RESEARCH ARTICLE

Sami Dogan[1]
Mehmet Fuat Cetin[1]
Omer Gunal[2]
Havva Erdem[3]

[1]Duzce University, Medical Faculty, General Surgery Department, Duzce, Turkey
[2]Marmara University, Medical Faculty, General Surgery Department, Istanbul, Turkey
[3]Ordu University, Medical Faculty, Pathology Department, Ordu, Turkey

Corresponding Author:
Mehmet Fuat Cetin
Düzce University Medical Faculty General Surgery Department, Duzce, Turkey
Tel: +90 5056706845
E-mail: mefuce@gmail.com

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konuralptipdergi@duzce.edu.tr
konuralptipdergisi@gmail.com
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Comparing the Effects of Antiadhesıve Materials after Abdominal Surgery

ABSTRACT

Objective: We aimed to evaluate and compare the effects of anti-adhesion materials, Seprafilm, Suprofilm, olive oil, and olive oil containing Vitamin E by measuring tension forces.

Methods: 60 male Wistar-Albino rats were divided into six groups. The front side of the cecum and right abdominal parietal peritoneal wall were abrased. The rats were euthanized on the 14th postoperative day. Adhesions between intestines, omentum, other abdominal organs, cecum, incisionsites, and abdominal anterior wall peritoneum were all evaluated. Adhesion strength was measured with dynamometer. Histopathological evaluations of the adhesion area was performed.

Results: Stage-I (0.43Newton) in Group-I, stage-IV (1.0540N) in Group-II, stage-II (0.6370N) in Group-III, stage-II in Group-IV (0, 5230N), stage-III (0.7620N) in Group-V, stage-IV (1.3560N) in Group-VI, were detected. A significant difference was found between these findings. P = 0.001, (p <0.05). Histopathological examination: It was found that GroupV-VI reduced inflammation, increased collagen production, fibroblastic activity and vascular proliferation.

Conclusions: More objective evaluation can be made by measuring the tension force of the adhesions. Suprafilm can also be effectively used as an antiadhesive, such as Seprafilm. Olive oil and vitamin E require more studies to be used as antiadhesives.

Keywords: Antiadhesive, Tension force, Adhesion, Abdominal surgery, olive oil

Abdominal Cerrahi Sonrası Antiadeziv Maddelerin Etkinliklerinin Karşılaştırılması

ÖZET

Amaç: Gerilme kuvvetlerini ölçerek yapışma önleyici malzemelerin, Seprafilm, Suprofilm, zeytinyağı ve E vitamini içeren zeytinyağının etkilerini değerlendirmeyi ve karşılaştırmayı amaçladık.

Gereç ve Yöntem: 60 adet Wistar-Albino erkek ratları altı gruba ayrıldı. Çekumun ön yüzü tarafı ve sağ alt kadran parietal peritoneal duvarı aşındırıldı. Ratları postoperatif 14. günde ötenazi uygulandı. Bağırsaklar, omentum, diğer abdominal organlar, çekum, insizyonlar ve abdominal ön duvar peritonu arasındaki adezyonlar değerlendirildi. Yapışma mukavemeti dinamometre ile ölçüldü. Adezyon alanının histopatolojik değerlendirmeleri yapıldı.

Bulgular: Grup-I'te evre-I (0,43Newton), Grup-II'de evre-IV (1,0540N), Grup-III'te evre-II (0,6370N), Grup-IV'te evre-II (0, 5230N), Grup-V'te evre-III (0,7620N), Grup-VI'da evre-IV (1,3560N), tespit edildi. Bu bulgular arasında anlamlı fark bulundu. P = 0,001, (p <0,05). Histopatolojik inceleme: GrupV-VI'da inflamasyon azalttığı, kollejen yapımı, fibroblastik aktivite ve damar proliferasyonunu artırtığı bulundu.

Sonuç: Yapışmaların gerilme kuvveti ölçülerek daha objektif bir değerlendirme yapılabilir. Suprafilm; Seprafilm gibi bir yapışma önleyici olarak etkili bir şekilde kullanılabilir. Zeytinyağı ve E vitamini, yapışma önleyici olarak kullana bilmesi için daha fazla çalışmayı gerektirir.

