Original Article

Comparison of antibiotic accumulation in appendix with various methods of its injection

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Abstract

Relevance of the problem: In respect that, lack dynamic of morbidity incidence of acute appendicitis and frequency of postoperative complications, against the backdrop of increasing the number of antibiotics. The problem of prevention of purulent-inflammatory complications during its surgical treatment remains relevant. ***Materials and methods*:** The authors compared the intensity of accumulation of ceftriaxone in the appendix tissues depending on the method of injection. ***Results:*** It turned out that with the intramuscular injection of ceftriaxone in 1–2 hours before the operation, its accumulation in appendix in an amount sufficient to delay the growth of the laboratory culture of Escherichia coli is not observed. After intravenous injection of the drug, accumulation occurs slowly, significantly far behind to the lymphotropic technique. With the lymphotropic injection of ceftriaxone, 1 hour before the operation, a dose of growth retardant culture test is already fixed, and with the intjection of 2 hours before the operation – the dose of ceftriaxone practically corresponds to the maximum possible, that is, the action of a "pure" antibacterial drug. ***Conclusions:*** The method of selecting antibiotic therapy for acute appendicitis is the introduction of ceftriaxone by lymphotropic route.

Keywords: appendix; method of injections; accumulation features.

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Introduction:

For many years, acute appendicitis remains the most common disease in urgent surgery of the abdominal cavity. The incidence of acute inflammation of the herbivorous sprout is 20,7 per 10 thousand of population [1,2,3,4]. In the case of acute appendicitis, 60–70 % of emergency surgical interventions are performed. [1,3,5]. However, despite many years of research related to this disease, not all issues remain resolved. [1,6,7]. The frequency of postoperative complications reaches 4–15 % [3,8,9]. Mortality for a long time remains at the level 0,1–0,5 % [8,9,10], and in complicated forms increases to 3–5 % [11,12]. Some authors say even 10 % [1,2]. From the hearth of inflammation, which is a hormonal sprout, is the digestion of pathogenic microorganisms of the abdominal cavity and postoperative wound, which leads to purulent septic complications, which often become the leading cause of death after surgery [13,14]. Complications more often develop in destructive forms of acute appendicitis. The most widespread among them are festering wounds (66,3 %), subaponeurotic abscess (15,6 %), abdominal abscess (11,7 %), intestinal fistula (9 %), limited peritonitis (7,1 %), appendicular infiltrate (5,8 %) [1,2,8,15,16]. All of these complications develop despite of broad-spectrum antibiotics use, which is one of the arguments for the relevance of the problem.

Relevance of the problem. The most important

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current problem is in the treatment of acute appendicitis, – prevention of the development of purulent complications during the process of surgical intervention and in the postoperative period remains. However, due to the influence on the complications and mortality the use of antibiotics even of the last generations, unfortunately, does not affect, as evidenced by the lack of dynamics of complications over many years [1,2,9,15,17]. However, the cost of treatment is prohibitive. And all this is against the backdrop of the growing financial insolvency of the population. Consequently, the fight against the spread of infections from inflamed hormonal sprouts is the leading vector in the treatment of patients with acute appendicitis [2,8,11,12,13], which determines the relevance of this problem.Various pathogens are found in remote cartilaginous germs, which regenerate in the intestine of a healthy person, and against the background of violations of immune reactivity become pathogenic [13,14]. More often, in this case, E.coli is detected in association with other microorganisms and polymicrobial anaerobic or aerobic gram-negative flora [5,11,13,14]. Antibiotic therapy before surgical intervention begins empirically, and only after the performed operation and studies of purulent contents of the sprout on the microflora and its antibiotic susceptibility, the therapy may become etiopathogenetically grounded, but this happens in most cases not earlier than 3 days, which is late , as complications at this time already have time to develop and they need to be treated, which significantly differs from the prevention [6,8,10,11]. It is known that the maximum effect of antibacterial drugs appears during the peak of their accumulation in the blood. However, the degree of saturation of blood antibiotics depends on the ways of introducing the latter into the body of a patient [8,18]. It is difficult to trace the same antibiotic into the body of the diseased organ, and in most cases it is possible only after surgery. There are comparative works on determining the accumulation of streptomycin in the meristic leaf of the pleura after intrathoracic and post lymphotropic introduction of it [19]. The accumulation of the drug by the authors was determined by the level of inhibition of the growth of laboratory microbial culture B. Mycoidis. It was established that the zone of growth retardation of a microbial culture under the action of the homogenate of the peritoneal pleura after the introduction of the antibiotic is lymphotropic exceeding this after intra-thyroid administration of streptomycin in 1,6 times. Similar results are obtained when studying the accumulation of ampicillin in the prostate [20]. In the human body, the first barrier to the spread of infection from any organ is the lymphatic system. The same hormonal sprout also belongs to lymphoid tissue. Consequently, the importance of the lymphatic system in the pathogenesis of acute appendicitis is evident. In view of this therapy, aimed at the rehabilitation of the regional lymphatic collector, should be considered as one of the leading pathogenetic links in the treatment of patients with acute appendicitis, especially its complicated forms. Since the existing methods of antibiotic therapy are not perfect, the clinic has developed and tested methods of regional lymphotropic therapy in diseases of small bowel organs, including those with acute appendicitis, which are based on the accumulation of antibiotics in the ileocecal region [17,21].

