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Improvement of enteral nutrition technologies in patients with a severe course of acute pancreatitis

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Abstract: *in the case of severe acute pancreatitis, the early start of enteral nutrition (24-72 hours from the moment of hospitalization) by means of nasogastric or nasojejunal administration of the mixture is considered appropriate, which is associated with a 24% decrease in the frequency of infectious complications and a 32% decrease in mortality. However, 30.5-65.7% of patients may develop intolerance to this type of nutritional support. The aim of the study was to improve the results of treatment of patients with severe acute pancreatitis by improving enteral nutrition technologies. There were 101 patients with severe acute pancreatitis took part in the study, who were divided into the main group, where enteral nutrition was carried out according to the improved protocol - 34 patients, comparison group No. 1, where standard nasogastric nutrition was carried out - 34 patients, and comparison group No. 2, where standard EN – 33 patients. The effectiveness of enteral nutrition in the studied groups was evaluated by analyzing and comparing biochemical indicators of blood serum, frequency of intolerance to nutritional support, infected local complications, mortality, duration of multiple organ failure and stay of patients in the hospital. When using the proposed protocol of enteral nutrition in patients with a severe course of acute pancreatitis, 14 days after the start of treatment, a significant difference was obtained between the content of albumin, creatinine, cholesterol and K+ blood serum ($p<0.05$) between patients of the main group and the comparison groups, as well as the content of Na+ in blood serum ($p<0.05$) between patients of the main group and the group of standard nasogastric tube feeding. Application of the proposed protocol of enteral nutrition significantly reduces the frequency of intolerance of nutritional support in the first 7 days of treatment by 23.6% ($\chi2=5.7$, 95% CI 4.41-41.56, $p=0.01$) compared to the control group patients, where standard nasogastric tube feeding is used, by 21.5% ($\chi2=4.87$, 95% CI 2.34-39.48, $p=0.02$) compared to the group of standard enteral tube feeding, as well as the duration of multiple organ failure from 12.2±1.7 days to 10.5±1.9 days in comparison with the group of patients where standard nasogastric tube feeding was used ($p=0.0002$) and from 11.5±1.9 days to 10.5±1.9 days compared to the group of standard enteral tube feeding ($p=0.03$). The use of the proposed technology of enteral nutrition in patients with a severe course of acute pancreatitis improves treatment results by reducing the duration of multiple organ failure and the frequency of intolerance to this type of nutritional support.*

Key words: acute pancreatitis, enteral nutrition, intestinal absorption, nutritional support, treatment.

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Introduction

Acute pancreatitis (AP) is a common disease that accounts for 5-10% of urgent pathologies of the abdominal cavity (Petrov et al., 2019). Particularly dangerous is the severe course of the disease, which is accompanied by the progression of hypermetabolism and hypercatabolism syndromes, a high risk of complications (up to 50%) and fatalities (40-70%) (Purschke et al., 2022). Timely application of nutritional support in this category of patients prevents the development of catabolic processes, leads to a decrease in inflammatory processes and improves treatment results. According to modern protocols of nutritional support in patients with AP with mild and moderate severity of the disease, fasting during the first 2–3 days is recommended, followed by oral fractional consumption of water (1–1.5 l/day), polymeric isocaloric isonitrogenous nutritional mixtures in an increasing volume (100 ml 6 times a day on the 1st day, 150 ml 6 times a day on the 2nd day) under the control of serum amylase level and a gradual transition to a gentle medical diet (Lakananurak et al., 2020). With a severe course of AP, early start of enteral nutrition (EN) (24-72 h from the moment of hospitalization) by nasogastric or nasojejunal administration of the mixture is considered appropriate, which is associated with a 24% decrease in the frequency of infectious complications and a 32% decrease in mortality (Arvanitakis et al., 2020). Polymeric, semi-elemental and elemental food mixtures are used for introduction into the enteral probe at the rate of 250 kcal/day, with a further increase to 1800 kcal/day for one week and constant monitoring of intra-abdominal pressure. However, according to literature data, when using EN in 30.5-65.7% of cases, intolerance to the latter may occur in the form of nausea, vomiting, abdominal distension, diarrhea, increased intra-abdominal pressure, which are reasons for stopping enteral nutritional support (Fan et al., 2021).

