

Pharmacological stimulation of mesh implant engraftment after ventral hernia repair

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Abstract

Aim. To study the effect of pyrimidine medication hydroxyethyl dimethyldihydropyrimidine on the systemic inflammation after prosthetic repair of the anterior abdominal wall hernia.

Methods. We prospectively analyzed two groups of patients aged between 18 and 80 years, who underwent prosthetic repair of the aponeurosis defect in the anterior abdominal wall hernia with a standard polypropylene mesh implant. The main group (n=16) was given 0.5 g hydroxyethyl dimethyldihydropyrimidine *per os* 3 times a day before meals for 5–7 days from the first day after the operation. In the control group (n=16), patients received basic therapy without hydroxyethyl dimethyldihydropyrimidine.

Results. The postoperative period in patients after elective prosthetic hernioplasty of anterior abdominal wall was associated with an imbalance of the immune system with a tendency to lymphocytopenia (count in blood changed by –27.0%; p=0.20, Wilcoxon criterion) without significant leukocytopenia (count in blood changed by –4.9%; p=1.00, Wilcoxon criterion) and an 82.8% increase in C-reactive protein content (p=0.2, Wilcoxon criterion) compared to baseline values before the surgery. The proposed pharmacological support of prosthetic hernioplasty of the anterior abdominal wall with hydroxyethyl dimethyldihydropyrimidine allowed to correct the postoperative lymphocytopenia (p=0.04, U-criterion) and reduce the concentration of C-reactive protein by 223.6% (p=0.03, U-criterion) compared with the control, which was also associated with a decrease in the number of local complications of prosthetic hernioplasty.

Conclusion. The use of hydroxyethyl dimethyldihydropyrimidine in patients after prosthetic hernioplasty is associated with a significant decrease in the C-reactive protein level, prevention of postoperative lymphocytopenia and a decrease in the number of local wound complications; C-reactive protein level can serve as one of the early and significant indicators of postoperative complications in this category of patients.

Keywords: pharmacological support, anterior abdominal wall hernioplasty, inflammation regulation, lymphocytes, C-reactive protein, hydroxyethyl dimethyldihydropyrimidine.

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Background. Problems associated with hernias of the anterior abdominal wall remain a serious concern. Inguinal and postoperative hernias account for up to 40% and 20%–26%, respectively, [1–4] of all hernias of the anterior abdominal wall. The incidence of complications with open grafts varies within the range of 8%–28% [5], and 7%–12% when using the laparoscopic approach [6].

Deterioration of the tissue repair potential in the area of surgical intervention is one of the key factors in local wound complications (suppuration, fistula, mesh rejection), which leads logically to an increase in material costs, patient delays in hospital, and lengthening of the rehabilitation period [7–99]. A significant contribution to deterioration of the repair mechanisms is made by the

general reaction of the body to foreign material, such as an implant, as well as suture material [10]. Despite the high biological inertness of synthetic implants, a paraprosthetic exudative reaction is registered in 50%–70% of cases in the postoperative period and develops more often on days 2–4 after surgery [11].

The leading mechanism for triggering and regulating such reactions is known to be the balance of cytokines synthesized by a significant count of active cells, namely endotheliocytes, fibroblasts, leukocytes, and local and systemic macrophages [6, 12–15]. In most cases, for some reason, the body is unable to respond adequately to surgical aggression and the introduction of foreign bodies, which causes dysregulation of both local and systemic immune responses, leading simultaneously to a pronounced disorder of vascular permeability and a decrease in local defenses.

The presence of an imbalance in the immune system, existing already before the surgery, for example in obesity or metabolic syndrome, aggravates pathological reactions significantly [16, 17]. This imbalance is especially pronounced in the first 4–5 days after surgery [18], and the most pronounced decrease in the count of lymphocytes is noted during the day [19]. It should be noted that up to 80% of patients with hernias of the anterior abdominal wall are of working age; therefore, research in the field of preventing complications after hernioplasty is of great importance in increasing the ability to work and reducing financial losses from each clinical case [3–4, 20–22].

