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ABSTRACT

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EXPERIMENTAL MODELING OF ADHESION DISEASE IN RATS

The persistent causes of adhesion formation in the abdominal cavity remain inflammatory processes, previous abdominal surgeries, blunt and sharp abdominal trauma, including those of military origin, and congenital adhesions. According to the literature, peritoneal adhesion disease remains common in emergency surgery, with its incidence showing no decline. Acute adhesive intestinal obstruction ranks first among causes of intestinal obstruction of various origins. The severity of complications and postoperative mortality related to this condition show no tendency to decrease.

Currently, there are no experimental methods for inducing adhesion formation in the abdominal cavity of rats that closely mimic practical surgical conditions.

Objective: To develop and study, in an experimental setting, the morphological manifestations of the adhesion process using our proposed method of inducing adhesions in the abdominal cavity of rats, which would be as close as possible to the current clinical requirements of operative surgery.

Materials and Methods: Laparotomy, macroscopic, microscopic, histological examination (preparation of slide specimens), staining with hematoxylin and eosin, statistical analysis using Fisher's exact test, determination of median adhesion formation frequency, interquartile range, and confidence interval for the median.

Results: No adhesions formed in animals of the control group. In the second group, on day 7 after adhesion induction, 90 % of rats showed thin membranous avascular adhesions that were easily disrupted. In the third group, on day 14, adhesions were observed in 90 % of animals; these were denser, partially vascularized, and required blunt or sharp dissection. In the fourth group, on day 21, 80 % of rats exhibited dense adhesive bands with high vascularization. Histologically, a transition was noted from granulation tissue with dense infiltration (day 7) to mature fibrous tissue with minimal signs of inflammation (day 21).

Conclusions: Injury to the parietal peritoneum alone during laparotomy does not lead to adhesion formation. In most rats, the adhesion process progressed sequentially from thin membranous formations to dense fibrous tissue with vascularization. The visceral peritoneum was more prone to adhesion formation compared to the parietal peritoneum. Involvement of uninjured organs in the adhesion process indicates a systemic pathological process extending beyond local injury.

Keywords: peritoneal adhesions, adhesion formation, rats, experimental model, wound healing, fibrosis, laparotomy.

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ЕКСПЕРИМЕНТАЛЬНЕ МОДЕЛЮВАННЯ ЗЛУКОВОЇ ХВОРОБИ У ЩУРІВ

Незмінними причинами виникнення злукового процесу в черевній порожнині залишаються запальні процеси, перенесені оперативні втручання на черевній порожнині, тупі та гострі травми живота, у тому числі воєнного походження, та вроджені злуки.

Згідно з даними літератури, злукова хвороба черевної порожнини продовжує залишатися поширеною в ургентній медицині і її частота не зменшується. Гостра злукова кишкова непрохідність посідає перше місце у структурі кишкової непрохідності різного походження. Тяжкість ускладнень та післяопераційна летальність з цього приводу не мають тенденції до зменшення.

На сьогоднішній день відсутні експериментальні методики формування злукового процесу у черевній порожнині щурів, які були б наближені до практичної хірургії.

Мета роботи: розробити в експерименті і вивчити морфологічні прояви злукового процесу запропонованої нами методики утворення спайкового процесу у черевній порожнині щурів, яка буде максимально наближеною до сучасних клінічних вимог оперативної хірургії.

Матеріали та методи дослідження: лапаротомія, макроскопічне, мікроскопічне, гістологічне дослідження (виготовлення плівкових препаратів), фарбування препаратів гематоксиліном та еозином, статистична обробка за методом Фішера, визначення медіани частоти злукоутворення, інтерквартильного розмаху та довірчого інтервалу для медіани.

Результати: у тварин контрольної групи злуки в черевній порожнині не утворювалися. У другій групі на 7 добу після моделювання злук у 90 % щурів спостерігались тонкі плівчасті злуки без васкуляризації, що легко руйнувались. У третій групі на 14 добу після ініціювання злук утвори виявлялися в 90 % тварин, вони були щільнішими, частково васкуляризованими та потребували механічного або гострого роз'єднання. У четвертій групі на 21 добу після моделювання злук у 80 % щурів спостерігалися щільні злукові тяжі з високою васкуляризацією. Гістологічно встановлено перехід від грануляційної тканини зі щільною інфільтрацією (7 доба) до зрілої фіброзної тканини з мінімальними ознаками запалення (21 доба).

