Iranian Journal of Veterinary Surgery

ORIGINAL ARTICLE

Effect of Platelet-Rich Plasma and Dexamethasone on Experimentally Induced Intraabdominal Adhesions in Rat

Mahan Sarebani, Soroush Sabiza ✉, Seyedeh Misagh Jalali

Department of Clinical Sciences, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran.

ARTICLE INFO

Article History:

Received: 9 October 2024
Revised: 27 October 2024
Accepted: 8 December 2024

Keywords:

Platelet rich plasma
Peritoneal adhesions
Dexamethasone
Adhesion induction
Rat

ABSTRACT

Following surgical trauma to the peritoneum, bleeding and increased vascular permeability occur, accompanied by the leakage of fibrinogen-rich fluids from the damaged surfaces. Peritoneal adhesions are observed in 60 to 93 percent of patients after abdominal surgeries and are one of the most common causes of long-term complications following such procedures. This study aimed to examine the combined effect of platelet-rich plasma (PRP) gel and the drug dexamethasone in preventing intra-abdominal adhesions following laparotomy in rats. In this research, 35 adult male Wistar rats, weighing between 250 and 300 grams, were selected. Fifteen rats were used to prepare PRP, and blood collection was performed after anesthesia with ketamine/xylazine. The remaining 20 rats were divided into four groups: the control group (C), the PRP-treated group (P), the dexamethasone-treated group (D), and the group receiving the combination of PRP and dexamethasone (PD). To induce adhesions, sterile tampon friction was applied to the serosal surface of the poorly vascularized descending colon area, and additional friction was created using a surgical blade on the peritoneal surface of the colon. The relevant treatments were then injected into each group. Results showed no significant differences in fibrinogen levels and leukogram between the groups ($p > 0.05$); however, macroscopic examination indicated a reduction in adhesions in the PRP group compared to the other groups ($p = 0.001$). According to the results of this research, it is concluded that the addition of dexamethasone to platelet-rich plasma will not have a significant effect on reducing the state of adhesion following abdominal surgery in rats.

Introduction

Peritoneal adhesions are abnormal fibrous bands that occur in 60 to 93 percent of cases following abdominal and peritoneal surgeries, often leading to significant complications. These adhesions can result in chronic pain, organ dysfunction, and second surgery.[1] Moreover, peritoneal adhesions are associated with infertility, pelvic pain, bowel obstruction, and increased postoperative costs.[2] Adhesions are observed in 79 to 90 percent of patients undergoing open abdominal surgery,[3] and 3 to 20 percent of these patients are rehospitalized within five years due to adhesion-related complications.[4]

Peritoneal tissue repair is a complex process involving various cells, cytokines, coagulation factors, and proteases that work together to restore tissue integrity.[5] Biochemical events, including inflammation, angiogenesis, and tissue repair, play a crucial role in controlling adhesion formation.[6] The fibrinolytic system is essential in peritoneal healing after surgery, as bleeding and increased vascular permeability occur immediately after trauma, allowing the release of

✉ Corresponding author. Email: s.sabiza@scu.ac.ir

https://doi.org/10.30500/ivsa.2024.482626.1417

fibrinogen-rich fluid.[7] Primary fibrinolysis, which occurs within five days, results in peritoneal healing without adhesion formation.[8] The main causes of intra-abdominal adhesions include physical or chemical injury to the peritoneal mesothelium, excessive handling of internal organs, and drying of the viscera due to prolonged surgery. Adhesion-related complications include chronic abdominal and pelvic pain, secondary infertility in women, and gastrointestinal tract narrowing.[9,10]

Several methods have been used to reduce postoperative adhesions, such as fibrinolytic agents, antibiotics, anti-inflammatory drugs, nanofiber membranes, and solid barriers.[11] These strategies aim to minimize peritoneal trauma, prevent fibrin formation, and employ physical barriers.[4] Various approaches, including abdominal cavity lavage, lytic agents, anti-inflammatory drugs, heparin, and green tea extract, have been studied for adhesion prevention.[12-16]

