EFFICACY OF INTRA-AND POST-OPERATIVE PERITONEAL LAVAGE IN PREVENTION OF EXPERIMENTAL POSTSURGICAL PERITONEAL ADHESIONS FORMATION IN DONKEYS*

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SUMMARY

This study was carried out on twenty two donkeys subjected to jejunal and cecal serosal stripping adhesion induction model followed by intra- and post-operative peritoneal lavage for the first three postinduction days. The chosen antiadhesive pharmaecuticals are dimethyl sulfoxide 20% solution; sodium chloride sterile solution containing 5000 IU heparin/liter; Ringer's lactate sterile solution containing 0.1% lavasept and 1% sodium carboxymethycellulose. From the quantitative macroscopic and histopathological adhesions score system and the clinicopathological findings insignificant differences was found in the postsurgical adhesions scores among peritoneal lavaged and control groups. The effectiveness of intraperitoneal lavage using dimethyl sulfoxide, heparin, lavasept and sodium carboxymethylcellulose in the prevention of adhesions cannot be scientifically supported because the results were controversial and lacked any implication for clinical use. No method has gained wide acceptance and surgeons must rely on meticulous surgical technique which can minimize tissue trauma and reducing the risk of postsurgical adhesions formation.

INTRODUCTION

Postoperative formation of peritoneal adhesions represents a major clinical problem after abdominal surgery. These adhesion were considered the most common cause for repeated episodes of abdominal pain and death in 18 to 22% of horses undergoing surgery for small inestinal lesions (Baxter et al, 1989, MacDonald et al, 1989; Risberg, 1997; DiZerega, 1997; Moll et al, 1991; Mueller et al, 2000; Diamond, 2001 and Treutner and Schumpelick, 2000). In addition, adhesions

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Thesis.

were the second most common reason for repeated laparotomy in horses with gastrointestinal disease (Parker et al, 1989; Smith et al, 2005 and Boland and Weigel, 2006).

The preventive strategies which developed to inhibit adhesion formation include minimization of tissue trauma by meticulous atraumatic surgery, hemostasis, inhibition of the inflammatory response, separation of serosal surfaces, enhancement of peristalsis, covering raw peritoneal surfaces, enzymatic digestion and inhibition of fibrin deposition (Ellis, 1971; Singer et al, 1996; Southwood and Baxter, 1997; Mueller et al, 2000; Otcu et al, 2003; Yagmurlu et al, 2003; Certin et al, 2004; Sullins et al, 2004; Bulbuloglu et al 2005; EL-Ghoul, 2005 and Sikkink et al, 2006).

Little is known about the causes and prevention of serosal adhesions in horses. The purpose of this study was to evaluate the reliability of serosal stripping model of abdominal adhesions and to investigate the efficacy of intra-and post-surgical peritoneal lavage using dimethyl sulfoxide, heparin, lavasept and sodium carboxymethylcellulose pharmaceuticals in prevention of experimentally induced intra-abdominal adhesions in donkeys.

MATERIAL AND METHODS

The study was carried out on twenty two, apparently healthy, donkeys of 5 years mean old and 125 kg mean body weight. This work was done in department of surgery, anesthesiology and radiology; department of medicine and department of pathology, faculty of veterinary medicine, Cairo university, Egypt. The donkeys were randomly

assigned to five groups; each containing 5 animals:

Donkeys in all groups were subjected to jejunal and cecal serosal stripping as a model for induction of adhesion.

- Group 0 (Control group): Donkeys were subjected to jejunal and cecal serosal stripping only without any treatment.
- Group 1 (Dimethyl sulfoxide group): Donkeys were subjected to intra-abdominal peritoneal lavage using dimethyl sulfoxide (DMSO) 20% solution (Aldrich, chemical company LTD Gillingham-England).
- Group 2 (Heparin group): Donkeys were subjected to intra-abdominal peritoneal lavage using sodium chloride sterile solution containing 5000 U heparin / liter (NILE Co. for pharamaceuticals and chemical industries. Cairo, Egypt).
- Group 3 (Lavasept group): Donkeys were subjected to intra-abdominal peritoncal lavage using Ringer's lactate sterile solution containing 0.1% lavasept (Fresenius, Stans, Switzerland).
- Group 4 (Sodium carboxymethycellulose group): Donkeys were subjected to intraabdominal peritoneal lavage using 1% sodium carboxymethycellulose (SCMC) (ADWIC, El-Nasr Pharmaceutical and chemicals Co. Cairo, Egypt).

Intraperitoneal lavage solutions were used in a dose of 7 ml/kg (Moll et al, 1991; Mueller et al, 1995 and Lopes et al, 1998/1999).

Surgical technique:

- Food was withheld for 12 hours before surgery and penicillin streptomycin antibiotic was admin-

istered intramuscular.

- The following anaesthetic regimen was used: xylazine hydrochloride (1.1 mg/kg, intravenously), followed by chloral hydrate narcosis (5 g/ 50 kg bwt, intravenously) and maintained with thiopental sodium (15 mg/kg bwt, intravenously). Donkeys were prepared for aseptic abdominal surgery.
- A ventral midline celiotomy was done followed by systematic exploration of the abdominal cavity to facilitate examination of the viscera.
- Induction of intra-abdominal adhesions: The jejunum was exteriorized and examined from the ileocecal orifice to the duodenocolic ligament. Intra-abdominal adhesions were created at the antimesentric border of the jejunum using serosal stripping method (El-Sayed, 1977). Also, the cecum was located and exteriorized from the abdomen and adhesions was created at three areas by serosal stripping. Two interrupted 3-0 chromic catgut sutures were placed through the seromuscular layer at the two end of each serosal stripped area (Fig. 1).

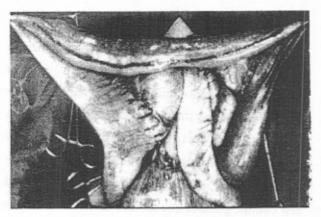


Fig. 1: Jejunal serosal stripping

 Intraoperative peritoneal lavage: was done in the peritoneal lavaged groups using the chosen pharmaceuticals after finishing from intestinal serosal stripping.

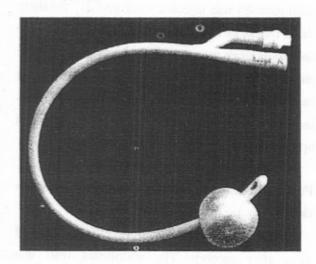


Fig.2: The catheter used for peritoneal lavage

Closure of the abdominal wall and Placement of Foley catheter:

In the peritoneal lavaged and control groups, before finishing the closure of the abdominal wall a 20 - F Foley catheter (Silkolatex® Rusch Gold® Balloon Catheter) was inserted into the peritoneal cavity and fixed in place through the last two sutures (Fig. 2). After closure of the abdominal incision, a sterile 20 ml syringe was used to inflate the Foley catheter.

