VIA MEDICA
ORIGINAL PAPER / GYNECOLOGY
Ginekologia Polska
2019, vol. 90, no. 9, 507–512

ISSN 0017–0011
DOI: 10.5603/GP.2019.0088

A comparison in an experimental rat model of the effects on adhesion formation of different hemostatic methods used in abdominopelvic surgery

Erkan Mavigök[1], Murat Bakacak[2], Fatih Mehmet Yazar[3], Zeyneb Bakacak[4], Aslı Yaylalı[5], Ömer Faruk Boran[6], Abdülkadir Yasir Bahar[7]

[1]Department of Obstetrics and Gynecology, Birecik State Hospital, Şanlıurfa, Turkey
[2]Department of Obstetrics and Gynecology, Kahramanmaraş Sütçü İmam University, School of Medicine, Turkey
[3]Department of General Surgery, Kahramanmaraş Sütçü İmam University, School of Medicine, Turkey
[4]Private Clinic, Kahramanmaraş, Turkey
[5]Department of Histology and Embriyology, Kahramanmaraş Sütçü İmam University, School of Medicine, Turkey
[6]Department of Anesthesiology and Reanimation, Kahramanmaraş Sütçü İmam University, School of Medicine, Turkey
[7]Department of Pathology, Kahramanmaraş Sütçü İmam University, School of Medicine, Turkey

ABSTRACT

Objectives: To evaluate the effects of different hemostasis methods used in abdominal surgery on the development of abdominal adhesion.

Material and methods: A total of 48 Wistar albino female rats were separated into six groups; Group 1 — Control group, Group 2 — Hemorrhage group, Group 3 — Electrocoautery group, Group 4 — Gel Spon-P®, Group 5 — PAHACEL®, and Group 6 — Ankaferd-Blood Stopper®. Adhesions that developed were scored according to the Knightly classification and the prevalence of adhesions according to the Linsky classification. The total adhesion score was calculated as the total of the severity and prevalence scores.

Results: The lowest total adhesion values were determined in Group 1 (control) and the highest adhesion values were in Group 2 (hemorrhage) group in terms of all parameters. The adhesion values in Group 3, where the rats were administered hemostasis with electrocautery were similar to those of Group 2 (hemorrhage). When the alternative methods were evaluated, the lowest adhesion scores were in Group 6 (Ankaferd-Blood Stopper®).

Conclusions: In cases of minor pelvic or abdominal bleeding, not providing hemostasis or applying hemostasis with electrocautery can increase the development of intra-abdominal adhesions. The use of alternative hemostatic materials instead of electrocautery for hemostasis may reduce the formation of adhesions.

Key words: intra-abdominal hemorrhage; abdominal adhesion; hemostatic agents; pelvic surgery; hemostasis

Ginekologia Polska 2019; 90, 9: 507–512

INTRODUCTION

Post operative adhesions may develop following any abdominal surgical procedure as a response to all foreign bodies in direct contact with the peritoneum, such as powder or sutures, or as an abnormal response of the organism to minor or major bleeding. Both minor and major intra-abdominal bleeding can cause significant morbidity and mortality in patients postoperatively. To avoid this, it is imperative that careful hemostasis is obtained during surgical procedures.

Various methods are used to prevent post operative bleeding, such as mechanical or thermal devices and topical hemostatic agents. Each technique has advantages and disadvantages. Minor bleeds are often seen in the post operative period, but generally can not be determined. Although this does not cause hemodynamic impairment, it does cause the collection and activation of thrombocytes in the peritoneal area and the accumulation of fibrinogen [1, 2].

Fibrinogen and thrombin interact to create fibrin monomers then polymers. When these fibrin polymers are not

Corresponding author:
Murat Bakacak
Kahramanmaraş Sütçü İmam University, School of Medicine, Department of Histology and Embriology, Kahramanmaraş, Turkey
muratbakacak46@gmail.com

removed from the region, they combine with coagulation factors such as Factor VIII, becoming insoluble, and create a fibrin gel matrix [2, 3]. Then, as a result of fibrin polymers combining with leukocytes, erythrocytes, thrombocytes, mast cells and other cells, the development of adhesions is caused with a fibrin gel matrix between two serosal surfaces [4].

