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FEATURES OF ANTIBIOTIC THERAPY IN PATIENTS WITH A COMPLICATED COURSE OF ACUTE PANCREATITIS

Kolosovych I.V. *https://orcid.org/0000-0002-2031-4897*
Hanol I.V. *https://orcid.org/0000-0002-3470-2102*

Bogomolets National Medical University, Department of Surgery №2, Kyiv, Ukraine

ganoli@ukr.net

Background. The most common cause of death among patients with acute pancreatitis in the late period of the disease is purulent-septic complications, which occur in 30-50% of cases.

Aim: To study of the spectrum of microorganisms in the complicated course of acute pancreatitis and justification of the appointment of antibiotic therapy, taking into account the role of Helicobacter pylori as a pathogenetic factor of the disease.

Materials and methods: 280 patients with acute pancreatitis participated in the study, who were divided depending on the treatment tactics into the main (n=140) and comparison group (n=139). To assess the effectiveness of surgical tactics in the studied groups, a comparative analysis of the frequency of development of purulent-septic complications and the species composition of microorganisms based on the results of bacteriological examination of biological fluids was carried out.

Results. The species composition of microorganisms in case of purulent-septic complications in patients with severe acute pancreatitis is represented mainly by gram-negative flora (Escherichia coli, Pseudomonas aeruginosa, Acinetobacter spp., Klebsiella pneumoniae) with low sensitivity to most antibiotics, with the exception of protected semi-synthetic broad-spectrum antibiotics from the group penicillins and imipenem-cilastatin. When analyzing the studied indicators in the main group, an increase in the content of immunoglobulin M to Helicobacter pylori was detected in 41.1% (39/95) of patients with a severe course of the disease within 3 weeks from the moment of hospitalization. The use of generally accepted schemes of antibacterial therapy in combination with proton pump inhibitors for the treatment of purulent-septic complications of acute pancreatitis, taking into account the sensitivity of Helicobacter pylori to them, is not inferior to standard anti-Helicobacter treatment in terms of eradication effect (eradication was achieved in 94.9% of patients).

Conclusions. The use of improved methods of diagnosis and treatment, including the justified appointment of antibiotic therapy taking into account Helicobacter pylori infection, made it possible to significantly reduce the frequency of development of purulent-septic complications by 18.1% ($\chi2=7.67$, 95% CI 5.30 -30.20, $p=0.005$) and the number of microbial associations in the studied biological fluids by 51.3% ($\chi2=37.62$, 95% CI 37.15-61.44, $p<0.0001$).

Key words: acute pancreatitis, purulent-septic complications, microflora, diagnosis, treatment.

Background. The peculiarity of acute pancreatitis (AP) is the high risk of developing complications, the mortality rate of which reaches 15%, and in the severe course of the disease varies within 40–70% [1]. Currently, the most common cause of death in the late stages of the disease is purulent-septic complications, which occur in 30-50% of patients with severe AP [2]. At the same time, it is generally accepted to prescribe antibacterial drugs in the case of the proven fact of the development of purulent-septic complications, taking into account the results of the sensitivity assessment of the released microorganisms and the peculiarities of the formation of the therapeutic concentration of antibacterial agents in the tissues of the pancreas or its secretion. Thus, in Europe, when examining the type of pathogens found in acute infected destructive pancreatitis, a mixed flora is determined in 68% of patients, while the most frequent pathogen is Pseudomonas aeruginosa (59%), associated with *Candida albicans* or *Candida glabrata* [3]. There have also been studies dedicated to the study of Helicobacter pylori (HP), as one of the possible etiopathogenetic factors of HP and its complications [4]. At the same time, it should be noted that antibiotic prophylaxis, routine antifungal prophylaxis, and the use of probiotics are not recommended [5]. However, some researchers suggest that prophylactic administration of antibiotics can prevent the development of infectious complications in patients with sterile pancreatic necrosis [6]. In addition, there are studies devot-

ed to the justification of antibiotic therapy taking into account the content of procalcitonin in blood serum (the content of procalcitonin ≥1 ng/ml is an indication for prescribing antibiotics) [7].

Aim: To study of the spectrum of microorganisms in the complicated course of acute pancreatitis and justification of the appointment of antibiotic therapy, taking into account the role of Helicobacter pylori as a pathogenetic factor of the disease.