Purpose of the work: To conduct a comparative analysis of the accumulation of the antibiotic ceftriaxone introduced by the lymphotropic method in the hormonal sprout with destructive forms of acute appendicitis with intravenous and intramuscular administration of the drug.

Materials and methods: Under our supervision there were 3 groups of patients. In the main group, we observed 17 people aged 20 to 79 years old, among whom there were male subjects – 7, and women – 10. The study group of this group, with their consent, was given antibacterial therapy by lymphotropic introduction of ceftriaxone for 1 to 2 hours to surgical intervention according to the method proposed by us [17]. The first comparison group consisted of 17 patients whose age was within the range of 23–69 years, male subjects in the group were 9, and female – 8. Antibiotics were administered intravenously to this group at the same time interval: 1 to 2 hours prior to surgery. The second group of comparison was made up of 17 patients, whose age was within the range of 22–65 years, male in the group was – 8, female – 9. Antibiotics in this group were injected intramuscularly for 1 to 2 hours before surgical intervention. After a surgical operation (appendectomy) under sterile conditions, for 30–40 minutes, a germ-borne germ was delivered to a bacteriological laboratory where it was homogenized under the same conditions. Homogenate was

harvested in the volume of 0,05 ml with the aid of an automatic pipette, diluted 1: 2 with a physiological solution, and injected into prepared juice with meat-peptone broth and agar-agar on which the culture of Escherichia coli was grown.

The acidity of the medium was maintained within the range of 6,1 ± 0,1. Turbidity – within 3 OD for Mac Farland. In each of the cups there were 4 dimples. One of them (control) was administered diluted antibiotic ceftriaxone in a dose of 1,0, in others - a homogenate of the removed sprout from its various sites, namely: the basis of the sprout (o), the tops (c), ripples (b). The results were evaluated in terms of diameter of the growth retardation zone (ZZR) culture test in mm around the amaranth agar-agar and test material in 48 hours. Clinical outcomes were evaluated based on the dynamics of the general patients condition, pain sensation in the operation zone, temperature response, drainage excretions, leucocytosis, ESR, nuclear shear index, and the number of large granular lymphocytes.

Ethical approval: The study was approved by the ethical committee of the Medical Institute of Sumy State University.

Research results: The results obtained during the study are presented in Table 1. According to the table, it is evident that the homogenate of the removed appendectomy of patients in group 1a, in which the antibiotic was administered lymphotropically 1 hour before the operation, inhibited the growth of Escherichia coli around the fossa with agar-agar in a diameter of 16,06 ± 1,3 mm, and in patients of group 1b, which antibiotic was administered lymphotropically for 2 hours. Before the operation, the growth of Escherichia coli around the fossa with agar-agar was inhibited in the diameter of 29,23 ± 1,3 mm, which was more than 1,8 times ($p < 0,05$). In the control flask of the studied patients 2 and 3 groups (2a and 2b, 3a and 3b), in which the antibiotic was administered at the same time, but intravenously and intramuscularly, the inhibition of the growth of the test culture was the same as in the studied main group (30,65 ± 1,1 mm), which is quite understandable. In the pits with homogenate of the appendix of group 2a, the inhibition of growth of Escherichia coli was 8,35 ± 1,22 mm, and in patients of the group 2b – 16,9 ± 1,7 mm, which is more than 2,0 times ($p < 0,05$) In all patients studied, 3 groups (3a and 3b) in the pits with homogenate of the appendix inhibited the growth of Escherichia coli at all without regard to the administration time.