Aim

Improving the results of treatment of patients with severe acute pancreatitis by improving the technologies of enteral nutrition.

Materials and methods

There were 101 patients with AP who were hospitalized at the clinic of the Department of Surgery #2 of Bogomolets National Medical University in the period from 2012 to 2022 and was approved by the Ethics Committee of Bogomolets National Medical University (December 15, 2011, protocol # 5). All patients signed informed consent for participation in the study and/or treatment at the clinic. The study included patients with a severe course of the disease (according to the classification of AP Atlanta 2012), who received EN. Prediction and assessment of the severity of the course of HP was carried out using the APACHE II scale (severe course -8 points and more). Exclusion criteria were chronic somatic diseases in the decompensation phase, the patient's refusal to participate in the study. Prediction and assessment of the severity of the course of AP was carried out using the APACHE II scale (severe course - 8 points and more). Exclusion criteria were chronic somatic diseases in the decompensation phase, the patient's refusal to participate in the study.

Depending on the specifics of the selected treatment tactics, the patients were divided into three groups: the main group, where EN was performed according to the improved protocol - 34 patients, comparison group No. 1, where standard nasogastric nutrition was performed - 34 patients, and comparison group No. 2, where standard EN was performed – 33 patients. Comprehensive conservative treatment of patients was carried out in intensive care and intensive care units in accordance with international treatment protocols. The improvement of the EN protocol was preceded by studies that were devoted to the study of the timing of the recovery of intestinal absorption, as one of the main criteria for the initiation of EN in patients with AP, the comparison of the effectiveness and safety of nasogastric administration of feeding mixtures, and the improvement of methods of preventing intestinal complications in patients with this pathology (Kolosovych and Hanol, 2022). Based on the results of the research, the use of a 3% solution of potassium iodide was proposed in order to determine the recovery of intestinal absorption as an indicator of the onset of EN in patients with severe AP (it was established that in most patients the recovery of intestinal absorption occurs only 48 hours after the start of treatment), it was proved, that naso-

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gastric feeding is an effective and safe method of introducing mixtures and can be considered as an alternative to enteral tube feeding, and the use of antiflatulents in the composition of the mixture was also proposed in order to reduce the frequency of EN intolerance. The local protocol for enteral nutrition in patients with severe AP developed in the clinic was based on own research and recommendations of the European Society of Clinical Nutrition and Metabolism (ESPEN) (Cañamares-Orbís et al., 2022) and included the following provisions:

in patients with a severe course of AP, EN is preferred compared to parenteral, while it should be started 48 hours after the start of treatment with a preliminary determination of the state of recovery of intestinal absorption by using a test with a 3% solution of potassium iodide;

contraindications to the start of EN are uncontrolled shock, hypoxemia, acidosis, gastrointestinal bleeding from the upper parts of the digestive tract, secretion of stagnant gastric contents in the amount of >500 ml/6 h, ischemic damage to the small intestine, intestinal obstruction, abdominal compartment syndrome;

EN should be started with nasogastric administration of the mixture, and in case of complications, use nasojejunal administration;

with an increase in intra-abdominal pressure >15 mm Hg. preference is given to nasojejunal administration of feeding mixtures at a rate of 20 ml/h, and with intra-abdominal pressure >20 mm Hg. EN should be stopped and parenteral nutrition should be started;

nutrition begins with drip administration of a glucose-electrolyte solution through a probe at a rate of 100 ml/hour, followed by control after 2 hours by the method of passive or active aspiration for 15 minutes. If the volume of the residual liquid exceeds 100 ml - the probe is used for decompression and injection of the solution in the lavage mode in the previous time mode. In the presence of a smaller amount of residual fluid - the volume of infusion increases by 50% with further monitoring every 3-4 hours;

on the second day of therapy, the introduction into the probe of a 20% solution of an oligomeric (elemental or semi-elemental) mixture for EN in the volume of up to 300 ml/day (1 kcal in 1 ml) with the introduction of simethicone emulsion in a dose of 2 ml (80 mg) is additionally prescribed 3- 5 times a day;

in the absence of complications associated with the use of oligomeric mixtures, their number increases by 2 times the next day (the rate of administration does not change). In case of complications, the rate of introduction of the mixture should be reduced by 2 times. In case of persistent intestinal dyspepsia, it is necessary to temporarily (for 12-24 hours) return to the introduction of only glucose-electrolyte solution;