- Postoperative peritoneal lavage: was done using the chosen pharmaceuticals through the placed intra-abdominal catheter for the first three days after operation then remove the catheters.
- Postoperative care and monitoring (Clinical assessment): After recovery from anesthesia,

donkeys were allowed access to water and were gradually returned to full feed during the next 24 hours. Penicillin-streptomycin antibiotic was administered for 5-7 days. Antiinflammatory agent (arthridine®) was injected intravenously for three days. Donkeys were monitored for attitude, pulse and respiratory rates, rectal temperature, signs of pain, and swelling or drainage associated with the incision. Donkey that had clinical signs of abdominal pain after surgery was examined and treated appropriately.

Postmortem examination (Necropsy examination):

- Donkeys in all groups were euthanatized 21 days after surgery. The abdominal wall was opened in a "U" shaped fashion to facilitate the inspection of the different structures within the abdomen. The abdominal incision, peritoneal cavity, the abdominal organs and the digestive tract were examined. The location of adhesions was noted and their nature characters were recorded Fibrinous adhesions were classified as those that pulled apart easily with minimal digital pressure while those that did not separate with moderate to strong digital pressure were considered as fibrous adhesions. The number, degree and extent of adhesions were recorded and classified according to the intra-abdominal adhesions scores and types (El-Sayed, 1977; Moli et al, 1992; Baxter et al. 1993; Diamond, 2001 and Ozel et al, 2005).
- Scores of adhesions: The stripped sites of jejunal and caecal adhesions were graded into the following scores: Score 0: No adhesions; Score 1:Minimal adhesions of 1-2 strands between vis-

cera; Score 2: Moderately dense but diffuse adhesions present without distortion of the mesentery or bowel; Score 3: Severe adhesions with twisting of the intestine and Score 4: Massive adhesions, with small bowel loops adhered to each other or to other parts of the intestinal tract.

- Types of adhesions: These were classified according to El-Sayed (1977) into:Intestinal adhesions (adhesions between coils of the intestine); Omental adhesions (adhesions between omentum and the antimesentric border of the intestine); Peritoneal adhesions (adhesions between peritoneum and the adjacent coils of intestine) and Laparatomy wound adhesions (adhesions between laparatomy wound and the adjacent structures).
- Histopathological examination: Tissue samples were collected from adhesions sites, scrosal stripped areas, intestine, liver, kidney, heart and lung. The samples were fixed in buffered 10% formalin, embedded in paraffin, sectioned at 3μm, and stained with hemotoxylin and cosin for subsequent evaluation (Bancroft and Cock, 1994). Toluidine blue stain used for detection of mast cells.

Clinicopathologic evaluation:

- Blood analysis: Venous whole blood, serum and plasma samples were collected from each donkey for haematological and biochemical analysis before and on the first, second, third, seventh, fourteenth and twenty one day postoperation. The examined hematological parameters are hemoglobin, hematocrit, red blood cell counts, white blood cell counts, platelet counts and differential leucocytic counts (Cowell and Tyler, 2002). The exam-

ined biochemical parameters are glucose, total protein, urea, total bilirubin, direct bilirubin, alkaline phosphatase, aspartate aminotransferase in serum and fibrinogen in plasma. The biochemical kits were supplied by Biocon, Germany. Fibrinogen concentration was determined by calculating the difference between total protein values of serum and plasma (Duncan et al, 1994).

- Peritoneal fluid analysis: On days 0, 1, 2, 3 and 21 two peritoneal fluid samples were obtained from each donkey (one with EDTA and the other without EDTA) for cytological and biochemical analysis. The examined cytological parameters are red blood cell counts, white blood cell counts, proportion of segmented neutrophils, lymphocytes, macrophages, mesothelial and mast cells (Cowell and Tyler, 2002). The examined biochemical parameters are glucose, total protein, urea, total bilirubin, direct bilirubin, alkaline

phosphatase, aspartate aminotransferase and fibringen.

Statistical analysis of the data was done by means of analysis of variance (ANOVA) for repeated measures. When the F-value was significant, a least-significant difference test was used to determine differences among means using SPSS (Statistical Product & Service Solutions) (Kuehl, 1994). All data were presented as mean ± standard error, and p< 0.05 was considered significant.

RESULTS

Macroscopic evaluation of adhesion:

The results of macroscopic evaluation of adhesions in and among the control and peritoneal lavaged donkeys using DMSO, heparin, lavasept and SCMC were showed in Fig. 3 & 4 and tabulated in table 1&2.

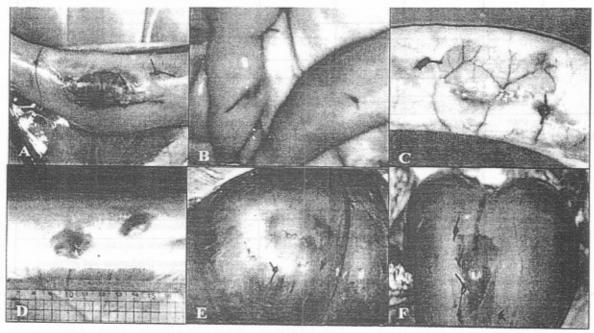


Fig. 3: Serosal stripping sites free from adhesions. Note that jejunum was free from adhesion and suture material was present without any inflammatory reaction (A&B). New vasculature formation at the jejunal stripped serosa (C). Inflammatory reaction around the stitch (D). Cecal serosal stripping site was free of adhesion and only slight inflammatory reaction was present (E&F).