In order to increase the regenerative capacity of tissues, pyrimidine preparations have been widely used for a long time in surgical practice. According to the literature, the inflammatory response in the form of an increase in the amount of interleukins-1 and -6, C-reactive protein (CRP), fibrinogen, and A-antitrypsin is most pronounced in the first 24 h after surgery and is normalized only on day 7 of the postoperative period [23–25], and hydroxyethyl dimethyldihydropyrimidine is able to have the greatest positive effect on the wound process within the first 5–7 days [26].

Based on our experimental studies, it has been established that hydroxyethyl dimethyldihydropyrimidine has the most favorable effect on interleukins-6 and -10, as well as CRP [27]. Based on the foregoing, we hypothesized that the use of hydroxyethyl dimethyldihydropyrimidine can improve the results of engraftment of the mesh prosthesis by regulating inflammation in the immediate postoperative period.

The study aimed to analyze the effect of the pyrimidine series drug hydroxyethyl dimethyldihy-

dropyrimidine on the systemic inflammatory process after prosthetic repair of hernias of the anterior abdominal wall.

Materials and methods of the study. The clinical prospective randomized study was conducted with enrollment of 32 patients in the E.L. Berezov City Clinical Hospital No.7, Nizhny Novgorod.

Inclusion criteria:

- 1) age from 18 to 80 years inclusive;
- 2) the presence of a nonincarcerated hernia of the anterior abdominal wall;
- 3) performing hernia repair with a standard polypropylene prosthesis;
- 4) voluntary informed written consent of the patient.

Criteria for exclusion from the study:

- 1) the presence of a malignant neoplasm at the time of the study;
- 2) an infection caused by the human immunodeficiency virus;
- 3) hypersensitivity to the study drug;
- 4) erythrocytosis at the time of study;
- 5) the period of pregnancy or lactation;
- 6) total points on the SOFA¹ scale greater than 3;
- 7) refusal to participate in the study.

The standard polypropylene prosthesis was selected as standard esfil, which fully complies with the International Endohernia Society recommendations of level A (synthetic non-absorbable mesh made of monofilament thread, strength greater than 16 N/cm², pore diameter 1–1.5 mm).

The surgical options for performing hernia repair used in the work included retromuscular ($n = 4$) and preperitoneal ($n = 5$) location of the prosthesis, transabdominal preperitoneal plastic repair ($n = 15$), and Lichtenstein inguinal hernia repair ($n = 8$). Despite the variability presented, the study groups were comparable in terms of the types of surgeries performed ($p = 0.83$, χ^2). Dressings were performed depending on the postoperative wound condition.

The study groups were statistically significantly comparable in terms of age ($p = 1.00$, U-test), gender ($p = 0.90$, χ^2), concomitant pathology (for systems of blood circulation, respiration, digestion, $p = 1.00$; χ^2), and blood counts before surgery (leukocytes, lymphocytes, platelets, CRP; $p = 1.00$, χ^2). Blood sampling was performed in patients of both groups in the interval from 3 to 5 days after surgery. The average age in the main and control groups was 57.0 and 59.5 years, respectively.

The study groups of patients differed in the use of pharmacological support of the postoperative period with pyrimidine drugs. Patients of group I (16

¹ SOFA — Sequential Organ Failure Assessment.

Table 1. Median blood plasma parameters of patients in the main (I) and control (II) groups before prosthetic hernial defect repair

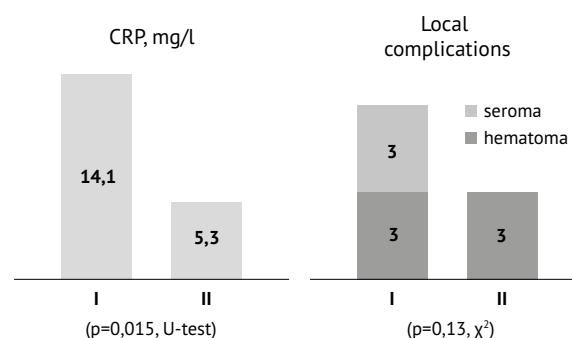
Indicator	Group		Difference in indicators, %	p, U-test
	I	II		
Leukocytes, $\times 10^9/l$	5.7	6.4	12.3	0.88
Lymphocytes, %	28.7	30.4	5.9	1.00
Platelets, $\times 10^{12}/l$	236.1	261.1	10.6	1.00
C-reactive protein, mg/l	6.1	7	14.8	0.96

