

# MODERN PRINCIPLES OF TREATMENT OF ACUTE DESTRUCTIVE PANCREATITIS

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## Abstract

**Objective.** To improve the results of endovideosurgical treatment of patients with acute destructive pancreatitis.

**Material and methods.** The research was carried out at the bases of the Nur-Sultan Multifunctional City Hospital №2 and the Nur-Sultan Multifunctional City Hospital №1. Statistical analysis of the results was carried out using the methods of variation statistics with the calculation of  $M \pm SD$ . Differences between comparison groups were analyzed using the Wilcoxon-Man-Whitney test and were considered statistically significant at  $p \leq 0.05$ .

From 2017-2021, 64 patients with acute destructive pancreatitis were treated according to the developed and implemented treatment algorithm:

Of these: AP without organ failure and local or systemic complications - 10 people. AP of moderate and severe form - 54 people. Lethal outcomes - 1; The average length of stay in the hospital is  $20.8 \pm 1.2$  days; The mean age was  $43 \pm 1.3$  years.

The control group - treatment of patients with moderate and severe acute biliary pancreatitis without the use of ulinostatin (hereinafter US) was  $n = 122$ ;

Lethal outcomes - 8.

An algorithm for the use of US was developed and implemented depending on the severity of the course of destructive pancreatitis in the complex treatment of patients with AP.

**Results.** 10 patients were treated conservatively. 54 - surgical treatment was combined with the appointment of US according to the developed scheme. Endoscopic surgery was performed in 51 patients; 3 patients were operated on by laparotomy. The average duration of hospital stay in the main group was  $3.5 \pm 0.34$  days less than in the control group.

**Conclusion.** The research results showed the high efficiency of the developed algorithm for endovideosurgical treatment of AP in combination with the use of the US. Received AC №14704 dated January 27, 2021 (www.kazpatent.kz).

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**Conflict of interest**

The authors declare that they have no conflicts of interest

**Keywords**

acute destructive pancreatitis, ulinostatin, endovideosurgical methods of treatment

## Жедел деструктивті панкреатитті хирургиялық емдеуді оңтайландыру

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## Аңдатпа

**Мақсаты.** Жедел деструктивті панкреатитпен ауыратын науқастарды емдеудің эндовидеохирургиялық әдісінің нәтижелерін жақсарту.

**Материал және әдістер.** Зерттеулер ҚР «№1 қалалық ауруханасы» ШЖҚ ММК базасында және ҚР «Нұр-Сұлтан қаласының №2 қалалық ауруханасы» ШЖҚ ММК базасында жүргізілді.

Нәтижелерді статистикалық талдау вариациялық статистика әдістерін қолдану арқылы  $M \pm SD$  есептей отырып жүргізілді. Салыстыру топтарының арасындағы айырмашылықтар Уилкоксон-Ман-Уитни тестінің көмегімен талданды және  $p \leq 0.05$  кезінде статистикалық маңызды деп саналды.

2017-2021 жылдар аралығында әзірленген және енгізілген емдеу алгоритмі бойынша жедел деструктивті панкреатитті бар 64 науқас емделді.

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**Мүдделер қақтығысы**

Авторлар мүдделер қақтығысының жоқтығын мәлімдейді

Олардың ішінде: орган жеткіліксіздігі және жергілікті және/немесе жүйелік асқынусыз ОП -10 адам

ЖП орташа және ауыр түрі – 54 адам. Өлімге әкелген жағдайлар-1. Ауруханада болған орташа ұзақтығы- 20,8±1,2 тәулік. Ерлер – 35 адам. (54,7%). Әйелдер – 29 адам. (45,3%) . Орташа жасы 43±1,3 жасты құрады.

Бақылау тобы- жедел деструктивті панкреатиті бар науқастарды улиностаинсіз емдеу – 122 науқас. Өлімге әкелген жағдайлар-8.

Жедел деструктивті панкреатиті бар науқастарды кешенді емдеуде деструктивті панкреатит ағымының ауырлығына байланысты улиностаинді қолдану алгоритмі әзірленді және енгізілді. Әзірленген схемаға сәйкес улиностаинді тағайындаумен біріктірілген.

**Нәтижелер.** 10 науқасқа консервативті ем жүргізілді. 54 - хирургиялық емдеу әзірленген схема бойынша улиностаин тағайындаумен біріктірілді. 54 науқастың 51-іне эндоскопиялық операция жасалды; 3 науқасқа лапаротомия әдісімен операция жасалды. Басты топ бақылау топқа қарағанда ауруханадан 3,5±0,34 тәулікке ертерек жазылып шыққан

**Қорытынды.** Зерттеу нәтижелері протеаза тежегіші улиностаинді қолданумен бірге жедел панкреатитті эндовидеохирургиялық емдеу алгоритмінің жоғары тиімділігін көрсетті. 2021 жылғы 27 қаңтардағы АС № 14704 ([www.kazpatent.kz](http://www.kazpatent.kz)) алынды.

