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Abstract

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THE FIRST EXPERIENCE OF LYMPHOTROPIC ANTIBACTERIAL THERAPY FOR ACUTE PANCREATITIS

Introduction. Acute pancreatitis remains one of the most common surgical diseases of the abdominal cavity. Its incidence has been constantly increasing in recent years. Mortality remains high with pancreatitis: 15–45%.

Objective. To study capacity for increasing the effectiveness of treatment of acute pancreatitis by lymphotropic administration of antibacterial and anti-inflammatory drugs.

Materials and methods. We observed 17 patients with acute pancreatitis, with the average age of 47.7 years; all patients were hospitalized within the first two days of the disease. The treatment was performed in addition to the infusion therapy in accordance with the order of the Ministry of Health of Ukraine No. 297 dated April 2, 2010, using lymphotropic administration of antibacterial therapy, which was tested at the Department of Surgery of SSU and differed in that antibacterial and anti-inflammatory drugs were injected regionally into the pancreas.

Results. In the first 4 days, according to the ultrasound findings, the size of the inflamed pancreas decreased from 31.25, 18.5, and 27.25 cm to 25.25, 15.75, and 18 cm, and the size of the spleen decreased from 262.64 cm^3 to 160.99 cm^3, which is the evidence of drug targeted effect on the pancreas and spleen.

Conclusions. Lymphotropic antibacterial and anti-inflammatory therapy used for 4 days reduced the size of the head, body and tail of the gland by 6.4, 3.9, and 7.0 cm. The reduction in the size of the gland contributed to the elimination of clinical signs of inflammation, especially pain, and leukocytes number decrease, which indicates the "targeted" effect of the drugs. The reduction in the size of the spleen from 308.9 cm^3 to 227.1 cm^3 proves the effect produced by lymphotropic use of drugs on the immune system. This is also supported by corrected immunoglobulin levels.

Keywords: acute pancreatitis, lymphotropic antibacterial and anti-inflammatory therapy.

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ПЕРШИЙ ДОСВІД ЛІМФОТРОПНОЇ АНТИБАКТЕРІАЛЬНОЇ ТЕРАПІЇ ГОСТРОГО ПАНКРЕАТИТУ

Актуальність. Гострий панкреатит залишається одним із найбільш поширених хірургічних захворювань органів черевної порожнини. Його частота в останні роки постійно збільшується. Смертність при панкреатиті залишається високою: 15–45 %. При інфікуванні залози, що звичайно відбувається на 1-му–3-му тижнях лікування сягає 70–80 %, що і визначає актуальність проблеми.

Мета. Вивчити можливості підвищення ефективності лікування гострого панкреатиту шляхом лімфотропного введення антибактеріальних і протизапальних препаратів.

Матеріали і методи. Під нашим спостереженням було 17 хворих на гострий панкреатит, середній вік обстежених 47,7 років, усі хворі були госпіталізовані у перші дві доби захворювання. Лікування проводили на тлі інфузійної терапії відповідно до наказу МОЗ України № 297 від 02 квітня 2010 р. за лімфотропною методикою антибактеріальної терапії, яка пройшла експериментальне випробування на кафедрі хірургії СумДУ і відрізняється тим, що антибактеріальні та протизапальні препарати вводили регіонально до підшлункової залози.

Результати. У перші 4 доби за даними УЗД розміри запаленої підшлункової залози зменшилися від 31,25–18,5–27,25 см до 25,25–15,75–18 см, а розміри селезінки – з 262,64 $см^3$ до 160,99 $см^3$, що є свідченням адресного впливу препаратів на підшлункову залозу і селезінку.

Висновки. Застосування лімфотропної антибактеріальної та протизапальної терапії протягом 4 діб вело до зменшення розмірів головки, тіла і хвоста залози на 6,4–3,9–7,0 см. Зменшення розмірів залози сприяло ліквідації клінічних ознак запалення, особливо болю і зменшення кількості лейкоцитів, що свідчить за «адресний» вплив введених препаратів. Зменшення розмірів селезінки від 308,9 $см^3$ до 227,1 $см^3$ підтверджує вплив лімфотропного застосування препаратів на імунну систему. Це саме підтверджує і корекція рівня імуноглобулінів.

Ключові слова: гострий панкреатит, лімфотропна антибактеріальна і протизапальна терапія.