The adhesions that develop restrict intestine movements post operatively and diminish qualty of life [2–4]. Various blood-stopping methods and materials are used to prevent bleeding [5–12]. Although the effects on adhesion development of some of these agents have been evaluated in literature, to the best of our knowledge, there has been no previous study that has collectively and comprehensively compared hemostatic agents with different mechanisms in respect of the inflammatory response and the later emergence of adhesions that have formed.

Objectives

Considering that it was necessary to evaluate the potential of hemostatic material to form abdominal adhesions and to determine which material formed the least adhesions, the aim of this study was to evaluate the effects on adhesion development of blood-stopping materials frequently used during surgical procedures.

MATERIAL AND METHODS

Approval for the current study was granted by the Local EthicsCommittee (decision no: 14.03.2017/02). The study was conducted in the Experimental Animals Reproduction and Research Center of Kahramanmaraş Sütçü Imam University in conformity with the principles of the National Institutes of Health Guide for the Care and Use of Laboratory Animals.

A total of 48 female adult Wistar albino rats, each weighing 300–350 g were used in the study. The animals were acclimatised to the laboratory conditions for one week before the experiment, at a temperature of 22 ± 2°C, and fed with Standard rodent food (SPRF) (Purina®). At 12 hours before the experiment, food was withdrawn but free Access to drinking water was continued. All the surgical procedures were conducted in the morning between 08.00 and 11.00.

The rats were randomly separated into 6 groups of 8, as follows:

- Group 1: Control group (n: 8),
- Group 2: Hemorrhage group (n: 8),
- Group 3: Electrocautery group (n: 8),
- Group 4: GelSpon-P® group (n: 8),
- Group 5: PAHACEL® group (n: 8),
- Group 6: Ankaferd-Blood Stopper® group (n: 8).

In the first operation, general anaesthesia for the surgical procedure was applied to all rats with an intramuscular injection of 50 mg/kg ketamine hydrochloride (Ketalar; Eczacibasi, Istanbul, Turkey) and 10 mg/kg xylazine hydrochloride (Rompun; Bayer Türk Ilaç Ltd., Istanbul, Turkey). When a sufficient depth of anaesthesia was obtained, the abdomen of each rat was shaved and cleaned with povidone iodine. The abdomen was entered with a midline incision and the uterus was visualised (Fig. 1A).

After making the abdominal incision, the rats in Group 1 were applied with 2cc saline into the abdomen and the abdomen was left open for 1 min (Fig. 1B). All the rats in all the other groups were traumatised using a no. 15 scalpel starting from the uterus bifurcation until petechial bleeding was observed macroscopically in a 1 cm serosa segment in both horns (Fig. 1C). The following procedures were then applied to the study groups. To Group 2, no coagulation procedure was applied (Fig. 1D). To Group 3, cauterisation was applied for a maximum of 5 seconds at 10 watt power until sufficient coagulation was obtained, using a manually controlled monopolar cautery, disposable high-temperature cautery device [low-temp fine tip 2200°F (1204°C)] (5115 Ulmerton Road Clearwater, Florida 33760 USA) (Fig. 1E).

To Group 4, a 2 × 1 cm absorbable hemostatic gelatine sponge (GelSpon-P®) (Eucare Pharmaceuticals Limited, Plot No. AC-25B, SIDCO Industrial Estate, Thirumudivakkam, Chennai-600 044. India) was placed over the incision (Fig. 1F). To Group 5, a 2 × 1 cm absorbable hemostatic oxidized regenerated cellulose patch (PAHACEL®) (Altaylar Medikal