Platelet-rich plasma (PRP) modulates the intra-abdominal environment by producing various growth factors, such as platelet-derived growth factor AB (PDGF-AB), transforming growth factor β1 (TGFβ-1), and vascular endothelial growth factor (VEGF). It attracts reparative cells to the site of tissue injury, which is essential for natural wound healing and leads to a reduction in the inflammatory process. Structurally, PRP gel is similar to a fibrin clot.[17] It has been shown that the topical application of PRP gel improves colon anastomosis in rat models.[18] Studies on rat models have demonstrated that PRP significantly reduces postoperative adhesion formation.[19,20]

Corticosteroids such as dexamethasone help reduce adhesions by decreasing vascular permeability and inhibiting cytokines and chemotactic factors involved in adhesion formation.[21] Dexamethasone effectively prevents early inflammation caused by trauma and chemical agents and, in the later stages of inflammation, inhibits fibroblast proliferation and reduces granulation tissue formation, thus preventing adhesions and scarring. Additionally, anti-inflammatory agents and antihistamines prevent adhesions by inhibiting fibroblast repair.[22]

Given the importance of the aforementioned issues, the objective of this study was to evaluate the effect of platelet-rich plasma and dexamethasone on experimentally induced intraabdominal adhesions in rats.

Materials and Methods

Animals

This study was conducted on 35 adult male Wistar rats, weighing between 250-300 grams and the study protocol approved by the Ethics Committee of the Veterinary Faculty at Shahid Chamran University of Ahvaz. The procedures were filed under the ethical code IR.SCU.REC.1402.040. Animal housing was in standard conditions of temperature (22 ± 3 °C), humidity (60 ± 5%), and a 12-hour light/dark cycle. They were fed on a standard pellet diet and tap water. Fifteen of the rats were chosen to prepare platelet-rich plasma (PRP). The remaining twenty rats were randomly divided into four equal groups. The control group (C) received normal saline and the second group (P), the third group (D), and the fourth group (PD) received PRP, dexamethasone, and combination of PRP and dexamethasone, respectively.

PRP Preparation

The fifteen rats were anesthetized using ketamine/xylazine (100/10 mg/kg). Blood was drawn using a sterile syringe and transferred into glass tubes containing sterile sodium citrate at a ratio of 9:1. Whole blood was collected by cardiac puncture and mixed with sodium citrate anticoagulant in sterile tubes, followed by centrifugation. After centrifugation at 1000 rpm for 15 minutes, the blood separated into three layers: plasma (upper layer), buffy coat (thin middle layer), and red blood cells (bottom layer). The upper plasma and buffy coat layers were transferred to an empty sterile tube and centrifuged again at 3000 rpm for 5 minutes at room temperature. The upper two-thirds of the supernatant, consisting of platelet-poor plasma (PPP), was removed, and the remaining one-third (lower portion) was considered PRP. To ensure platelet count, the PRP dissolved in phosphate-buffered saline (PBS) was counted per volume unit using an automated cell counter. The prepared PRP was then frozen at -70 °C until use.[23]

Surgery

All animals were anesthetized by intraperitoneal injection of a mixture of ketamine (100 mg/kg) and xylazine (10 mg/kg). A standard midline abdominal incision was made, and the entire abdominal cavity was inspected to ensure the absence of any previous lesions or adhesions. To induce adhesions in the peritoneal cavity, the serosal surface of the descending colon in the avascular area was abraded using dry sterile gauze until petechiae appeared on the serosal surface. Additionally, abrasions were made on the peritoneal surfaces of the left abdominal wall near the descending colon using a No. 15 surgical blade.[24] After inducing the adhesion model and before closing the abdominal incision, each group received its respective treatment. The control group received 1 ml of normal saline sprayed over the abdominal viscera. In the PRP group, 1 ml of platelet-rich plasma was used. The dexamethasone group received 0.2 mg/kg of dexamethasone diluted in 5 ml distilled water, and 1 ml of the solution was used. In the fourth group, 0.5 ml of PRP and 0.5 ml of dexamethasone were administered. In all groups, the total injection volume was

adjusted to 1 ml using normal saline. Additionally, a single dose of subcutaneous enrofloxacin (5 mg/kg) was administered postoperatively to prevent secondary infection.