#### Түйін сөздер

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## Оптимизация хирургического лечения острого деструктивного панкреатита

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#### Аннотация

**Цель.** Улучшить результаты эндовидеохирургического метода лечения пациентов с острым деструктивным панкреатитом.

**Материал и методы.** Исследование проводилось на базах РГК на ПХВ «Городская больница №1» и РГП на ПХВ «Городская больница №2» города Нур-Султан РК.

Статистический анализ результатов проводили с использованием методов вариационной статистики с расчетом  $M \pm SD$ . Различия между группами сравнения анализировали с использованием критерия Вилкоксона-Мана-Уитни и считали статистически значимыми за  $p \leq 0,05$ .

С 2017-2021гг. пролечено по разработанному и внедренному алгоритму лечения 64 пациентов с острым деструктивным панкреатитом:

Из них: ОП без органной недостаточности и местных и/или системных осложнений -10 чел. ОП средней и тяжелой формы -54 чел.

Летальные исходы-1; Средняя продолжительность нахождения в стационаре-20,8±1,2 суток; Средний возраст составил - 43 ± 1,3 лет.

Контрольная группа - лечение больных с средним и тяжелым острым билиарным панкреатитом без использования улиностаина (далее УС) составила  $n = 122$ ; Летальные исходы-8.

Разработан и внедрен алгоритм применения улиностаина в зависимости от степени тяжести течения деструктивного панкреатита в комплексном лечении больных с острым деструктивным панкреатитом.

**Результаты.** 10 больных пролечено консервативно. 54 – хирургическое лечение сочеталось с назначением улиностаина по разработанной схеме. Из 54 пациентов, эндоскопические операции были произведены 51 пациентам; 3 пациента были прооперированы с помощью лапаротомии. Средняя продолжительность нахождения в стационаре у основной группы была на 3,5±0,34 суток меньше, чем контрольной.

**Заключение.** Результаты исследований показали высокую эффективность разработанного алгоритма эндовидеохирургического метода лечения острого панкреатита в сочетании с применением ингибитора протеаз улиностаина.

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#### Ключевые слова

острый деструктивный  
панкреатит, улиностаин,  
эндовидеохирургические  
методы лечения

### Relevance:

Despite the progressive development of modern medicine, the relevance of the treatment of patients with acute pancreatitis remains, as the mortality rate with this pathology is growing steadily. Today, this is a rather serious problem and requires considerable attention.

Numerous publications of endovideosurgical methods for the treatment of acute pancreatitis in combination with drug treatment indicate that surgeons are constantly searching for the optimal integrated approach to the treatment of this severe surgical disease.

The introduction of new drugs and technologies is necessary to improve treatment. The incidence of acute pancreatitis both abroad and in Kazakhstan tends to increase. The proportion of patients with destructive pancreatitis is 15-20%. At the same time, mortality, depending on the volume and severity of the pathology, remains at the level of 20% and above. The incidence of acute pancreatitis since 2000 in the Russian Federation has come out on top, accounting for 35-45% in the structure of acute surgical diseases of the abdominal organs (Kovalenko A.A., 2007; Vashetko R.V., 2012; Gostishchev V.K., 2012; Ostrovsky A.G., 2012; Bagnenko S.F., 2013), and the upward trend in the number of patients continues. In 15 - 20% of cases, the development of acute pancreatitis is destructive (Saveliev V.S., 2008). Among patients with acute pancreatitis, men average 55 - 75%, and women - 25 - 45% (Kuznetsov N.A., 2004). Most cases occur in people of working age from 21 to 60 years (65%). Among patients under 45 years old (76%) are men, which is mainly associated with alcohol abuse. A high incidence rate (up to 80%) among women over 60 years of age is associated, first of all, with a history of often exacerbating cholecystitis, as a manifestation of cholelithiasis (Shapovalyants S.G., Mikhailusov S.V., 2000). An increase in the number of patients with acute pancreatitis has led to an increase in the frequency of its destructive forms and their complications. So the formation of infected pancreatic necrosis is almost 60% of cases, parapancreatitis - more than 45%, omentobursitis - almost 30% (Tolstoy A.D., 2003).

