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## THE USE OF ANTI-ADHESION DRUGS IN PREGNANT WOMEN WITH STRANGULATED POSTOPERATIVE HERNIAS AND ACUTE ADHESIVE SMALL INTESTINAL OBSTRUCTION

### Summary

Adhesion disease of the peritoneum is one of the difficult and unsolved problems of surgery. The number of patients is constantly increasing, which is due to the increase in the number and volume of surgical interventions on the organs of the abdominal cavity.

**Aim.** The study aimed to investigate and compare the outcomes of treatment in pregnant women with peritoneal adhesions following emergency surgical interventions, where adhesiolysis was performed and hyaluronic acid was used.

**Materials and methods.** Between 2012 and 2024, 80 pregnant women aged 21 to 42 years with adhesive disease underwent adhesiolysis and were included in the study. The patients were divided into four groups: 1) Control Group: 20 patients who received urgent surgical treatment, adhesiolysis, and conservative management using standard protocols for strangulated postoperative hernias; 2) Second Group: 20 patients who underwent surgical intervention for strangulated ventral hernias and adhesiolysis with the application of hyaluronic acid; 3) Third Group: 20 patients who underwent urgent enterolysis without the use of hyaluronic acid for acute adhesive small intestinal obstruction; 4) Fourth Group: 20 patients who underwent urgent enterolysis with the application of hyaluronic acid for acute adhesive small intestinal obstruction. For statistical analysis, the following methods were used: the Mann-Whitney U coefficient, the correlation coefficient ( $r$ ), Spearman's rank correlation coefficient ( $\rho$ ), and Confidence Intervals. Statistical analysis was performed using the MedCalc program, version 23.0.2

**Results.** In the second group, following surgical interventions and the application of hyaluronic acid, favorable short-term and long-term outcomes were observed, with a follow-up period extending up to 6 years. However, in the fourth group of patients who underwent urgent enterolysis with the use of the drug, an improvement in short-term results was noted, although the long-term outcomes were nearly indistinguishable from those in the third group.

**Conclusions.** The study confirmed the efficacy of hyaluronic acid in treating adhesions during surgical procedures for postoperative hernias. However, its effectiveness was not observed in emergency surgeries for acute adhesive intestinal obstruction. Superior outcomes can be attained through a comprehensive approach to the prevention and management of peritoneal adhesive disease, incorporating the use of modern and innovative anti-adhesion agents.

**Keywords:** Adhesive Peritoneal Disease in Pregnant Women; Acute Adhesive Small Intestinal Obstruction; Hyaluronic Acid Preparation; Adhesion Separation.

### Introduction

Adhesion disease of the peritoneum is one of the difficult and unsolved problems of surgery. The number of patients is constantly increasing, which is due to the increase in the number and volume of surgical interventions on the organs of the abdominal cavity. After secondary laparotomies, the number of patients with peritonitis and its complications is increasing. However, under certain conditions of violation of fibrinolysis, a fibrous disease of the peritoneum is formed in varying degrees of prevalence and severity of adhesions. Peritoneal adhesions are found in 93-100% of patients operated on the abdominal cavity, most of them have an asymptomatic course. Adhesions are a major cause of acute or chronic pelvic pain, infertility in gynecology, abdominal pain, and adhesive bowel obstruction in surgery. In 5-18% of operated patients, clinical manifestations of various degrees of expression associated with the adhesion process in the abdominal cavity are observed, about 3.8% of these patients require re-hospitalization and surgical interventions. Enterolysis in clinically manifested adhesion disease of the peritoneum is a necessary and routine procedure, but it causes the formation of new adhesions, and 12-19% of patients require repeated operations [3, 10].

Prevention of adhesion disease is of critical importance. One of the key strategies for preventing postoperative adhesions is the development and application of new anti-adhesion drugs [10, 32]. The most widely

recognized anti-adhesion agents are compounds based on carboxymethylcellulose and hyaluronic acid, which are polysaccharides that create a physical barrier between abdominal organs, preventing fibrin deposition and subsequent adhesion formation.