Discussion: Thus, we have evidence that after intravenous administration of ceftriaxone, its penetration into the worm sprout in an amount sufficient to inhibit the growth of the test culture of Escherichia coli is not observed either after an hour or two.Consequently, surgical intervention in this

Table 1: Zone dynamic of retardation growth of test culture

Group	Way of ceftriaxone injection	Number of patients	Growth retardation zone
Control	In a hole with agar agar	7	30,65 ± 1,11 mm
1 b	Limfotropic therapy 2 hours before operation	10	29,23 ± 1,3 mm
1 a	Limfotropic therapy 1 hour before operation	7	16,06 ± 1,03 mm
2 b	intravenous administration 2 hours before operation	8	16,9 ± 1,7 mm
2 a	intravenous administration 1 hour before operation	9	8,35 ± 1,22 mm
3 b	intramuscular administration 2 hours before operation	9	Absent
3 a	intramuscular administration 1 hour before operation	8	Absent

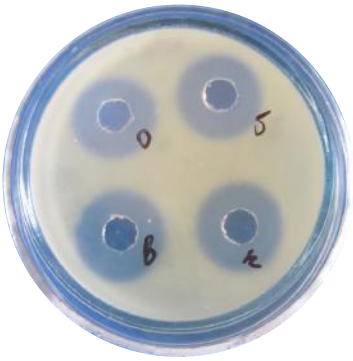

Fig. 1 The zones of growth retardation of the Escherichia coli laboratory culture of group 1b

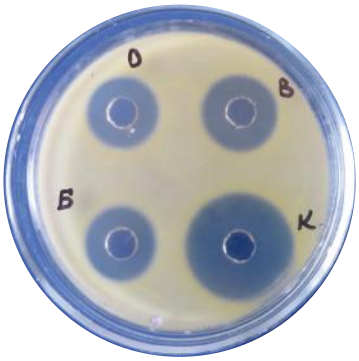

Fig. 2 The zones of growth retardation of the Escherichia coli laboratory culture of group 1b

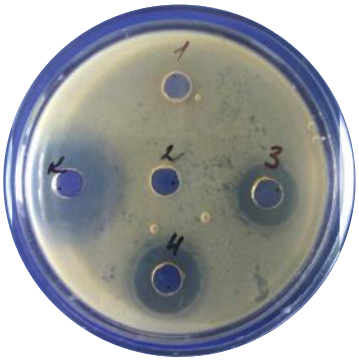

Fig. 3 The zones of growth retardation of the Escherichia coli laboratory culture of group 2b

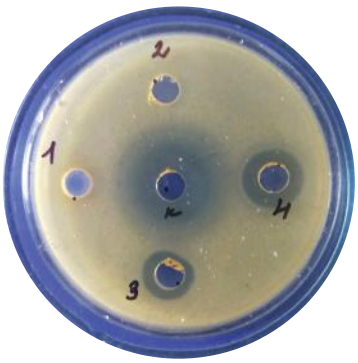

Fig. 4 The zones of growth retardation of the Escherichia coli laboratory culture of group 2a

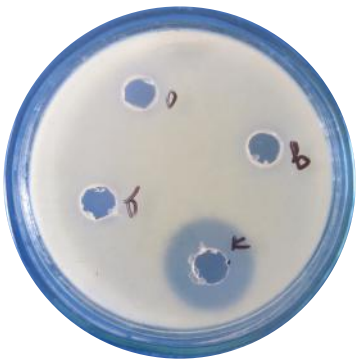

Fig. 5 The zones of growth retardation of the Escherichia coli laboratory culture of group 3b

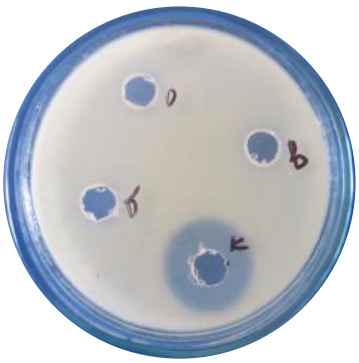

Fig. 6 The zones of growth retardation of the Escherichia coli laboratory culture of group 3a