The search and introduction of new drugs in combination with endovideosurgical technologies are necessary to improve the treatment and increase the effectiveness of the treatment of severe complications of acute pancreatitis.

### Scientific novelty:

For the first time in the Republic of Kazakhstan, on the basis of the Nur-Sultan Multifunctional City Hospital №2 and the Nur-Sultan Multifunctional City Hospital №1, scientific studies were carried out on the use of the infusion solution "Ulinastatin". An algorithm for the treatment of acute destructive pancreatitis with endovideosurgical interventions in combination with the use of a protease inhibitor has been developed, depending on the severity of the course of the disease. The use of ulinastatin in patients of the main group was carried out according to the developed algorithm: AC No. 14704 dated January 27, 2021.

### Purpose of the study.

To improve the results of endovideosurgical treatment of patients with acute destructive pancreatitis.

### Materials and methods.

The study was conducted on the basis of the Nur-Sultan Multifunctional City Hospital №2 and the Nur-Sultan Multifunctional City Hospital №1 of the Republic of Kazakhstan.

CT, MRI, ZORING unit, Karl Stors endoscopic stand, Karl Stors argon-plasma coagulator, GelPort (Applied Medical), abdominal radiography, abdominal ultrasound, ERCP; clinical and laboratory research. Statistical analysis of the results was carried out using the methods of variation statistics with the calculation of  $M \pm SD$ . Differences between comparison groups were analyzed using the Wilcoxon-Mann-Whitney test and considered statistically significant at  $p \leq 0.05$ .

From 2017-2021, 64 patients with acute destructive pancreatitis were treated according to the developed and implemented treatment algorithm:

Of these: AP without organ failure and local and / or systemic complications -10 people. AP of moderate and severe form -54 people.

Lethal outcomes-1; The average length of stay in the hospital is  $20.8 \pm 1.2$  days;

Men - 35 (54.7%), women – 29 (45.3%) . The mean age was  $43 \pm 1.3$  years.

The control group - treatment of patients with moderate and severe acute biliary pancreatitis without the use of ulinostatin (hereinafter US) was  $n = 122$ ;

Lethal outcomes-8; The average duration of stay in the hospital is  $24.3 \pm 1.6$  days.

Patients of the main group - in addition to traditional therapy received US (Bharat Serums and Vaccines Ltd., India) twice a day at 10:00 and 22:00 at a dose of 100 thousand IU for 5 days, no later than 48 hours after moment of hospitalization

Of these, 37% (20 people) of patients underwent ERCP;

13% (7 people) of patients were operated on (laparoscopy, open surgery);

50% (27 people) treatment of patients is limited conservatively: drug treatment + EPST (Fig. 1).

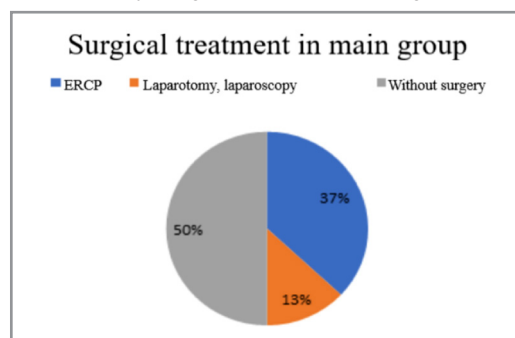
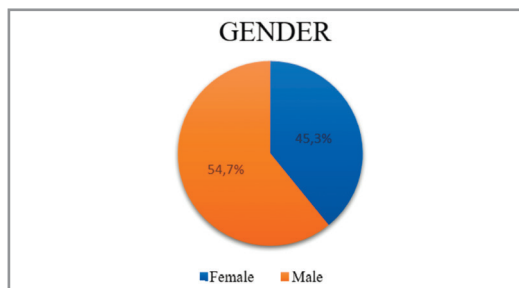


Figure 1.  
Types of treatment  
in the main group

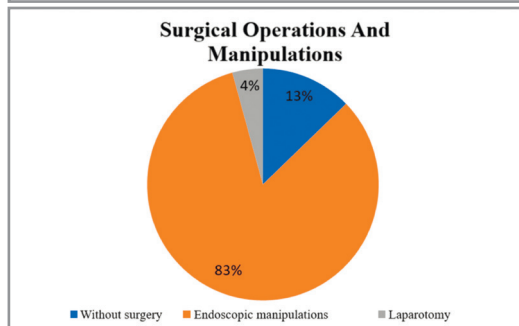
### Results:

According to the developed algorithm, 54 patients with acute biliary pancreatitis of moderate and severe severity were treated. Of these, 29 were women and 35 were men (Fig. 2). The mean age of the patients was  $43 \pm 1.3$  years. All patients received therapy in accordance with the approved clinical protocol «Acute