MATERIALS AND METHODS

This research was conducted between 2016–2023 and was approved by the Commission on Bioethical Expertise and Ethics of Scientific Research at Bogomolets National Medical University (protocol No.169 dated 03/20/2023). It involved the examination of 280 patients who were treated in the clinic of the Department of Surgery No.2 of Bogomolets National Medical University. Inclusion criteria were patients of both sexes aged 18 years and older who were admitted to the hospital by emergency care with a diagnosis of AP, exclusion criteria were chronic somatic diseases in the decompensation phase, patient refusal. Depending on the treatment tactics, the patients were divided into the main group (141 people) and the comparison group (139 people). The patients of the two groups probably did not differ in age, sex, duration of the disease before admission to the hospital, etiology of the disease, degree of severity and accompanying pathology (p>0.05) (Table 1).

Examination and treatment of patients with AP in the studied groups was carried out in accordance with the «Local protocols of medical care for patients with acute pancreatitis» approved in medical institutions, which were based on the recommendations of the «Adapted evidence-based clinical guideline» of the Ministry of Health of Ukraine (M.P. Komarov, 2016) and «International Consensus on Integrative Diagnosis and Treatment of Acute Pancreatitis» [8]. Indications for antibiotic therapy were the development of purulent-septic complications, taking into account the data of bacteriological examination. It should be noted that bacteriological examination of biological fluids was carried out in all patients in case of suspicion of the development of infectious complications, as well as in the case of the use of invasive methods of diagnosis and treatment, regardless of the established fact of infection. The assessment of the effectiveness of antibiotic therapy and the decision to stop it were made based on the analysis of clinical and laboratory indicators.

Table 1

Characteristics of patients in the studied groups

Demographic indicators	Main group (n=141)	Comparison group (n=139)
Age (years)	50,7±6,4	49,9±7,3
Sex: male female	 87 (61,7%) 54 (38,3%)	 80 (57,6%) 59 (42,4%)
Duration of illness before hospitalization (hours)	29,1±14,7	28,9±15,6
Etiological factors: alcoholic biliary traumatic idiopathic	 71 (50,4%) 52 (36,9%) 2 (1,4%) 16 (11,3%)	 74 (53,2%) 48 (34,5%) 3 (2,2%) 14 (10,1%)
Degree of severity of the course of the disease: mild moderate severe	 28 (19,9%) 18 (12,8%) 95 (67,4%)	 30 (21,6%) 17 (12,2%) 92 (66,2%)
The sum of points according to the Charlson comorbidity index	0,8±0,7	0,9±0,7

In the patients of the main group, improved surgical tactics were applied, based on the diagnosis of the severity of AP, taking into account changes in calcium-phosphorus metabolism, the content of vitamin D in blood serum and the use of a developed mathematical model for predicting the severity of the course of AP, clinical and laboratory monitoring of indicators of the hemostasis system and fibrinolysis, improved technologies of nutritional support and a staged approach to the correction of intra-abdominal hypertension in patients with a severe course of the disease, implementation of own endoscopic and minimally invasive methods of surgical treatment [9]. At the same time, an additional indication for carrying out antibiotic therapy in patients of the main group was taking into account the data of a fecal test for Helicobacter infection followed by a serological examination of patients regarding the content of immunoglobulin M to HP in blood serum. In the case of an increase in the content of immunoglobulin M to HP in blood serum ≥1.24 IU/ml, it was considered as a likely predictor of the development of purulent-septic complications (sensitivity is 86.4%, specificity - 100.0%) and antibiotic therapy was started with preliminary implementation bacteriological examination of the biopsy material of the mucous membrane of the antral part of the stomach (the material was additionally obtained during fibrogastroduodenoscopy) [10].

To assess the effectiveness of surgical tactics in the studied groups, a comparative analysis of the frequency of development of purulent-septic complications and the species composition of microorganisms based on the results of bacteriological examination of biological fluids was carried out.

Statistical analysis was performed using the programs Statistica 12 (Serial Number: STA999K347150-W) and MEDCALC® (Internet resource with open access, https://www.medcalc.org/calc/). The normality of data distribution was determined using the Shapiro-Wilk test. Differences between groups were determined using the Student's t-test for independent samples and the Mann-Whitney U-test. Differences in the sample distribution were assessed using the $\chi 2$ test.