Висновки: ушкодження лише парієтальної очеревини під час лапаротомії не призводить до утворення злук. У більшості щурів після моделювання злук зафіксовано послідовне прогресування спайкового процесу від плівчастих утворів до щільної фіброзної тканини з васкуляризацією. Вісцеральна очеревина виявилася більш схильною до злукоутворення порівняно з парієтальною. Залучення неушкоджених органів у злуковий процес свідчить про системний характер патологічного процесу, що виходить за межі локального ушкодження.

Ключові слова: злуки очеревини, формування злук, щури, експериментальна модель, загоєння ран, фіброз, лапаротомія.

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INTRODUCTION

The main causes of adhesion formation in the abdominal cavity remain inflammatory processes, previous surgical interventions in the abdominal cavity, blunt and penetrating abdominal trauma, including those of military origin, as well as congenital adhesions [1–10]. Adhesion disease of the abdominal cavity continues to be a common issue in emergency medicine, with no tendency toward decline. Acute adhesive intestinal obstruction ranks first among the causes of intestinal obstruction of various origins [2–8]. The number of complications and postoperative mortality related to this condition also shows no tendency to decrease [3, 4, 7–10]. The formation of adhesions between the parietal and visceral peritoneum leads to impaired function of abdominal organs, especially the intestines [4]. In addition, adhesions in the abdominal cavity affect the outcomes of possible future surgeries, limit physical activity, worsen overall well-being, and reduce patients' quality of life.

Since the identification of this problem by Richard Bright in 1835 [5], efforts have been continuously made to find methods of preventing adhesion disease [1], as any surgical intervention in the abdominal cavity results in the development of adhesions in 67–93 % of patients [1–4, 6–11]. This is largely due to the absence of a clearly defined and universally accepted etiopathogenesis of the disease.

Several theories of adhesion formation are currently known. The inflammation theory explains the development of adhesions as a result of fibrin exudation, followed by the adhesion of the serosal surfaces of the peritoneum, which is likely in the presence of a concomitant infectious process [6, 7].

Risk factors for adhesion formation include postoperative intestinal paresis with delayed peristaltic activity [8].

There is also a view regarding the role of intestinal wall ischemia in the development of adhesive processes. H. Ellis experimentally demonstrated that in cases where bleeding from injured peritoneal areas stops spontaneously without the use of hemostatic agents, the damage heals by primary intention without adhesion formation. In contrast, tissue crushing and the application of surgical sutures cause impaired blood supply, which contributes to the development of adhesions [6, 8, 9, 11].

It has been suggested that autoimmune and hyperergic reactions of connective tissue may contribute to adhesion formation [9, 10].

To investigate the mechanisms of adhesion development and to test potential preventive measures and agents, a reliable experimental model of the adhesive process in the abdominal cavity is necessary [6]. Surgeons are familiar with a variety of factors that damage the peritoneum and initiate adhesion formation. In experimental surgery, several methods for modeling adhesion formation have been developed using mechanical, biological, chemical, and implant-based factors. However, all of them exhibit certain local limitations in their applicability [10–20].

In our opinion, current trends in modeling abdominal adhesions should aim for the closest possible approximation to the clinical treatment algorithms currently used in surgery and gynecology.

Below, we present a general overview of proposed experimental models of adhesion disease in rats [10–20, 25–27].

Peritoneal mesothelial injury typically involves mechanical damage to the peritoneum via crushing, scarification, incision, or coagulation. Studies have shown that mechanical injury to the peritoneal epithelium promotes inflammation and the activation of fibrinogenesis, which authors consider a key initiating factor in the development of intra-abdominal adhesions [25, 27]. Research by Kim et al. (2022) confirmed that

the intensity of adhesion formation correlates with the degree of mechanical injury [28].

In chemical induction of adhesions, chemical agents such as alcohols or acids are used. According to several authors, barium and talc may also provoke adhesion formation. For this purpose, intraperitoneal injection of barium sulfate suspension or talc suspension has been employed [10, 21]. In particular, the study by Zhang Y.D. et al. (2002) demonstrated that administration of 95 % ethanol induced intense adhesion formation [12].

In the infectious method of adhesion induction, bacterial agents such as *Escherichia coli* or *Staphylococcus aureus* are introduced into the abdominal cavity via microlaparotomy [29].

Some experimental studies combined mechanical injury to the visceral peritoneum of the small intestine with treatment of the damaged area using kaolin solution containing infectious components [11].