Anahtar Kelimeler: Antiadhesive, Gerilme kuvveti, Adhesion, Abdominal cerrahi, zeytinyağı

INTRODUCTION

Peritoneal adhesions formed between organs or tissues in the abdominal cavity can be defined as abnormal fibrous bands. Postoperative adhesions affect millions of people around the world by leading to serious problems, such as bowel obstruction, difficult reoperative surgery, chronic abdominal and pelvic pain, and female infertility (1). Approximately 19% of patients with previous abdominal surgery are at risk of further unintentional enterotomy. Peritoneal ischemia, aggressive manipulation of the tissues, infection, and inadequate hemostasis were the most common reasons for intraperitoneal adhesion formation (2).

13.86% of rectosigmoid operations, 12.19% of colonic operations, 3.94% of non-colonic intestinal operations, 2.25% of other abdominal regions operations and 1.5% of appendectomized patients need second operations due to mechanical intestinal obstructions (3).

There have been numerous studies performed for the prevention of adhesions. Seprafilm (Genzyme, Cambridge, MA, USA), used in this study, reduces the frequency, extent, and severity of the adhesion after laparotomy as also determined at prospective, randomized, multicenter, and controlled studies (4).

Seprafilm was designed to provide a mechanical barrier to prevent the formation of adhesions after operations. These are components which act as a physical barrier to help prevent adhesion formation (5).

In recent years, another mechanical barrier, Suprafilm (chitin) has also been used in the same way. Chitin is converted to chitosan by de-acytilation. The structure of Chitosan is a polymer composed of glucosamine and N-acetyl-glucosamine monomers connecting with β-1,4 position (6). Chitin decreased the frequency and phase of postoperative peritoneal adhesions in rats (7). It is reported that less intraperitoneal adhesions are occurred and a significant reduction in the incidence and severity of postoperative adhesions is observed in rats exposed to high doses of vitamin E (8).

According to this information, this study was designed to compare the effectiveness of olive oil, which has vitamin E, and two different antiadhesive barriers (Seprafilm and Suprofilm).

MATERIAL AND METHODS

In this experimental study, a total of 60 male Wistar albino rats weighing 250-360 grams were used. The approval was obtained from the Animal Research Ethics Committee at Abant Izzet Baysal University and the experiments were carried at the Laboratory of Animal Experiments which is parterned with the Faculty of Medicine at Duzce University. The principles from the Declaration of Helsinki Rules regarding laboratory animals were strictly applied during the whole study. Rats were fed with standard rat chow and were drinking water normally—creating a life style of a 12-hour light-dark cycle.

The rats were divided into 6 groups as follows:

Group 1: Sham group; did nothing.
Group 2: Control group; adhesion induction with abrasive sandpaper to the anterior wall of abdominal parietal peritoneum and right face of the cecum.
Group 3: Seprafilm placement of 3x3cm in diameter.
Group 4: Suprofilm placement of 3x3cm in diameter.
Group 5: 3cc olive oil administration intraperitoneally.
Group 6: 3cc olive oil with 20mg Vitamin E administration intraperitoneally.

Anesthesia and Surgery: After 12 hours of fasting, the rats were anesthetized with 25 mg/kg ketamine hydrochloride (Ketalar, Pfizer Pharmaceuticals Lmt. Corporation, Istanbul, Turkey) and injected intraperitoneally. After anesthesia, the abdomen was shaved and the skin was washed with povidone-iodine. A 4cm midline laparotomy incision was made, and the adhesion-abrasion model of Günal et al was performed between the cecum and anterior abdominal Wall (9).

The aim of this operation was to create a broad spectrum of adhesion. After making the midline incision, 40 mm of layers were passed; through the abdomen and skin—then the musculo-peritoneal was entered. The cecum segment of the colon was taken out of the abdomen. The cecum and small intestine carefully lie on a wet gas and application of abrasion was performed to the anterior side of the cecum and the right anterior wall of the abdomen. Then, the skin was closed after the replacement of the cecum into the abdomen. Seprafilm in group 3, and Suprofilm in group 4, were put over the abrasion area in 3x3cm diameters. Olive oil in group 5, and olive oil containing vitamin E in group 6, were administered into the abdominal cavity.

All the animals were allowed to resume their diets until the 14th day after the first surgery. The animals were euthanized with an inhalation overdose and ketamine hydrochloride. Then the abdominal wall has opened with an "inverted U" incision and the adhesions were classified according to the staging systems of the Evans model and the adhesion force was measured by the dynamometer (Table 1).

For this purpose, according to the model of Evans, the adhesions were graded by severity scores 0, 1, 2, and 3. In addition, five different regions (surgical wound, a traumatized area of the

anterior wall of the lower right abdomen, omentum, cecum, and omentum-in other organs from the intestines) were examined one by one to see whether adhesions occurred and the complete localization of adhesion of these regions.