study was not just on the inflamed sprout, but on the body with purulent content. And although this occurs, its removal, manipulation on it, including the intersection in the base area, took place under conditions of bacterial saturation with a variety of microflora [6,11,13] and purulent transformation, which inevitably, in a percentage of cases, is accompanied by infection with the crossing zone of the sprout and surrounding ones fabrics. It is clear why the postoperative period in a large part of the patients runs with a number of the above complications. At the same time, with the lymphotropic administration of the drug according to the proposed method, the hormonal sprocket after an hour accumulates an antibiotic in sufficient quantity (53,3 %) from the maximum possible inhibition of growth of the test culture observed with the introduction of a «pure antibacterial drug. Two hours later, the accumulation of the drug is practically no different from the control, which appears to be practically the same area of growth retardation Escherichia coli. When the intravenous route of administration of the drug is also observed accumulation of antibiotic in the tissue of the hormonal sprout, but this is much slower, namely: after 1 hour by 27,8 % of the maximum possible, and after 2 hours – by 56,3 %. And all this despite the fact that the intravenous administration of the antibiotic causes its maximum accumulation in the blood after several minutes, which depends on the rate of administration of the drug. In view of this, it can be thought that the antibiotic accumulated in the blood after intravenous or intramuscular administration is evenly distributed in all organs and tissues, including in the worm. Thus, after intravenous administration of the drug after 1 hour in the germ, its amount is accumulated that can slow down the growth of the microflora by 27,8 % of the maximum possible, and in two hours – by 56,3 %. At the same time, after the “targeted” administration of the antibiotic (ceftriaxone), which we believe is a lymphotropic

method, its accumulation in the inflamed germ in one hour inhibits the growth of the microflora by 53,3 % of the maximum possible, which is greater than after intravenous administration in 1,9 times, and in two hours – more than 1,8 times. Accordingly, the possibility of bacterial contamination and the risk of complications in the lymphotropic introduction of ceftriaxone decreased in the figures indicated.

Before surgery in the peripheral blood of all three groups of patients, there was a significant increase in the number of leukocytes, which was within the range of 8,7–14,1x10^9/l, there was an acceleration of the ESR to 27–40 mm per year, an increase of the index of nuclear shear to 0,3–0,5, reduction of the number of large granular lymphocytes to 1–2 %. In the postoperative period in the studied main group as a result of the use of lymphotropic therapy, the level of leukocytes started to decrease already for 18–20 hours, reaching 7,6–10,3x10^9/l, and 3-4 days – to 5,6–6,4x10^9/l ($p<0,05$). In the 2nd comparison group, where the antibiotic was administered intravenously, a decrease in leukocytosis after surgery was observed for 3–4 days to 7,3–8,5x10^9/l. In the 3rd comparison group, where the antibiotic was administered intramuscularly, reduction of leukocytosis for 3–4 days was observed up to 8,8–9,3x10^9/l. Similarly, the general condition of the patients also changed. The raised body temperature in patients with the main group was maintained for 2–3 days at the level of 37,3–37,7 C, in patients of the 2 groups of comparison – within 4–5 days at the level of 37,4–38,0 C, and in patients 3 comparison groups – for 4–5 days at the level of 37,8–38,5 C. During lymphotropic therapy, from the first day after surgery, there was a decrease in ESR to 12–15 mm per year and a nuclear shear index of 0,1-0,2. When treated with standard techniques, the improvement of these indicators was observed only 3 days after surgery. The number of large granular lymphocytes increased to 4–5 % in patients with the main group for 3–4 days, and in patients of both groups of comparison, even at the time of discharge from the hospital (5–6 days), no increase in the number of granular lymphocytes was observed. Selection of drainage in patients with the main group decreased progressively, which allowed them to be removed already 2–3 days after surgery. In patients of the first control group, drainage was carried out for 4–5 days, and in patients of the second control group 5–6 days after surgery. The formation of infiltrates in the idiopathic region and in the area of postoperative suture in patients with the main group was not. In the operated second group, the infiltration of the idiopathic area was recorded in 2 (5,9 %) persons, and the post-surgical wound infiltration was 5 (14,7 %), which forced the patients to be detained in the hospital for an additional 3–5 days and used the modified antibiotic therapy and physiotherapy procedures.

Conclusions: Traditional intravenous administration of ceftriaxone within 1–2 hours prior to the operation is not accompanied by its accumulation in a wormhole in a dose sufficient for bactericidal or bacteriostatic action, which is manifested in the absence of inhibitory growth of the laboratory test culture of Escherichia coli and leads to a number of inflammatory postoperative complications. Intravenous administration of an antibiotic is accompanied by its accumulation in the tissues of the cartilage germ, but rather slowly and in a lower braking dose. Along with this, the administration of the antibiotic according to the proposed method contributes to its accumulation in the tissues of the sprout much faster and in an amount sufficient for optimal antibacterial action, which is equivalent to such in the culture of the pathogen itself antibiotic.

Prospects for further researches: Considering the etiology and pathogenesis of acute appendicitis associated with the regional lymphatic system and the lymphoid nature of the hormonal sprout, the empirical rehabilitation of the regional lymphatic system of the sprout by lymphotropic introduction of ceftriaxone should start 1–2 hours prior to surgical intervention that facilitates regression local inflammation and prevention of complications in the ileocecal region, which is especially important in the destructive forms of acute appendicitis.

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