Various surgical approaches have been used in rat models of peritoneal adhesion formation. For instance, Zhang Y.D. et al. (2002) performed a midline laparotomy under sterile conditions. Two centimeters of the distal cecum were placed on moist gauze and rubbed on the anterior surface with dry gauze up to ten times until petechial hemorrhages appeared. Then, five drops of 95 % ethanol were applied to the altered cecal wall [12]. However, this method is highly artificial and distant from clinical surgical practice.

Yilmaz H.G. et al. (2005) performed a 3 cm midline laparotomy. The anterior surface of the cecum was scratched until bleeding occurred, after which the injured site was sutured with 5/0 silk. The cecum was returned to the abdominal cavity in its natural position. A 1 cm^2 defect was created in the parietal peritoneum of the right abdominal wall. The laparotomy was closed in a single layer using continuous 3/0 silk sutures. This technique appears artificial at all stages and, moreover, silk is not used in clinical surgery for suturing the cecum [13].

Rasti M. et al. (2007) performed a 3 cm lower midline laparotomy. On the right abdominal wall, ten longitudinal incisions were made, and on the left side, a 2 cm^2 parietal peritoneal excision was carried out [14]. While the experiment was successful, it was considered excessively artificial and traumatic.

Yetkin G. et al. (2009) used a sponge to rub the serosal surface of the cecum until it lost its sheen and pinpoint bleeding appeared. Ethanol drops were applied to stimulate adhesion formation. Hemostasis of the adjacent parietal peritoneum was then performed, and the cecum was fixed to the right iliac region using 3/0 silk sutures [15]. This approach is not representative of clinical surgery since silk is not typically used for cecal suturing.

Pryor H.I. et al. (2009) injured a 1 × 2 cm area of parietal peritoneum above the cecum by rubbing, and the cecum was mobilized and further abraded until pinpoint hemorrhages occurred. The injured bowel was left to air dry for 10 minutes [16]. This technique is quite conditional, although it simulates the conditions of practical surgery.

Lalountas M.A. et al. (2010) opened the abdominal cavity via a 4 cm midline incision under aseptic conditions. The cecum was exteriorized and rubbed until hemorrhagic spots appeared [17].

Whang S.H. et al. (2011) created adhesions in four groups of rats. Group 1: midline laparotomy with peritoneal excision to the muscle layer on the left abdominal wall. Group 2: damage to the parietal peritoneum for 1 minute using a brush. Group 3: placement of four 2/0 Prolene sutures on the parietal peritoneum. Group 4: abrading the visceral peritoneum of the ileocecal region using sandpaper. This method is time-consuming and highly traumatic, especially considering the small size of laboratory animals [18].

Kraemer B. et al. (2014) induced adhesions in six groups of rats. Group 1: brushing of the abdominal wall peritoneum and uterine horns. Group 2: brushing of the abdominal wall peritoneum. Group 3: surgical excision of the parietal peritoneum and suturing with interrupted sutures. Group 4: ischemia induction via clamping, followed by suturing with Vicryl. Group 5: bipolar electrocauterization of the peritoneum. Group 6: electrocauterization followed by suturing with Vicryl. This protocol is complex and traumatic, making it difficult to replicate [19].

Raisi et al. (2021) performed three transverse and longitudinal incisions (1.5 cm each) on the right parietal peritoneum and excised a 1.5 × 1.5 cm portion on the left side [20]. This approach is complex, traumatic, and overly artificial.

Paydarkina A.P. and Kushch O.H. (2024) induced adhesions by intraperitoneal injection of 0.5 ml of 20 % talc suspension [10]. Since modern surgery excludes the presence of talc in the abdominal cavity, this model is suitable for experimental use only.

The consequences of abdominal adhesions include intestinal obstruction and female infertility [1, 3, 4, 6, 7, 9, 21]. The most common manifestation in surgical practice is acute adhesive small bowel obstruction (AASBO), which requires emergency surgical intervention and remains one of the most challenging abdominal surgical conditions [4, 6–8, 10, 11]. The incidence of AASBO among all causes of intestinal obstruction ranges from 2 % to 55 % 3, 4, 6–8, 10, 11, 22]. Mortality due to this complication ranges from 4 % to 9.3 %, reaching 11.3 % to 20 % in early postoperative cases [6 – 9, 11, 22, 23]. Despite numerous efforts to

prevent adhesion formation, their incidence remains persistently high at 55–66 % according to various authors [1, 4, 6, 8, 11, 22–24].

Adhesion formation in the abdominal cavity is a natural protective and adaptive response to external and internal stimuli exceeding physiological thresholds and is accompanied by mesothelial damage to the peritoneum [1–11, 22–24].

