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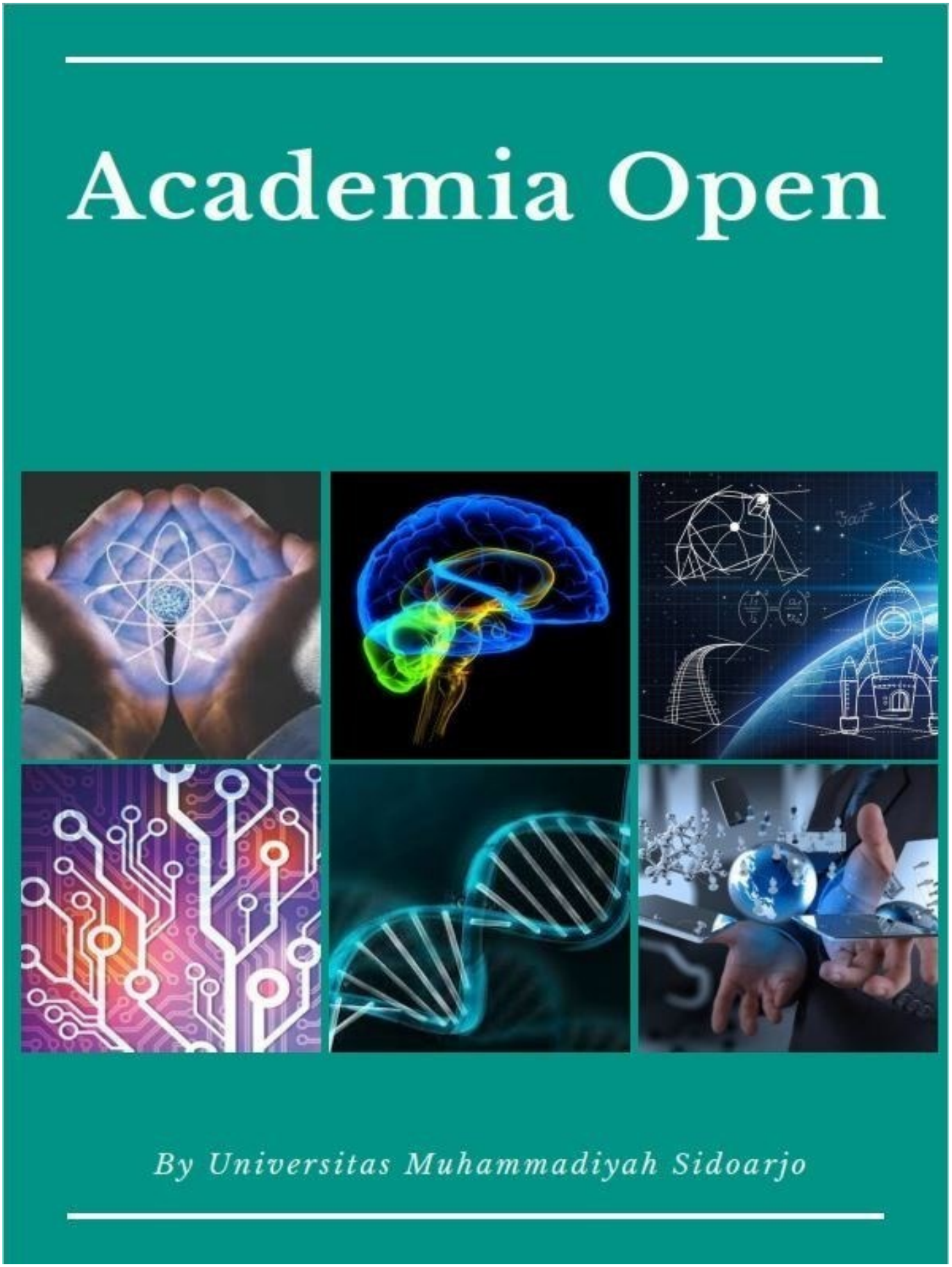

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Table Of Contents

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Endolymphatic Drug Delivery Improves Outcomes in Persistent Postoperative Peritonitis