Assessments

Fourteen days after surgery and adhesion induction, cardiac blood collection was performed under ketamine/xylazine anesthesia. Blood was collected into EDTA-containing tubes and sterile glass tubes containing sodium citrate at a ratio of 9:1. Complete blood samples were analyzed for hematological evaluations using an automated cell counter, and the plasma obtained by centrifugation at 3000 rpm for 15 minutes was used to measure fibrinogen levels via the coagulation-based Von Clauss method, which measures fluid viscosity.

At the end of the study, euthanasia was carried out using a dosage five times more than that of the anesthesia induction dose, and exploratory laparotomy was performed. The extent and quality of adhesions to the tissues in the surgical area were evaluated. The number of adhesion bands was scored using the Nair scoring method (Table 1), and the difficulty of separating the adhesions was assessed using the Adachi scoring method (Table 2).

Data Analysis

The data was analyzed using version 27 of SPSS (IBM Corporation, NY, USA). A one-way ANOVA test followed by LSD post-hoc was used to compare leukogram and fibrinogen measurements between the study groups. The Kruskal-Wallis test was employed to compare adhesion scores between groups. For leukogram and fibrinogen data, results were presented as mean ± standard deviation (SD), while adhesion scores were shown as median (min-max). A *p*-value of less than 0.05 was considered statistically significant.

Table 1. Nair scoring method based on the number of adhesion bands.[25]

Grade	Adhesion Severity
0	No adhesions observed
1	One adhesion band between organs or between an organ and the abdominal wall
2	Two adhesion bands between organs or between an organ and the abdominal wall
3	More than two adhesion bands between organs or between an organ and the abdominal wall
4	Complete adherence of organs to the abdominal wall with no visible separation (regardless of the number of bands)

Table 2. Adachi scoring method based on adhesion separation difficulty.[26]

Grade	Adhesion Severity
0	No adhesions observed
1	One adhesion, separable by blunt dissection*
1.5	Multiple adhesions, separable by blunt dissection
2	One adhesion, requiring sharp dissection**
2.5	Multiple adhesions, requiring sharp dissection
3	Omentum adhesion requiring sharp dissection at the surgical incision site

*Blunt dissection: Separation without surgical instruments, using only the surgeon's hands and no bleeding involved. **Sharp dissection: Separation requiring surgical instruments, such as scissors.

Results

According to the Adachi adhesion scoring system, the highest adhesion levels were observed in the C group, showing statistically significant differences compared to the D group ($p = 0.005$), P group ($p = 0.001$), and PD group ($p = 0.003$). The lowest adhesion levels were observed in the P group, which exhibited significant differences compared to the C group ($p = 0.001$), D group ($p = 0.024$), and PD group ($p = 0.037$) (Table 3 and Figure 1).

Based on the Nair adhesion scoring system, the highest adhesion levels were observed in the C group, with significant differences found when compared to the D ($p = 0.001$), P ($p = 0.001$), and PD groups ($p = 0.001$). The lowest adhesion levels according to the Nair method were found in the P and PD groups, which had significant differences compared to the C group (Table 3 and Figure 2). By examining the leukogram profile of the studied animals, despite differences in the values of white blood cells, monocytes, lymphocytes, and granulocytes and fibrinogen levels no statistically significant differences

Table 3. Median (minimum - maximum) adhesion scores in rats receiving saline (C), dexamethasone (D) (0.2 mg/kg), PRP (P), and a combination of dexamethasone and PRP (PD) (n = 5).

Group	Adachi Scoring System (0-3)	Nair Scoring System (0-4)
C	2.5 (1-3)	3 (2-4)
D	1 (0-1.5)	0.5 (0-2)
P	0 (0-0)	0 (0-0)
DP	1 (0-2)	0 (0-2)