RELEVANCE OF THE PROBLEM

To date, both researchers and the surgical community have made numerous attempts to prevent the formation of adhesions in the abdominal cavity. These efforts have included various pharmaceutical agents, locally acting barriers based on hyaluronic acid or collagen, and other therapeutic measures. Recent studies indicate that the use of biomaterial-based barriers is considered the most promising method for the prevention of adhesion formation. However, even these methods are not sufficiently reliable in preventing the development of this complex pathological process [6]. All experimental approaches aimed at inducing adhesions typically involve creating them in a specific, artificially selected area of the abdominal cavity. Consequently, the interventions are applied precisely to that selected site, and the resulting response is, therefore, of a local nature.

A significant number of the experimental models we have analyzed demonstrate that the problem of adhesion disease remains unresolved and continues to be a subject of ongoing scientific investigation, which underscores the relevance of the issue.

AIM OF THE STUDY

1. Based on the above, we concluded that there is a need for a simple and practical method for inducing adhesions that may occur under various conditions, regardless of the underlying disease. The adhesion induction model should closely reflect the clinical realities of modern surgical practice.

2. Therefore, the aim of our study was to develop an experimental model and examine the morphological features of adhesion formation using our proposed method of inducing adhesions in the abdominal cavity of rats. This model is designed to closely resemble the clinical scenarios encountered in modern operative surgery and to reflect adhesion formation that may arise after any surgical intervention.

MATERIALS AND METHODS

The study on rats was conducted at the laboratory of the Educational and Scientific Medical Institute of Sumy State University. A total of 40 healthy male albino Wistar rats, weighing 250–300 g and aged 8 to 10 weeks, were used. The animals had not previously undergone any surgical procedures or received any medications. The rats were housed in the vivarium of Sumy State University under standard conditions: a 12-hour light/dark cycle, humidity of 65 % ± 3 %, and temperature of 22 ± 2 °C. They had free access to water and pellet food. The research was conducted in compliance with the standards of the Council Convention on Bioethics (1997), the European Convention for the Protection of Vertebrate of Europe Animals Used for Experimental and Other Scientific Purposes (Strasbourg, 1986), Council Directive of Europe 86/609/EEC (1986), and the Law of Ukraine No. 3447-IV «On the Protection of Animals from Cruelty».

The animals were divided into four groups. The comparison group (Group 1) included 10 rats (n = 10). These animals underwent a midline laparotomy without additional trauma to the parietal or visceral peritoneum. Groups 2, 3, and 4 also consisted of 10 rats each (n = 10). In these groups, the rats underwent midline laparotomy followed by mechanical trauma to the parietal peritoneum of the right abdominal wall by scraping an area 3 cm long and 1 cm wide to the point of «bloody dew2 (8–10 vertical strokes).

All surgical procedures (n = 40) were performed under pharmacological anesthesia by intramuscular injection of Telazol (20 mg/kg) and Xylazine (5 mg/kg). Surgeries were performed under sterile conditions, therefore, no antibacterial prophylaxis was administered. During the procedures, respiration rate and heart rate were monitored every 2 minutes. After anesthesia, the rats were placed in a supine position and fixed using adhesive tape. The operative area was shaved and disinfected with a 10 % povidone-iodine solution. A midline incision up to 4 cm was made through the skin, muscles, and parietal peritoneum. In the comparison group, layered suturing of the peritoneum, abdominal wall muscles, and skin was performed. In Groups 2, 3, 4, the surgical site was covered with sterile gauze, and adhesion formation was induced by scraping the parietal peritoneum of the right abdominal wall using abrasive material (emery sponge) № 80 (3 cm × 1 cm, 8–10 vertical strokes) until «bloody dew» appeared. A small amount of blood accumulated in the abdominal cavity during scraping and was not removed. The abdominal cavity was closed in layers. To prevent rats from chewing on the sutures, intradermal stitches were applied. The postoperative wound was treated with 10 % povidone-iodine solution, covered with an aseptic dressing, and an elastic bandage was applied around the torso. Postoperatively, the animals were kept in a warm, dark environment with controlled temperature until recovery. After surgery, the rats were monitored dynamically with an assessment of clinical vital signs–respiratory rate and heart rate. All rats that underwent laparotomy received intramuscular analgesia

with Dexketoprofen at a dose of 5 mg/kg body weight twice a day for three days.