Table 1: Postmortem observation of adhesions

Groups	Donkeys	Observation	Score of	Length of	Type of adhesion
		period (day)	adhesion	adhesion	
	case 1	21 day	2 score	5 cm	Adhesion between stripped caecal serosa and
Control	:				laparotomy wound (Abdominal wall adhesion)
group	case 2	21 day	2 score	5 cm	Adhesion between stripped caccal serosa and
					laparotomy wound (Abdominal wall adhesion)
Ì	case 3	21 day	0 score		Absence of adhesion
	case 4	7 day	1 score	1-2 cm	Adhesion between stripped caecal serosa and
)					laparotomy wound (Abdominal wall adhesion)
	case 5	10 day	0 score		Absence of adhesion
DMSO	case 1	21 day	1-2 score	7 cm	Adhesion between stripped seosa of caecum and
group					jejunum (Intestinal adhesion)
j	case 2	3 day	******		Absence of adhesion
	case 3	8 day	4 score	20-30 cm	Adhesion between stripped serosa of caecum,
Ì					jejunum & colon and taparotomy wound
				l	(Abdominal wall adhesion)
1	case 4	21 day	1 score	5 cm	- Adhesion between caecum stripped scrosa and
				d E	colon (Intestinal adhesion)
			} 		- Adhesion of stripped caecal serosa and
					łaparotomy wound (Abdominal wall adhesica)
	case 5	1 day	0 score		Absence of adhesion
	case 1	13 day	2 score	6 cm	- Adhesion between stripped caecal serosa and
Heparin			Ì		laparotomy wound (Abdominal wall adhesion)
group		Í		ļ	- Adhesion between colon and ileum
]		<u> </u>	(Intestinal adhesion)
	case 2	14 day	2 score	25 cm	Adhesion of the stripped caecal serosa, colon and
				<u> </u>	laparotomy wound (Abdominal wall adhesion)
	case 3	G day	0 score		Absence of adhesion
	case 4	4 day	0 score		Absence of adhesion
	case 5	10 day	0 score		Absence of adhesion
	case 1	10 day	0 score	******	Absence of adhesion
Lavasept	case 2	24 day	2 score	15 cm	Adhesion between stripped caecal serosa and
group					laparotomy wound (Abdominal wall adhesion)
	case 1	1 day	0 score		Absence of adhesion
SCMC	case 2	15 day	1 score	7 cm	Adhesion between stripped caecal serosa and
group					laparotomy wound (Abdominal wall adhesion)
Ì	case 3	14 day	0 score		Absence of adhesion
	case 4	14 day	2 score	10 cm	Adhesion between stripped caecal serosa and
					laparatomy wound (Abdominal wall adhesion)
	case 5	14 day	0 score		Absence of adhesion

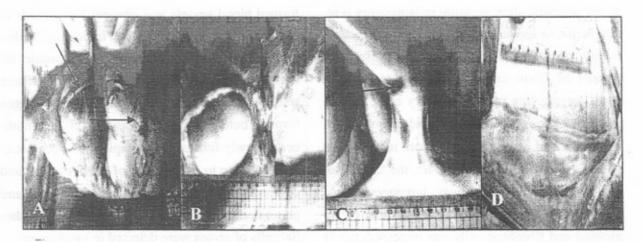


Fig. 4: Intestinal adhesion between jejunum and caecum (A) and colon and caecum (B). Note the excessive fibrin present on the cecal serosa (arrow). Abdominal wall adhesion with the jejunum (C) and caecum (D). Note that the suture material was included in the adhesion (arrow).

Table 2: Intra-abdominal adhesion scores in the examined groups.

	Control group	DMSO group	Heparin group	Lavasept group	SCMC group
Observation period (days)	16.0 ± 3.0	10.8 ± 4.0	11.6 ± 2.6	9.4 ± 1.9	15.5 ± 5.5
Score of adhesion (0-4 score)	1.6 ± 0.3	3.0 ± 1.0	1.5 ± 0.5	2.0 ± 0.01	2.0 ± 0.01
Length of adhesion (cm)	3.66 ± 1.3	14.0 ± 8.0	6.5 ± 0.5	24.5 ± 0.5*	15.5 ± 0.5
Number of adhesions	3	2	2	1	2

Microscopic evaluation of adhesion

Histopathological examination revealed insignificant difference in the microscopical picture among the examined groups. There was a constant finding of inflammatory reaction and granulation tissue formation at site of adhesion and in small and large intestine. There were desquamation of the epithelial lining of the mucosa of jejunum, cecum and colon. Some cases showing increasing in numbers and activity of goblet cells in villi and crypt of luberkuhen. Lamina propria exhibit a signs of inflammatory reaction represented by congestion of blood vessels, edema and aggregation of inflammatory cells mainly macrophages, lymphocytes and mast cells. The submucosa revealed the presence of edema, fibrin thrombus in most of the blood vessels, areas of hemorrhages in some cases and inflammatory cells as neutrophils, macrophages, eosinophils, mast cells and lymphocytes (Fig. 5).

At the adhesion sites, an acute inflammatory reaction began to appear at the first week after induction of adhesion, the reaction represented by large amount of fibrin exudate, hemorrhage in some cases, aggregation of inflammatory cells, as neutrophils, eosinophils mast cells and macrophages. Fibroblast and angioblast cells were recorded but in small numbers. Two week later, the fibrin exudate decreased in its amount, lymphocytes and plasma cells began to appear, the number of angioblast and fibroblast cells was increased, newly formed blood vessels was obvious and strands of collagen fibers were detectable. In donkeys euthanized three weeks postoperation, a chronic inflammatory reaction was predominant. There were an increase numbers of mature collagen forming bundles in some areas (Fig. 6), less number of newly formed blood capillaries were notices in addition to less amount of fibrin exudate and aggregation of macrophages, lymphocytes and plasma cells were detected. Regenerated mesothelial cells of serosa were detected in some cases.

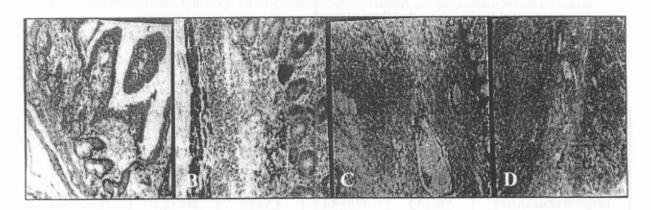


Fig. 5: Small intestine of donkey showing the presence of edema and aggregation of inflammatory cells (A) (H&E X 66) and of large numbers of mast cells (B) (Toludine blue X 33) in lamina propria; Submucosa of large intestine showing fibrin thrombus accompanied by aggregation of inflammatory cells and fibrin (C); Submucosa of jejunum showing desqumation of epithelial lining, areas of hemorrhage and congested blood vessels (D) (H&E X 33).