RESULTS AND DISCUSSION

Local complications of AP were observed in 92% (104/113) patients of the main group, in 88.9% (97/109) of the comparison group ($\chi 2$=0.616, 95% CI -4.86-11.27, p= 0.43), of which 22.1% (23/104) and 40.2% (39/97) of patients were infected, respectively ($\chi 2$=7.67, 95% CI 5.31-30.21, p=0.005).

In the comparison group, 193 studies were conducted, a positive result was obtained in 52.8% (102/193) cases. 165 strains of microorganisms were identified, under these circumstances monoculture was found in 41.2% (42/102), microbial associations were found in 58.8% (60/102) (two-component microbial associations were found in 95% (57/60), three-component – in 5% (3/60) cases). The results of bacteriological studies are presented in the Table 2.

When the species composition of microorganisms was studied, in 72.1% (119/165) cases, gram-negative flora was observed among the detected strains. Among gram-negative bacteria, non-fermenting gram-negative bacteria prevailed (*Pseudomonas aeruginosa* in 33.9% (56/165), *Acinetobacter spp.* - in 5.5% (9/165) cases) and the Enterobacteriaceae family (*Klebsiella pneumoniae* - in 13.3% (22/165) and *Escherichia coli* - 15.8% (26/165), *Enterobacter spp.* - in 2.4% (4/165), *Citrobacter spp.* - in 1.2% (2/165) of cases). Gram-positive flora was detected in 25.5% (42/165) of cases, namely, in 17.6% (29/165) of cases, microorganisms of the Enterococcus family (*Enterococcus faecalis* - in 10.3% (17/165), *Enterococcus faecium* - in 7.27% (12/165) cases), in 6.7% (11/165) cases, microorganisms of the Staphylococcus family (*Staphylococcus aureus* - in 3.6% (6/165), *Staphylococcus saprophyticus* - in 1.2% (2/165), *Staphylococcus epidermidis* - in 1.8% (3/165) of cases), in 1.2% (2/165) of cases, microorganisms of the Streptococcus family (*Streptococcus pneumoniae* - in 0.6% (1/165), *Streptococcus viridans* - in 0.6% (1/165) of cases). Fungal infection (*Candida spp.*) was detected in 2.4% (4/165) of cases.

It should be noted that with the extension of the treatment period of patients in the intensive care unit and intensive care unit, against the background of the use of antibiotic therapy, a change in the species composition of the microflora oc-

Table 2

Bacteriological examination of biological fluids in patients of the comparison group

Biological material	The number of conducted studies	The number of studies with detected growth of microorganisms
Exudate from the abdominal cavity and/or retroperitoneal space	84 (43,5%)	54 (64,3%)
Exudate from a postoperative wound	16 (8,3%)	9 (56,3%)
Exudate from the pleural cavity	13 (6,7%)	5 (38,5%)
Urine	31 (16,1%)	14 (45,2%)
Sneezing	35 (18,1%)	15 (42,9%)
Blood	14 (7,3%)	5 (35,7%)
In total	193 (100%)	102 (52,8%)

curred. Thus, at the beginning of treatment, when examining exudate from the abdominal cavity and/or retroperitoneal tissue, Escherichia coli prevailed, and subsequently an increase in the number of hospital strains was found. Most often, Pseudomonas aeruginosa, Acinetobacter spp., Klebsiella pneumoniae, which had low sensitivity to most antibiotics, were detected. In addition, the appearance of mixed microflora (microbial associations) and the detection of opportunistic microflora were observed. Bacteremia was detected in 5 (3.7%) patients with clinical signs of generalized infection, Escherichia coli was determined in 60% (3/5) of cases. At the same time, the species composition of microorganisms in the blood did not correspond to the microflora from the exudate from the abdominal cavity.

Determining factors that influenced the choice of antibacterial drugs in case of deterioration of clinical and laboratory indicators and progression of the disease were: the severity of the general condition of the patients, the species composition of microorganisms according to the results of bacteriological research taking into account the results of their sensitivity assessment, the presence and duration of previous antibiotic therapy, the duration of the patient's stay in the hospital , the presence of local and extra-abdominal infected complications, features of the formation of a therapeutic concentration of antibacterial agents in the tissues of the pancreas or its secretion. Thus, in case of a severe course of the disease, development of local complications, refusal to take antibiotics the day before, duration of stay in the hospital less than 5 days, monotherapy was carried out in the form of intravenous administration of cephalosporins of the II and III generations (the sensitivity of microorganisms to these drugs was observed in 46.1% (47/ 102) cases). In the absence of a clinical effect within three days, the presence of septic complications, a stay in the hospital for more than 5 days, taking antibacterial drugs the day before, combined therapy combining cephalosporins of the III generation and metronidazole, or fluoroquinolones (ciprofloxacin) and metronidazole (the sensitivity of the microflora was observed in 77, 5% (77/102) of cases). Reserve drugs included carbopenems (imipenem-cilastatin, meropenem) (the sensitivity of the microflora was observed in 93.1% (95/102) of cases).

