MINISTRY OF EDUCATION AND SCIENCE OF UKRAINE
SUMY STATE UNIVERSITY
MEDICAL INSTITUTE

Eastern Ukrainian Medical Journal

2, Rymskogo-Korsakova st., Sumy 40007, Ukraine
e-mail: EUMJ@med.sumdu.edu.ua
eumj.med.sumdu.edu.ua
ISSN: 2663-5909 (print)

ABSTRACT

DOI: https://doi.org/10.21272/eumj.2023;11(1):14-20

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JUSTIFICATION OF LYMPHOTROPIC ANTIBACTERIAL THERAPY BENEFITS BASED ON THE CHANGES IN SPECIFIC IMMUNITY PARAMETERS IN ACUTE PANCREATITIS

Introduction. The incidence and features of acute pancreatitis stimulate the scientific community and clinicians to look for new antibiotics and new algorithms for their use in treating this disease, which is the world's third most frequent acute surgical disease.

Despite this, acute pancreatitis mortality indicates the need for better approaches, especially in conditions of microbial resistance to antibiotics, which determines the urgency of the problem.

The **objective** of the paper was to justify lymphotropic antibacterial therapy as an alternative method of treatment of acute pancreatitis based on the changes in specific immunity parameters, which will make it possible to increase the effectiveness of treatment of the disease and potential complications.

Materials and methods were based on the study of the leukocyte index of intoxication, the hematological index of intoxication, and some other parameters of immunity on lymphotropic and standard antibacterial therapy. With this in mind, patients were divided into two groups.

Results. It was established that under the influence of lymphotropic antibacterial therapy, the leukocyte index of intoxication decreased by 0.3392 units on early admission and by 0.4128 units on late admission compared to standard antibacterial therapy. LAT appeared to be more effective in terms of the effect on HII – by 1.1214 units on early admission and by 1.0537 units on late admission. The effect on cellular immunity with LAT was more pronounced than that with standard antibacterial therapy.

Discussion. Purulent-infectious foci in acute pancreatitis lead to profound disturbances in the immune system as they develop intensively and quickly, and already after 24 hours of manifestation, they significantly exceed those that develop within 24 hours. Lymphotropic antibacterial therapy adjusts these changes bringing them closer to the control ones, while standard antibacterial therapy fails to do so.

Conclusions. Changes in the immune system parameters, which tend towards the control ones, suggest that lymphotropic antibacterial therapy is an alternative to standard therapy.

Keywords: acute pancreatitis, parameters of the immune system, alternative method of treatment.

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ОБҐРУНТУВАННЯ ПЕРЕВАГ ЛІМФОТРОПНОЇ АНТИБАКТЕРІАЛЬНОЇ ТЕРАПІЇ ЗА ДИНАМІКОЮ ДЕЯКИХ ПОКАЗНИКІВ ІМУНІТЕТУ ПРИ ГОСТРОМУ ПАНКРЕАТИТІ

Вступ. Частота і особливості гострого панкреатиту змушують наукову спільноту та лікарів-практиків шукати нові антибіотики та відшукувати нові алгоритми їх застосування при лікуванні третього за частотою гострого хірургічного захворювання, яким є гострий панкреатит.

Незважаючи на це летальність при гострому панкреатиті змушує чекати кращого, особливо в умовах мікробної резистенції до антибіотиків, що визначає актуальність проблеми.

Мета роботи обґрунтувати доцільність лімфотропної антибактеріальної терапії як альтернативної методики лікування гострого панкреатиту на підставі динаміки деяких показників імунітету, що дасть змогу підвищити ефективність лікування гострого панкреатиту і його ускладнень.

Матеріали і методи базувались на вивченні лейкоцитарного індексу інтоксикації та гематологічного індексу інтоксикації і деяких інших показників імунітету на тлі лімфотропної і стандартної антибактеріальної терапії. З огляду на це хворі розділені на дві групи.

Результати. Встановлено, що під впливом лімфотропної антибактеріальної терапії лейкоцитарний індекс інтоксикації при ранній госпіталізації зменшувався порівняно зі стандартною антибактеріальною терапією на 0,3392 ум.од., а порівняно з пізньою – на 0,4128 ум.од. Різниця по впливу на ГІІ була на користь ЛТТ у 1,1214 ум.од. при ранній госпіталізації і на 1,0537 ум.од. при пізній госпіталізації Вплив на клітинний імунітет при ЛТТ перевершував такий при стандартній антибактеріальній терапії на свою користь.

