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ABSTRACT

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EFFECTIVENESS OF LYMPHOTROPIC THERAPY IN THE PATIENTS WITH ACUTE APPENDICITIS AND ITS COMPLICATED FORMS

Introduction. Despite using the latest generations of antibiotics and modern methods of their introduction in the surgical treatment of acute appendicitis, purulent-septic complications keep occurring, accounting for 45% of fatal outcomes in the patients operated on for this disease.

Materials and methods. Patients were divided into two groups. The main group included patients who were administered antibiotics and pathogenetic drugs locally to the ileocecal zone by means of lymphotropic administration. The comparison group included patients who received standard antibiotic therapy.

Results. On the 5th day of the postoperative period, the level of IgA in the main group was 1.16 ± 0.7 mg/ml, and in the comparison group – 1.54 ± 0.8 mg/ml. The level of elastase in the operated patients of the main group decreased to 111.797 ± 21.39 nmol/min × ml, i.e., by 2.4 times ($p < 0.001$), and in patients of the comparison group – to 179.605 ± 26.79 nmol/min × ml, i.e., by 1.5 times ($p < 0.05$). Under the influence of lymphotropic administration of the antibiotic, the volume of the spleen decreased by the 5-th day to 281.22 ± 18.8 cm^3, i.e., 145.44 cm^3, and with standard administration of antibiotics, the spleen decreased within the period to 344.71 ± 21.13 cm^3, i.e., by 79.54 cm^3, which is less by 66 cm^3, or 1.8 times ($p < 0.05$) vs. main group.

Conclusions. The proposed method of antibiotic therapy is a preventive measure against purulent-septic complications, especially in its destructive forms, improves the results of treatment of patients with acute appendicitis, and shortens their term of staying in the hospital, which has a positive impact on financial status.

Keywords: lymphotropic therapy, acute appendicitis, appendicular infiltrate.

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РЕЗЮМЕ

ЕФЕКТИВНІСТЬ ЛІМФОТРОПНОЇ ТЕРАПІЇ В ЛІКУВАННІ ХВОРИХ НА ГОСТРИЙ АПЕНДИЦИТ ТА ЙОГО УСКЛАДНЕНІ ФОРМИ

Вступ. Незважаючи на застосування антибіотиків останніх поколінь і сучасних методик їх введення при оперативному лікуванні гострого апендициту, продовжують траплятися гнійно-септичні ускладнення, які бувають причиною смерті 45 % оперованих у структурі летальності після оперативного втручання з приводу цього захворювання.

Матеріали і методи. Хворі були розподілені на дві групи. До основної групи увійшли хворі, яким введення антибіотиків та патогенетичних препаратів проводилося регіонально до ілеоцекальної зони лімфотропним шляхом. До групи порівняння увійшли хворі, яким проводилася стандартна антибіотикотерапія.

Результати. На 5 добу післяопераційного періоду рівень IgA в основній групі становив 1,16 ± 0,7 мг/мл, а в групі порівняння – 1,54 ± 0,8 мг/мл. Рівень еластази у оперованих основної групи зменшився до 111,797 ± 21,39 нмоль/хв × мл, тобто у 2,4 разу ($p < 0,001$), а у хворих групи порівняння – до 179,605 ± 26,79 нмоль/хв × мл, тобто у 1,5 рази ($p < 0,05$). Під впливом лімфотропного введення антибіотика об'єм селезінки зменшувався на 5 добу до 281,22 ± 18,8 см³, тобто на 145,44 см3, а при стандартному введенні антибіотиків селезінка у досліджений термін зменшилася до 344,71 ± 21,13 см³, тобто на 79,54 см3, що менше, ніж в основній групі на 66 см³, або у 1,8 разу ($p < 0,05$).

Висновки. Запропонована методика антибіотикотерапії є методом профілактики гнійно-септичних ускладнень, особливо при його деструктивних формах, покращує результати лікування хворих на гострий апендицит, скорочує термін перебування їх у стаціонарі, що відбивається позитивним чином на фінансових проблемах.

Ключові слова: лімфотропна терапія, гострий апендицит, апендикулярний інфільтрат.