The next aim of the study was to assess the prevalence and severity of peritoneal adhesion formation and perform a morphological evaluation in all experimental groups. In Group 2, the abdominal cavity was examined on day 7 after adhesion modeling. In Group 3, the examination was performed on day 14, and in Group 4 on day 21 post-operation. For this purpose, relaparotomy was performed. During the procedure, the abdominal organs and peritoneal changes were assessed. The number of adhesions, their spread in the abdominal cavity, their maturity, and adhesion strength were recorded. Adhesion changes were documented using a SONY Cyber-shot digital camera. The data were analyzed statistically using Statistica software to determine the p-value, which was used to assess the significance of the test results. Results were considered statistically significant at $p < 0.05$. Additionally, for each group, the median frequency of adhesion formation, interquartile range, and confidence interval for the median were calculated.

The degree of adhesion spread in the abdominal cavity was assessed by the percentage of the peritoneal surface covered by adhesions (from 0 % to > 75 %). The maturity and strength of adhesions were assessed based on adhesion density, vascularization type, and ease of separation. Morphological changes in the peritoneum were evaluated using a visual-descriptive method, which included a system for transforming qualitative characteristics of adhesions into quantitative scores. The extent of adhesion formation was documented using the classification by Diamond et al. (1987) (Table 1). Changes in the abdominal cavity were evaluated by two independent experts blinded to the experimental conditions but trained in assessing adhesion severity [30]. Additionally, histomorphological analysis was performed on all animals at the corresponding time points.

Table 1– Diamond Scale for the Extent and Maturity of Peritoneal Adhesions

Extent of Adhesion Coverage in the Abdominal Cavity	**Score**
0 % of the surface covered with adhesions	0
< 25 % of the surface covered with adhesions	1
25–50 % of the surface covered with adhesions	2
50–75 % of the surface covered with adhesions	3
> 75 % of the surface covered with adhesions	4
Adhesion Maturity and Strength of Adhesion	
No adhesions present	0
Thin, filmy adhesions without blood supply, easily separable	1
Moderately dense adhesions with minimal vascularization	2
Dense, vascularized adhesions requiring moderate mechanical force to separate	3
Very dense, massive adhesions invading tissues, bleed during blunt dissection	4

RESULTS

A comprehensive analysis of the data obtained from the animals in the comparison group revealed no adhesion formations either in the abdominal cavity or between the abdominal organs and the postoperative scar – 0 % (n = 0). The site of parietal peritoneal injury after the initial laparotomy was completely remesothelialized. Relaparotomy in this group of rats was performed on the 21st day after the surgical intervention.

The macroscopic assessment of postoperative adhesion formation in group 2 was performed on day 7, in group 3 on day 14, and in group 4 on day 21 after adhesion induction, using the classification proposed by Diamond et al. (1987). The macroscopic evaluation criteria included the number of adhesions, their density, distribution in different abdominal regions, and the presence and intensity of vascularization (Table 2).

On day 7, in animals of the second (2nd) main group (n = 10), adhesion formation in the abdominal cavity was observed in 9 out of 10 rats (90 %) following adhesion induction. The median adhesion frequency was 1.00 [interquartile range (IQR): 1.00–1.00], with a 95 % confidence interval (CI): 1.00–1.00. This indicates a high incidence of adhesion formation in the majority of animals in this group. All 9 animals (100 %) exhibited thin, film-like adhesions: delicate, homogeneous structures that were easily separated using a blunt instrument (swab), which resulted in bleeding upon separation, suggesting the early stage of fibrous tissue organization. In all animals (100 %), adhesions were found between the omentum and intestines.

Table 2 – Adhesion Process Characterization According to the Diamond Extent Scale

Number of Animals		Group 2 (n=10)	Group 3 (n=10)	Group 4 (n=10)
Number of Adhesion Formation Cases		9 (90 %)	9 (90 %)	8 (80 %)
Extent of Adhesion Coverage in the Abdominal Cavity	**Score**	**Number of Cases**		
< 25 %	1	3	4	3
< 50 %	2	4	3	3
< 75 %	3	2	2	2
> 75 %	4	-	-	-
		p = 0,0003	p = 0,0005	p = 0,0017
Adhesion Maturity and Strength of Adhesion				
Thin, filmy adhesions without blood supply, easily separable	1	9	-	-
Moderately dense adhesions with minimal vascularization	2	-	9	-
Dense, vascularized adhesions requiring moderate mechanical force to separate	3	-	-	-
Very dense, massive adhesions invading tissues, bleed during blunt dissection	4	-	-	8
		p = 0,00009	p = 0,0001	p = 0,0002