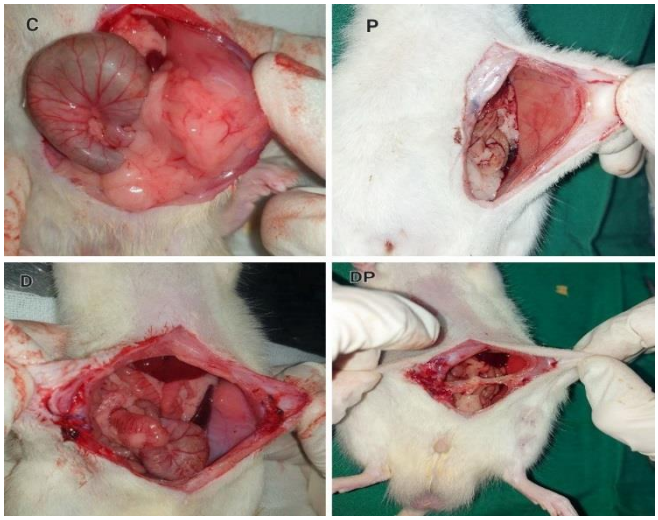

Figure 1. Dissection and evaluation two weeks after surgery, based on Adachi's table.

were observed between the groups ($p > 0.05$) (Tables 4 and 5).

Discussion

The peritoneum has a unique structure and mechanism that, when injured, such as during surgery or inflammation, can initiate the adhesion process. This adhesion occurs as part of the peritoneum's healing response following damage, and it is clinically significant because it presents one of the major challenges for physicians and surgeons after abdominal surgeries. Following any injury to the peritoneum, inflammatory mediators are released, leading to the accumulation of inflammatory cells such as neutrophils and increased blood flow to the site. Peritoneal healing may occur with or without adhesion formation, depending on the activity of the fibrinolytic system.[27]

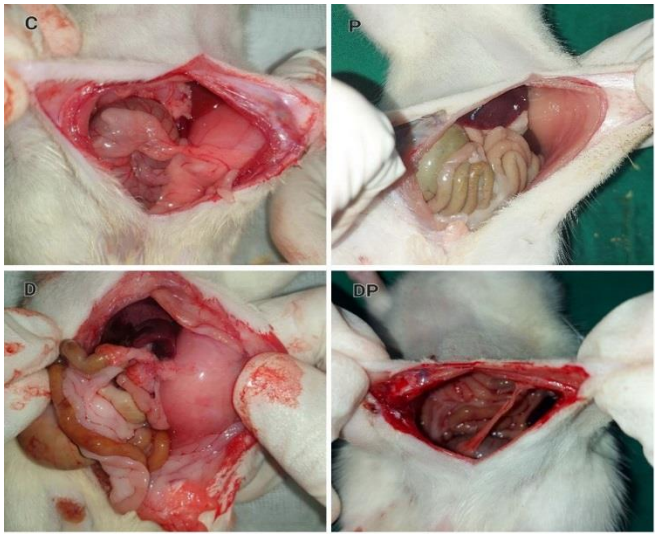

Figure 2. Dissection and evaluation two weeks after surgery, based on Nair's table.

Table 4. Mean ± standard deviation of the leukogram after the induction of experimental abdominal adhesions in the groups receiving saline (C), dexamethasone (D) (0.2 mg/kg), PRP (P), and a combination of dexamethasone and PRP (PD) in rats (n = 5).

Group	White Blood Cells ($\times 10^3$)	Monocytes ($\times 10^3$)	Lymphocytes ($\times 10^3$)	Granulocytes ($\times 10^3$)
C	14.7 ± 4.6	0.4 ± 0.1	9.1 ± 2.2	5.1 ± 2.3
D	9.9 ± 1.7	0.2 ± 0.2	5.3 ± 3.4	4.4 ± 3.7
P	10.9 ± 5.0	0.3 ± 0.1	6.1 ± 3.6	4.4 ± 1.5
DP	9.7 ± 1.0	0.2 ± 0.0	5.4 ± 1.0	4.0 ± 0.9

Table 5. Mean ± standard deviation of fibrinogen levels after the induction of experimental abdominal adhesions in the groups receiving saline (C), dexamethasone (D) (0.2 mg/kg), PRP (P), and a combination of dexamethasone and PRP (PD) in rats (n = 5).