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INTRODUCTION / ВСТУП

Acute appendicitis is the most common urgent surgical disease with various manifestations and complications [8, 13]. In developed countries, the incidence of acute appendicitis occurs in 5.7–89 patients per 100,000 population, with a peak at the age of 10–30 years [7, 11]. There is evidence that the risk of acute appendicitis is 9% in the United States, 8% in Europe, 2% in Africa [6, 11]. In Ukraine, the incidence rate ranges from 13.8 to 31.1 patients per 10,000 population [9]. Between surgical interventions on the abdominal organs, appendicitis accounts for 20–30% of operations [9]. Postoperative mortality is in the range of 0.1–0.5% [7]. In the presence of

concomitant complications and neglected processes, it increases to 3–5% [4, 7]. Complications of inflammation of the appendix may be in the form of appendicular infiltrate, which occurs in 3.7% [2]; typhoid fever – in 7.01%; local abscesses of the abdominal cavity (intestinal, pelvic, subphrenic, subhepatic) – in 2.1–5.3% [4, 6]; peritonitis in 14.9%, and in destructive forms of appendicitis – in 22–65% [2]. In the postoperative period, purulent-septic complications are registered in 5.5–18.8% of the operated [9, 10, 12], and colonic fistula in – 0.08–6%.

The urgency of the problem. Purulent-septic complications in the structure of mortality after surgery continue to occur in 65.0–77.0% of patients [2]. These complications require the use of modern antibiotics, increasing the daily dose, often requiring repeated changes and a combination of several drugs. Despite this, the number of purulent complications and mortality rates in acute appendicitis remains constant [4]. The modern generation of antibacterial drugs and the ways of their introduction into the body of patients are unable to improve the situation.

The aim of the study: To improve the effectiveness of treatment of patients with acute appendicitis and its complication – appendicular infiltrate.

Materials and Methods. We analyzed the immediate and long-term results of the treatment of patients with acute appendicitis and appendicular infiltrate. The respective groups were divided into two subgroups. The main subgroup included patients who received lymphotropic antibiotic therapy during treatment. The comparison subgroup included patients who received standard antibiotic therapy, according to which antibiotics were administered intramuscularly or intravenously.

In order to prevent purulent complications, patients were offered the method of lymphotropic administration of antibacterial drugs proposed by the department. The method is based on the use of lymphoretic drugs that stimulate lymph formation and lymph outflow with sequential administration of antibiotics [3]. The algorithm of lymphotropic antibacterial therapy was as follows: Lidase (32–64 units) is injected into the right iliac region along the inner edge of the wing of the iliac bone by 1.5–2 cm with an intramuscular needle, after which No-Spa is injected every 5 minutes, heparin (5000 units), lidocaine 0.5–1% – 2 ml, ceftriaxone (1.0). The needle remains in place at all times. In addition, a non-specific anti-inflammatory resorbable drug, Dicloberl, was administered lymphotropically.

The results of treatment were evaluated by the dynamics of the general condition of patients, the temperature response, the reduction of the infiltration and some changes in laboratory parameters (leukocytosis, ESR, nuclear shift index), which we had been studied for 3–5 days, and then we did it according to the indications. In addition, the number of CD3, CD4, CD8 and large granular lymphocytes (LGL) was determined. These indicators were studied when patients were admitted to the clinic and on the 5th day after surgery. Along with this, the volume of the spleen was simultaneously examined using ultrasound of the abdominal cavity.

It is known that in various reactions of inflammation and tissue destruction, the leading place is occupied by proteolysis processes [5]. As one of the main proteolytic enzymes, we studied neutrophil elastase (NE). An increase in the level of this enzyme is known in various inflammatory processes. Given the above, considering the proteolytic system involved in the pathogenesis of inflammatory diseases induced by the microflora, we conducted a systematic study of neutrophilic elastase in the hospitalization of patients and in the dynamics.

Statistical analysis of the results of the study was performed using the software product STATISTICA 6.1 (StatSoftInc., Serial № AGAR909E415822FA). Analysis of the normality of data distribution was performed according to the Shapiro-Wilk test. The results of descriptive statistics in the normal type of distribution of quantitative characteristics are presented as the arithmetic mean (M) and standard error of the arithmetic mean (m). When the distribution of quantitative traits other than normal was determined by the median and interquartile range (Me (25.0%; 75.0%)). The Mann-Whitney (U) test was used to compare two unrelated samples with an abnormal distribution. The reliable level of statistical significance (p) was < 0.05 [1].