During the analysis of the studied indicators in the main group, an increase in the content of immunoglobulin M up to HP was found in 41.1% (39/95) of patients with a severe course of the disease within 3 weeks from the moment of hospitalization, the specified patient underwent bacteriological examination of the biopsy material of the mucous membrane of the antral part of the stomach according to the proposed method. The results of the study of the sensitivity of the sown HP strains to antibiotics are presented in the Table 3.

In addition to antibiotic therapy, proton pump blockers were also prescribed to these patients. After the completion of the course of antibacterial therapy, according to international recommendations, the patients were examined for the presence

of HP by a molecular biological method, eradication was achieved in 37 (94.9%) patients.

Bacteriological examination of biological fluids in patients of the main group was performed in order to substantiate and control the effectiveness of antimicrobial therapy in the event of the development of purulent-septic complications and the use of invasive methods of diagnosis and treatment. Thus, 116 microbiological studies were conducted and microflora was detected in 53 (45.7%) samples, of which monoculture in 92.5% (49/53) and two-component microbial associations – in 7.5% (4/53) of cases (Table 4).

According to the results of the study, 57 strains of microorganisms were identified, of which 66.7% (38/57) were gram-negative flora. Among gram-negative bacteria, Pseudomonas aeruginosa was identified in 21.1% (12/57), Acinetobacter spp. – in 3.5% (2/57), Klebsiella pneumoniae – in 17.5% (10/57) and Escherichia coli – 19.3% (11/57), Enterobacter spp. – in 3.5% (2/57), Citrobacter spp. – in 1.8% (1/57) of cases. Gram-positive flora was

Table 3

Sensitivity of Helicobacter pylori to antibiotics in vitro

Sensitivity HP / Antibiotic	Sensitive	Moderately sensitive	Resistant
Ceftriaxone	35 (89,7%)	2 (5,1%)	2 (5,1%)
Ceftazidime	36 (92,3%)	2 (5,1%)	1 (2,6%)
Cefoperazone	34 (87,2%)	3 (7,7%)	2 (5,1%)
Cefatoxime	36 (92,3%)	2 (5,1%)	1 (2,6%)
Cefepime	37 (94,9%)	1 (2,6%)	1 (2,6%)
Amoxicillin/clavulanate	33 (84,6%)	3 (7,7%)	3 (7,7%)
Imipenem/cilastatin	37 (94,9%)	1 (2,6%)	1 (2,6%)
Meronem	37 (94,9%)	1 (2,6%)	1 (2,6%)
Amikacin	33 (84,6%)	3 (7,7%)	3 (7,7%)
Vancomycin	34 (87,2%)	3 (7,7%)	2 (5,1%)
Ticarcillin/clavulanic acid	36 (92,3%)	2 (5,1%)	1 (2,6%)
Piperacillin/tazobactam	37 (94,9%)	2 (5,1%)	0 (0%)
Ciprofloxacin	33 (84,6%)	3 (7,7%)	3 (7,7%)
Levofloxacin	34 (87,2%)	3 (7,7%)	2 (5,1%)

Table 4

Bacteriological examination of biological fluids in patients of the main group

Biological material	The number of conducted studies	The number of studies with detected growth of microorganisms
Exudate from the abdominal cavity and/or retroperitoneal space	74 (63,8%)	41 (55,4%)
Exudate from a postoperative wound	5 (4,3%)	2 (40%)
Exudate from the pleural cavity	7(6%)	1(14,3%)
Urine	5 (4,3%)	2 (40%)
Sneezing	16 (13,8%)	6 (37,5%)
Blood	9 (7,8%)	1 (11,1%)
In total	116 (100%)	53 (45,7%)

detected in 29.8% (17/57) of cases, namely Enterococcus faecalis in 12.3% (7/57), Enterococcus faecium in 8.8% (5/57), Staphylococcus aureus in 3.5% (2/57), Staphylococcus saprophyticus – in 1.8% (1/57), Staphylococcus epidermidis – in 1.8% (1/67) of cases), Streptococcus pneumoniae – in 1.8% (1/ 57) cases. Fungal infection (Candida spp.) was detected in 3.5% (2/57) of cases.