Group	Fibrinogen (mg/dl)
C	192.3 ± 16.7
D	175.6 ± 50.3
P	155.3 ± 15.9
DP	170.1 ± 16.7

The mechanism of intra-abdominal adhesion formation after surgery involves several complex stages. Initially, injury to the peritoneum triggers an acute inflammatory response, which results in the release of cytokines and growth factors. These factors attract neutrophils and macrophages to the injury site. While these immune cells secrete enzymes to aid in tissue repair, they can also contribute to the formation of fibrotic tissue and adhesions.[28] Next, fibroblasts and mesenchymal cells migrate to the site, producing extracellular matrix and collagen. An excessive production of these substances can lead to the formation of scar tissue and adhesions. The reduced activity of matrix metalloproteinases (MMPs), which are responsible for breaking down the extracellular matrix, also contributes to this process. Adhesions can cause internal organs to stick together, leading to complications such as pain, bowel obstruction, and organ dysfunction.[29] Other factors, such as local hypoxia and oxidative stress, also play a role in exacerbating adhesions. Hypoxia enhances adhesion formation by activating hypoxia-inducible factor (HIF) signaling pathways and increasing the production of pro-inflammatory and fibrotic factors. Additionally, oxidative stress promotes the inflammatory and fibrotic processes through the production of free radicals and cellular damage.[30]

During surgeries, reduced blood flow and oxygen supply to the tissue lead to an increase in plasminogen activator inhibitors and suppression of the fibrinolytic system, allowing fibrin strands to remain at the site. In the presence of collagen, these fibrin strands transform into resistant structures, leading to adhesion formation. Adhesions occur in 66% of abdominal surgeries and are associated with complications such as bowel obstruction and infertility, particularly in women.[31] This condition is observed in 79% to 90% of patients undergoing open abdominal surgery.[3]

According to studies by Erang *et al*., dexamethasone is a steroidal anti-inflammatory drug that works by suppressing the body's inflammatory and immune responses. This drug reduces cytokine production and inhibits the activity of inflammatory cells, which can help reduce inflammation and, consequently, the formation of intra-abdominal adhesions. Dexamethasone effectively controls the inflammatory process by inhibiting the production of prostaglandins and leukotrienes, which are the main mediators of inflammation.[32]

Mariano *et al*. have shown that fibrinogen, a key protein in the blood coagulation process, plays a significant role in the formation of peritoneal adhesions. This protein is converted to fibrin in response to tissue injury and helps form fibrin clots, contributing to the development of tissue adhesions. Additionally, fibrinogen aids in tissue repair and the formation of new adhesions

by activating platelets and releasing growth factors. Therefore, reducing fibrinogen levels or inhibiting its conversion to fibrin could lead to a reduction in peritoneal adhesions.[33]

Stratakis *et al*. demonstrated that platelet-rich plasma (PRP) is an effective method for reducing peritoneal adhesions following surgery. In a study conducted on 27 rats, the animals were divided into three groups: a control group that received normal saline, a group that received hyaluronic acid, and a group that received PRP. The results indicated that PRP significantly reduced the extent, severity, and size of the adhesions, while also reducing inflammation, fibrosis, and neutrophil infiltration. These findings suggest that PRP can be used as an effective method for reducing post-surgical adhesions.[20]

Makarichian *et al*. found that the use of platelet-rich PRP alone had the greatest effect in preventing post-surgical adhesions in animal models. In a study conducted on 60 rats, the groups that received PRP showed a significant reduction in adhesion severity compared to the groups that received silver nanoparticles or heparin. PRP reduces peritoneal adhesion formation by improving inflammatory and physiological processes, enhancing hemostatic properties, and promoting wound healing. It has been identified as an effective agent in preventing post-surgical adhesions.[19]

Fibrinogen is a critical precursor in the formation of adhesions, and measuring its levels in plasma can serve as an appropriate indicator of the presence of adhesions. In this study, fibrinogen levels were measured across different groups, and no statistically significant differences were observed between them. The present study also examined the leukogram profile of the animals under investigation. Despite variations in the levels of white blood cells, monocytes, lymphocytes, and granulocytes, no statistically significant differences were found between the groups. In a study conducted by Sui *et al*. in 2021, the blood parameters of 119 COVID-19 patients were analyzed. The results showed that among 80 individuals, severe inflammatory responses were observed. These patients exhibited increased levels of plasma fibrinogen, white blood cells, neutrophils, and hemoglobin, while the number of lymphocytes was significantly reduced.[34]

Based on existing studies and research, PRP has emerged as a promising approach for reducing intra-abdominal adhesions following surgery. PRP, with its growth factors and anti-inflammatory properties, can accelerate tissue healing and reduce inflammation. While some studies have demonstrated that PRP can reduce adhesions, the results of other research have indicated no significant effect or even a lack of reduction in adhesions. These conflicting results suggest that PRP can be used without increasing the risk of further adhesions, but more extensive and thorough research is required to reach definitive and reliable conclusions. Therefore, the use of PRP in reducing peritoneal adhesions is considered a potentially safe method, but it necessitates further investigation to fully prove its effectiveness.