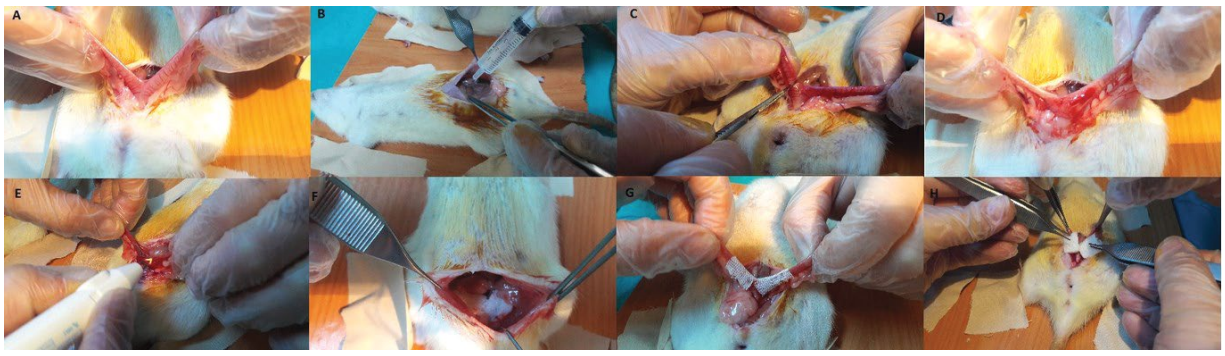

Figure 1. Operations applied to the study groups

Tıbbi Malz. İnş. Teks. Gıda İth. İhr San ve Tic. Ltd. Şti ATB İş Merk. No: 222 Yenimahalle, Ankara, Turkey) was placed over the incision (Fig. 1G). To Group 6, a 2 × 1 cm wet pad blood stoper (Ankaferd-Blood Stopper®) (İmmun Gıda İlaç Kozmetik San. Ve Tic. Ltd. Şti. Kireçburnu Cd. Raifbey Sk. No: 8/A Kireçburnu Sarıyer/Istanbul, Turkey) was placed over the incision and when hemostasis was obtained, was removed from the abdomen (Fig. 1H).

In all the rats, the abdominal wall was then closed with 3-0 silk sutures and the operations were completed. On the 14th day, decapitation was applied and the development of adhesions was examined with second-look laparotomy using the same incision. The adhesion scoring was applied according to the Knightly classification [13] for adhesion severity and according to the Linsky classification [14] for adhesion prevalence. A total adhesion score was obtained from the total of these verity and prevalence scores. The histopathological evaluation of adhesions was applied using the Zühlke microscopic adhesion classification system [15].

Data obtained in the study were analysed statistically using IBM SPSS for Windows, version 22.0 software (IBM statistics for Windows version 22, IBM Corporation, Armonk, NY, USA). Data were presented as mean ± standard deviation (SD). Variance analysis (Repeated measures ANOVA with Bonferroni correction) was applied to repeated measurements. In the comparisons of paired groups, the Tukey HSD method was used. A value of $p < 0.05$ was accepted as statistically significant.

RESULTS

The adhesion severity score was determined to be statistically significantly higher in all the study groups than in the control group ($p < 0.01$). No statistically significant difference was determined between Group 2 and Group 3 in respect of the severity score ($p = 0.994$). A statistically significant difference was determined between the severity scores of the groups where hemostatic agents were used (Group 4, Group 5, Group 6) and those of Group 1, Group 2, and Group 3 ($p < 0.01$ for all). The lowest adhesion severity score of the groups where hemostatic agents were used was determined in Group 6, but no significant difference was determined between these groups ($p > 0.05$) (Tab. 1) (Fig. 2A).

No statistically significant difference was determined between the groups where hemostatic agents were used in respect of the adhesion prevalence scores ($p > 0.05$ for all). Compared to the control group, the adhesion prevalence scores were determined to be statistically significantly higher in all the study groups ($p < 0.01$ for all). No significant difference was determined between Group 2 and Group 3 in respect of adhesion prevalence scores ($p = 0.915$). Compared to Group 2 and Group 3, the adhesion prevalence scores of the groups where hemostatic agents were used were statistically significantly higher ($p < 0.01$ for all) (Tab. 1) (Fig. 2B).

According to the Zühlke histological scoring system, the values of all the study groups were statistically significantly higher than those of the control group ($p < 0.01$ for all). In the evaluation of all the adhesion groups, no statistically significant difference was seen ($p > 0.05$). The results are shown in Table 1 and Figure 2C. The fibrosis and inflammation scores are shown in Table 1.

DISCUSSION

The results of the current study demonstrated that the lowest adhesion values were seen in Group 1, as expected. The highest adhesion values in respect of all the parameters were determined in the hemorrhage group. In the rats applied with hemostasis with electrocautery, the adhesion values were seen to be similar to those of the hemorrhage group. When the alternative methods were evaluated, the lowest adhesion values were determined in the Ankaferd Blood Stopper group.

The development of post operative adhesions starts on days 5–7 following the surgical procedure [16], and therefore, it is most appropriate for evaluation to be made after-day 7 [5]. In the current study, adhesions were evaluated on post operative day 14.