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Introduction/Вступ

Acute inflammation of the pancreas, acute pancreatitis, belongs to polyetiological diseases of destructive-inflammatory nature based on autoenzymatic necrobiosis secondary to endogenous infection. The microflora that accompanies inflammation, in most cases has a combined nature, which limits the use of antibacterial drugs [1, 2]. Swelling of the gland accompanied by pancreatic necrosis, which in most

cases is due to the proteolytic enzymes removal from the vascular bed, spreads to the surrounding tissues of the abdominal cavity and retroperitoneal space [3]. In recent years, there has been a steady trend towards an increase in the incidence of this condition, in particular, its severe destructive forms [4]. Despite the achievements of pharmacotherapy, the relevant mortality remains at 15–42% [5]. Contamination of necrobiotic areas under certain conditions usually occurs within 1 to 3 weeks [3, 5]. When the pancreatic necrosis zone is infected, the mortality amounts to 70–80% [3, 6].

Rationale. As the area of pancreatic necrosis expands, the likelihood of infection also increases. The adverse outcomes were reported to occur at an earlier stages of infection [7], with infectious complications being the most common cause of death (the proportion of them reaches 20–85.7%). However, there is no common view as for the advisability and effectiveness of antibiotic use in patients with acute pancreatitis. Apart from that, antibiotic therapy for this disease is not considered mandatory according to the Order of the Ministry of Health of Ukraine No. 297 dated April 2, 2010. The above-listed factors accompanied by the high mortality rates and ever-increasing pathogen resistance to antibacterial drugs substantiates the rationale.

Study Objectives. To share the first experience of acute pancreatitis treatment using lymphotropic method of antibacterial and anti-inflammatory drugs administration [8, 9].

Materials and methods. We studied the results of treatment of patients with acute pancreatitis using infusion therapy as the basic method of treatment according to the Protocol of the Ministry of Health of Ukraine. The therapy approach involved antibiotics (ceftriaxone) and anti-inflammatory drugs administered in early hospitalization by means of lymphotropic methods.

We observed 17 patients aged 22 to 70 years, with the average of 44.9 ± 13.2 years. Among them there were 5 (29.4%) females and 12 (70.6%) males. Most patients (15 - 88.24%) were admitted on the first day of the disease, and 2 (11.74%) patients – on the second day. In all these patients, gross nutritional disorders were the trigger of inflammation.

To compare the effectiveness of treatment of patients in the main group, we used data of the appropriate number of patients (17) who had received treatment in the previous year (in the end of 2020) according to the protocol of the Ministry of Health of Ukraine.

The patients were examined according to generally accepted methods. During history taking, special attention was paid to the nature and localization of pain. It turned out that girdle pain occurred with an enlargement of any part of the gland. Apart from the gland size, the size of the spleen was also examined.

Full blood counts were performed according to the standard method. Particular attention was paid to the indicators of inflammatory response, with the leukocyte index of intoxication (LII) being the key one. Blood glucose and amylase levels were measured. When needed, the standard chest x-ray examination was performed, for which suspected pleural effusion was the main indication.

Results and discussion. The frequency and nature of complaints was as follows: 100% of patients presented with girdle pain; girdle pain with predominantly left-sided localization was observed in 83.3%; weakness was reported in 94% of patients, dry mouth – in 17.7%, bloating – in 16.7%, nausea – in 76.5%, and vomiting – in 35.3% of patients. Ultrasonoscopy at admission demonstrated that individual parts of the pancreas were increased up to the following dimensions: the head – 31.2 ± 5.35 mm, the body – 20.2 ± 4.9 mm, the tail – 24.2 ± 4.4 mm. After the second session of lymphotropic therapy (Day 2) the patients felt much better; girdle pain concentrated in the epigastria region within the first two days and became of a dull or aching nature. On day 4, pain remained in the epigastrium in 7 (41.2%) subjects, mainly on palpation. During this period, the size of the head, body and tail decreased to 23.8 ± 4.4, 16.3 ± 3.9, and 17.2 ± 2.3 mm, respectively. Thus, in fact, the size decreased by 6.4, 3.9, and 7.0, respectively, while in the comparison group, the size of the head of the gland decreased only in 2 people: by 2 and 3 mm, respectively, which can be regarded as a technical error. The reduction of the gland, in our opinion, led to the reduction of pain. The number of leukocytes by this time (Day 4) decreased from 10.5 ± $3.8x10^9$/L to 6.6 ± $2.4x10^9$/L, i.e. by 3.9 ± $1.9x10^9$/L, while in the comparison group this value decreased from 9.7 ± $3.4x10^9$/L to 8.8 ± $2.9x10^9$/L. ESR decreased from 17 ± 7.1 mm to 8.4 ± 3.1 mm, while in the comparison group the value decreased from 22 ± 3.1 mm/h to 18 ± 5.2 mm/h. The leukocyte index of intoxication (LII) in patients of the study group decreased from 4.73 ± 1.42 units to 1.23 ± 0.9 units,