Results and Discussion. At the hospitalization in the department of patients with appendicular infiltrate, there were signs of intoxication, which exceeded those in acute appendicitis (general weakness, fatigue, loss of appetite, dry mouth), body temperature ranged from 37.8 to 39.2 °C. In the right iliac region, immobile painful formation 10–12 to 15–18 cm in a longer dimension (ultrasound) was palpated. In the laboratory blood test, there was leukocytosis from 8,5 to 15 x 10^9/L, accelerated ESR in the range of 17–41 mm/h and the increased nuclear shift index (0,6–0,9).

As early as on the 3rd day, in patients with appendicular infiltrate, when using regional lymphotropic antibiotic therapy, it was possible to achieve rapid positive dynamics in relation to the laboratory parameters: leukocytosis decreased to (6.5–10) x 10^9/L, ESR – to 7–20 mm/h, nuclear shift index – to 0.3–0.5.

In patients of the comparison group, who were treated according to the traditional scheme, during the same period (3 days), there was a slight improvement in laboratory parameters, but it was not significant ($p > 0.05$).

An important resorption of appendicular infiltrate in the main group began on Day 2–3, and in patients of the comparison group – on Day 8–9 ($p < 0.05$). The patients of the main group were discharged under the supervision of an outpatient surgeon for 6–7 days, when the infiltrate was practically not palpated, and during ultrasound examination, additional formations in the right iliac region were not detected. Patients of the comparison group were discharged from the department for 12–14 days. Among patients of the main group, 15 (43%) were operated on within 1.5–2 months as planned. Residual phenomena in the form of an adhesive process in the right iliac region were not revealed practically. Postoperative complications from the abdominal cavity and postoperative wound were not observed. The bed-day was 6.8 ± 1.15. Other patients in this group, 20 (57%) did not come to the surgeon's examination on their own, which, in our opinion, indicated their satisfactory condition and the absence of clinical manifestations of the disease. 13 (37%) respondents answered the questionnaire (there were no complaints). In the comparison group, 20 (57%) people underwent planned surgery, which is 1.3 times more than in the main group. The reason for the intervention was an aching periodically spastic pain in the right iliac region. 14 (70%) persons had the residual phenomena in the form of adhesions of various degrees of maturity; infiltration abscess occurred in 7 (20%) operated patients ($p<0.05$). The average bed-day of this group was 14,1.

At the hospitalization of patients with acute appendicitis, the level of ESR was within 7–42 mm/h (average value – 14,47 ± 4,4 mm/h) in patients of the main group (103 persons) and within 7–39 mm/h (average value – 13,89 ± 4,6 mm/h) ($p > 0,05$) in patients of the comparison group (105 individuals). On the third day of the postoperative period in the study of ESR, it was found a decrease in this indicator in the main group from 6 to 27 mm/h (mean value – 11.86 ± 3.6 mm/h). In the comparison group, changes in this period occurred in the range of 7–36 mm/h (mean value – 14.54 ± 4.3 mm/h). On the fifth day of the postoperative period in the main group, the average ESR was recorded at a value of 8.39 ± 2 mm/h, and in the comparison group – at a value of 11.83 ± 4.8 mm/h. Given that ESR reflects the ratio of different protein fractions, where the main role is given to globulins as inflammatory proteins, the above reliably testifies to the positive effect of the lymphotropic use of antibiotics on the general inflammatory reaction in acute forms of appendicitis due to a decrease in the number of inflammatory proteins – globulins.

In patients with acute appendicitis, there was a decrease in the amount of CD3 to 53.22 ± 5.39%, CD4 to 35.89 ± 1.21% and LGL to 2 ± 0.69%, with an increase in the amount of CD8 to 43.36 ± 3.83%. The volume of the spleen, as an immunocompetent organ that responds to any infectious aggression, in the hospitalization of patients with destructive forms of acute appendicitis was increased and amounted to 426.66 ± 47.9 cm³ (with a norm of 244.4±16.2 cm³).

