mucous foam, rather than the physiological effect on the biochemistry of the digestive process [9]. The use of antifatulants before ETF, as well as their addition to the enteral mixtures allowed to reduce the incidence of intestinal complications in the first two days after treatment by 32.1 % ( $p = 0.001$ ), for 3–4 days – by 36.4 % ( $p = 0.0004$ ) and 7 days – by 23.3 % ( $p = 0.004$ ).

## Conclusions

1. The criterion for the appointment of ETF is the preserved function of absorption of the small intestine, which can be determined using the proposed screening technique, which has a high diagnostic efficiency (sensitivity – 87.36 %, specificity – 81.5 %.)
2. It is established that the recovery of intestinal absorption (at the peak of exacerbation of the inflammatory process of the pancreas or in the early postoperative period) occurs at  $2.2 \pm 0.3$  days, and membrane digestion – at  $4.1 \pm 0.5$  days from the start of treatment, that is, the ETF should be started no earlier than 48 hours.

3. The application of the proposed method of prevention of intestinal complications on the background of the appointment of ETF allowed to reduce the incidence of intestinal complications in the first two days after treatment by 32.1 % ( $p=0,001$ ), for 3–4 days – by 36.4 % ( $p=0.0004$ ) and 7 days – by 23.3 % ( $p=0.004$ ).

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