Обговорення. Гнійно-інфекційні подразнення при гострому панкреатиті ведуть до глибоких порушень в імунній системі, як розвиваються інтенсивно і швидко і вже після 24 год маніфестації процесу значно перевершують такі, що розвиваються до 24 год. Лімфотропна антибактеріальна терапія корелює ці зміни наближаючи до контрольних, а при стандартній антибактеріальній терапії це не вдається.

Висновки Зміни показників імунної системи в процесі антибактеріальної терапії, які наближаються до контрольних є підставою вважати лімфотропну антибактеріальну терапію альтернативною до стандартної.

Ключові слова: гострий панкреатит, показники імунної системи, альтернативна методика лікування.

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How to cite / Як цитувати статтю: Duzhyi I, Kononenko M, Shymko V, Sytnik O, Kravets O**.** Justification of lymphotropic antibacterial therapy benefits based on the changes in specific immunity parameters in acute pancreatitis. *EUMJ*. 2023;11(1):14-20
DOI: https://doi.org/10.21272/eumj. 2023;11(1):14-20

INTRODUCTION / ВСТУП

Human interaction with the microworld has various components and, accordingly, various consequences. A person carries many microorganisms in and on his body, but in most cases, they do not cause pathological processes. However, some of the human diseases which were sporadic some 30–40 years ago are more widespread in today's conditions, even though the social conditions and quality of life in the predominant number of countries, especially in Europe, Asia, and North America, have significantly improved. However, in recent decades, acute pancreatitis has ranked third among other urgent surgical diseases in terms of its incidence, course, and complications [1]. It is known that the disease in the first stages of its course and after the manifestation remains aseptic, and as the enzymatic invasion and pancreatic necrosis areas appear, which can occur already in the first hours of the disease, the infection of the gland increases hourly: from 46.0% on Day 1 to 100% on Day 4–5 [2]. The keywords here are "in a larger number of patients" and "often." The frequency of these complications is 40–60%, while preoperative and postoperative mortality reaches 70% and even 85% [3, 4]. Consequently, in some patients with this disease, the inflammatory process resolves favorably despite the "relatively standard" treatment [5]. How does this happen? It is clear that the body managed to “pull itself together" and ensure the appropriate level of immune response to bacterial aggression and defeat it. This is what we will try to prove in this study.

It is known that the resultant of the relationship between a microorganism and a macroorganism involves the factors of the external and internal environment of the organism. The influence of external factors on the risk of disease development in all patients is relatively equal and we cannot change them, but they affect the macroorganism in different ways through changing or not changing various components of the immune system, which according to our hypothesis can prevent the development of purulent-inflammatory diseases or change their course and affect possible complications. This determines the relevance of the problem in acute pancreatitis.

Study Objective. The objective was to compare the changes in specific immunity parameters in acute pancreatitis and justify the benefits of lymphotropic antibacterial therapy as an alternative method for acute pancreatitis treatment.

Materials and Methods. Considering the inadequacy of standard antibacterial therapy in the treatment of acute pancreatitis despite the use of newer strong antibiotics, we studied and compared the effect of standard antibacterial therapy and an alternative method of lymphotropic antibacterial therapy (LAT) on some parameters of immunity [6, 7]. The study included 165 patients who were undergoing inpatient treatment for acute pancreatitis. The method of randomization was used. 82 patients (comparison group) received an antibiotic (ceftriaxone) according to the standard method along with the pathogenetic therapy. The experimental group (83 subjects) was treated with antibiotics using the proprietary developed method. Using the ultrasound examination, the patients' spleen volume was measured. We calculated the leukocyte index of intoxication (LII), hematological index of intoxication (HII), the number of CD-3, CD-4, CD-8 lymphocytes, and LGLs. The study was conducted in the clinical and diagnostic laboratory of the Sumy Regional Clinical Hospital of Sumy Regional Council. The indicated parameters of immunity were evaluated in both groups on the first day at admission and on the 5th day of treatment. Also, 30 apparently healthy individuals were examined to obtain control values. The two-sided Fisher's exact test was used to determine the significant difference between the groups.

Results. The first reaction of the immune system to any stimulus, including infectious agents, is the leukocyte system reaction, which is comprehensive

and determines not only the leukocyte index of intoxication of the body (LII), but also the features of the immune response to the stimulus activity.