On the 5th day after the operation in the main group, the number of CD3 – lymphocytes increased to 69.4 ± 1.81%, i.e., by 16.18% from baseline, while in the comparison group, this figure increased to 61.47 ± 1.51%, i.e., at 8.05% ($p <0.05$). The level of CD4 in the main group increased to 43.64 ± 1.31%, which is 121.59% of the initial, and in the comparison group, this figure increased to 39.38 ± 1.25%, which is 108.67% of the initial equal ($p <0.05$). The number of CD8 – lymphocytes after lymphotropic therapy in the main group decreased in the programmed period to 29.96 ± 3.4%, i.e., by 13.4%, and in the comparison group to 38.51 ± 3.13%, i.e., by 5.5% ($p <0.05$). The number of LGL increased 2.4 times, almost reaching the normal value in the main group ($p<0.05$). In the studied comparison group, the number of LGL increased only 1.4 times.

At hospitalization of patients, the level of NE as one of the links of the inflammatory process exceeded 3.8 times an indicator of the control group (M – 70.08 ± 9.98 nmol/min × ml) and 267.245 ± 26.27 nmol/min × ml in the main group and 265.848 ± 26.75 nmol/min × ml in the comparison group ($p >0.05$). During treatment, the level of elastase decreased to 111.797 ± 21.39 nmol/min × ml for 5 days in the main group, and in the comparison group – to 179.605 ± 26.79 nmol/min × ml ($p < 0.001$). In our opinion, the decrease in the activity of the proteolytic system, along with the activation of the

elements of the immune system, indicates a positive effect of lymphotropic administration of antibacterial drugs not only on the inflammatory process but also on the immune system. We believe that inhibition of the proteolytic system restrained the necrobiotic effect of inflammatory agents, which contributed to the prevention of complications in the postoperative period.

After appendectomy and resorption of inflammatory appendicular infiltrate under the influence of antibacterial therapy, which is carried out by lymphotropic administration of the antibiotic on the 5th day of the postoperative period, the volume of the spleen decreased to 281.22 ± 18.8 cm³, i.e., 145.44 cm^3, which indicated a decrease infectious-toxic load on the immune system, the main representative of which is the spleen, due to its more effective sanitation. At the same time, with standard administration of the antibiotic, the spleen in the studied period decreased to 344.71 ± 21.13 cm³, i.e., by 79.54 cm^3, which is less than in the main group by 66 cm³, or 1.8 times ($p < 0.05$).

At hospitalization of patients with acute appendicitis, the level of IgA exceeded the control values by 2.6 times ($p <0.05$). On the 5th day of the postoperative period, its level in the main group was 1.16 ± 0.7 mg/ml, and in the comparison group – 1.54 ± 0.8 mg/ml, i.e., in the main group 1.3 times faster was observed normalization of indicators. When studying the dynamics of IgM parameters before surgery, the value of 1.74 ± 0.5 mg/ml was recorded, which exceeded the control values (1.08 ± 0.18 mg/ml) by 1.6 times. On the 5th day of the postoperative period, its level decreased to 1.21 ± 0.28 mg/ml. In the comparison group, the changes in IgM level were significantly less indicative, namely: 1.78 ± 0.4 mg/ml before surgery and 1.58 ± 0.3 mg/ml – on the 5th day after surgery, which is less than 1.3 times. IgG values were determined at hospitalization at the level of 6.7 ± 1.2 mg/ml in the main group, which is 1.3 times less than in the control group (8.7 ± 0.9 mg/ml). On the 5th day of the postoperative period, the level of IgG was – 8.2 ± 2.33 mg/ml. In the comparison group, the level of this globulin ranged from 6.44 ± 1.1 mg/ml (in hospitalization) to 7.6 ± 1.9 mg/ml (5 days after surgery).