starting from the third day, ⅔ of the injected volume can be polymer mixtures, while the amount of nutritional support for patients for 5–6 days should be 20–25 kcal/kg and protein 1–1.2 g/kg per day (nitrogen-conserving effect in the first three days, it is achieved by parenteral administration of 150 g/day of 10% glucose solution and 25-50 g/day of lipids in the form of 10-20% fat emulsions), in case of persistent hyperglycemia over 10 mmol/l, specialized polymer mixtures should be used;

removal of probes and transition to oral fractional use of mixtures for EN by the sipping method (more often it is 6-7 days), as well as the subsequent transition to a gentle medical diet is possible in the absence of signs of gastroduodenostasis, enteropathy and amylasemia, elimination of endotoxicosis phenomena, stabilization of the patient's condition, presence of appetite, preservation of swallowing function.

The general characteristics of the patients in the studied groups are presented in the table. 1.

Patients of the three groups did not differ significantly in terms of age, sex, etiology, and prognostic indicators (sum of points on the APACHE II scale) of the severity of the course of the disease at the time of hospitalization. The frequency of surgical interventions in the main group and the group of standard nasogastric tube feeding was the same and amounted to 73.5% (25 patients), in the group of standard enteral tube feeding, surgical interventions were performed in 26 (78.9%) patients.

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Table 1. Characteristics of patients in the studied groups

Demographic data		Main group (n=34)	Group of standard nasogastric tube feeding (n=34)	Group of standard enteral tube feeding (n=33)
Age (year)		52,0±9,5	51,6±5,7#	50,8±7,3#
Sex	**Male**	19 (55,9%)	19 (55,9%)#	19 (57,6%)#
	Female	15 (44,1%)	15 (44,1%)#	14 (42,4%)#
Etiological factors:	**alcoholic**	19 (55,9%)	19 (55,9%)#	19 (57,6%)#
	biliary	11 (32,4%)	11 (32,4%)#	10 (30,3%)#
	idiopathic	4 (11,8%)	4 (11,8%)#	4 (12,1%)#
The sum of points on the APACHE II scale at the time of hospitalization		13,5±3,1	13,2±1,9#	12,9±2,7#

Note: # - p>0.05 when compared with the main group.

Evaluation of the effectiveness of EN in the studied groups was carried out by analyzing biochemical indicators of blood serum 7 and 14 days after the start of treatment, namely, the content of total protein, albumin, total bilirubin, creatinine, glucose, cholesterol, C-reactive protein, Na+ and K+ serum was determined of blood. We also analyzed the frequency of complications that were associated with EN and were manifested by increased pain in the epigastric area, projection of the small and/or large intestine, the occurrence of vomiting, regurgitation, diarrhea in the first 24 hours and 7 days after the use of EN, compared intra-abdominal pressure, frequency of infected local complications during the course of AP, mortality, duration of multiple organ failure, and hospital stay of patients.

Statistical analysis was performed using the programs Statistica 10 (Serial Number: STA999K347150-W) and MEDCALC® (Internet resource with open access, https://www.medcalc.org/calc/).

Results

To evaluate the effectiveness of EN, a comparative analysis of biochemical indicators of blood serum in patients in the studied groups was carried out. The evaluation of the indicated indicators was carried out before the start of EN use (Table 2), after 7 days (Table 3) and after 14 days after its start (Table 4).

No significant difference was found in the analysis of biochemical indicators of blood serum at the time of treatment initiation in the studied groups (p>0.05).