Properties of hyaluronic acid include: 1) mechanical effect: acts as a barrier; 2) moisturizing properties: high capacity for water binding; 3) healing properties: promotes normalization of cell migration and proliferation; 4) auxiliary function: interrupts the tissue inflammation cascade.

Despite their potential benefits, the indications for using anti-adhesion drugs remain unclear, and there are no standardized algorithms or guidelines for their application in general surgery. As a result, many surgeons are hesitant to use these agents [9].

**Aim.** The study aimed to investigate and compare the outcomes of treatment in pregnant women with peritoneal adhesions following emergency surgical interventions, where adhesiolysis was performed and hyaluronic acid was used.

### Materials and methods

Between 2012 and 2024, 80 pregnant women aged 21 to 42 years with adhesive disease underwent adhesiolysis and were included in the study. The average age of the patients was  $31.1 \pm 11.4$  years ( $m = 1.25$ ). Participants had a body

mass index (BMI) ranging from 17.0 to 39.9. The groups were statistically comparable in terms of age and BMI. None of the women had harmful habits such as smoking or alcohol consumption. The gestational period was up to 6 months, and no abnormalities were observed during pregnancy.

1) Control Group: 20 patients who received urgent surgical treatment, adhesiolysis, and conservative management using standard protocols for strangulated postoperative hernias; 2) Second Group: 20 patients who underwent surgical intervention for strangulated ventral hernias and adhesiolysis with the application of hyaluronic acid; 3) Third Group: 20 patients who underwent urgent enterolysis without the use of hyaluronic acid for acute adhesive small intestinal obstruction; 4) Fourth Group: 20 patients who underwent urgent enterolysis with the application of hyaluronic acid for acute adhesive small intestinal obstruction.

Only the small intestine was coated with a hyaluronic acid solution. Depending on the patient's constitution and body weight, 300 to 400 ml of the solution were used. Initially, larger quantities were applied, but this led to complications such as abdominal seroma and issues with midline laparotomy wounds. As a result, the solution is now exclusively used for intestinal coating and is not administered through drains. Following enterolysis, the abdominal cavity was drained using a tube, which was

removed within 2 days to prevent adhesions at the drainage site.

The severity of adhesions was evaluated using the Peritoneal Adhesion Index (PAI), which includes at least 5 out of 9 abdominal regions affected by adhesions [1]. The inflammatory process was graded according to the classification by Q. Zeng et al. [10, 36]:

Grade 0: No adhesions.

Grade 1: Mild – thin, avascular, transparent, loose adhesions easily separated by blunt dissection.

Grade 2: Moderate – medium thickness and transparency, partially vascularized adhesions.

Grade 3: Severe – dense, highly vascularized adhesions.

Only patients with Grade 2 and Grade 3 adhesions were included in the study.

Outcomes were assessed using a scoring system: good result – 2 points; satisfactory result – 1 point; unsatisfactory result – 0 points.

The postoperative outcomes and statistical scores are presented in Table 1:

Evaluation of short-term, intermediate, and long-term results of treatment, along with corresponding points for statistical analysis, is presented in Table 2:

Evaluation of short-term, intermediate, and long-term results of treatment, along with corresponding points for statistical analysis, is presented in Table 3:

**Table 1**

**The postoperative outcomes and statistical scores**

Criteria	Result		
	Good (2 points)	Satisfactory (1 point)	Unsatisfactory (0 points)
Abdominal pain	-	mild intensity	medium or severe intensity
Nausea	-	mild intensity	medium or severe intensity
Recovery (appearance) of peristalsis	up to 1 day	up to 2 day	after 2 days
Passage of gases	up to 2 day	up to 3 day	after 3 days
The first independent bowel movement	up 3-4 days	up to 5-6 days	after 5-6 days

**Table 2**

**Evaluation of short-term, intermediate, and long-term results of treatment, along with corresponding points for statistical analysis**