Table 3. Median blood counts in patients of the main (I) and control (II) groups on days 3–5 after prosthetic hernial defect repair

Indicator	Group		Difference in indicators, %	p, U-test
	I	II		
Blood leukocytes, $\times 10^9/l$	7.4	6.1	–17.6	0.56
Lymphocytes, %	38.4	23.8	–38.0	0.04
Platelets, $\times 10^{12}/l$	195.1	247.6	26.9	0.33
C-reactive protein, mg/l	12.6	40.8	223.6	0.03

Table 2. Dynamics of the median blood plasma parameters in patients of the main (I) and control (II) groups before prosthetic hernial defect repair and after surgery

Indicator	Group		p, U-test
	I	II	
Leukocytes, $\times 10^9/l$	23.0	–4.9	1.00
Lymphocytes, %	25.3	–27.7	0.20
Platelets, $\times 10^{12}/l$	–21.0	–5.5	1.00
C-reactive protein, mg/l	51.6	82.8	0.02

**Fig. 1.** Comparison of the level of C-reactive protein (CRP) and local wound complications

people) received hydroxyethyl dimethyldihydropyrimidine in tablets at a dose of 0.5 g 3 times a day [28]. The drug intake began immediately after the first meal after the surgery and lasted for 5–7 days, depending on the time of discharge from the hospital. Patients of group II did not receive hydroxyethyl dimethyldihydropyrimidine.

According to the recommendations of Rebrova (2002), the computer program StatSoft Statistica 12 was used for statistical processing of the data obtained. The study used a 5% confidence interval. The normality of the distribution of quantitative traits was not tested, since all the data obtained were considered as nonparametric. In order to assess the distribution of continuous values in unrelated groups, the Mann–Whitney U-test was used, and in the related groups, the Wilcoxon test was used. A χ^2 criterion was used to compare discrete values. Patients were distributed into groups by a simple alternate method of randomization.

Results and discussion. It was revealed that in the blood plasma of patients of group I, the concentration of CRP was statistically significantly increased by 52%, there was a tendency toward an increase in blood counts of leukocytes by 23% and lymphocytes by 25%. In the group II, the opposite tendency was noted, namely a decrease in blood counts of leukocytes by 4.9% ($p = 1.00$, Wilcoxon's

test) and lymphocytes by 27.7% ($p = 0.20$, Wilcoxon's test). The CRP level in group II increased by 82.8% ($p = 0.02$, Wilcoxon's test) (Tables 1, 2).

When studying the difference in blood plasma parameters before the surgery and on days 3–5 after surgery (Table 3) in both groups, a decrease in the count of lymphocytes by 38% and an increase in CRP level by 224% were noted. It was also revealed that the level of CRP was associated with the number of postoperative complications in the site of implantation, which amounted to 3 (3 seromas) in the main group and 6 (3 seromas and 3 hematomas) in the control group (Fig. 1).

The results obtained were confirmed by the studies by Pochhammer et al. (2020), which they previously published in the journal *hernia*. In the present article, the authors conclude that (citation): “Serum CRP levels following mesh-reinforced ventral hernia repair may predict infectious complications” [29]. According to the Clavien and Dindo (2004, 2009), grade IIIa complications (invasive intervention without general anesthesia) were established in 5 cases in the control group of patients, and in 1 case in the main group ($p = 0.084$, χ^2).

CONCLUSIONS

1. Days 3–5 after prosthetic hernioplasty for external ventral hernia in comparison with the indices before surgery are associated with a tendency

toward lymphocytopenia (27%) and an increase in CRP by 83%.

2. Pharmacological support of prosthetic hernial defect repair in external ventral hernias with hydroxyethyl dimethyl dihydropyrimidine within 5 days after surgery enables avoidance of postoperative lymphopenia and reduces the level of CRP in blood plasma by 223.6%, compared with the control, which is associated with a tendency to decrease local wound complications.

3. C-reactive protein can be used as a marker of wound complications after prosthetic hernial defect repair in external ventral hernias.

Author contributions. S.G.I. was the work supervisor; E.E.L., S.N.B., A.A.B., and A.A.M. conducted the research; A.G.I., O.S.K., D.A.E., and T.V.V. were responsible for collecting and analysis of the results.

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Conflict of interest. The authors declare no conflict of interest.

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