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Abstract

Postoperative peritonitis remains a critical challenge in contemporary surgery, with persistent complications despite conventional antibiotic therapy leading to increased mortality and prolonged recovery periods. This study investigates the therapeutic efficacy of direct endolymphatic drug therapy (TTBET) in managing persistent postoperative peritonitis following acute appendicitis. The research examined 66 patients with appendicular peritonitis treated in Tashkent surgical clinics, divided into a main group receiving endolymphatic therapy via catheterized peripheral lymphatic vessels (n=36) and a control group receiving conventional treatment (n=30). Immunological parameters including T-lymphocytes, B-lymphocytes, immunoglobulins (IgG, IgA, IgM), and neutrophil phagocytic activity were measured at baseline and day 14 post-treatment using standardized biochemical and immunological assays. Results demonstrated statistically significant improvements in the endolymphatic therapy group, with T-lymphocyte counts increasing 1.41-fold compared to controls (p=0.0022), IgG levels rising 1.7-fold versus 1.49-fold in controls, and neutrophil phagocytic activity improving 1.68-fold versus negligible change in the control group. This study provides novel evidence that endolymphatic administration achieves superior drug concentration at inflammatory sites while simultaneously modulating immune responses through direct lymphatic system engagement. The findings suggest endolymphatic therapy represents a pathogenetically sound approach for managing persistent peritonitis, offering reduced antibiotic doses, enhanced immunological recovery, and improved clinical outcomes, warranting broader clinical implementation in surgical infection management protocols.

Keywords : Endolymphatic Drug Administration, Postoperative Peritonitis Management, Lymphatic System Therapeutics, Immunomodulation Surgical Infections, Regional Antibiotic Delivery, Purulent-Septic Complications

Highlight :

- Endolymphatic therapy significantly increases T-lymphocytes, immunoglobulins IgG/IgM, and neutrophil phagocytic activity
- Main group shows 1.41-fold T-lymphocyte increase versus minimal improvement in control group
- Treatment normalizes microcirculation and reduces postoperative complications in appendicular peritonitis patients.

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Introduction

Over the last several years, the prevention and treatment of not only several acute surgical inflammatory diseases but also a wide range of postoperative complications, such as surgical sepsis and septic shock as a result of various infections, have become a priority issue (Savelyev V.S., 2019, 2020). This has further led to the exploration of good ways of delivering antibacterial and other drugs in different routes.

In the recent past, there has been a decline in the effectiveness of the antibacterial therapy as a result of various factors, some of which are the rapid development of the antibiotic-resisting strains of microbes, the increasing prevalence of the inflammatory diseases of the surgical type, the increased number of surgical operations in patients in critical conditions, the irrational use of the antibiotics, difficulties in the creation of treatment regimens, and the lack of the adequate antibiotic concentrations at the pathologic focus (Loxvitskiy S.V. et al., Seeking rational solutions to the treatment of antibacterial therapy stimulates the creation of pathogenetically based strategies and is particularly relevant in the treatment of purulent-septic complications after the long-term use of antibiotics (Golbraikh V.A., 1998).

Most recently, endolymphatic administration of drugs by passing a catheter through peripheral lymphatic vessels has been formulated and introduced. This direct controlled endolymphatic antibiotic therapy (TTBET) method, in its inclusion into the overall approach to treating acute abdominal organ pathology, proves to be significantly effective in terms of treating the diseases, enables the reduction of cumulative antibiotic doses, purulent-septic complications, and, best of all, results in the rapid recovery of a patient (Yarema I.V. et al., 1993, 2008; Virenkov Yu.E. et al., 1987; Ashurmetov A)

Nevertheless, not all aspects of the treatment of pathological processes directly influenced by lymphatics and the mechanism of the body's response to TTBET are fully studied, which is why there is a need to conduct more in-depth scientific research (V.I. Vtorenko et al., 2008). The literature does not provide clear guidelines and contraindication criteria of TTBET, such as the daily and course dosage of fluids, the onset time, and the number of endolymphatic therapy.

Objective. To design an algorithm for delivering antibiotics and other drugs through lymphatic vessels in patients with peritonitis and to apply it on a large scale.

Tasks:

1. A retrospective study on risk factors that cause purulent complications in peritonitis.

2. Determine clinical, biochemical, and immunological changes of patients with peritonitis, before and after TTBET.

3. Measure the intoxication indices (LII, NDI) in patients with peritonitis.

Materials and Methods. Sixty-six patients who were treated in the surgical units of the Tashkent clinics with appendicular peritonitis were studied in the sample. All the patients were separated into two groups. The initial group (main group) was provided with endolymphatic treatment due to the complexity of the treatment. The second group (control group) was one that was not subjected to lymphogenic interventions. Each patient was examined dynamically on biological fluids (blood, urine, lymph). Biochemical tests were also performed, such as the total protein, sub-fractions of protein, nitrogenous wastes, creatinine, cholesterol, diastase and other values. They included immunological parameters, toxic indicators (LII, NDI), and clinical parameters (SAPS-II, APACHE-II).