Adhesions between loops of the small intestine and the parietal peritoneum of the right lateral abdominal wall (n = 3; 33 %) covered up to 25 % of the abdominal cavity. In 4 animals (44 %), adhesions between loops of the small intestine occupied up to 50 % of the abdominal cavity. In 2 animals (22 %), adhesions fixed part of the intestine to the subhepatic region, occupying up to 75 % of the abdominal cavity. In all 9 cases (100 %), the adhesions were thin and avascular. Overall, by day 7 after adhesion induction, the initial stages of active adhesion tissue formation were observed, without signs of vascularization (Fig. 1). On day 14, in animals of the third (3rd) main group (n = 10), adhesion formation in the abdominal cavity was observed in 9 out of 10 rats (90 %) following adhesion induction. The adhesions were notably denser compared to those in the second group and required either more forceful blunt dissection or sharp excision for removal, which resulted in moderate bleeding. The median adhesion frequency was 1.00 [interquartile range (IQR): 1.00–1.00], with a 95 % confidence interval (CI): 1.00–1.00, indicating a high incidence of adhesive disease. In all 9 (100 %) animals, the greater omentum was involved in the formation of adhesions. In 4 rats (44 %), adhesions were found between loops of the small intestine, occupying up to 25 % of the abdominal cavity. In 3 animals (33 %), adhesions between the cecum, small intestine, and the parietal peritoneum of the right lateral abdominal wall occupied up to 50 % of the abdominal cavity. In 2 animals (22 %), in addition to adhesions between small intestinal loops, adhesions were identified in the pelvic area, specifically between the sigmoid colon and the urinary bladder, with the entire adhesion process occupying up to 75 % of the abdominal cavity. In all 9 animals (100 %), the adhesions demonstrated slight vascularization (Fig. 2).

During relaparotomy in rats of the fourth (4th) main group on day 21 after adhesion induction and abdominal organ revision, adhesion formation at the site of mechanical peritoneal trauma was observed in 8 out of 10 animals (80 %). The median adhesion frequency was 1.00 [interquartile range (IQR): 0.75–1.00], 95 % confidence interval (CI): 1.00–1.00, indicating a tendency toward a high frequency of adhesion formation in this experimental setting. In all 8 rats, the previously uninjured cecum and greater omentum exhibited pathological changes. In 5 animals (62.5 %), the small intestine was also affected. The walls of these organs were connected to the ventral layer of the parietal peritoneum at the site of mechanical injury.

In 3 rats (37.5 %), the adhesions were flat, dense, and up to 1.5 cm in length. In 5 animals (62.5 %), adhesive changes were represented by dense fibrous bands. In 5 (62.5 %) experimental animals, the lateral wall of the cecum adhered to the parietal peritoneum at the site of injury, forming fibrous bands measuring 0.2–0.5 cm in length, which could only be separated using sharp dissection. In the remaining 4 rats (50 %), the adhesions appeared as cord-like or flat fibrous bands connecting the parietal peritoneum to the cecum (Fig. 3).

The maturity of the adhesions varied. Flat adhesions were identified in 3 rats (37.5 %), and firm connections between the cecum and the ventral parietal peritoneum were observed in 5 animals (62.5 %). In one case, the previously intact cecum was divided by adhesions into two compartments. Depending on the maturity of the adhesions, the degree of vascularization also varied.

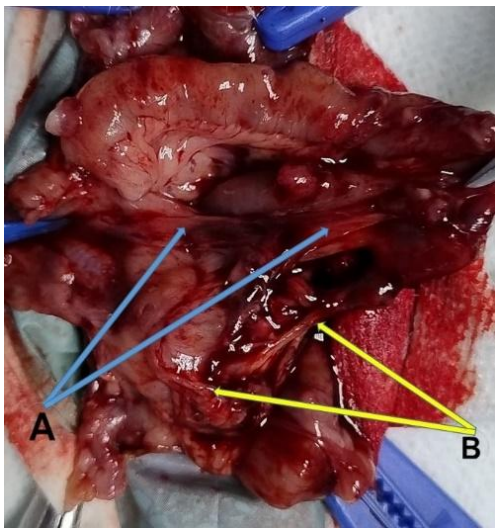

Figure 1 – Visceral-parietal (A) and visceral-visceral (B) adhesions of the small intestine on day 7 after adhesion induction