The duration of hyperthermia in patients of the main group was 1.7 ± 0.8 days, and in patients of the comparison group – 3.4 ± 1.4 days, which is 2 times more ($p <0.05$). Drainage in patients of the main group had been kept at 2.6 ± 0.6 days, and in patients of the comparison group – 3.9 ± 1.27 days, which is 1.5 times longer ($p<0.05$). The duration of antibiotic therapy in patients of the main group is 3.7 ± 0.77 days, and in patients in the comparison group – 6.7 ± 1.1 days, which is 1.8 times longer ($p <0.05$). The average bed-day in patients of the main group was 5.8 ± 1.15 days, and in patients of the comparison group – 8.6 ± 1.5 days, which is 1.5 times longer ($p <0.05$). Remembering that there were financial costs behind this, the advantages of lymphotropic administration of antibacterial drugs and pathogenetic drugs became obvious.

In the early postoperative period, complications were recorded in 13 (6.25%) operated subjects. Among patients of the main group, complications occurred in 3 (2.9%) persons. In the comparison group, they occurred in 10 (9.5%) operated patients. In particular, postoperative wound suppuration occurred in 2 patients of the main group (1.9%) and in 6 (5.7%) patients of the comparison group, which is 3 times more ($p <0.05$). Postoperative wound infiltrate was recorded in 1 patient of the main group (0.97%) and in 4 (3.8%) patients of the comparison group ($p <0.05$), which is more often 4 times. In the remote period during the 1 year, complications occurred in 7 (3.4%) convalescents. Among the operated people of the main group, it happened in 1 (0.97%) person, among the patients of the comparison group – in 6 (5.7%). Ligature fistula was observed in 1 patient of the main group (0.97%) and in 3 patients of the comparison group (2.9%). In 2 operated comparison groups (1.9%), there was a colonic fistula. One patient from the comparison group (0.95%) in 3 months after surgery was hospitalized with the phenomena of adhesive intestinal obstruction.

Summing up, we can emphasize that the introduction of antibiotics and pathogenetic drugs by lymphotropic regionally to the ileocecal zone provides adequate accumulation in the tissues of the vermiform process, which is not observed with their traditional introduction, which provides reliable antibacterial sanitation of this zone. This has a positive effect on the leukocyte response and the state of the proteolytic system, as well as on the immunological reactivity of the organism, which is manifested by the corresponding reaction of the spleen and immunocompetent lymphocytes. The proposed method of antibiotic therapy improves the results of treatment of patients with acute appendicitis, and reduces their length of stay in the hospital, which has a positive impact on financial problems.

Keeping in mind the etiology and pathogenesis of acute appendicitis, as well as the lymphoid nature

of the worm-like appendix, we consider the sanitation of the regional lymphatic system of the worm-like appendix by lymphotropic antibiotic therapy appropriate and justified pathophysiologically and clinically. The use of lymphotropic therapy in acute appendicitis is a method of prevention of purulent-septic complications, especially in its destructive forms, which improves the results of treatment of patients with acute destructive appendicitis. After lymphotropic antibacterial therapy, 43% of patients with appendicular infiltrate underwent surgery in the absence of any complaints; the other 57% did not seek medical help. Those who answered the questionnaire had no complaints. Given this, surgery after sanitation of the appendicular infiltrate in the absence of complaints is not necessary. But much more research needs to be done to definitively resolve this issue.

CONCLUSIONS / ВИСНОВКИ

1. The use of regional lymphotropic antibacterial therapy according to the proposed method in acute appendicitis provides reliable antibacterial sanitation of the abdominal cavity by actively affecting the cellular and humoral parts of the immune system, which effectively eliminates secondary immunodeficiency caused by acute disease. Regulation of immunity is achieved by stimulation of the immune system, a fragment of which is lymphatic, which is manifested by a reaction of the spleen (decrease) and an increase in fractions of immunocompetent lymphocytes.

2. Lymphotropic therapy has a positive effect on the imbalance of the proteolytic system by reducing its proteolytic activity.

3. The proposed method for appendicular infiltrates, reduces the time of resorption of the infiltrate and the length of stay of the patient in the hospital by an average of 7 days.

4. The proposed method of antibiotic therapy improves the results of treatment, reduces the length of stay of the patient in the hospital and, saves financial costs for treatment, ensures the timely return of the operated to socially useful work.

CONFLICT OF INTEREST / КОНФЛІКТ ІНТЕРЕСІВ

The authors declare no conflict of interest.

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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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