Peripheral lymphatic vessels were catheterised in the lower third of the leg or foot in the main group and in the region of the Les Franc joints, the standard procedure applied in our surgical department since 1982.

The separation of the patients into two groups was done depending on the inclusion of the lymphogenic methods in the treatment complex. The key sample comprised 36 patients who were treated to receive endolymphatic therapy as part of the treatment complex. The control group consisted of 30 patients who did not receive lymphogenic interventions. The patients who were chosen to be observed had manifestations of peritonitis, which followed acute appendicitis as a complication.

Dynamic laboratory analysis of the biological fluids (blood, urine, lymph) was performed on all patients. The identification of total protein and protein fractions, urea, creatinine, cholesterol, diastase, and blood glucose was performed artificially by biochemical analysis.

The first group involved the catheterisation of peripheral lymphatic vessels in the lower third of the leg or foot, and the Les-Frank joint area. Five patients who were severely intoxicated underwent thoracic lymphatic duct (TLD) drainage as per the standard procedure utilised in our department since 1989.

According to the clinical and laboratory parameters, antibiotics, proteolytic enzyme inhibitors, heparin and rheological agents were delivered into the catheterised peripheral lymphatic vessels. The doses and the volumes of the drugs were based on the severity and aetiology of peritonitis and the state of the patient.

The main immunological parameters were examined before treatment and on day 14 after treatment and included the relative and absolute numbers of total T-lymphocytes (E-ROK) and the T and B-cell-mediated immunity in rosette reactions, the major subpopulation of which was identified. The A.M. Zemskov method was used to measure phagocytic activity. The essential biochemical indicators were studied as per V.S. Kamyshnikov.

The statistical processing was carried out with the help of the STATISTICA software package (Windows, version 11). All the numerical data were statistically computed to determine reliability. The standard error (m) and mean (M) of all the populations were determined. The non-parametric tests were used to determine important differences, and the following were the criteria: the dynamics of indicators in the study and control groups, paired comparisons, the Wilcoxon signed-rank test, and the Mann-Whitney U-test between one indicator in the study and control groups. All tests of statistics were done at two-tailed significance. The statistically significant difference was taken to be below p=0.05..

Results and Discussions

The lymphatic system is essential in the pathogenesis of the destructive processes at the inflamed site. The pathway of processes that results in the oedema of the inflammatory focus is linked to the augmented blood vessel exudation and lapsed reabsorption of fluid and colloidal substances via

the interstitial spaces of the lymphatic system. In such a case, the progressive oedema contributes greatly to the impairment of the tissue trophism of the inflammatory focus to produce poorly oxidised metabolic products and cell necrosis, which in turn leads to the increase of the systemic toxin load.

Those conditions were the foundation of the choice of endolymphatic drugs applied in our research. Indicatively, in the case of administration of antibiotics alone without the presence of complementary agents, it is not always possible to guarantee penetration of the antibiotics into the inflammatory focus and lymph nodes of the region. Nonetheless, when the identical antibiotics are given following lymphatic heparinization, the chances of traversing the biological fluids through the lymphatic routes are high. As did we (and many other authors) observe, endolymphatic infusions hasten the movement of lymph along the great lymphatic vessels. This effect was confirmed in clinical practise of endotoxicosis: several hours after endolymphatic infusion of antibiotics, the increase in body temperature and even the worsening of a state of intoxication are often observed because of the dumping of toxic lymph into the blood.

Lymph nodes play an active role in immunological defence in addition to their barrier and detoxification functions. Every subpopulation of lymphocytes is maintained and multiplied. This aids the destruction of microorganisms and their toxins, and degenerative changes of lymph nodes, acts as an etiological factor, and indirectly leads to the restoration of immunological reactivity of the body. But, in other instances, especially in extreme lymphopenia, immunogenesis has to be activated. Thus, when the lymphocyte numbers are low and decreased in relation to the T-lymphocyte subpopulation, the T-activin was given endolymphatically, having previously suppressed the acute inflammation at the site of the lesion.