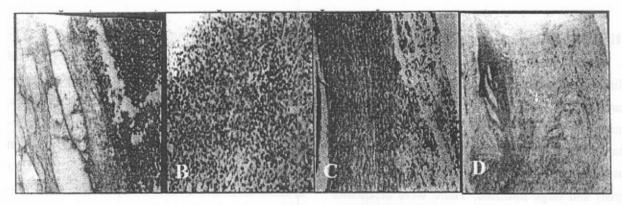


Fig. 6: Site of adhesion in cecum at 13 days post treatment showing large amount of fibrin exudate and aggregation of inflammatory cells mainly neutrophils in submucosa and serosa (A) (H&E X 33). Submucosa of cecum 23 days postoperation showing aggregation of large numbers of eosinophils (B) (H&E X 66); Site of adhesion showing presence of angioblast, fibroblast and immature collagen fiber in cecum (C) (H&E X 66) and collagen fiber in jejunum (D) (H&E X 33).

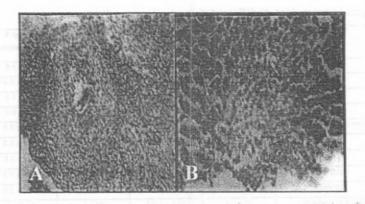


Fig. 7: Intestinal serosa showing granulome consists of suture material, inflammatory cells and connective tissue capsule (A) and liver showing areas of centrolobular necrosis (H&E X66).

Some cases at sites of abrasion showed foreign body granulome, formed from suture material, inflammatory cells as neutrophils, macrophages, lymphoctes and finally connective tissue capsule. The liver of some cases especially heparin group showed centrolobular necrosis (Fig. 7).

The score of the evaluated histopathological variables was 13 degree in the control group; 20 degree in DMSO group; 15 degree in DMSO group; 17 degree in heparin group and 22 degree in lavasept group.

Clinicopathologic findings:

Hematological parameters in the control and peritoneal lavaged donkeys using DMSO, heparin, lavasept and SCMC were presented in table 3.

Biochemical blood parameters in the control and peritoneal lavaged donkeys using DMSO, heparin, lavasept and SCMC were presented in table 4.

The results of peritoneal fluid parameters in the control and peritoneal lavaged donkeys using DMSO, heparin, lavasept and SCMC before induction of adhesions, and at the first, second and third postoperative days and at the euthanization day were showed in table 5.

Table 3: Hematological parameters at different times in the examined groups

Examined	Sampling	Group 0	Group 1	Group 2		·
Parameters	Time	(Control)	(DMSC)	(Heparin)	Group 3 (Lavasept)	Group 4 (SCMC)
Name debia						
Hemoglobin (g/dl)	0 day	10.1 ± 0.8	9.5 ± 0.7	10.3 ± 0.7	7.5 ± 1.6	9.3 ± 0.45
(9/04)	1 <u>si</u> waek	9.6 ± 0.8	11.3 ± 1.8	9.6 ± 0.45	10.2 ± 0.4	9.6 ± 0.8
ļ	2 <u>nd</u> week	10.2 ± 0.9	10.3 ± 0.5	9.6 ± 0.64	8.3 ± 1.6	10.4 ± 1.6
į	3 <u>rd</u> week	9.9 ± 0.9	10.2 ± 1.7	9.7 ± 0.54	9.7 ± 0.5	10 ± 1.6
	Day of euthanization	11.4 ± 1.1	6.0 ± 2.0 °	9.2±0.71	10.4 ± 0.6	10,11 ± 1.8
Hematocrite	0 day	31.0 ± 2.1	30 ± 1.7	28.8 ± 0.86	28.5 ± 6.3	31.8 ± 2.4
(vol %)	1 <u>st</u> week	32.2 ± 2.6	33.7 ± 2.6	28.4 ± 1	32.8± 3.5	31.5 ± 2
ĺ	2 <u>nd</u> week	30.7 ± 1.1	29.8 ± 1.6	28.8 ± 1.6	30.2 ± 2.3	31.6 ± 2.8
ſ	3 <u>rd</u> week	31.2 ± 1,7	33.3 ± 3.9	27.5 ± 0.3	29.8 ± 2.6	33.3 ± 0.3
ſ	Day of euthenization	36 ± 1.5	20.5 ± 7.5 °	27 ± 5	36.5 ± 2	31.5 ± 1.5
Red Blood Celt	0 day	4.2 ± 0.9	4.7 ± 0.5	4.2 ± 0.4	4.1 ± 0.7	3.6 ± 0.5
(لبر X10 ⁶)	1 st week	4.9 ± 0.6	5.8 ± 0.6 °	5 ± 0.3	4.3 ± 0.7	5.6 ± 0.9
	2 nd week	4.5 ± 0.9	3.7 ± 0.3	5.2 ± 0.3	4.2 ± 0.9	5 ± 1.5
ļ	3 <u>(d</u> week	4.4 ± 0.9	5.2 ± 0.6	4.5 ± 0.4	3.7 ± 0.5	4.4 ± 1.5
ĺ	Day of euthanization	3.9 ± 0.5	2.6 ± 1.1 *	4.4 ± 0.1	4 ± 0.3	3.8 ± 0.3
White blood	0 day	11.6 ± 1.45	17.2 ± 1.8	13.5 ± 1.9	12.9 ± 1.5	16.6 ± 2.1
ceil (X10 ³ µl)	1 <u>si</u> week	9.0 ± 1.9	14.0 ± 1.9	9.3 ± 2.3	10.4 ± 4.2	12.6 1 1.7
	2 <u>nd</u> week	9.3 ± 1.3	10.8 ± 1.8 °	8.9 ± 2.3 °	11.5 ± 4.6	7.5 ± 1.4 °
	3 rd week	9.5 ± 1.6	8.2 ± 1.9 *	8 ± 0.98 *	7.6 ± 2.2	8.8 ± 1.6 °
	Day of euthanization	13.3 ± 0.9	10.5 ± 2.9 °	19.6 ± 5.3	13 ± 2.1	10.3 ±0,35°
Segmented	0 day	13.7 ± 5	42 ± 4.7	23.0 ± 3.6	42.0 ± 17	34.0 ± 8
neutrophil (%)	1 st week	12.3 ± 4.3	45 ± 9.6	27.3 ± 1.7	35 ± 7.5	54.6 ± 9.6
	2 nd week	23.3 ± 12.3	20.2 ± 3	18 ± 2	41.3 ± 23.1	29 ± 19
	3 rd week	23.3 ± 9.2	26 ± 8.7	18 ± 2	54.5 ± 7.4	35.0 ± 5
	Day of euthanization	36 ± 16	19 ± 15 *	52.0 ± °	21.3 ± 7.6	35 ± 15
Lymphocyte (%)	0 day	72 ± 4.3	58 ± 3.8	74.3 ± 1.2	49.3 ± 12.6	64 ± 8.6
Lymphocyte (w)	1 st week	83.3 ± 3.3	50 ± 3.8	62.6 ± 1.3 *	56.6 ± 11.6	42 ± 9.4
,	2 <u>nd</u> week	71.3 ± 13.9	72.5 ± 8.5	80±0°	53.3 ± 23.5	67 ± 23
	3 rd week	73.3 ± 11.6	63.3 ± 14.5	82 ± 2.0 °	44 ± 8	63 ± 7
	Day of euthanization	55 ± 11	81 ± 15	24 ± 0.11°	67 ± 12	61 ± 18.5
14		<u></u>	0 0			01 ± 16.5
Monocytes (%)	0 day	2.75 ± 0.9		1.3 ± 1.3	2.6 ± 2.6	<u> </u>
	1 <u>st</u> week	2,3 ± 1.4	1 ± 0.1	7 ± 0.3 *	2.6 ± 2.6	0.6 ± 0.6
	2 <u>nd</u> week	1,3 ± 1.3	1.25 ± 1.2	2 ± 0.2	1.3 ± 1.3	2 ± 2
	3 <u>rd</u> week	2 ± 2	0	0	1.3 ± 1.3	4.5 ± 0.5 *
	Day of euthanization	7 ± 1.7	1.3 ± 1.3		4.6 ± 2.9	1 ± 0.1
Immature	0 day	0	0	0	2.6± 2.6	1 ± 0.1
neutrophil (%)	1 <u>st</u> week	1.3 ± 1.3	2.7 ± 2.7	4 ± 2.3	1.3± 1.3	2.7 ± 0.7
	2 <u>nd</u> week	2.6 ± 1.3	6 ± 0.6	0	0	2 ± 0.2
	3 <u>rd</u> week	0	10.6 ± 10.7	0	Ó	0
	Day of euthanization	2 ± 0.2	0	0	5.3 ± 5.3	1,5 ± 1.5
Eosinophils (%)	0 day	3 ± 1.2	1.3 ± 1.3	1.3 ± 0.3	3.3 ± 1.3	1.5 ± 0.9
	1 st week	0.6 ± 0.6	0	0	4.3 ± 4.3	0
	2 <u>nd</u> week	1.3 ± 1.3	0	0	1.3 ± 1.3	0
	3 <u>rd</u> week	1,3 ± 1.3	1 ± 0.2	0	0	0
	Day of euthanization	0	4 ± 1.4*	0	1.6 ± 0.6	0
Platelet	Q day	255.8 ± 63	274,6 1 94	142 ± 63	106.7 ± 44	215 ± 59
counts	1 st week	335 ± 97	100 ± 100	242.6 ± 82	208.5 ± 96	209.7 ± 11
(thousand/mi)	2 <u>nd</u> week	261 ± 82	105 ± 60	206.7 ± 76	258.5 ± 33	218.7 ± 7
	3 rd week	218.7 ± 102	80 ± 15.6	229.2 ± 31	287.7 ± 64	289.7 ± 1