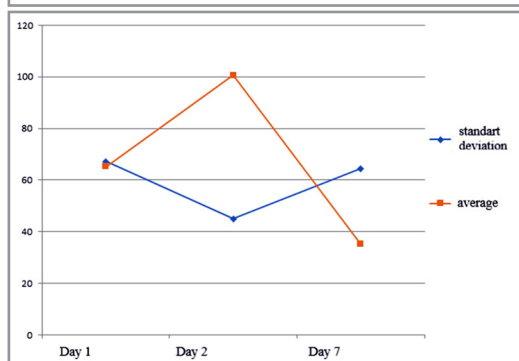
**Figure 2.**  
Distribution of patients  
by gender



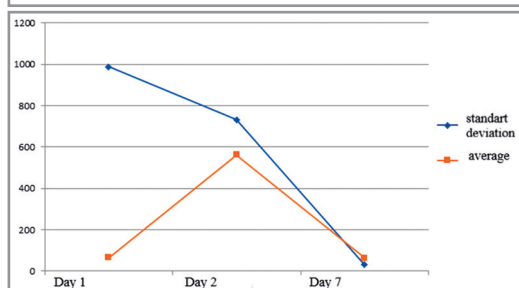
**Figure 3.**  
Types of Surgical  
treatment



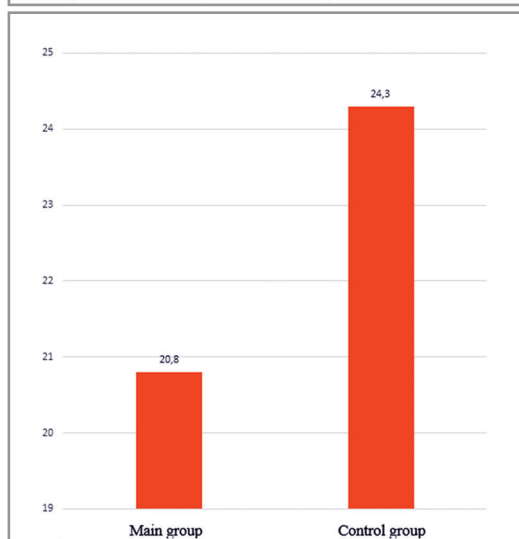
**Figure 4.**  
The level of total bilirubin in  
dynamics



**Figure 5.**  
Amylase level in dynamics



**Figure 6.**  
Average duration of  
hospitalization of the main and  
control groups



pancreatitis» (dated March 29, 2019, Protocol №. 60, Ministry of Health of the Republic of Kazakhstan), clinical protocol «Chronic pancreatitis» (dated December 14, 2017 Protocol №. 35 of the Ministry of Health of the Republic of Kazakhstan).

### Surgical operations and manipulations

10 patients were treated conservatively. 54 people have – surgical treatment combined with the appointment of ulinostatin according to the developed scheme.

Of the 54 patients, endoscopic surgery was performed in 51 patients. Only 3 patients were operated on in an open manner using laparotomy (Fig. 3).

Patients underwent a biochemical blood test at least three times: on admission, 1 day after the start of treatment, control tests at discharge. As a result: the average value of the level of total bilirubin after treatment decreased from 65 µmol/l at admission to 35 µmol/l with an equal statistical deviation (Fig. 4). The mean post-treatment amylase level decreased from 65 U/L on admission to 63 U/L (Fig.5). The drug has proven itself on the good side, it showed the highest efficiency after ERCP and EPST were performed in patients.

The average length of stay in the hospital in the main group was 3.5±0.34 days less, which also correlates with the dynamics of biochemical blood tests.

### Algorithm for the use of ulinostatin depending on the severity of the course of destructive pancreatitis

The drug has established itself as an active inhibitor of pancreatic proteases; showed the highest efficiency after ERCP and EPST were performed in patients.

Our clinical studies have revealed: in moderate pancreatitis, it is effective and safe to administer Ulinastatin 100,000 units 2 times intravenously dissolved in saline or 5% glucose solution 100.0 ml for 1-3 days. In severe pancreatitis - 100,000 units x 2 times per 100.0 ml of saline solution or 5% glucose solution intra-arterially selectively for 5-7 days in combination with endovideosurgical interventions in the hepatopancreatoduodenal zone.

**Conclusions:** The results of our studies showed the high efficiency of the developed algorithm for the endovideosurgical method for the treatment of acute pancreatitis in combination with the use of the protease inhibitor ulinostatin.

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