Table 1. Staging of adhesions by tension forces

Stage 0: No adhesions
Stage 1: leaving of adhesion with low tension force between 0-0.44 N
Stage 2: leaving of adhesion with tension force between 0.45-0.74 N
Stage 3: leaving of adhesion with high tension force between 0.74-1.04 N (needed partial dissection)
Stage 4: leaving of adhesion with tension force higher than 1.05 N (needed dissection)

Evaluation of Adhesions: A model of intra-abdominal adhesions after surgery was divided into five types:

a- adhesion of intestines and omentum to the abdominal incision.

b- adhesion of intestines and omentum to the traumatized anterior abdominal wall.

c-omentum adhesions to the cecum.

d-omentum adhesions to other organs.

e-adhesions between the intestines.

The distribution of types of adhesions was examined in all groups. The evaluation was based on average breaking strength. We created a staging of adhesions by measuring the tensile forces. This measurement was made with the help of the device from Sundoo instruments; a model SH-100 digital force gauge. Once I installed stand dynamometer, the measurements were performed digitally. For these measurements, a complete block of adhered tissue was removed. The tissue hung out with 2/0 vicry to the end of the apparatus of the dynamometer. After fixation of adhesion, tissue formed on both sides the digital indicator and was followed by turning the dynamometer force arm. The largest tensile strength was noted. This way, the force was measured.

Our evaluation as a method that was not performed previously at the literature, the tensile strength, was done qualitatively like below:

Histopathological Evaluation: For the histopathological examination, 2-3 cm^2 surface of the front wall of the cecum and adhesions on it were excised and the specimens were fixed in 10% buffered formalin containers. After dehydration, the classic laboratory method, the specimens were embedded into paraffin block, five micrometer thick sections were stained with hematoxylin-eosin and they were examined by light microscopy. The specimens were investigated by the pathologis who did not know what each group received. The histopathological evaluation was graded with the criteria shown in table 6 below:

Statistical Analysis: For statistical analysis, the SPSS version 15.0 (SPSS Inc., Chicago, IL) statistical software package was used. To test the forces of attraction between the two groups, the One-way ANOVA test was used for comparison. To find out which group is different between the two groups, the LSD test of post hoc tests was used and significant differences were interpreted. Between the groups, Pearson's Chi-Square test was used to compare all parameters. The data mean (μ) and the standard deviation (mean ± SD) were carried out. The statistical significance at $P < 0\ 05$ was adopted.

RESULTS

Evaluation According To the Adhesion Frequency: The adhesion at the incision site was different between the groups.

All other groups had fewer adhesions than the control group. This was not statistically significant. Group 5 and 6 had the same number of adhesions n:3 (30%). Group 4 had a fewer number of adhesions than the control group n:2 (20%). Adhesion to the incision site was not seen in group 3 and the sham group.

In the area of the traumatized anterior abdominal wall, adhesions in all groups were lower than the control group—except group 6. The control group adhesion ratio was 50%. 80% of group 3 and group 4 had no investigated adhesions. The adhesion ratio for group 5 was significantly lower than the control group (40%), and group 6 had more adhesions than the control group (70%).

The omentum adhesion ratio in all groups to the cecum was also close, or the same, and at times even more than the control group (90%). So, it was detected that none of the antiadhesive materials prevent adhesions. The Suprofilm group had the lowest adhesion ratio (60%).

Adhesion between the intestines was significantly less in all groups than the control group. In the olive oil + vitamin E group and in the Suprofilm group, adhesions never happened. In group 5, one adhesion (10%) and in group 3, two adhesions (20%) were observed. That was also found to be statistically significant.

Evaluation of Adhesions According To the Staging Frequency of the Rupture Forces: Group 1 was excluded from the study because only one rat, including all subgroups, had adhesions.

This evaluation method has never been done before. The incidence of the adhesion stage according to breaking strength was measured. All groups compared to the adhesion tensile strength, easy to leave (stage I) and less strongly allocated (stage II). The incision site adhesions were allocated under a force of 0.74 N. The traumatized area of the anterior abdominal wall adhesions and breaking tensile strength in group 5 and 6 were

higher than the control group. Adhesions in these groups strongly needed dissection, over 1.05N (stage 4). It means that group 5 and 6 did not prevent the adhesion formation and the increasing tensile strength. Groups 3 and 4 were close to each other.