In the first subgroup (the patients hospitalized and examined within 24 hours after the manifestation of acute pancreatitis) of the experimental group, LII was 0.8226 ± 0.1341 units on admission (Day 1), and after 5 days of lymphotropic antibacterial therapy, it decreased almost to the level of apparently healthy subjects (0.4884 ± 0.1268 units). In the first subgroup of the comparison group (the patients hospitalized within 24 hours after the manifestation of acute pancreatitis), LII was 0.9873 ± 0.0207 units on admission (Day 1), and after 5 days of standard antibacterial therapy, it decreased to 0.8276 ± 0.0416 units. Thus, after 5 days of antibacterial therapy, the LII value decreased in the first subgroup of the experimental group by 0.375 units, while in the first subgroup of the comparison group, the value decreased only by 0.160 units, which was 2.1 times less ($p < 0.001$).

In the second subgroup of the experimental group (the patients hospitalized after 24 hours of acute pancreatitis manifestation), LII was 0.8462 ± 0.1441 units on admission (Day 1), and after 5 days of antibacterial therapy, it decreased to 0.7298 ± 0.0760 units, that is by 0.117 units. In parallel with this, in the second subgroup of the comparison group, LII was equal to 1.2662 ± 0.1218 units on admission (Day 1), and after 5 days of antibacterial therapy, this value decreased to 1.1426 ± 0.0416 units, that is by 0.124 units (Table 1).

Table 1 – The correlation between antibacterial therapy and indicators of intoxication (progression of intoxication syndrome under the influence of antibacterial therapy)

Indicators of intoxication	**Apparently healthy subjects**	**Experimental group (lymphotropic antibacterial therapy)**				**Comparison group (standard antibacterial therapy)**			
		At admission		After 5 days		At admission		After 5 days	
		Subgroup I	Subgroup II	Subgroup I	Subgroup II	Subgroup I	Subgroup II	Subgroup I	Subgroup II
Leukocyte index of intoxication (LII, units)	0.4238 ± 0.0105	0.8226 ± 0.1341	0.8462 ± 0.1441	0.4884 ± 0.1268	0.7298 ± 0.0760	0.9873 ± 0.0207	1.2662 ± 0.1218	0.8276 ± 0.0416	1.1426 ± 0.0416
Hematological index of intoxication (HII, units)	0.8692 ± 0.1112	2.2637 ± 0.2466	2.3667 ± 0.3268	0.9130 ± 0	1.5351 ± 0	2.2644 ± 0.4240	2.6680 ± 0.2880	2.0644 ± 0.5888	2.5888 ± 10

The hematological index of intoxication (HII) among the patients of the first subgroup (hospitalized within 24 hours after the manifestation of acute pancreatitis) in the experimental group was 2.2637 ± 0.2466 units, and after 5 days of LAT decreased to 0.9130 ± 010 units, i.e., by 1.351 units.

In the first subgroup of the comparison group, HII decreased from 2.2644 ± 0.4240 units to 2.0644 ± 0.5888 units, that is by 0.2 units, while among the patients of the second subgroup, HII decreased from 2.6680 ± 0.2880 units to 2.5888 ± 10 units, that is by 0.08 units. It indicates a 2.5 times greater effectiveness of therapy at early hospitalization ($p < 0.05$).

Discussion. LII and HII intoxication indices correlated unambiguously with acute inflammation of the pancreas; namely: the index increased significantly, especially after 24 hours of inflammation development. On the other hand, the regulatory effect of lymphotropic therapy on the immune system was much more effective. The antibacterial therapy provided a significantly greater effect in patients admitted within 24 hours after disease manifestation. Moreover, the impact of lymphotropic antibacterial therapy was more effective compared to the standard one. In terms of LII, the efficacy of lymphotropic antibacterial therapy was 2.1 times higher than that of standard therapy at early hospitalization.

At late hospitalization, the decrease of HII with lymphotropic therapy was more significant than with standard antibacterial therapy by 2.5 times ($p < 0.05$).

When studying cellular immunity in patients with acute pancreatitis, we observed inhibition of CD-3 and CD-4 cell formation, namely: at hospitalization of patients of the experimental group, the level of CD-3 was 53.1 ± 5.3%; after 5 days of lymphotropic antibacterial therapy, the value increased to 69.4 ± 1.8%, i.e. by 16.3 %, while after standard antibacterial therapy, the value increased from 53.02 ± 6.1% to 61.5 ± 1.5%, that is, by 8.48%, which was almost 2 times less than after LAT (Table 2).