When determining the sensitivity of microorganisms to antibiotics, the following results were obtained. So Escherichia coli, Enterobacter spp. and Citrobacter spp. in 90% of cases were sensitive to imipenem-cilastatin, in 80% to meropenem, in 40% to levofloxacin, in 20% to amikacin; Staphylococcus aureus, Staphylococcus saprophyticus and Staphylococcus epidermidis showed the highest sensitivity to vancomycin and imipenem/cilastatin (100% of cases); Klebsiella pneumoniae was sensitive in 90% of cases to ticarcillin/clavulanic acid, in 70% of cases to cefipim, levofloxacin, in 60% to amikacin; Streptococcus pneumoniae showed high sensitivity to cefaperazone and cefipime; Enterococcus faecalis and Enterococcus faecium were sensitive to cefipim and vancomycin in 100% of cases. When studying the sensitivity of Pseudomonas aeruginosa and Acinetobacter spp. in patients with purulent-septic complications of acute pancreatitis, resistance to ceftazidime and cefipime was 50% of isolated strains. Similar sensitivity (50%) was determined to meropenem, sensitivity to imipenem-cilastatin and amikacin was 100%. It should also be noted the 100% level of resistance of isolated strains of Pseudomonas aeruginosa to ciprofloxacin and levofloxacin.

The occurrence of purulent-septic complications in patients with AP is associated with such risk factors as the patient's age, biliary etiology of the disease, pancreatic tissue necrosis >50%, late start of enteral nutrition, persistent multiple organ failure, long-term invasive artificial lung ventilation [11]. In our study, the frequency of development of purulent-septic complications in patients of the comparison group was 40.2%, which corresponds to the statistical data of other researchers [12]. However, including the well-founded appointment of antibiotic therapy in patients of the main group, taking into account the infection of patients with HP with the help of the diagnostic technique of HP developed in the clinic and determining its sensitivity to antibiotics, it was possible to reliably reduce the frequency of the development of infection of local complications to 22.1% ($\chi2$=7, 67, 95% CI 5.30–30.20, p=0.005).

An increase in the content of immunoglobulin M to HP was detected in 41.1% (39/95) of patients of the main group with a severe course of the disease, while eradication of HP against the background of the prescribed therapy was achieved in 94.9% (37/39) of patients, which corresponds to the requirements of the Maastricht Consensus (the eradication scheme is considered effective if eradication is achieved in more than 80% of cases) [13]. When comparing the species composition of microorganisms according to the results of bacteriological examination of biological fluids in the studied groups, no probable difference was obtained, among the detected strains gram-negative flora prevailed (the main group – 66.7%, the comparison group – 72.1%) ($\chi2$=0.65, 95 % CI –7.49–19.48, p=0.41), which coincides with the results of studies by other researchers [14]. Under these circumstances, at the initial stage, Escherichia coli was most often detected, later – Pseudomonas aeruginosa, Acinetobacter spp., Klebsiella pneumoniae, which had a low sensitivity to most antibiotics (the pathogens showed the highest sensitivity to protected semi-synthetic broad-spectrum antibiotics from the group of penicillins and imipenem-cilastatin). However, in patients of the main group, a decrease in the number of microbial associations was observed by 51.3% ($\chi2$=37.62, 95% CI 37.15–61.44, p<0.0001).

We believe that the obtained data allow us to consider HP as one of the factors in the pathogenesis of AP. At the same time, it should be noted that at a certain stage of the development of purulent-septic complications, nosocomial and opportunistic infections, which are characterized by high resistance to antibiotics, are joined. In turn, the effectiveness of antibiotic therapy and, accordingly, increasing the probability of a favorable outcome of the disease largely depends on the correct use of information about the microbiological situation in a specific case, and the application of the proposed method of bacteriological examination of the biopsy material of the mucous membrane of

the antral part of the stomach makes it possible to ensure a justified regimen of antibiotic use and to reduce the rate of growth of antibiotic resistance. In addition, of course, the resistance of microbial agents to antibiotics increases over time, therefore, permanent and systematic monitoring of antibiotic resistance and timely replenishment of drug formularies with effective antibacterial drugs are indispensable conditions for the complex treatment of patients with AP.