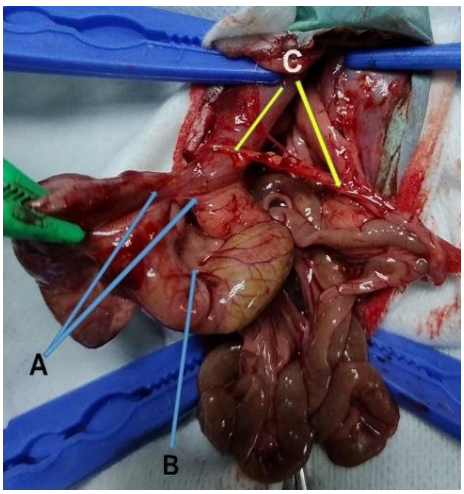

Figure 2 – Horseshoe-shaped caecum with visceral-parietal (A) and visceral-visceral (B) adhesions, omental-parietal and omental-intestinal adhesions (C) on day 14 after adhesion induction

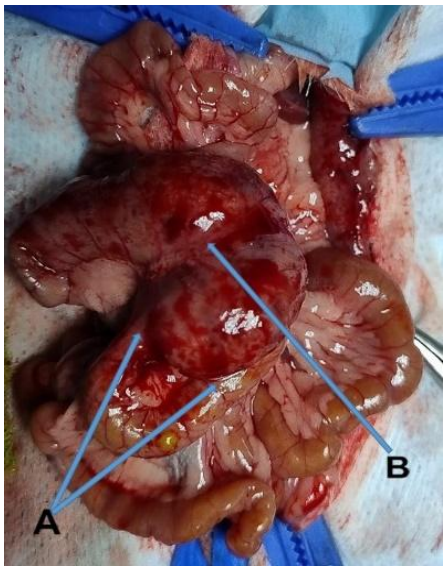

Figure 3 – Visceral-visceral adhesions between the dome of the caecum and a loop of the small intestine (A), adhesion between the dome and the body of the caecum (B) on day 21 after adhesion induction

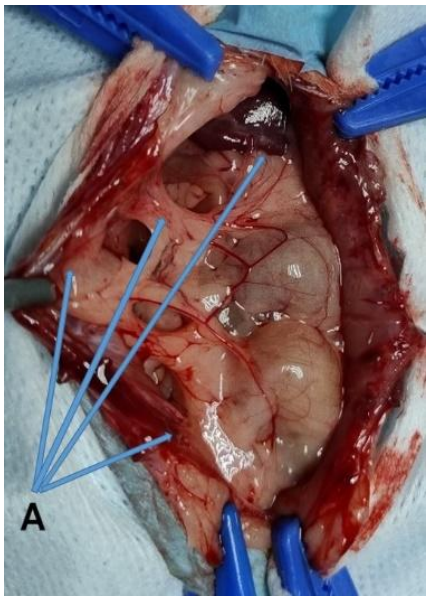

Figure 4 – Visceral-parietal adhesions (A). The adhesion process involves up to 75 % of the abdominal cavity on day 21 after adhesion induction

A high level of vascularization was noted in the flat, cord-like adhesions (n=4; 50 %) and in the flat adhesions connecting the cecum to the parietal peritoneum of the right ventral abdominal wall (n=5; 62.5 %). Moderate vascularization was observed in the adhesions of 7 animals (87.5 %). In 3 animals (37.5 %), the adhesive process was limited to the right lateral abdominal area, while in 5 animals (62.5 %), it extended to other anatomical regions of the abdominal cavity. In 2 rats (25 %), the adhesion process affected up to 75 % of the abdominal cavity (Fig. 4). During adhesiolysis, the fibrous formations in these animals could only be separated by sharp dissection.

During histological examination of adhesion biopsies on day 7 after the start of the experiment, the structure of the adhesions revealed loose granulation tissue. The stroma of the adhesions was rich in young fibroblasts and individual fibrocytes; collagen fibers were thin and insufficiently organized. Dense inflammatory infiltration was observed, mainly consisting of lymphocytes, macrophages, and occasional neutrophils. The histomorphological picture corresponded to the stage of active inflammation and the early phase of repair (Fig. 5).

On day 14 of the experiment, the adhesions were predominantly composed of mature granulation tissue

with a moderate number of fibroblasts and increasing collagen production. Collagen fibers were significantly more organized compared to day 7. The inflammatory infiltration was less pronounced, with lymphocytes and macrophages predominating. The morphological picture corresponded to the proliferative stage of repair and partial organization of adhesion tissue (Fig 6).

By day 21 of the experiment, the histological specimens of adhesions were characterized by dense fibrous connective tissue with well-formed collagen fibers. The stroma of the adhesions contained a moderate number of fibroblasts and fibrocytes, occasional blood vessels, and minimal or absent infiltration by lymphocytes and macrophages, indicating process stabilization and resolution of chronic inflammation (Fig 7).