The endolymphatic therapy was performed on the basis of the traditional treatment performed to correct the metabolism of water-electrolytes, proteins, and vitamins, stabilise acid-base equilibrium, and avoid the complications of vital organs and body systems. The indications were to administer antibiotics, heparin, antienzymatic agents, and T-activin through the endolymphatic route only. There were differences in the amount of the drugs quantitatively constituting the drugs, the amount of the injected solutions, the order of the infusions of the endolymphatic circulation and the time when the therapy should start in each patient, which depended on the severity and stage of illness. Overall, the primary group of patients was categorised into two subgroups: 1) localised peritonitis, and 2) diffuse peritonitis. The second subgroup of patients normally got admitted after being discharged with postoperative period complications despite multiple courses of antibiotic treatment and minimal intervention.

The endolymphatic therapy was initiated in the early postoperative period, and sometimes even before the surgical treatment in the first subgroup of patients, and 4-6 days or even later after the manifestation of disease in the second subgroup. The TTBET plan of these subgroups encompassed the antibiotic treatment, the use of proteolytic enzyme inhibitors, the correction of the microcirculatory disorders, and the detoxification therapy when needed. In the case of generalised peritonitis, the variation in the approach was that endolymphatic antibiotic treatment was associated with the conventional antibiotics with dissimilar mechanisms of action. In case there was no positive outcome even after 3-4 days (e.g. restoration of normal temperatures, decreasing leukocytosis, and intestinal peristalsis is restored), the medication was rotated. Following catheterisation of the peripheral lymphatic vessels, 2.0 ml of 2,500 IU of heparin saline solution was administered first, followed by 0.5-0.6 ml per minute (0.5-0.6 ml initially). We used the broad-spectrum cephalosporins and aminoglycosides in our choice of antibiotics. Namely, on the III-IV days, cephalosporins were used, 1.0g per day, and gentamicin 80mg/day in a 2ml solution, which is three times less in comparison to intramuscular administration with metrogyl (50mg/day).

This regimen was added with 1520 ml of reosorbilact endolymphatic infusion in patients with severe intoxication syndrome 6-8 hours after antibiotics or protease inhibitors to avoid drug interactions. Reosorbilact was administered in a slow bolus (2530 minutes). The number of infusions was 3–4 per course of the treatment.

In case of lymphopenia less than 17, T-activin was given endolymphatically within 1-1.5 hours of antibiotics at a dosage of 100 mg, thrice or four times a day, 1-2-5 days as an emergency.

Analysis of Immunological Parameters in Patients with Appendicular Peritonitis Using the TTBET Method in Comparative Groups

Table 1. Main Immunological Parameters in Comparative Groups on the 14th Day of Treatment in Patients with Peritonitis (M ± m)

Parameter, Measurement Unit	Normal values (n = 66)	Comparison groups	
		Main group	14th day of treatment
T-lymphocytes, total (E-ROK), abs. ×10⁹/L	1,15±0,2	(I) 0,63±0,1	0,89±0,09
		(II) 0,64±0,08	0,67±0,1
		z=0,39; p=0,69	z=3,06; p=0,0022
T-helper cells, abs. ×10⁹/L	0,72±0,04	(I) 0,42±0,07	0,63±0,06
		(II) 0,41±0,06	0,47±0,06
		z=0,2; p=0,85	z=2,96; p=0,003
T-suppressor cells, abs. ×10⁹/L	0,52±0,03	(I) 0,36±0,02	0,41±0,09
		(II) 0,37±0,08	0,49±0,05
		z=0,14; p=0,89	z=0,74; p=0,46
B-lymphocytes (M-RC), abs. ×10⁹/L	0,15±0,03	(I) 0,11±0,02	0,18±0,03
		(II) 0,11±0,05	0,12±0,02
		z=0,07^=0,93	z=2,42;
			p=0,016

IgG, g/L	11,3±0,6	(I) 12,4±0,3 (II) 12,5±0,8	21,6±1,1 8,4±0,2
		z=1,21; p=0,23	z=2,35; p=0,018
IgA, g/L	1,9±0,07	(I) 2,3±0,04 ...	2,1±0,04
		z=0,13; p=0,896	z=2,5; p=0,013
IgM, g/L	1,2±0,03	(I) 0,9±0,03 (II) 0,89±0,02	1,1±0,03 0,7±0,02
		z=0,46; p=0,67	z=3,56; p=0,0037
Neutrophil phagocytic activity, %	60,2±2,7	(I) 41,7±2,56 ...	69,9±4,3 ...
		z=0,09^=0,93	z=2,4; p=0,017