The omentum adhesion force to the cecum was less than the control group in all groups (stage II: 0 45-0.74 N) and that has been found to be statistically significant.

Likewise, similar results were found in the tensile adhesion strength of the omentum to the other organs.

In the staging of breaking strength of adhesions between the omentum to other organs, half of those adhesions were at stage I (0-0.44 N easily separated). The tensile strength of adhesion did not occur in the control group so it was decided that it was an inappropriate evolution. It wasn't found to be statistically significant.

The staging of adhesions breaking strength between the intestines was statistically significantly lower than the control group. More than 60% of adhesion was between stage I-II (under 0.74). It means that antiadhesive substances decreased the tensile strength of adhesions between the intestines.

Statistical Evaluation of Average Adhesion Tensile Forces: Including all types, in group 1 only one rat had adhesion. In the sham group, the adhesion tensile strength, according to the average variation within groups, was high and it was expected to close the gap between the groups so the sham group was statistically excluded from the study. The other five groups were evaluated. In group 2 stage 4 (1.0540 N) adhesion, in group 3 stage 2 (0.6370 N) adhesion, in group 4 stage 2 (0.5230 N) adhesion, group 5 stage 3 (0.7620 N) adhesion, and group 6 stage 3 (1.3560 N) adhesion were determined. That was statistically significant between the average forces. (P = 0.001)

As seen in Table 2, with the evaluation of the adhesion breaking strength mean and standard deviation, there was a statistically significant difference between the control group, group 3, and group 4. (P = 0.001)

In group 6, the higher tensile strength was determined in comparison to groups 2, 3, 4, and 5.

Accordingly, compared to the control group in terms of tensile strength, there was a statistically significant decrease in groups 3 and 4. In groups 5 and 6, there was an increase in tensile strength but it was not statistically significant. The last group had no antiadhesion effect. Furthermore, the tensile strength was found to have increased.

In general, there was a statistically significant difference between the groups in terms of the tensile strength of adhesions (P = 0.001, Table 2).

Table 2. Adhesion tensile strength comparison in groups

Groups	ADHESION TENSILE STRENGTH COMPARISON				
	Mean (Newton)	Std. Deviation	Minimum (Newton)	Maximum (Newton)	P/Sig.
Group 2 (Control)	1.0540[ac]	.58308	.38	2.20	.001
Group 3 (Sepra)	.6370[b]	.27793	.35	1.25	
Group 4 (Supro)	.5230[b]	.19362	.30	.90	
Group 5 (O. Oil)	.7620[ab]	.28894	.46	1.29	
Group 6 (O. Oil + Vit-E)	1.3560[c]	.64371	.55	2.45	

Evaluation of Adhesions by Evans scoring: According to the evaluation of adhesions by Evans, adhesion to incision site was 50% in the control group, and all of them were at stage I. Other than the control group, all groups except for group 3 were at the same stage. According to Evans, 10% of group 5 and 6 were at stage II. This was not statistically significant. Group 3 was found to be at the same stage as the sham group.

In regards to the adhesions to the traumatized area of the anterior abdominal wall, groups 3 and 4 were compared to the control group and were found to be low (20%, only two rats). Groups 5 and 6 were found to be high according to Evans (grade III), and the tensile strength was at grade 4 (1.05 N). It was found to be statistically significant. P = 0.027

Adhesions of the traumatized area of the cecum and the omentum in all groups were close to the control group. Even compared to other parameters, the maximum adhesion was seen in the control group. Group 4 was lower than the other groups. It was found to be statistically significant. P = 0.001

The omentum adhesion to other organs was not seen in the control group. The Evans score of 2 and 3 was mostly in group 5. Most of the adhesion was observed in order, as groups 4 and 6. It was found to be statistically significant. P = 0.038

Adhesions between the intestine were significantly less in all other groups when compared to the control group. In groups 4 and 6 there was no adhesion. Twenty percent of group 3 and ten percent of group 5 had adhesions. It was found to be statistically significant. (P = 0.01)

Histopathological Evaluation: The 2-3cm² front wall of the cecum was excised and fixed in 10% of buffered formalin. Afterwards, the

dehydration samples were embedded in paraffin blocks. Following which, five micrometer thick sections were mounted on slides, stained with hematoxylin-eosin and examined by light microscopy. The pathologist did not know which samples were
obtained from which group. A histopathological evaluation was performed according to the criteria in Table 3.