Criteria	Result		
	Good (2 points)	Satisfactory (1 point)	Unsatisfactory (0 points)
Pain syndrome	-	mild intensity	severe
Bowel passage	up to 1 day	up to 2 day	after 2 days
A feeling of intestinal discomfort	-	mild intensity	severe
Asthenic syndrome	-	mild intensity	severe
Inpatient treatment	-	1-2 cases in therapeutic department	surgical treatment

**Table 3**

**Evaluation of short-term, intermediate, and long-term results of treatment, along with corresponding points for statistical analysis**

Criteria	Result		
	Good (2 points)	Satisfactory (1 point)	Unsatisfactory (0 points)
Pain syndrome	-	mild intensity	severe
Bowel passage	up to 1 day	up to 2 day	after 2 days
A feeling of intestinal discomfort	-	mild intensity	severe
Asthenic syndrome	-	mild intensity	severe
Inpatient treatment	-	1-2 cases in therapeutic department	surgical treatment

For statistical analysis, the following methods were used: the Mann-Whitney U coefficient, the correlation coefficient ( $r$ ), Spearman's rank correlation coefficient ( $\rho$ ), and Confidence Intervals. Statistical analysis was performed using the MedCalc program, version 23.0.2/

## Results

According to TASC (2000), the evaluation of treatment outcomes was conducted at standardized time intervals recommended by surgeons and cardiovascular surgeons: immediate results – within 30 days post-surgery; short-term

results – from 1 to 6 months post-surgery; intermediate results – from 12 to 24 months post-surgery; long-term results – from 2 years post-surgery.

Criteria for evaluating the immediate results of treatment. The criteria for assessing treatment outcomes within 30 days after surgery included: bowel passage (evacuation of contrast after 24 hours as the primary criterion); duration of inpatient treatment; recovery of work capacity.

The results of treatment of groups of patients are shown in Table 4:

**Table 4**

**The results of treatment of groups of patients**

Results		Good (2 points)	Satisfactory (1 point)	Unsatisfactory (0 points)
Postoperative period and immediate	I	6 (30%)	12 (60%)	2 (10%)
	II (20±0,09)	16 (80%)	4 (20%)	-
	III (20 (20±0,13) ± 0,18)	6 (30%)	7 (35%)	7 (35%)
	IV (20 ± 0,1535)	11 (55%)	7 (35%)	2 (10%)

Mann-Whitney U for the first and second groups = 96.00 ( $p=0.0013$ ).

Correlation coefficient ( $r$ ) = 0.5833 ( $p=0.0069$ ).

Spearman's rank correlation coefficient ( $\rho$ ) = 0.548 ( $p = 0.0124$ ).

95% Confidence Interval for  $\rho$ : 0.139 to 0.797. These results indicate a statistically significant difference in treatment outcomes between the first and second groups.

Mann-Whitney U for the third and fourth group = 132.5 ( $p = 0.05$ ).

Correlation coefficient ( $r$ ) = 0.7849 ( $p<0.0001$ ).

Spearman's rank correlation coefficient ( $\rho$ ) = 0.823 ( $p<0.0001$ ).

95% Confidence Interval for  $\rho$ : 0.597 to 0.927. These results show a statistical difference in treatment outcomes between the third and fourth groups, although the data are on the borderline of statistical significance.

Criteria for evaluating short-term, intermediate and long-term results of treatment. The definitive criteria for evaluating the treatment of adhesions in the intermediate and long-term periods include: bowel passage (contrast evacuation after 24 hours), intestinal dysfunction (constipation, flatulence), a feeling of intestinal discomfort, the presence

of pain syndrome, asthenic syndrome, inpatient treatment in a therapeutic or surgical department due to adhesion disease, absence of repeated surgical interventions for adhesion-related obstructions or recurrent ventral hernias.