Note: (I) - main group (n=36); (II) - comparison group (n=30)

In the assessment of the immunological indicators of patients with peritonitis, the absolute number of total T-lymphocytes (E-RC) in the baseline population (I) and the comparison population (II) was found to be lower than the normal values to the extent of 1.83 and 1.79, and there is no significant difference between the groups (Z = 0.39; p = 0.69) (Table 3). This indicator in group I was more likely to increase by 1.41 times compared to group II patients with peritonitis (z = 3.06; p = 0.0022). The difference in the absolute number of total T- lymphocytes between normal values and by day 14 was reduced by 22.6 and 41.7% in groups I and II, respectively.

The absolute value of T-helper cells in groups I and II were lower than it was in normal conditions, 1.71 and 1.76 times lower, respectively, and the groups did not differ significantly (z = 0.2; p = 0.85). Group I increased 1.5 times by day 14, whereas in group II it was only 12.8%. In comparison with normal values, the reduction in the absolute numbers of T-helper by day 14 was relative = -12.5% in group I and -34.7 in group II.

The baseline absolute number of T-suppressor cells in groups I and II were 1.44 and 1.4 times less than normal, with no marked difference between the groups (z = 0.14; p = 0.89). By day 14, the percentage of T-suppressors increased in group I was not significant, +12.2, and in group II was +24.5, which can be taken to mean the nature of the lesion and the dynamics of the destructive processes in the purulent-septic complications.

Humoral immunity was analysed and demonstrated that in both groups the base absolute number of B-lymphocytes (M-RC) was reduced 1.36 times without significant differences (z = 0.07; p = 0.93). On day 14, the absolute number of B-lymphocytes in group I improved by 30.9% and in group II, it improved by only 8.3%, possibly because of the lack of differentiation, activation of the antigen-presenting cells, and inhibition of the antibody-producing activity of the immune system of patients with peritonitis.

The IgG levels of both groups were slightly above normal by 8.9 and 9.6, with no significant differences (z = 1.21; p = 0.23). On day 14, group I saw 1.7 times in IgG and group II saw 1.49 times in IgG, or 1.35 times compared to normal. The comparison of the levels of IgG in the groups was more than 2.4-fold (z = 2.35; p = 0.0018).

The baseline level of IgA and IgM was not significantly different between the comparison groups (p = 0.896; p = 0.64). IgA levels were increased 1.21- and 1.22-fold above normal and may have been through the expression of antigen-presenting B- lymphocyte regions in the gastrointestinal mucosa. Group IgA levels were almost back to normal by day 14, but they were still 2.1 times lower than normal in group II (z = 2.5; p = 0.013). The levels of IgM baseline were 1.33 and 1.34 times lower than normative in both groups (p = 0.64). On day 14, IgM reliably rose 1.55x in group I, which is just above normal levels, whereas in group II, IgM was still below normal by 41.7 per cent. By day 14, the level of IgM in the groups was two-fold (z = 3.56; p = 0.0037).

In the case of phagocytic immunity, at the baseline of phagocytic activity, neutrophils from both groups exhibited the same status (z = 0.09; p = 0.93), with values of -30.4% of normal. Group 1 day 14 neutrophil phagocytic activity improved 1.68 times in group I and only 9.7 times in group II, which was still below normal levels of -22.9.

Conclusion

TTBET is intended to bring about hypocoagulation repair, antibacterial, detoxifying, and immunostimulatory activity in patients with postoperative persistent peritonitis. Endolymphatic drug therapy does not have any practical contraindications. 2. It augments the total amount of total T-lymphocytes and T-helper cells, augments the rise in IgG and IgM of immunoglobulins and augments phagocytic activity of immunocytes. 3. Endolymphatic injections of solutions stimulate the lymph movement in the lymphatic system and its entry into the blood, which helps in the normalisation of the microcirculatory system..