The sham group was close to the control group in terms of inflammation. Ninety percent of group 4 had grade 2 inflammation. Groups 5 and 6 had less inflammation compared to the control group. Fibroblastic activity was found to be higher in groups 5 and 6. Foreign body reaction was also found to be higher in groups 5 and 6 than the other groups. Collagen production was higher in group 5 than in the other groups. The proliferation of blood vessels was also found to be higher in groups 5 and 6 but it was not statistically significant. Inflammation and foreign body reaction were statistically significant compared to the other groups. (Table 3).

Table 3. Percentage of the affected area in groups of microscopic adhesion rating criteria

	Inflammation, percentage of the affected area	fibroblastic activity	foreign body reaction	collagen production	vascular proliferation
Grade 0	None	None	None	None	None
Grade 1	0-25%	Mild	Rare	Mild	Mild
Grade 2	26-50%	Moderate	Moderate	Moderate	Moderate
Grade 3	51%- ↑	Prominent	Prominent	Prominent	Prominent

Although it was not statistically significant, a decrease in inflammation and an increase in collagen production, fibroblastic activity, and vascular proliferation were determined via histopathological evaluation in groups 5 and 6. The reason for this should be clarified with more detailed studies.

DISCUSSION

Postoperative intra-abdominal adhesions are an undesirable result. The incidence of peritoneal adhesions is 67-93% of abdominal surgery patients and 97% of gynecological pelvic surgery patients. In 70% of small bowel obstructions, adhesion was identified. Intestinal obstruction was found after 10% of appendectomy, 6.4% of cholecystectomy, 10-25% of intestinal surgery, 17-25% of proctocolectomy (10,20). 15-20% of secondary infertility rates in women are due to adhesions (11). Mortality in small bowel obstruction due to adhesions ranged from 3% to 30%. In a study conducted in the US, it was found that annual health spending due to adhesion is over one million dollars (12). In this experimental study, we found adhesions in 100% of the control group in different anatomical locations over the incidence mentioned above. Seprafilm was widely used in several studies (10-15) as an adhesion barrier and so it became a comparison element in our study. Seprafilm completely prevented adhesion to the incision site in our study. All other groups had adhesions. The adhesion between the intestine declined by 60% than in the control group. Suprofilm is a product that's been studied recently and it's known that the adhesions are markedly decreased (16-17). In a study, Seprafilm is compared with Suprafilm, and it has been found that Suprofilm makes less adhesion (18). In our study, adhesion to the traumatized cecum was the same as the Seprafilm group. Seprafilm was more effective than Suprofilm in adhesion to the incision site. Suprofilm made little or no adhesion between the intestine. There was nonabsorbed Suprofilm in the abdominal cavity on the 14th postoperative day. We have determined that Suprofilm is absorbed in three weeks. Groups 5 and 6 were found to be effective in adhesion between intestine alone, unlike the others, antiadhesion activity in other regions could not be shown. Unlike our study, the studies emphasized that olive oil and oliveoil + vitamin E significantly reduced the adhesion (15,19,20). In a comparative study with 10% fat emulsion, it reduced adhesion but it was not statistically significant. These results are correlated in our study. Olive oil tensile strength of adhesion was not significantly different from the control group. Olive oil + vitmin E tensile strength of adhesion was more than the control group.

CONCLUSION

Abdominal adhesion is one of the most important side effects of intra-abdominal surgical operations and despite advances in the prevention, it was still seen as incompetent. Use and investigation of many substances to prevent adhesion continues. In our study, we saw that it is not easy to create intra-abdominal adhesions in rats. Although it was not statistically significant, Suprofilm was superior to Seprafilm, in terms of adhesions between the intestine, cecum omentum adhesion, and the tensile strength of adhesion between them. Fourteen days after operation, Seprafilm was totally absorbed but Suprofilm remained, particularly in the abdominal cavity. Suprofilm completely disappeared three weeks after the first operation. This result showed us that Suprofilm could be used to prevent adhesion.

As a liquid barrier and antioxidant, olive oil was found to be ineffective in the prevention of

adhesion at the incision site and in the field of trauma. However, it was evident that olive oil prevented adhesion between the intestines.

Olive oil + vitamin E had no effect on adhesion in the study. Inflammation was reduced compared to the others, but collagen production and fibroblastic activity were increased. As a result, much more rupture force was detected than the others. The foreign body reaction was markedly more than the others. As a result, more objective evaluation can be made by measuring the tension force of the adhesions. Suprafilm can also be effectively used as an antiadhesive, such as Seprafilm. Olive oil and vitamin E require more studies to be used as antiadhesives.

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