One mechanism in the formation of adhesions is the inflammatory response associated with increased leukocytes and insufficient tissue oxygenation caused by metabolites

Table 1. Comparison of the adhesion severity, adhesion prevalence, Zuhlke histology, fibrosis and inflammation scores of the groups

	Group 1 (n: 8)	Group 2 (n: 8)	Group 3 (n: 8)	Group 4 (n: 8)	Group 5 (n: 8)	Group 6 (n: 8)
Adhesions everity score	0.25 ± 0.462	3.87 ± 0.353[b]	3.75 ± 0.462[b]	2.62 ± 0.517[b-d-f]	2.75 ± 0.462[b-d-f]	2.50 ± 0.534[b-d-f]
Adhesion prevalence score	0.25 ± 0.462	3.75 ± 0.462[b]	3.50 ± 0.534[b]	2.50 ± 0.534[b-d-f]	2.75 ± 0.462[b-d-e]	2.50 ± 0.534[b-d-f]
Zuhlke Histological score	0.5 ± 0.534	2.50 ± 0.755[b]	2.37 ± 0.517[b]	1.50 ± 0.534[b-c-e]	1.62 ± 0.517[b-c]	1.37 ± 0.517[a-d-e]
Fibrosis score	0.25 ± 0.462	2.75 ± 0.707[b]	2.25 ± 0.462[b]	1.37 ± 0.517[b-d-e]	1.87 ± 0.640[b-c]	1.25 ± 0.462[b-d-f]
Inflammation score	0.37 ± 0.517	2.87 ± 0.640[b]	2.75 ± 0.886[b]	1.62 ± 0.744[b-d-e]	1.62 ± 0.517[b-d-e]	1.37 ± 0.517[a-d-e]

[a] — $p < 0.05$difference between the group and the control group; [b] — $p < 0.01$ difference between the group and the controlgroup; [c] — $p < 0.05$ difference between the group and the hemorrhage group; [d] — $p < 0.01$ difference between the group and the hemorrhage group; [e] — $p < 0.05$ difference between the group and the electrocautery group; [f] — $p < 0.01$ difference between the group and the electrocautery group