Table 2. Initial biochemical indicators of blood serum in the studied groups

Laboratory indicators	Rate	Main group (n=34)	Group of standard nasogastric tube feeding (n=34)	Group of standard enteral tube feeding (n=33)	F	P
Total serum protein, g/l	65-85	47,4±2,5	47,4±2,0	47,8±1,9	0,40	0,75
Serum albumin, g/l	35-50	27,4±1,1	27,3±0,8	27,7±1,1	0,91	0,43
Total bilirubin, μmol/l	3,4-20,8	38,5±13,1	39,9±13,5	37,5±13,5	0,19	0,89
Creatinine, μmol/l	62-115	152,3±13,0	152,7±9,4	151,0±12,7	0,28	0,83
Glucose, mmol/l	3,5-5,5	8,2±2,1	8,9±2,4	8,0±1,9	2,06	0,10
C-reactive protein, mg/l	0,8-8	69,2±20,6	69,8±28,6	70,6±26,4	0,03	0,99
Serum cholesterol, mmol/l	2,9-5,17	5,0±0,6	5,3±0,7	5,0±0,6	2,0	0,12
Na+ serum, mmol/l	130-149	136,9±7,5	137,1±8,1	136,6±7,6	0,95	0,42
K+ serum, mmol/l	3,5-5,4	3,4±0,1	3,4±0,2	3,4±0,1	0,62	0,59

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Table 3. Dynamics of biochemical parameters of blood serum in the studied groups 7 days after the use of enteral nutrition

Laboratory indicators	Rate	Main group (n=34)	Group of standard nasogastric tube feeding (n=34)	Group of standard enteral tube feeding (n=33)
Total serum protein, g/l	65-85	52,9±1,6	50,7±2,4*	51,7±2,6
Serum albumin, g/l	35-50	29,8±1,3	28,3±1,1*	28,8±1,6*
Total bilirubin, μmol/l	3,4-20,8	27,7±7,5	29,8±6,5	26,8±7,1
Creatinine, μmol/l	62-115	137,9±16,5	146,9±13,7*	141,0±12,4
Glucose, mmol/l	3,5-5,5	6,1±0,7	6,2±0,9	6,2±0,6
C-reactive protein, mg/l	0,8-8	105,5±49,7	109,6±51,4	103,5±60,7
Serum cholesterol, mmol/l	2,9-5,17	4,6±0,3	4,1±0,7*	4,3±0,4*
Na+ serum, mmol/l	130-149	140,9±3,1	140,1±4,8	140,5±5,2
K+ serum, mmol/l	3,5-5,4	3,9±0,2	3,7±0,2*	3,7±0,1*

*Note: * - p<0.05 when compared with the main group.*

When analyzing the results after 7 days from the moment of application of EN, a significant difference was obtained in the content of albumin, cholesterol and K+ blood serum (p<0.05) between the patients of the main group and the comparison groups, as well as the content of total protein and creatinine (p<0, 05) between patients of the main group and the group of standard nasogastric tube feeding.

When analyzing the results after 14 days from the moment of application of EN, a significant difference was obtained between the content of albumin, creatinine, cholesterol and K+ in the blood serum (p<0.05) between patients of the main group and the comparison groups, as well as the content of Na+ in the blood serum (p< 0.05) between patients of the main group and the group of standard nasogastric tube feeding.

A comparative analysis of the frequency of intolerance to EN in patients of the main group and the group of standard nasogastric tube feeding on the first day after the use of EN was performed (41.2% and 58.8%, respectively ($\chi 2$=2.07, 95% CI -5.87 -38.55, p=0.15), the main group

Table 4. Dynamics of biochemical parameters of blood serum in the studied groups 14 days after the use of enteral nutrition

Laboratory indicators	Rate	Main group (n=34)	Group of standard nasogastric tube feeding (n=34)	Group of standard enteral tube feeding (n=33)
Total serum protein, g/l	65-85	58,4±3,8	56,3±3,7	56,7±3,6
Serum albumin, g/l	35-50	32,7±1,8	30,1±1,2*	30,6±1,6*
Total bilirubin, μmol/l	3,4-20,8	21,1±2,1	23,4±2,7	22,4±4,8
Creatinine, μmol/l	62-115	107,9±10,8	127,9±14,7*	119,9±12,1*
Glucose, mmol/l	3,5-5,5	5,4±0,3	5,6±0,6	5,5±0,8
C-reactive protein, mg/l	0,8-8	101,6±54,5	121,5±56,2	116,6±77,6
C-reactive protein, mg/l	2,9-5,17	4,7±0,4	4,0±0,5*	4,0±0,4*
Na+ serum, mmol/l	130-149	142,2±1,8	140,7±2,7*	141,3±2,5
K+ serum, mmol/l	3,5-5,4	4,1±0,2	3,9±0,2*	3,9±0,1*