Studies have shown that both PRP and dexamethasone can individually contribute to reducing peritoneal adhesions; however, their combination, as suggested by recent studies, appears to neutralize each other's effects. PRP functions by enhancing growth factors and accelerating tissue repair processes, while dexamethasone exerts its effects by reducing inflammation and inhibiting fibroblast proliferation. Combining these two may interfere with the mechanisms of tissue repair and inflammation reduction, potentially leading to adverse outcomes. For instance, the growth factors in PRP might weaken the anti-inflammatory effect of dexamethasone, and vice versa. This interference could diminish the efficacy of both agents and ultimately have no impact on reducing adhesions. In this study, pathology evaluation was not done, although the use of sampling from adhesion areas and performing staining and examination of histopathology sections could improve the quality of evaluations.

Based on the above findings, this study, which focused on preventing peritoneal adhesions using platelet-rich plasma, dexamethasone, and a combination of both, demonstrated that adding dexamethasone to platelet-rich plasma did not have a significant effect on reducing adhesion severity following abdominal surgery in rats when compared to platelet-rich plasma alone. However, the addition of dexamethasone to PRP showed a significant reduction in adhesions compared to the control group.

Acknowledgments

The authors would like to thank members of Surgery Division, Veterinary Hospital, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Iran.

Conflict of Interest

The authors declare that they have no competing interests.

References

1. Fatehi Hassanabad A, Zarzycki AN, Jeon K, Dundas JA, Vasanthan V, Deniset JF, Fedak PW. Prevention of post-operative adhesions: A comprehensive review of present and emerging strategies. *Biomolecules*. 2021; 11(7): 1027. doi: 10.3390/biom11071027
2. Ward BC, Panitch A. Abdominal adhesions: current and novel therapies. *Journal of Surgical Research*. 2011; 165(1): 91-111. doi: 10.1016/j.jss.2009.09.015
3. Stommel MW, Ten Broek RP, Strik C, Slooter GD, Verhoef C,