Table 4: Biochemical parameters at different times in the examined groups

Examined	Sampling	Group 0	Group 1	Group 2	Group 3	Group 4
Parameters	time	(Control)	(DMSO)	(Heparin)	(Lavasept)	(SCMC)
Total protein	0 day	G r 0.47	6.0 ± 0.16	5.3 ± 0.5	6.8 t 0.6	6.5 ± 0.6
(g/dl)	1 <u>st</u> week	7:1 1.7	6.1 ± 0.06	5.6 ± 0.3	9.8 ± 3.4°	5.4 ± 1.6
,	2 <u>rid</u> week	5± 0.4	5.1 ± 0.8	6.3 ; 2.5	6.9 ± 0.5	7.3 ± 2.8
	3 <u>rd</u> week	5 ± 0.7	5,9 ± 0.1	not analyzed	6.0 ± 0.2	4.3 r 1.6
	Day of euthanization	5 ± 0.6	7.3 ± 2.3°	not analyzed	6.6 + 0.3	4.1 ± 1,5
Fibrinogen	0 day	2.85 t 1.8	2.04 ± 0.12	1.7 ± 1.1	1.8 ± 0.4	2.2 ± 0.9
(g/dI)	1 si week	1.35 ± 0.15	0.83 ± 0.27	1.3 + 0.2	13 ± 0.3*	2.1 = 0.2
4.	2 <u>nd</u> week	2.0 ± 0.5	0.93 ± 0.70	1.0 ± 0.02	1.9 ± 0.1	1.2 = 0.2
	3 <u>rd</u> week	0.3 ± 0.05	1.4 = 0.30	not analyzed	1.7 = 0.9	0.3 + 0.05*
	Day of euthanization	not analyzed	0.5 + 0.06	nol analyzed	0.9 ± 0.05°	not analyzed
Glucose	0 day	58.7 ± 6.4	63.4 ± 4	53.5 ± 11.1	57.3 + 1.6	54 ± 17.4
(mg/dl)	1 <u>si</u> week	89 ± 3.04	78.3 ± 6	63.3 ± 14.3	130 : 19.7*	84 ± 12.5
	2 <u>nd</u> week	67.2 ± 6.7	55.0 ± 13.4	54 1 14.3	75.5 ± 5.5°	65 ± 12.4
	3 <u>rd</u> week	60.3 ± 10.3	69.0 ± 23	not analyzed	94.5 = 2.5*	30 ± 9.2
	Day of euthanization	46 ± 8.5	79.5 ± 0.5	riol analyzed	60.0 ± 10.4	not analyzed
Úrea	0 day	16. 8 ± 5.8	27.8 : 1.7	24.5 ± 4.1	27.3 ± 2.2	28.1 11.9
(mg/di)	1 si week	21.1 1 1.6	38.6 ±12.8	26.5 ± 5.4	34.7 17.2	25 ± 5.2
	2 rkl week	26.7 1 6.2	32,3 ±14.7	54.9 ± 3.8°	25.0 1 3,4	14.7 ± 4.2
	3 rd week	21.5 1 5.6	19.7 ± 2.4	not analyzed	14.7 ± 3.9	30.6 ± 6.4
	Day of euthanization	41 3 = 13.4	16.3 ± 2.1	not analyzed	22.4 ± 3.7	19.3 ± 3.5
Total	0 day	1.8 = 1.7	0.062 ± 0.01	0.135 ± 0.04	0.23 ± 0.08	0.13 』 0.03
bilirubin	1 st week	0.08 + 0.03	0.063 ± 0.02	0.090 ± 0.02	0.05 + 0.01	0.220 ± 0.1
(lb\gm)	2 nd week	0.108 ± 0.03	0.270 ± 0.09°	0.435 ± 0.42	0.05 ± 0.02	0.110 ± 0.01
	3 <u>rd</u> week	0.488 ± 0.04	0.670 ± 0.08*	not analyzed	0.253 ± 0.1	0,220 ± 0.1
	Day of euthanization	0.110 ± 0.04	0.080 ± 0.03	not analyzed	0.92 ± 0.3*	0.860 ± 0.2°
Direct	0 day	0.253 ± 0.08	0.548 + 0.13	0.505 ± 0.22	0.187 ±0.04	0.12 + 0.07
Bilirubin	1 st week	0.25 ± 0.09	0.340 1 0.04	0.240 = 0.10	0.39 ± 0.09	0.41 ± 0.2
(mg/dl)	2 nd week	0.087 + 0.05	0.275 ± 0.06	0.270 ± 0.02	0.39 + 0.19	0.96 ± 0.1*
	3 rd week	0.070 ± 0.01	0.275 = 0.27	not analyzed	0.03 ± 0.03	0.41 ± 0.01
	Day of euthanization	0.960 ± 0.05°	1.10 1 0.2"	not analyzed	1.2 ± 0.07'	0.27 ± 0.01
Alkaline	0 day	111,1± 21.2	110.0 ± 14.2	103.7 ± 4.2	283 ± 53.5	168 : 14 9
phosphatase	1 st week	88.2 ± 35.2	71.5 ± 4.3	86.3 ± 8.4	102.9 ± 22*	200 ± 42.5
(U/L)	2 <u>nd</u> week	78.8 ± 5.4	56.9 ± 23.9°	28.5 ± 33.9	91.7 1 10*	91.2 ± 14.5
	3 rd week	61.3 ± 3.7°	45.8 ± 6.2*	not analyzed	71.5 ± 5.4*	67.6 ± 9.6
	Day of outhanization	52.9 ± 8.6	76.5 1 26.5	not analyzed	68.B± 8.9*	45.8 ± 10.1°
Aspartate	0 dəy	117.2 1 24.8	181.1 ± 10.5	146.9 = 29.5	169 : 17.6	135 ± 16.3
aminotransf-	1 st week	62.8 ± 15.7	150.0 ± 11.4°	113.4 ± 14.9	204.2 ± 45	172.7 ± 60.3
erase (U/L)	2 nd week	105.7± 14.6	91.6 ± 6.6*	77.1 ± 17	204 ± 47.1	151.8 : 51.6
	3 rd week	67.9 ± 12.1	61.4 ± 0.7*	not analyzed	193.7 ± 40	109.9 ±22,4
	ļ		<u> </u>			
	Day of euthanization	89.0 ± 15.2	0.82 ± 0.01	not analyzed	94.2 ± 6.0	151.8 ± 33