CONCLUSION

1. The species composition of microorganisms in the event of purulent-septic complications in patients with severe acute pancreatitis is represented mainly by gram-negative flora (Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae) with low sensitivity to most antibiotics, with the exception of protected semi-synthetic broad-spectrum antibiotics from the group of penicillins and imipenem-cilastatin.
2. The use of generally accepted schemes of antibacterial therapy in combination with proton pump inhibitors for the treatment of purulent-septic complications of acute pancreatitis, taking into account the sensitivity of Helicobacter pylori to them, is not inferior to standard anti-Helicobacter treatment in terms of eradication effect (eradication was achieved in 94.9% of patients).
3. The use of improved methods of diagnosis and treatment, including the justified appointment of antibiotic therapy taking into account Helicobacter pylori infection, made it possible to significantly reduce the frequency of development of purulent-septic complications by 18.1% ($\chi2$=7.67, 95% CI 5.30 –30.20, p=0.005) and the number of microbial associations in the studied biological fluids by 51.3% ($\chi2$=37.62, 95% CI 37.15–61.44, p<0.0001).

Conflict of interest. The authors of this manuscript claim that there is no conflict of interest during the research and writing of the manuscript.

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ОСОБЛИВОСТІ АНТИБІОТИКОТЕРАПІЇ У ПАЦІЄНТІВ З УСКЛАДНЕНИМ ПЕРЕБІГОМ ГОСТРОГО ПАНКРЕАТИТУ

Колосович І.В., Ганоль І.В.

Національний медичний університет імені О.О. Богомольця, Київ, Україна

ganoli@ukr.net

Актуальність. Найбільш частою причиною летальних випадків серед пацієнтів з гострим панкреатом у пізньому періоді захворювання є гнійно-септичні ускладнення, що зустрічаються у 30–50% випадків.

Ціль: вивчення спектру мікроорганізмів при ускладненому перебігу гострого панкреатиту та обгрунтування призначення антибіотикотерапії з урахуванням ролі Helicobacter pylori як патогенетичного чинника захворювання.

Матеріали та методи. У дослідженні взяли участь 280 хворих на гострий панкреатит, що були розділені в залежності від лікувальної тактики на основну (n=140) та групу порівняння (n=139). Для оцінки ефективності хірургічної тактики в досліджуваних групах був проведений порівняльний аналіз частоти розвитку гнійно-септичних ускладнень та видового складу мікроорганізмів за результатами бактеріологічного дослідження біологічних рідин.

Результати. Видовий склад мікроорганізмів у разі виникнення гнійно-септичних ускладнень у пацієнтів з тяжким гострим панкреатитом представлений переважно грамнегативною флорою (Escherichia coli, Pseudomonas aeruginosa, Acinetobacter spp., Klebsiella pneumoniae) з низькою чутливістю до більшості антибіотиків за виключенням захищених напівсинтетичних антибіотиків широкого спектра дії з групи пеніцилінів та іміпенему-циластатину. При аналізі досліджуваних показників в основній групі підвищення вмісту імуноглобуліну М до Helicobacter pylori було виявлено у 41,1% (39/95) пацієнтів з тяжким перебігом захворювання в терміни до 3 тижнів від моменту госпіталізації. Використання загальноприйнятих схем антибактеріальної терапії в комбінації з інгібіторами протонної помпи для лікування гнійно-септичних ускладнень гострого панкреатиту, з урахуванням чутливість до них Helicobacter pylori, не поступається за ерадикаційним ефектом стандартному антихелікобактерному лікуванню (ерадикація була досягнута у 94,9% пацієнтів).

Висновки. Застосування удосконалених методів діагностики та лікування, в тому числі обґрунтоване призначення антибіотикотерапії з урахуванням інфікованості на Helicobacter pylori дало змогу вирогідно зменшити частоту розвитку гнійно-септичних ускладнень на 18,1% ($\chi2$=7,67, 95% ДІ 5,30-30,20, p=0,005) та кількість мікробних асоціацій в досліджуваних біологічних рідинах на 51,3% ($\chi2$=37,62, 95% ДІ 37,15–61,44, p<0,0001).

Ключові слова: гострий панкреатит, гнійно-септичні ускладнення, мікрофлора, діагностика, лікування.