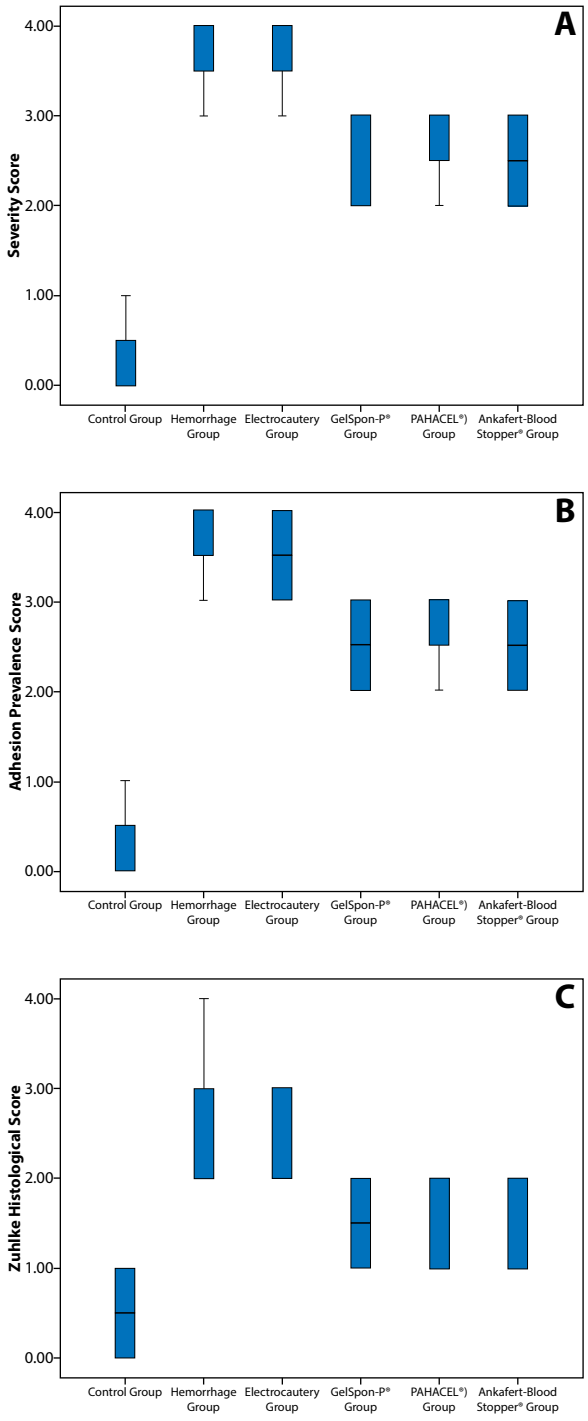

Figure 2. Comparison graph of the adhesion severity, adhesion prevalence, and Zuhlke histology scores of the group

of free oxygen radicals [6]. The high levels of free oxygen radicals that emerge cause an increase in vascular permeability, trigger the formation of exudate, and cause fibrosis. In a study by Pellicano M et al. [7], which compared sutures and electrocautery used for hemostasis, the abdominal adhesions in the subjects applied with electrocautery were seen to have formed at a statistically significantly higher level. Wallwiener CW [8] reported that deep electrocoagulation increased the development of abdominal adhesions compared to superficial electrocoagulation. Therefore, in the current study, the hemostasis method with deep electrocautery was used as a control group, as this has been shown in previous studies to be a model causing widespread abdominal adhesions.

The other control group in the current study was the hemorrhage group. The basic approach in forming this group was to evaluate the effect of bleeding on fibrosis development and to be able to more clearly evaluate the benefit of using blood stopping agents. The results of the current study showed that the most significant fibrosis values occurred in the hemorrhage group in respect of both the scoring systems and the histopathological evaluation results, and the development of fibrosis in the electrocautery group was seen to be similar to that of the hemorrhage group.

Ankaferd Blood Stopper® (ABS) is a plant-origin topical hemostatic agent, which has started to be used in recent years. It helps the formation of a fibrin gel matrix in the bleeding area. Recent studies have emphasized that ABS has antiinflammatory and antineoplastic features, decreases the development of tissue necrosis and the potential for the development of foreign body reaction is minimal [17–19]. Conflicting results have been reported in studies evaluating the effects of ABS on the development of adhesions. In an experimental rat study by Cömert et al, the effect of the abdominal application of a single-dose of ABS was evaluated, with one group applied with saline to the open abdomen, two groups were applied with ABS to uterine and peritoneal injuries, and one group was not applied with any treatment to uterine and peritoneal injuries. The adhesions in the subjects applied with ABS were reported to be at a significantly lower rate than those that were not treated [9].

In an other study that evaluated the effect of ABS and calcium alginate on the development of peritoneal adhesions, there was reported to be less development of adhesions in rats applied with ABS [10]. In a liver laceration model in rats, Akarsu et al reported that similar effects were seen from saline and ABS in respect of the histopathological effects on intra-abdominal adhesion formation [11]. In the current study, with the exception of the control group, the lowest values in respect of all the parameters were seen to be in the rats applied with ABS. When the Zühlke histological scoring results and the inflammation values were compared with those of the control group applied with saline, the results were statistically significantly different but the level of significance was seen to be weak ($p = 0.040$, $p = 0.041$, respectively).

The other alternative agent used in this study to stop intra-abdominal bleeding was a gelatine sponge (GelSpon-P®). This is made from a gelatine-based material such as colla-

gen, and is in the form of a hard, porous sponge in various sizes. It can absorb blood up to 45 times its own weight because of the porous structure. The hemostatic effect occurs by allowing thrombocytes to adhere to the smooth porous structure [20]. However, it has been reported that an inflammatory response occurs during the absorption process, and the absorption of a gelatine sponge placed in the subdural area of rabbits was reported to cause granulomatous inflammation [12].

In the current study, the rats applied with gelatine sponge were determined to have developed adhesions at a significantly high rate compared to the control group. However, the level of adhesions was significantly lower compared to Groups 2 and 3 (Tab. 1). When the alternative treatment methods were compared with each other, the adhesion values in Group 4 were higher than in Group 6, and lower than in Group 5, but no statistically significant difference was determined between these groups ($p > 0.05$).