*Note: * - p<0.05 when compared with the main group.*

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and the group of standard enteral tube feeding (41.2% and 51.5%, respectively ($\chi2$=0.7, 95% CI -12.96-32.09, p=0.4), and after 7 days: 8.8% and 32.6%, respectively ($\chi2$=5.7, 95% CI 4.41-41.56, p=0.01) and 8.8 % and 30.3%, respectively ($\chi2$=4.87, 95% CI 2.34-39.48, p=0.02). When comparing the intra-abdominal pressure in patients of the main group and the group of standard nasogastric tube feeding on the first day from the moment of application of EN, this indicator was 10.6±2.9 and 11±2.9 mm Hg. (p=0.57), in the main group and the group of standard enteral tube feeding 10.6±2.9 and 10.9±3.1 mm Hg. (p=0.57) respectively; after 7 days – 10.3±2.4 and 11.8±2.8 mm Hg. (p=0.02), 10.3±2.4 and 11.4±1.9 mm Hg. (p=0.04) respectively; after 14 days – 9.3±2.0 and 10.1±2.2 mm Hg. (p=0.12), 9.3±2.0 and 10.2±1.9 mm Hg. (p=0.06) respectively. The frequency of developing infected local complications of the course of AP in the main group and the group of standard nasogastric tube feeding was also analyzed (32.4% and 35.3%, respectively ($\chi2$=0.063, 95% CI -18.85-24.28, p=0, 8), in the main group and the group of standard enteral tube feeding (32.4% and 33.3%, respectively ($\chi2$=0.006, 95% CI -20.70-22.48, p=0.9), duration of multiple organ failure (10.5±1.9 [8-16] days and 12.2±1.7 [8-16] days, respectively (p=0.0002), as well as 10.5±1.9 [8-16] days and 11.5±1.9 [6-16] days, respectively (p=0.03)), duration of hospital stay (50.7±28.8 [23-124] days and 55.5±30.5 [27-124] days, respectively (p=0.5), as well as 50.7±28.8 [23-124] days and 54.9±32.6 [20-119] days, respectively (p=0.5)) and fatal cases (11.8% and 14.7%, respectively) ($\chi2$=0.123, 95% CI -14.10-19.88, p=0.7), as well as 11.8% and 12.1%, respectively ($\chi2$=0.001, 95% CI -16.25-17.07, p=0, 9)).

Discussion

EN is an important component of complex therapy in patients with a severe course of AP. The issues of the time of onset and the method of introduction of the food mixture into the gastrointestinal tract remain debatable, which is associated with the opinion of the need for «pancreatic rest» in the early period of the disease and the high frequency of development of intolerance to EN (Li et al., 2019). At the same time, there are studies that prove the safety and absence of a reliable difference in the frequency of complications when using the nasogastric or nasojejunal method of introducing a mixture for nutrition in patients with AP (Jabłońska et al., 2021). We have improved the EN protocol in patients with a severe course of AP, which is based on the determination of the timing of restoration of intestinal absorption as one of the main criteria for the initiation of enteral tube feeding in patients of this category, the use of antiflutal agents to prevent the development of intestinal complications in EN, and the safety of nasogastric administration of mixtures for enteral food. According to the results of our study, 14 days after the start of treatment, when using the proposed EN protocol in patients with a severe course of AP, a significant difference was obtained between the content of albumin, creatinine, cholesterol and K+ blood serum (p<0.05) between patients of the main group and comparison groups, as well as the content of Na+ in blood serum (p<0.05) between patients of the main group and the group of standard nasogastric tube feeding. It has also been proven that the use of the proposed protocol of nutritional support significantly reduces the frequency of EN intolerance in the first 7 days of treatment by 23.6% ($\chi2$=5.7, 95% CI 4.41-41.56, p=0.01) in compared with the group of patients where standard nasogastric tube feeding is used, by 21.5% ($\chi2$=4.87, 95% CI 2.34-39.48, p=0.02) compared with the group of standard enteral tube feeding, as well as the duration of multiple organ failure from 12.2±1.7 days to 10.5±1.9 days in comparison with the group of patients where standard nasogastric tube feeding was used (p=0.0002) and from 11.5±1, 9 days to 10.5±1.9 days compared to the group of standard enteral tube feeding (p=0.03).

Conclusions

Determination of the terms of restoration of intestinal absorption is one of the main criteria for the initiation of enteral nutrition in patients with severe acute pancreatitis.