Grünhagen DJ, van Duijvendijk P, Bemelmans MH, den Dulk M, Sietses C, Van Heek TN. Multicenter observational study of adhesion formation after open-and laparoscopic surgery for colorectal cancer. *Annals of Surgery*. 2018; 267(4): 743-748. doi: 10.1097/SLA.0000000000002175
4. Schnüriger B, Barmparas G, Branco BC, Lustenberger T, Inaba K, Demetriades D. Prevention of postoperative peritoneal adhesions: A review of the literature. *American Journal of Surgery*. 2011; 201(1): 111-121. doi: 10.1016/j.amjsurg.2010.02.008
5. Holmdahl L, Ivarsson ML. The role of cytokines, coagulation, and fibrinolysis in peritoneal tissue repair. *European Journal of Surgery*. 1999; 165(11): 1012-1019. doi: 10.1080/110241599750007810
6. Reed KL, Fruin AB, Bishop-Bartolomei KK, Gower AC, Nicolaou M, Stucchi AF, Leeman SE, Becker JM. Neurokinin-1 receptor and substance P messenger RNA levels increase during intra-abdominal adhesion formation. *Journal of Surgical Research*. 2002; 108(1): 165-172. doi: 10.1006/jsre.2002.6533
7. Cheong YC, Shelton JB, Laird SM, Richmond M, Kudesia G, Li TC, Ledger WL. IL-1, IL-6 and TNF-α concentrations in the peritoneal fluid of women with pelvic adhesions. *Human Reproduction*. 2002; 17(1): 69-75. doi: 10.1093/humrep/17.1.69
8. Sulaiman H, Dawson L, Laurent GJ, Bellingan GJ, Herrick SE. Role of plasminogen activators in peritoneal adhesion formation. *Biochemical Society Transactions*. 2002; 30(2): 126-131.
9. De Wilde RL, Devassy R, Broek RP, Miller CE, Adlan A, Aquino P, Becker S, Darmawan F, Gergolet M, Habana MA, Khoo CK. The future of adhesion prophylaxis trials in abdominal surgery: an expert global consensus. *Journal of Clinical Medicine*. 2022; 11(6): 1476. doi: 10.3390/jcm11061476
10. Gumán-Valdivia-Gómez G, Tena-Betancourt E, de Alva-Coria PM. Postoperative abdominal adhesions: pathogenesis and current preventive techniques. *World Journal of Surgery and Surgical Research*. 2019; 1: 1008. doi: 10.24875/ciru.18000511
11. Chen CH, Chen SH, Mao SH, Tsai MJ, Chou PY, Liao CH, Chen JP. Injectable thermosensitive hydrogel containing hyaluronic acid and chitosan as a barrier for prevention of postoperative peritoneal adhesion. *Carbohydrate Polymers*. 2017; 173: 721-731. doi: 10.1016/j.carbpol.2017.06.019
12. Wang XC, Gui CQ, Zheng QS. Combined therapy of allantoin, metronidazole, dexamethasone on the prevention of intra-abdominal adhesion in dogs and its quantitative analysis. *World Journal of Gastroenterology*. 2003; 9(3): 568. doi: 10.3748/wjg.v9.i3.568
13. Reijnen MMPJ, Bleichrodt RP, Van Goor H. Pathophysiology of intra-abdominal adhesion and abscess formation, and the effect of hyaluronan. *Journal of British Surgery*. 2003; 90(5): 533-541. doi: 10.1002/bjs.4141
14. Schindler AE. Gonadotropin-releasing hormone agonists for prevention of postoperative adhesions: an overview. *Gynecological Endocrinology*. 2004; 19(1): 51-55. doi: 10.1080/09513590410001725495
15. Aldemir M, Öztürk H, Büyükbayram H, Erten G. The preventive effect of Rofecoxib in postoperative intraperitoneal adhesions. *Acta Chirurgica Belgica*. 2004; 104(1): 97-100. doi: 10.1080/00015458.2003.11978403
16. Parsaei P, Karimi M, Asadi SY, Rafieian-Kopaei M. Bioactive components and preventive effect of green tea (*Camellia sinensis*) extract on post-laparotomy intra-abdominal adhesion in rats. *International Journal of Surgery*. 2013; 11(9): 811-815. doi: 10.1016/j.ijsu.2013.08.014
17. Fernández-Barbero JE, Galindo-Moreno P, Ávila-Ortiz G, Caba O, Sánchez-Fernández E, Wang HL. Flow cytometric and morphological characterization of platelet-rich plasma gel. *Clinical Oral Implants Research*. 2006; 17(6): 687-693. doi: 10.1111/j.1600-0501.2006.01179.x
18. Yamaguchi R, Terashima H, Yoneyama S, Tadano S, Ohkohchi N. Effects of platelet-rich plasma on intestinal anastomotic healing in rats: PRP concentration is a key factor. *Journal of Surgical Research*. 2012; 173(2): 258-266. doi: 10.1016/j.jss.2010.10.001