Surgicel absorbable hemostat is a material made from oxidised regenerated cellulose, the main component of which is poly anhydro glucoronic acid. Woven in the form of threads, it is prepared to resemble gauze. As it has a pH of 3, when compared with a substance such as thrombin, it destroys that substance. By swelling when in contact with blood, it adheres to blood vesels and wound edges. Thus, the clots that form provide hemostasis within 2–3 mins [21]. In a study by Günay et al. [22], Surgicel and quercetin were used in an experimental abdominal adhesion model, and the highest inflammation and fibrosis values were determined in the Surgicel group, and were reported to be significantly lower than the results of the control group. Ateş et al. [23] compared Interceed and double layer Surgicel, and reported that compared to the control group, adhesions in the study groups were significantly reduced. In the current study, consistent with previous findings in literature, although the adhesion values of the Pahacel group were significantly lower than those of the hemorrhage group and the electrocautery group, in the comparison with the gelatine sponge and ABS groups, the highest adhesion values were determined in the Pahacel group.

That this was an experimental study conducted on rats was the most significant limitation. However, it was not possible to conduct a study of this design on humans, but as this is the first study to compare the effect on adhesion development of blood stopping agents commonly used in humans, this is a step in a positive direction.

CONCLUSIONS

In conclusion, the results of this study showed the effect of minor abdominal bleeding on adhesion development and that according to objective criteria, it is necessary to apply hemostasis in these types of bleeds. In accordance with previous findings in literature, adhesions developing as a result of hemostasis applied with electrocautery were determined to be similar to the group where no hemostasis was applied. In addition, adhesions were observed at a statistically significantly lower rate in the alternative hemostasis method groups of Gel Spon-P®, Pahacel®, Ankafert-Blood Stopper® compared to the groups where no hemostasis was applied and the group applied with hemostasis with electrocautery. Thus, it was determined that in patients requiring hemostasis, alternative treatment methods should be preferred rather than electrocautery.

In cases with minor pelvic or abdominal bleeding, not applying hemostasis or applying hemostasis with electrocautery can increase the development of intra-abdominal adhesions. The use of alternative hemostatic materials instead of electrocautery for hemostasis can reduce the formation of adhesions.

REFERENCES

1. Boland GM, Weigel RJ. Formation and prevention of postoperative abdominal adhesions. J Surg Res. 2006; 132(1): 3–12, doi: 10.1016/j.jss.2005.12.002, indexed in Pubmed: 16457846.
2. Arung W, Meurisse M, Detry O. Pathophysiology and prevention of postoperative peritoneal adhesions. World J Gastroenterol. 2011; 17(41): 4545–4553, doi: 10.3748/wjg.v17.i41.4545, indexed in Pubmed: 22147959.
3. Ward BC, Panitch A. Abdominal adhesions: current and novel therapies. J Surg Res. 2011; 165(1): 91–111, doi: 10.1016/j.jss.2009.09.015, indexed in Pubmed: 20036389.
4. Kamel RM. Prevention of postoperative peritoneal adhesions. Eur J Obstet Gynecol Reprod Biol. 2010; 150(2): 111–118, doi: 10.1016/j.ejogrb.2010.02.003, indexed in Pubmed: 20382467.
5. Karaca G, Aydin O, Pehlivanli F, et al. Effect of ankaferd blood stopper in experimental peritoneal adhesion model. Ann Surg Treat Res. 2016; 90(4): 213–217, doi: 10.4174/astr.2016.90.4.213, indexed in Pubmed: 27073792.
6. ten Broek RPG, Wilbers J, van Goor H. Electrocautery causes more ischemic peritoneal tissue damage than ultrasonic dissection. Surg Endosc. 2011; 25(6): 1827–1834, doi: 10.1007/s00464-010-1474-3, indexed in Pubmed: 21140171.
7. Pellicano M, Bramante S, Guida M, et al. Ovarian endometrioma: postoperative adhesions following bipolar coagulation and suture. Fertil Steril. 2008; 89(4): 796–799, doi: 10.1016/j.fertnstert.2006.11.201, indexed in Pubmed: 17953954.
8. Wallwiener CW, Kraemer B, Wallwiener M, et al. The extent of adhesion induction through electrocoagulation and suturing in an experimental rat study. Fertil Steril. 2010; 93(4): 1040–1044, doi: 10.1016/j.fertnstert.2008.12.002, indexed in Pubmed: 19147134.
9. Cömert M, Karakaya K, Barut F, et al. Does intraabdominal use of Ankaferd Blood Stopper cause increased intraperitoneal adhesions? Ulus Travma Acil Cerrahi Derg. 2010; 16(5): 383–389, indexed in Pubmed: 21038113.
10. Tuncal SD, Kismet K, Kilicoglu B, et al. Evaluation of intraabdominal adhesion generating potentials of ankaferd and calcium alginate used as hemostatic agents. Bratisl Lek Listy. 2014; 115(9): 544–549, indexed in Pubmed: 25318912.
11. Akarsu C, Kalaycı MU, Yavuz E, et al. [Comparison of the hemostatic efficiency of Ankaferd Blood Stopper and fibrin glue on a liver laceration model in rats]. Ulus Travma Acil Cerrahi Derg. 2011; 17(4): 308–312, indexed in Pubmed: 21935827.
12. Barbolt TA, Odin M, Léger M, et al. Pre-clinical subdural tissue reaction and absorption study of absorbable hemostatic devices. Neurol Res. 2001; 23(5): 537–542, doi: 10.1179/016164101101198794, indexed in Pubmed: 11474811.
13. KNIGHTLY JJ, AGOSTINO D, CLIFFTON EE. The effect of fibrinolysin and heparin on the formation of peritoneal adhesions. Surgery. 1962; 52: 250–258, indexed in Pubmed: 14457251.