References

1. A. M. Usarov, “Immunological Foundations of Lymphatic Drug Administration in Appendicular Peritonitis,” Miasto Przyszłości Kielce, vol. 53, no. 4, pp. 795–800, 2024. [Online]. Available: https://miastoprzyszlosci.com.pl/index.php/mp/article/view/4937
2. D. A. Abdurazzakova, A. M. Ashurmetov, and M. N. Agzamova, “Efficiency of Endolymphatic Drug Administration,” Young Scientist, no. 9, pp. 61–62, 2018. [Online]. Available: https://moluch.ru/archive/
3. M. N. Agzamova, D. A. Abdurazzakova, and F. M. Ismailov, “Study of Microbial Flora in Peritonitis,” Young Scientist, no. 1, pp. 33–34, 2018. [Online]. Available: https://moluch.ru/archive/
4. M. N. Agzamova, K. F. Zuparov, and T. Z. Zikrilla, “Oxidative Status During Alloplasty in Patients With Postoperative Ventral Hernia,” Infection, Immunity and Pharmacology, vol. 1, no. 1, pp. 5–9, 1999.
5. M. D. Akhmedov, A. I. Akhmedov, and A. A. Tursumetov, “Cytochrome Oxidase Activity of Liver Parenchyma at Various Periods of Ischemia and Obstructive Jaundice,” European Science, no. 2, vol. 44, pp. 71–75, 2019. [Online]. Available: [https://euro-

science.org](https://euro-science.org)
6. A. M. Ashurmetov, D. A. Abdurazzakova, and S. N. Navruzov, “Lymphoimmunostimulation in Diffuse Purulent Peritonitis,” Young Scientist, no. 7, pp. 103–105, 2018. [Online]. Available: https://moluch.ru/archive/
7. Kh. M. Jafarov, K. M. Zhafarov, and I. S. Melnik, “Method of Treating Purulent-Inflammatory Diseases in Patients With Diabetes Mellitus,” Palliative Medicine and Rehabilitation, no. 2–3, pp. 110–113, 2002.
8. F. M. Ismailov, M. N. Agzamova, and S. R. Mekhmonov, “Causes of Death in Emergency Conditions of the Abdominal Organs,” Young Scientist, no. 8, pp. 44–46, 2018. [Online]. Available: https://moluch.ru/archive/
9. S. N. Navruzov, Sh. R. Mekhmonov, and K. S. Dolimov, “Extended and Combined Surgeries for Large Bowel Obstruction,” Bulletin of the Association of Physicians of Uzbekistan, vol. 3, no. 1, pp. 20–23, 2003.
10. A. Abdumajidov, J. K. Mirzakhidovich, and T. A. Abdumalikovich, “Complex Treatment of Pyo-Inflammatory Diseases in Patients With Diabetes Mellitus,” Central Asian Journal of Pediatrics, vol. 2, no. 3, pp. 57–59, 2019.
11. A. I. Akhmedov, A. A. Tursumetov, and K. M. Zhafarov, “Features of Allohernioplasty for Postoperative Ventral Hernias in the On-Lay Position Under Conditions of Infection,” European Journal of Molecular and Clinical Medicine, vol. 7, no. 3, pp. 3897–3905, 2020. [Online]. Available: https://ejmcm.com
12. V. M. Buyanov, G. V. Rodoman, and L. A. Laberko, “Modern Methods for Assessing Endogenous Intoxication in Diffuse Peritonitis,” in Proceedings of the 1st Moscow International Congress of Surgeons, Moscow, Russia, 1995, pp. 16–17.
13. A. S. Ermolov, E. E. Udovskiy, and A. R. Grigoryan, “Nonspecific Humoral Immunity Status in Endolymphatic Antibiotic Therapy of Surgical Infections,” Khirurgiya, no. 1, pp. 76–79, 1987.
14. V. A. Golbraikh, Endolymphatic Therapy in the Complex Treatment of Patients With Purulent-Inflammatory Diseases of the Abdominal Organs, Ph.D. dissertation abstract, Moscow, Russia: Sechenov First Moscow Medical Institute, 1998.
15. K. M. Zhafarov and I. S. Melnik, “Immediate Results of Surgical Treatment of Patients With Strangulated Ventral Hernia of the Anterior Abdominal Wall,” Asian Pacific Journal of Environment and Cancer, vol. 4, no. S1, pp. 13–14, 2021. doi: 10.31557/apjec.2021.4.S1.13
16. J. K. Mirzakhidovich, T. A. Abdumalikovich, and A. A. Ibrogimovich, “Prevention of Postoperative Wound Complications in Rapped Abdominal Hernia,” Annals of the Romanian Society for Cell Biology, vol. 25, no. 6, pp. 6473–6484, 2021. [Online]. Available: https://annalsofrscb.ro