Application of the proposed protocol of enteral nutrition significantly reduces the frequency of intolerance of nutritional support in the first 7 days of treatment by 23.6% ($\chi2$=5.7, 95% CI 4.41-41.56, p=0.01) compared to the control group patients, where standard nasogastric tube feeding is used, by 21.5% ($\chi2$=4.87, 95% CI 2.34-39.48, p=0.02) compared to the group of standard enteral tube feeding.

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There is no significant difference between the frequency of local infectious complications, the duration of multiple organ failure, the duration of hospital stay, and deaths when comparing nasogastric and enteral feeding mixtures in patients with severe acute pancreatitis.

The use of the proposed protocol of enteral nutrition in patients with severe acute pancreatitis leads to a decrease in the duration of multiple organ failure from 12.2±1.7 days to 10.5±1.9 days in comparison with the group of patients who used standard nasogastric tube feeding (p= 0.0002) and from 11.5±1.9 days to 10.5±1.9 days in comparison with the group of standard enteral tube feeding (p=0.03).

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Conflict of interests

Authors have no conflict of interest to declare.

Consent for publication

All authors have read and approved the final version of this manuscript. All authors agreed to publish this manuscript.

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Удосконалення технологій ентерального харчування у хворих з тяжким перебігом гострого панкреатиту

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Анотація: при тяжкому перебігу гострого панкреатиту доцільним вважається ранній початок ентерального харчування (24-72 год від моменту госпіталізації) шляхом назогастрального або назоеюнального введення суміші, що асоціюється зі зниженням частоти інфекційних ускладнень на 24% та смертності на 32%. Однак, у 30,5-65,7% пацієнтів може виникати непереносимість даного виду нутритивної підтримки. Метою дослідження було покращення результатів лікування хворих на тяжкий гострий панкреатит шляхом удосконалення технологій ентерального харчування. В дослідженні приймали участь 101 хворий на тяжкий гострий панкреатит, що були розділені на основна групу, де проводилось ентеральне харчування за удосконаленим протоколом – 34 пацієнти, група порівняння №1, де проводилось стандартне назогастральне харчування – 34 пацієнти та група порівняння №2, де проводилось стандартне ЕХ – 33 пацієнти. Оцінку ефективності ентерального харчування в досліджуваних групах проводили шляхом аналізу та порівняння біохімічних показників сироватки крові, частоти виникнення непереносимості нутритивної підримки, інфекованих локальних ускладнень, летальності, тривалості поліорганної недостатності та перебування пацієнтів в стаціонарі. При використанні запропонованого протоколу ентерального харчування у хворих з тяжким перебігом гострого панкреатиту через 14 діб з моменту початку лікування було отримано достовірну різницю між вмістом альбуміну, креатиніну, холестерину та К+ сироватки крові ($p<0,05$) між пацієнтами основної групи та груп порівняння, а також вмістом Na+ сироватки крові ($p<0,05$) між пацієнтами основної групи та групи стандартного назогастрального зондового харчування. Застосування запропонованого протоколу ентерального харчування достовірно зменшує частоту виникнення непереносимості нутритивної підтримки в перші 7 діб лікування на 23,6% ($\chi2=5,7$, 95% ДІ 4,41-41,56, $p=0,01$) в порівнянні з групою хворих, де застосовується стандартне назогастральне зондове харчування, на 21,5% ($\chi2=4,87$, 95% ДІ 2,34-39,48, $p=0,02$) в порівнянні з групою стандартного ентерального зондового харчування, а також тривалості поліорганної недостатності з 12,2±1,7 діб до 10,5±1,9 діб в порівнянні з групою хворих, де застосовувалось стандартне назогастральне зондове харчування ($p=0,0002$) та з 11,5±1,9 діб до 10,5±1,9 діб в порівнянні з групою стандартного ентерального зондового харчування ($p=0,03$). Використання запропонованої технології ентерального харчування у хворих з тяжким перебігом гострого панкреатиту покращує результати лікування шляхом зменшення тривалості поліорганної недостатності та частоти виникнення непереносимості даного виду нутритивної підтримки.

Ключові слова: гострий панкреатит, ентеральне харчування, кишкова абсорбція, нутритивна підтримка, лікування.