19. Makarchian HR, Kasraianfard A, Ghaderzadeh P, Javadi SMR, Ghorbanpoor M. The effectiveness of heparin, platelet-rich plasma (PRP), and silver nanoparticles on prevention of postoperative peritoneal adhesion formation in rats. *Acta Cirurgica Brasileira*. 2017; 32: 22-27. doi: 10.1590/s0102-865020170103
20. Stratakis K, Arkoumanis T, Liakea A, Nikiteas N, Zargaran D, Zargaran A, Kontzoglou K, Kyriakopoulou P, Perrea D. Platelet-rich plasma gel versus hyaluronic acid on prevention of peritoneal abdominal adhesion formation in rats. *Chirurgia (Bucur)*. 2022; 117(5): 585. doi: 10.21614/chirurgia.2737
21. Syahputra DA, Mashudy A. The effect of addition of dexamethasone into normal saline irrigation solution on prevention of intraperitoneal adhesion post laparotomy in Wistar rats (*Rattus norvegicus*). *Annals of Medicine and Surgery*. 2020; 59: 57-63. doi: 10.1016/j.amsu.2020.08.053
22. P, Takhtfooladi MA, Jahanshahi A, Sotoudeh A. Effects of dexamethasone, piroxicam, and sterile *aloe vera* extract on the prevention of postoperative peritoneal adhesion formation in rat. *Advances in Environmental Biology*. 2012; 6: 2851-2865.
23. Zarin M, Karbalaei N, Keshtgar S, Nemati M. Platelet-rich plasma improves impaired glucose hemostasis, disrupted insulin secretion, and pancreatic oxidative stress in streptozotocin-induced diabetic rat. *Growth Factors*. 2019; 226-237. doi: 10.1080/08977194.2020.1735382
24. Avsar FM, Sahin M, Aksoy F, Avsar AF, Aköz M, Hengirmen S, Bilici S. Effects of diphenhydramine HCl and methylprednisolone in the prevention of abdominal adhesions. *American Journal of Surgery*. 2001; 181(6): 512-515. doi: 10.1016/s0002-9610(01)00617-1
25. Lin LX, Yuan F, Zhang HH, Liao NN, Luo JW, Sun YL. Evaluation of surgical anti-adhesion products to reduce postsurgical intra-abdominal adhesion formation in a rat model. *PLoS One*. 2017; 12(2). doi: 10.1371/journal.pone.0172088
26. Morshedi M, Bahramifar A, Nabizadeh A. Comparison of the effects of atorvastatin, hyaluronic acid and oxidized cellulose (Interceed) on reducing intestinal adhesions postoperative after open abdominal surgery in animal models: effects of atorvastatin, hyaluronic acid and oxidized cellulose on intestinal adhesions. *Iranian Journal of Pharmaceutical Sciences*. 2019; 15(3): 81-90. doi: 10.22037/ijps.v15.40495
27. Tabibian N, Swehli E, Boyd A, Umbreen A, Tabibian JH. Abdominal adhesions: a practical review of an often overlooked entity. *Annals of Medicine And Surgery*. 2017; 15: 9-13. doi: 10.1016/j.amsu.2017.01.021
28. Holmdahl L, Risberg B, Beck D. Adhesions: pathogenesis and prevention–panel discussion and summary. *European Journal of Surgery*. 1997 1(577):56-62.
29. DiZerega GS. Peritoneum, peritoneal healing, and adhesion formation. In: *Peritoneal Surgery*. New York, NY: Springer New York; 2000; 3-37.
30. Attard JAP, MacLean AR. Adhesive small bowel obstruction: epidemiology, biology and prevention. *Canadian Journal of Surgery*. 2007; 50(4): 291.
31. Tang CL, Jayne DG, Seow-Choen F, Ng YY, Eu KW, Mustapha N. A randomized controlled trial of 0.5% ferric hyaluronate gel (Intergel) in the prevention of adhesions following abdominal surgery. *Annals of Surgery*. 2006; 449-455. doi: 10.1097/01.sla.0000207837.71831.a2

32. Arung W, Meurisse M, Detry O. Pathophysiology and prevention of postoperative peritoneal adhesions. *World Journal of Gastroenterology*. 2011; 17(41): 4545. doi: 10.3748/wjg.v17.i41.4545
33. Mariano RS, Uscategui RA, Nociti RP, Santos VJ, Padilha-Nakaghi LC, Barros FF, Silva MA, Malta CA, Bonato DV, Vicente WR, Teixeira PP. Intraperitoneal lidocaine hydrochloride for prevention of intraperitoneal adhesions following laparoscopic genitourinary tract surgery in ewes. *Veterinární Medicína*. 2015; 60(8): 403-406. doi: 10.17221/8414-VETMED
34. Sui J, Noubouossie DF, Gandotra S, Cao L. Elevated plasma fibrinogen is associated with excessive inflammation and disease severity in COVID-19 patients. *Frontiers in Cellular and Infection Microbiology*. 2021: 11: 734005. doi: 10.3389/fcimb.2021.734005