The results of treatment of groups of patients are shown in Table 5:

**Table 5**

**The results of treatment of groups of patients**

Results		Good (2 points)	Satisfactory (1 point)	Unsatisfactory (0 points)
Short-term, intermediate and long-term	I (20±0,15)	9 (45%)	9 (45%)	2 (10%)
	II (20±0,099)	15 (75%)	5 (25%)	-
	III (20±0,19)	8(40%)	6(30%)	6(30%)
	IV (20±0,19)	9(45%)	7(35%)	5(35%)

Mann-Whitney U for the first and second groups = 135.00 ( $p = 0.0412$ ).

Correlation coefficient ( $r$ ) = 0.6623 ( $p = 0.0015$ ).

Spearman's rank correlation coefficient ( $\rho$ ) = 0.631 ( $p = 0.0029$ ).

95% Confidence Interval for  $\rho$ : 0.261 to 0.831 These results indicate a statistically significant difference in treatment outcomes between the first and second groups.

Mann-Whitney U for the third and fourth groups = 187 ( $p = 0.7071$ ).

Correlation coefficient ( $r$ ) = 0.93 ( $p < 0.0001$ ).

Spearman's rank correlation coefficient ( $\rho$ ) = 0.935 ( $p < 0.0001$ ).

95% Confidence Interval for  $\rho$ : 0.841 to 0.974. These results show no statistically significant difference in treatment outcomes between the third and fourth groups.

Here is the rephrased version of the text, maintaining the academic and scientific tone and adhering strictly to your request to preserve the original formatting and structure, without adding new elements or using bold formatting:

The table demonstrates the efficacy of the anti-adhesion drug hyaluronic acid in Group II patients following

surgery for ventral hernias. However, in the fourth group of patients, who underwent urgent enterolysis with the use of the drug, an improvement in immediate outcomes was observed, but the long-term results were nearly identical to those in the third group.

Thus, ventral hernias and acute adhesive obstructions differ in both their pathogenesis and treatment approaches.

A differentiated strategy is essential for managing these conditions.

## Discussion

One of the approaches to preventing postoperative adhesions involves not only the development of modern surgical techniques, the use of high-quality suture materials, and advanced implants but also the exploration of new methods for adhesion prevention through the application of anti-adhesion drugs.

Among the most widely recognized anti-adhesion agents are compounds based on carboxymethylcellulose and hyaluronic acid, which are polysaccharides that create a physical barrier between abdominal organs, preventing fibrin deposition and subsequent adhesion formation [11, 13, 14].

Interceed (oxidized regenerated cellulose, Ethicon) is an absorbable membrane that degrades into monosaccharides within two weeks after application. It does not require fixation with sutures. Randomized clinical trials have demonstrated that the use of Interceed following laparoscopic and open surgeries reduces the adhesion process by 50-60%, although it does not completely eliminate adhesions. It is approved for use in the United States.

Sepracoat (Genzyme) is a hyaluronic acid solution that dissolves within five days after being introduced into the abdominal cavity. Currently, its primary application is in operative gynecology. It is approved for use in some European countries but has not received FDA approval in the United States.

Seprafilm (Genzyme) is a biodegradable membrane composed of hyaluronic acid and carboxymethylcellulose. Its use is limited to laparotomy procedures, as it degrades rapidly and requires careful handling. A large multicenter randomized study in the United States, involving 1,701 patients divided into two groups (with and without the membrane), found no statistically significant difference in the development of adhesion disease between the groups.

Gore-Tex Surgical Membrane (W. L. Gore Corp.) is a non-absorbable membrane made of thin sheets (0.1 mm) of polytetrafluoroethylene, with an average pore diameter

of less than 2 micrometers. Unlike other materials, it can be secured to tissues using sutures. Studies have shown that polytetrafluoroethylene is more effective than oxidized regenerated cellulose. However, the material requires suturing and must be removed during the postoperative period.

Spraygel (Confluent Surgical) is a polyethylene glycol-based product applied as a spray onto the peritoneum. It adheres to the peritoneal surface within seconds. Currently, the drug is in the clinical trial phase, and initial results indicate its effectiveness.