Table 5: Peritoneal fluid parameters at different times in the examined groups

Examined	Sampling	Group 0	Group 1	Group 2	Group 3	Group 4
Parameters	time	(Control)	(DMSO)	(Heparin)	(Lavasept)	(SCMC)
Red blood cell	Operation day	63.3 ± 53.3	85 ± 38.8	40 ± 10	60 ± 20	122 ± 60
counts (X10 ³	1 st day postoperation	150 ± 66.9	323,3±50,4°	113 ± 46.6	386.6 ± 26	242 ± 114
μl)	2 nd day postoperation	56.6 ± 23.3	120 ± 67	70 ± 30	90 ± 40	215 ± 155
	3 rd day postoperation	60.0 ± 5.8	265 ± 71.8	65.8 ± 64.1	60 ±10.5	800 ± 53*
	Day of euthanization	50.0 ± 14.8	90 ± 15.7	70 ± 4.9	not analyzed	0
White blood	Operation day	4.51 ± 1.2	7±1	1.9 ± 0.7	4.4 ± 2.3	3.2 ± 1.1
cell counts	1 st day postoperation	18.9 ± 13.5	89.9 ± 28.9	51.7 ± 24.6	106.5 ±5.1	62.2 ± 29*
(X10 ³ μl)	2 <u>nd</u> day postoperation	24.4 ± 5.5	99.7 ± 34.5*	20.5 ± 11.5	34 ± 8.3	130 ± 78°
	3 <u>rd</u> day postoperation	19.0 ± 2.8	138.6±41.9*	13.3 ± 5.6	19±4	352 ± 31°
	Day of euthanization	6.1 ± 0.2	12.8 ± 3.5	50.4 ± 25.6	not analyzed	7 ± 1.8
Segmented	Operation day	46 ± 6.4	60.5 ± 8	43.6 ± 25	68.8 ± 8	56 ± 13.5
neutrophils	1 st day postoperation	81.0 ± 13.3*	94.7 ± 1.8*	88 ± 7	92 ± 9.2	82 ± 6
(%)	2 <u>nd</u> day postoperation	88.0 ± 11.5*	82.7 ± 11°	87.5 ± 7.5	94 ± 12.1	96.5 ± 1.5°
	3 rd day postoperation	85.0 ± 6.0*	86.3 ± 4.1*	72.5 ± 12.5	78 ± 16	91 ± 17.9
	Day of euthanization	54.0 ± 9.8	60.0 ± 9.4	75 ± 15.3	not analyzed	48 ± 10.1
Lymphocytes	Operation day	40.6 ± 20.2	36 ± 9	27.5 ± 17.5	22 ± 2	35 ± 13.6
(%)	1 st day postoperation	19.0 ± 11.5	2.5 ± 0.24°	10.7 ± 7.6	5.5 ± 1.5°	12.5 ± 4.6
	2 <u>nd</u> day postoperation	8.6 ± 3.6	8.7 ± .3.9*	11±9	3 ± 0.2*	3 ± 2.0
	3 rd day postoperation	7.0 ± 3.6	4.3 ± 0.3°	27.5 ± 12.5	8 ± 2*	6 ± 1.1
	Day of euthanization	36.0 ± 6.8	36 ± 8.6	25 ± 7.1	not analyzed	24 ± 4.8
Other cells (%)	Operation day	3.0 ± 1.5	3 ± 1.9	9.0 ± 9	10 ± 10	8.5 ± 4.7
(mast cell/	1 st day postoperation	. 0	2.25 ± 1	1.3 ± 0.88	2.5 ± 1.5	6.5 ± 4.5
macrophages)	2 nd day postoperation	1.0 ± 0.1	0.25 ± 0.25	1.5 ± 1.5	3 ± 1.0	0.5 ± 0.5
	3 <u>rd</u> day postoperation	7.3 ± 6.3	9.3 ± 9.3	0	14 ± 14	3.0 ± 0.9
	Day of euthanization	4.0 ± 1.7	36.0 ± 10.0	0	not analyzed	28.0 ± 6.2
Total protein	Operation day	2.8 ± 1.5	0.79 ± 0.39	1.7 ± 0.63	3.3 ± 0.4	2.5 ± 0.7
(g/di)	1 st day postoperation	2.06 ± 0.8	5.6 ± 2.0*	4.9 ± 1.2*	3.8 ± 0.9	3 ± 0.9
	2 <u>nd</u> day postoperation	2.53 ± 0.2	1.9 ± 1.12	3.4 ± 1.7	0.8 ± 0.01	2,4 ± 1.1
	3 rd day postoperation	3.2 ± 1.1	4.3 ± 2.1	2.06 ± 0.9	not analyzed	4.7 ± 1.5
	Day of euthanization	not analyze	0.9 ± 0.04	not analyzed	not analyzed	2 ± 0.4
Fibrinogen	Operation day	0.65 ± 0.25	0.27 ± 0.07	0.2 ± 0.01	0.15 ±0.05	0.9 ± 0.1
(g/dl)	1 st day postoperation	3.0 ± 1.1°	0.775±0.18*	0.5 ± 0.1	0.7 ± 0.1	0.9 ± 0.2
	2 <u>nd</u> day postoperation	0.4 ± 0.05	0.6 ± 0.1	0.5 ± 0.2	0.55 ±0.35	0.4 ± 0.01
1	3 rd day postoperation	0.75 ± 0.02	0.33 ± 0.6	0.4 ± 0.01	0.4 ± 0.01	0.9 ± 0.02
	Day of euthanization	0.7 ± 0.02	0.1 ± 0.01°	not analyzed	not analyzed	not analyzed