while in the comparison group LII decreased from 4.58 ± 1.4 units to 3.9 ± 0.68 units. The LII difference between the groups equaled 2.85 ± 0.4 units in favor of the study group, which was a significant manifestation of reduced intoxication after lymphotropic administration of antibiotics and anti-inflammatory drugs.

The level of immunoglobulins (A and M) decreased from 2.4 ± 0.8 mg/ml to 1.2 ± 0.2 mg/ml and from 1.7 ± 0.5 mg/ml to 1.3 ± 0.2 mg/ml, respectively. The level of immunoglobulins G increased from 6.7 ± 1.2 mg/ml to 8.2 ± 2.33 mg/ml, and the part of large granular lymphocytes (LGL) increased from 2.0 ± 0.69% to 4.3 ± 0.41%, i.e. by 2.2 times ($p < 0.05$). In the comparison group, the change in immunoglobulins was as follows: from 2.2 ± 0.6 mg/ml to 2.15 ± 0.5 mg/ml and from 1.6 ± 0.75 mg/ml to 1.5 ± 2 mg/ml, respectively, while immunoglobulin G level increased from 6.6 to 1.2 mg/ml to 6.8 ± 1.1 mg/ml. Thus, the improvement of laboratory signs of the general inflammatory process (i. e. decreased level of leukocytes and reduced ESR, decreased level of immunoglobulins A and M secondary to the increase in immunoglobulins G and LGL) in patients of the main group demonstrated the benefits of antibacterial and anti-inflammatory drugs administered using targeted lymphotropic technique, which prevents bacterial contamination of the gland in the early period. According to most authors, bacterial contamination is prognostically unfavorable and in a significant percentage of cases (up to 80%) ends in death [3, 6].

The level of amylase as compared to the level at admission (500 ± 15 units/L) decreased to 50 ± 5 units/L. Such progression with regard to the amylase level (10-fold, $p < 0.05$) indicated amelioration of inflammation and, accordingly, reduced edema and necrobiotic manifestations. In the comparison group, this enzyme decreased slightly: by 80 units/L. Clinical manifestations in this group regressed, but not significantly. The level of blood glucose changed slightly: 6.7 mmol/L at hospitalization, 6.5 mmol/L on the 4th day. In the comparison group, there was no difference in this parameter.

The reaction of the spleen as the basic immunocompetent organ to lymphotropic antibacterial and anti-inflammatory therapy manifested through a significant reduction in its size is the evidence of the significant impact of this technique on the course of acute pancreatitis. The size of the spleen decreased from 308.91 ± 21.5 cm^3 (baseline value at hospitalization) to 227.15 ± 10.1 cm^3 (on the 4th day of the therapy). Therefore, an absolute reduction amounted 81.76 ± 12.2 cm^3, i.e. 1.4-fold ($p < 0.05$). Such reaction of the spleen being the organ responsible for the course of the inflammatory process clearly indicates regression of pancreas inflammation and, thus, the effectiveness of lymphotropic antibacterial and anti-inflammatory therapy, which substantiates making it a targeted treatment [9].

Conclusions/Висновки

1. Lymphotropic method of administration of antibiotics and anti-inflammatory drugs is targeted, which is confirmed by a decrease in the size of the head, body and tail of the pancreas by 6.4, 3.9, and 7.0 cm, respectively.

2. The anti-inflammatory effect of lymphotropic antibacterial therapy is confirmed by a decrease in the number of leukocytes by 3.9 ± 1.9 × 10^9/L and a decrease in the leukocyte index of intoxication from 4.73 ± 1.42 units up to 1.23 ± 0.9 units.

3. The immunocorrection effect of antibacterial therapy is confirmed by a decrease in the size of the spleen from 308.9 cm^3 to 227.1 cm^3 and improvement of immunoglobulin levels.

Prospects for future research/Перспективи подальших досліджень

Collection of data to be continued with subsequent comparison of the effectiveness of lymphotropic drug administration in acute pancreatitis with standard protocol techniques.

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Conflict of interest/Конфлікт інтересів

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