At present, according to European publications, there are no combined anti-adhesion drugs available. Specifically, there is no combination of anti-adhesion agents with antiseptics to reduce microbial contamination. The indications for using anti-adhesion drugs remain unclear, and there are no standardized algorithms or guidelines for their application in general surgery. As a result, many surgeons avoid their use [8].

Some publications have overemphasized the role of hyaluronic acid. There is a lack of literature addressing the differential effects of hyaluronic acid in adhesiolysis for patients with incisional hernias compared to those with acute intestinal obstruction. Our study highlights the varying efficacy of hyaluronic acid in different types of surgeries. There is a need to explore new drugs or combinations of drugs for use in surgeries addressing acute intestinal obstruction.

## Conclusions

The study has demonstrated that hyaluronic acid is effective in treating adhesions during surgeries for postoperative hernias in pregnant women. However, its efficacy is limited in emergency surgeries for acute adhesive intestinal obstruction. It is essential to differentiate between patients with adhesive peritoneal disease and severe small intestinal obstruction and those with postoperative ventral hernias. Better outcomes can be achieved through a comprehensive approach to the prevention and treatment of adhesive peritoneal disease, including the use of modern and innovative anti-adhesion drugs.

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## ЗАСТОСУВАННЯ ПРОТИСПАЙКОВИХ ПРЕПАРАТІВ У ВАГІТНИХ ЖІНОК ПРИ ЗАЩЕМЛЕНИХ ПІСЛЯОПЕРАЦІЙНИХ ГРИЖАХ І ПРИ ГОСТРІЙ СПАЙКОВІЙ ТОНКОКИШКОВІЙ НЕПРОХІДНОСТІ

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### Резюме.

Спайкова хвороба очеревини є однією зі складних і невирішених проблем хірургії. Кількість хворих постійно зростає, що обумовлено збільшенням кількості та обсягів оперативних втручань на органах черевної порожнини.

**Мета** – вивчити та порівняти результати лікування вагітних жінок зі спайками очеревини після невідкладних оперативних втручань, при яких проводили роз'єднання спайок і використовували препарат гіалуронової кислоти.

**Матеріали і методи.** За період з 2012 по 2024 рр. обстежено та проліковано 80 вагітних жінок із спайковою хворобою, які перенесли роз'єднання спайок, віком від 21 до 42 років. Хворих розподілено на наступні групи: 1) контрольна – 20 хворих, яким проведено ургентне оперативне лікування, роз'єднання спайок та консервативне лікування загальноприйнятими методами при защемлених післяопераційних грижах; 2) друга група – 20 пацієнтів, яким проведено оперативне втручання у зв'язку із защемленими вентральними грижами та роз'єднання спайок із застосуванням препарату гіалуронової кислоти; 3) третя група – 20 пацієнтів, яким проводили терміновий ентероліз без застосування препарату гіалуронової кислоти, з гострою спайковою тонкокишковою непрохідністю; 4) четверта група – 20 хворих, яким проводили терміновий ентероліз із застосуванням препарату гіалуронової кислоти, з гострою спайковою тонкокишковою непрохідністю.

**Результати.** У другій групі після оперативного втручання і застосування препарату гіалуронової кислоти отримані добрі найближчі та віддалені результати з терміном спостереження до 6 років. Однак у четвертій групі пацієнтів після термінового ентеролізу та застосування препарату спостерігається поліпшення найближчих результатів, але віддалені результати практично не відрізнялися від третьої групи пацієнтів.

**Висновки.** Доведено, що гіалуронова кислота ефективна при лікуванні спайок під час операцій у пацієнтів з післяопераційними грижами. Однак гіалуронова кислота не ефективна в екстрених операціях при гострій спайковій кишковій непрохідності. Досягти кращих результатів можливо при комплексному підході до профілактики та лікування спайкової хвороби очеревини, застосуванні сучасних і нових протиспайкових препаратів.

**Ключові слова:** спайкова хвороба очеревини у вагітних жінок; гостра спайкова тонкокишкова непрохідність; препарат гіалуронової кислоти; роз'єднання спайок.

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