Table 2 – Cellular immunity status in patients with acute pancreatitis

Immunity parameter	Groups				
	Apparently healthy subjects	Experimental group		Comparison group	
		preoperative	Day 5	preoperative	Day 5
CD 3 (%)	74.14 ± 5.5	53.1 ± 5.3	69.4 ± 1.8	53.02 ± 6.1	61.5 ± 1.5
CD 4 (%)	48.86 ± 3.95	35.9 ± 1.2	43.7 ± 1.3	36.12 ± 1.5	39.3 ± 1.3
CD 8 (%)	25.79 ± 2.58	43.3 ± 3.9	30.1 ± 3.5	44.1 ± 2.3	38.4 ± 3.3
LGL (%)	5 ± 0.58	2.02 ± 0.7	4.7 ± 0.84	2.1 ± 0.7	3.2 ± 0.9
Spleen volume (cm^3)	244.4 ± 16.2	457.5 ± 273.8	242.7 ± 115	462.2 ± 341	444.1 ± 348

The CD-4 level after five-day LAT increased from 35.9 ± 1.2% to 43.7 ± 1.3%, i.e. by 7.8%, while after standard antibacterial therapy, it increased from 36.12 ± 1.5% to 39.3 ± 1.3%, that is, by 3.2%, which was 1.7 times less than after lymphotropic therapy (4.6%) ($p < 0.05$).

The CD-8 level decreased under the influence of lymphotropic therapy from 43.3 ± 3.9% at admission to 30.1 ± 3.5%, that is, by 13.2%, while after standard antibacterial therapy, the value decreased from 44.1 ± 2.3% to 38.4 ± 3.3%, that is, by 5.7%. Thus, lymphotropic therapy was 2.3 times more effective ($p < 0.05$).

The number of LGLs in patients of the experimental group increased from 2.02 ± 0.7% to 4.7 ± 0.84%, i.e., by 2.68%, while in patients of the comparison group, it increased from 2.1 ± 0.7% to 3.2 ± 0.9%, i.e., by 1.1% or 2.4 times.

The volume of the spleen, the leading immune organ, which was increased to 457.5 ± 273.8 cm^3 due to the infectious process, decreased to 242.7 ± 115 cm^3 after LTT, which almost corresponded to the values in apparently healthy subjects. The volume reduction reached 214.8 cm^3 at most.

In patients of the comparison group (treated with standard antibacterial methods), the volume of the spleen decreased from 462.2 ± 341 cm^3 to 444.1 ± 348 cm^3, i.e., by 18.1 cm^3. Therefore, the indirect effect of LAT on the immune system via the spleen was 11.9 times more effective.

CONCLUSIONS / ВИСНОВКИ

The difference in the effectiveness of LAT and standard antibacterial therapy in terms of reduction of intoxication syndrome (LII) after five days of treatment comprised 0.375 units on early admission and 0.117 units on late admission. In the experimental group, LAT showed a 2.1 times greater effect on the intoxication syndrome vs. standard antibacterial therapy on early admission and after five days of treatment. On late admission, the difference in the effect of antibacterial therapy on intoxication syndrome was not significant between groups.

The effect of lymphotropic antibacterial therapy on the cellular composition of the immune system was mainly represented by an increase in CD-3, CD-4, and LGL levels. Moreover, after LAT, CD-8 level decreased by 13.2%, which is 2.3 times more effective than after standard antibacterial therapy (5.7%).

Purulent-inflammatory complications requiring surgical interventions occurred in 5 (6.0%) patients treated with lymphotropic antibacterial therapy, with no negative consequences. In those receiving standard antibacterial therapy, surgical intervention was performed in 11 (12.9%) subjects, 2 (18.2%) patients died after surgery. Among non-operated patients, 2 (2.4%) subjects on standard antibacterial therapy died, while there were no fatal cases with lymphotropic therapy. Therefore, the obtained data concerning the effect of lymphotropic antibacterial therapy vs. standard (traditional) therapy indicate the superiority of lymphotropic therapy. This substantiates the feasibility of lymphotropic therapy in the treatment of acute pancreatitis, which is very important in wartime conditions.

CONFLICT OF INTEREST / КОНФЛІКТ ІНТЕРЕСІВ

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS / ПОДЯКА

We thank all co-authors and staff who have contributed to the study. Special thanks to senior assistants O. Nemtsova and O. Melnyk.

FUNDING / ДЖЕРЕЛА ФІНАНСУВАННЯ

None.

AUTHOR CONTRIBUTIONS / ВКЛАД АВТОРІВ

All authors substantively contributed to the drafting of the initial and revised versions of this paper. They take full responsibility for the integrity of all aspects of the work.

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Received 24.02.2023
Accepted 14.03.2023

Одержано 24.02.2023
Затверджено до друку 14.03.2023

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