DISCUSSION

Different methods had been tried to induce adhesions in animal model; serosal abrasions (Moll et al, 1991; Heidrick et al, 1994; Wurster et al, 1995; Vural et al, 1998; Mueller et al, 2000 and Hay et al, 2001); ischemic defects (Mueller et al, 2000); denudation (Ryan and Sax, 1995); electrocautery (Basbug et al, 1998 and Certin et al, 2004); cutting, scratching and scrapping (Haney and Doty, 1994) and stripping (El-sayed, 1977). In this study, intestinal serosal stripping adhesion model of the antimesentric border of jejunum and caecum lead to development of adhesions with different grades of severity and extent in the examined donkeys.

Visual and histopathological assessment of adhesions in the control donkeys revealed that adhesion was formed at approximately 60% of the stripped area. Adhesions was formed at 57% of the sites after electrocautery, 100% after cutting and scratching and 0% after scrapping (Haney and Doty, 1994); 100% after serosal stripping (El-Sayed, 1977); 29% after serosal injury increased to 91% when accompanied by subserosal injury. The degree and severity of adhesions would depend on the extent of the destruction produced during serosal stripping. In areas with massive serosal and subserosal damage healing of the denuded part took place with formation of adhesions and in areas with minimal destruction smooth healing occurs without adhesions (El-Sayed, 1977). The placed sutures act as foreign bodies and can cause tissue ischemia, thereby increasing the probability of adhesions development (Moll et al, 1991). Variability in the degree and extent of adhesions was attributed to the inadvertence during serosal stripping, low grade of infection, or individual variation in the tendency to form adhesion.

The selected materials used for intra-and postoperative peritoneal lavage in this study were dimethylsulfoxide, heparin in saline solution, lavasept in Ringer's lactate and carboxymethylcellulose. The selection of these materials was based on the current, empirical use of these substances in equine colic patients to prevent postoperative adhesions formation (Baxter, 1991) and its reported ability to prevent adhesions of the gastrointestinal and reproductive tracts of laboratory animals (EL-Ghoul, 2005).

Intraperitoneal lavage using DMSO had failed to prevent adhesion formation in the donkeys. Nonsteroidal antiinflammatory drugs were shown to reduce peritoneal adhesions in a variety of animal models after intraperitoneal lavage at the time of surgery in rat (Tayyar and Basbug, 1999), preoperative systemic administration in rabbits (Siegler at al, 1980), rats (Tsimoyiannis et al, 1989) and postoperative administration (Rodgers et al, 1996). However, Holtz (1982) demonstrated that it had no impact on adhesion prevention when given postoperatively. Anti-inflammatory drugs reduce adhesions by modulating fibrinolytic activity of resident macrophages and macrophages present in the early postsurgical period. It has been suggested that inflammation may be a contributory cause of serosal fibrin deposition, fibrosis and serosal adhesions in horses (Sullins et al. 1991) and ponies (Baxter et al, 1991b). DMSO was the first nonsteroidal anti-inflammatory discovered since aspirin. It reduces inflammation by its antioxidant activity and as a scavenger of the free radicals that gather at the site of injury (Shirley et al, 1978 and Bulbuloglu et al, 2005).

Peritoneal lavage using heparin diluted in sodium chloride solution lead to decrease in adhesion formation in donkeys (three donkeys are free and two had adhesion). This result was in agreement with Sahin and Saglam (1994) and Tayyar and Bashug (1999) who found that the extent, severity and total scores of adhesion formation were found to be reduced in rats when given heparin intraperitoneally or systematically with no harmful effect on hemostasis or wound healing. Subcutaneous heparin lead to significant decrease in adhesion formation in rats (Vela et al, 1999) dogs (Gupta and Jain, 1985) and ponies (Parker et al, 1987). Heparin is a potent inhibitor of several steps on the intrinsic coagulation pathway through its effect on a plasma cofactor and antithrombin III. Irrigation solutions containing the anticoagulant heparin have been used during surgery to reduce fibrin deposition on injured tissues. However, the increased risk of hemorrhage associated with heparin use has restricted clinical research in this area (Jansen, 1988). On the other hand the use of heparin to irrigate the peritoneal serosa during elective operations was found to have no important action in reducing the development of peritoneal adhesions in controlled clinical study in women (Jansen, 1988) and in rats (Diamond et al, 1991 and Sagol et al, 1999).

In lavasept peritoneal lavaged group; one donkey developed adhesions and the other one was free of adhesions. Lavasept is a noval antiseptic solution containing the polymeric biguanide polyhexanide was used as bactericidal antiseptic for peritoneum in 0.01% concentration (Willenegger, 1994 and Schmit-Neuerburg et al, 2001) and for antiinfective lavage of body cavities inclusively for peritoneal lavage in 0.05% concentration (Kramer et al, 1998).