CONCLUSIONS

1. Injury to the parietal peritoneum by laparotomy incision alone is insufficient to initiate and form adhesions (0 %).

2. In the second, third, and fourth groups of rats, adhesion formation was observed in 26 animals (87 %). On the 7th day after adhesion induction, delicate-type structures were observed: thin, film-like, and homogeneous, without vascularization, easily separated with a swab, which caused minor bleeding. These changes indicated the early stage of fibrous tissue organization. On day 14, additional formations showed a noticeably denser structure compared to the second group, had moderate vascularization, and were removed by «aggressive» blunt dissection or sharp incision with minor bleeding. By day 21 after adhesion modeling, mature adhesions were observed, characterized by dense fibrous connective tissue with pronounced collagenization and vascularization.

3. The visceral peritoneum is more prone to adhesion formation in the postoperative period compared to the parietal peritoneum. Following mechanical injury to the parietal peritoneum in rats, uninjured organs such as the cecum (8–31 % of cases), small intestine with mesentery (23–88 %), and greater *omentum* (26–100 %) were involved in the adhesion process. The affected organs lost elasticity and mobility; their walls became thickened and dense by day 21 after the experiment.

4. The adhesion process involved areas of the small and large intestines and the greater *omentum.* The involvement of other abdominal organs that were not directly subjected to mechanical trauma indicates that the adhesion process is not merely localized but systemic.

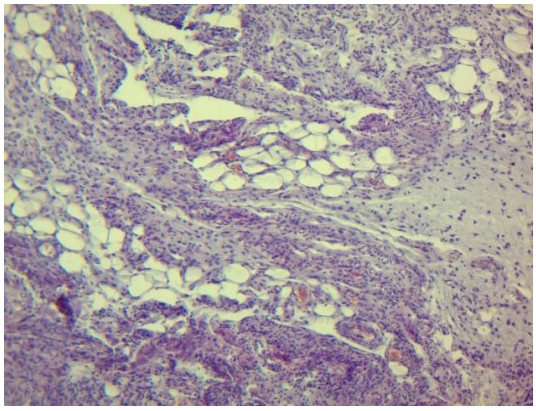

Figure 5 – Histological specimen of adhesion tissue on day 7 after adhesion induction

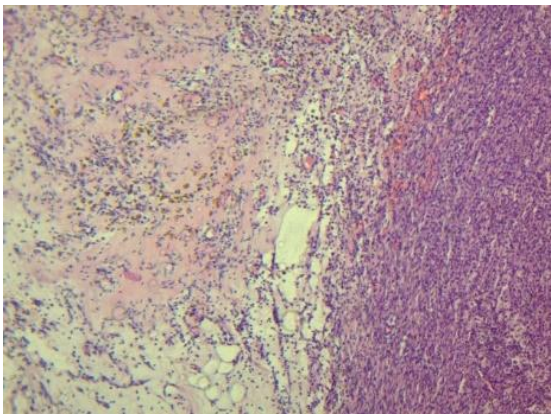

Figure 6 – Histological specimen of adhesion tissue on day 14 after adhesion induction

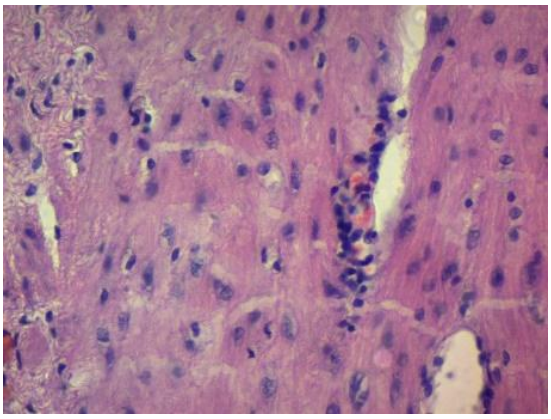

Figure 7 – Histological specimen of adhesion tissue on day 21 after adhesion induction

PROSPECTS FOR FUTURE RESEARCH

Prospects for future research is to explore specific aspects of the pathogenesis of adhesion formation. Our further research will focus on the possibilities of systemic prevention of adhesion development and translation of the results into clinical practice.

AUTHOR CONTRIBUTIONS

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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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest regarding this study, including financial, personal, or authorship-related interests that could have influenced the study and its results as presented in this article.

ARTIFICIAL INTELLIGENCE DISCLOSURE

The authors confirm that artificial intelligence technologies were not used in the preparation of this manuscript.

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