14. Linsky CB, Diamond MP, Cunningham T, et al. Adhesion reduction in the rabbit uterine horn model using an absorbable barrier, TC-7. J Reprod Med. 1987; 32(1): 17–20, indexed in Pubmed: 3560059.
15. Zühlke HV, Lorenz EM, Straub EM, et al. [Pathophysiology and classification of adhesions]. Langenbecks Arch Chir Suppl II Verh Dtsch Ges Chir. 1990: 1009–1016, indexed in Pubmed: 1983476.
16. Holmdahl L, al-Jabreen M, Risberg B. Experimental models for quantitative studies on adhesion formation in rats and rabbits. Eur Surg Res. 1994; 26(4): 248–256, doi: 10.1159/000129342, indexed in Pubmed: 7957461.
17. Turhan N, Kurt M, Shorbagi A, et al. Topical Ankaferd Blood Stopper administration to bleeding gastrointestinal carcinomas decreases tumor vascularization. Am J Gastroenterol. 2009; 104(11): 2874–2877, doi: 10.1038/ajg.2009.431, indexed in Pubmed: 19888263.
18. Tasdelen Fisgin N, Tanriverdi Cayci Y, Coban AY, et al. Antimicrobial activity of plant extract Ankaferd Blood Stopper. Fitoterapia. 2009; 80(1): 48–50, doi: 10.1016/j.fitote.2008.09.006, indexed in Pubmed: 18930120.
19. Işler SC, Demircan S, Cakarer S, et al. Effects of folk medicinal plant extract Ankaferd Blood Stopper on early bone healing. J Appl Oral Sci. 2010; 18(4): 409–414, doi: 10.1590/s1678-77572010000400015, indexed in Pubmed: 20835578.
20. Tomizawa Y. Clinical benefits and risk analysis of topical hemostats: a review. J Artif Organs. 2005; 8(3): 137–142, doi: 10.1007/s10047-005-0296-x, indexed in Pubmed: 16235029.
21. Johnson WS, Blanton EE. An evaluation of 9-aminoacridine/Gelfoam to reduce dry socket formation. Oral Surg Oral Med Oral Pathol. 1988; 66(2): 167–170, doi: 10.1016/0030-4220(88)90086-2, indexed in Pubmed: 3174049.
22. Güney G, Kaya C, Oto G, et al. Effects of quercetin and surgicel for preventing adhesions after gynecological surgery: A rat uterine horn model. J Obstet Gynaecol Res. 2017; 43(1): 179–184, doi: 10.1111/jog.13185, indexed in Pubmed: 27943594.
23. Ates U, Ata B, Ortakuz S, et al. Prevention of adhesion formation following ovarian surgery in a standardized animal model: comparative study of Interceed and double layer Surgicell. J Obstet Gynaecol Res. 2008; 34(1): 12–17, doi: 10.1111/j.1447-0756.2007.00684.x, indexed in Pubmed: 18226123.