Peritoneal lavage using 1% sodium carboxymethylcellulose solutions lead to prevention of adhesions formation in 50% of the examined donkeys which did not differ significantly between the SCMC treated group and the control group. Variable results have been reported following SCMC intraperitoneal lavage. SCMC has been found to reduce postoperative adhesions formation in intestinal and reproductive models in horses (Hay et al, 2001); ponies (Moll et al, 1991; Murphy et al, 2000 and Eggleston et al, 2004.), rats (Sahin and Saglam, 1994 and Sousa et al, 2001) ewes (Moll et al, 1992) and in rabbits (Diamond et al, 1987). On the other hand intraperitoneal instillation of SCMC failed to reduce postsurgical adhesion formation in rabbits (Gehlbach et al, 1994), rats (Yaacobi et al, 1993), ewes (Mansour et al, 1999) foals (Sullins et al, 1991) and in horses (Lopes et al, 1998). Diamond et al (1987) found an inverse correlation between either the concentration or the volume of SCMC employed and the extent of adhesion formation.

Carboxymethylcellulose is a substituted polysaccharide, water -soluble polymer that can provide a viscous barrier between serosal surfaces. The mechanism by which SCMC was able to reduce adhesion formation is uncertain. It may be a hydroflotation or siliconizing effect or coating of adhesiogenic tissues. The ionic nature of SCMC make the polymer strands repel each other in water, therefore, remaining freely soluble for longer time at the site of application and reduce adhesion formation. The efficacy of SCMC has not been proven in clinical studies (Diamond et al, 1987 and Southwood et al, 1997).

The results of this study emphasized the inconsistency of adhesion prevention by high molecular weight substances infused into the peritoneal cavity (Singer et al, 1996). The difference noted in the efficacy of SCMC in prevention of adhesions among animal species may be due to species variation in the pathophysiology of adhesion formation, the level of activity of plasminogen activator or activator inhibitor or the severity of the induction model (Singer et al, 1996).

In this study the observation period was 21 days, meanwhile some donkeys were dead before this time and the average observation period was 16 days in the control group; 10.8 days in DMSO group; 11.6 days in heparin group, 9.4 days in lavasept group and 15.5 days in SCMC group. Similarly, Ustun et al (1998) and Muller et al (2003) scored adhesions 21 days after surgery. Meanwhile adhesions were scored 3-7 days (Haney and Doty, 1994); 10 days (Hay et al, 2001); 12-14 days (Moll et al, 1992); 14 days (Diamond et al, 1987; Baxter et al, 1993 Hauge et al, 1998 and Sagol et al, 1999) and 45 days after surgery

(Otcu et al, 2003).

Postmortem examination in this study revealed that the most common site of postsurgical adhesions occurred between stripped jejunal and cecal serosa and laparotomy wound (abdominal wall adhesions) followed by adhesions between loops of intestine (intestinal adhesions). This was in close agreement with the observation of Menzies and Ellis (1990) and Ivarsson et al (1997).

Histopathological variables revealed that the adhesion scores were significantly higher in DMSO and lavasept groups and insignificantly higher in heparin and SCMC groups in comparison with the control group. Subjectively, higher adhesion scores were usually associated with a greater inflammatory response and more fibroplasia. The more mature fibrous adhesions had less inflammatory cell infiltration and thus lower the total histologic scores (Baxter et al, 1993).

The classic pathway for adhesion formation involved peritoneal injury, ischemia and foreign bodies which lead to peritoneal inflammation and production of plasminogen activator inhibitors. These inhibitors result in the loss of normal mesothelial fibrinolytic activity, and if prolonged, this allows the organization of fibrinous adhesions into permanent fibrous adhesions (Ellis, 1971/1980; Dijkstra et al, 2000 and Mutsaers, 2004). Horse is more sensitive to adhesion promoting factors (ischaemic tissue, infection, serosal trauma and foreign materials) and thus more prone to fibrous adhesion formation (Baxter, 1992 and Vegad, 1995).

The erythrogram showed that in DMSO group, the hemoglobin, hematocrit and red blood cell count were significantly decreased at the day of euthanization. This may caused by anemia due to peritonitis (Morris, 2002). Red blood cell count was significantly increased one week after induction of adhesion, with insignificant increase in hemoglobin and hematocrit values. Similar results were reported in horses (Semard, 1990; Lopes et al, 1999 and Dabareiner, 2002). This may caused by hemoconcentration and dehydration (Morris, 2002).

Regarding leukogram, significant leukopenia was recorded in DMSO, heparin and SCMC groups. Significant lymphocytosis was seen in the second and third week postoperation and a significant lymphopenia was noticed at the first week and at the day of euthanization in the heparin treated donkeys. Significant monocytosis was found in the heparin and SCMC group. Semard (1990); Darbareiner (2002) and Morris (2002) mentioned that in peritonitis white blood cell counts may be normal or a neutrophilic leukocytosis may be seen.

In lavasept and DMSO treated donkeys, the total protein was significantly increased at the first week after induction of adhesion. Hyperproteinemia may be due to dehydration or may result from increased immunoglobulin production (Dabareiner, 2002). Hypofibrinogenemia was observed at first week and day of euthanization in lavasept group and at the third week in SCMC group. Hyperfibrinogenemia was expected as a normal response to inflammation as mentioned by Johnston

and Morris (2002). Significant hyperglycemia was recorded at the first, second and third week after induction of adhesion in lavasept treated donkeys which may be a result of abdominal pain induced by surgery which result from release of endogenous epinephrine or corticosteroid in response to stress and can be expected with abdominal pain, regardless the cause (Coffman, 1980 and Moll et al, 1991). Serum urea level was significantly increased at the second week after adhesion induction in heparin treated donkeys. The reduced renal perfusion caused by hypovolemia due to dehydration produce elevation of urea (Carlson, 2002).

Peritoneal fluid reflects the pathophysiological state of parietal and visceral peritoneal surfaces (Hanson et al, 1992). Serial peritoneal fluid evaluation is a useful indicator for assessing the response of peritonitis and abdominal viscera trauma and various disease status to medical treatment (Hoogmoed et al, 1999).

The significant increased number of peritoneal red blood cell on the first day after adhesion induction in DMSO treated group and at the euthanization day in SCMC treated donkeys may have resulted from erythrocyte diapedesis through inflammed vessels (Schneider et al, 1988 and Cowell and Tyler, 2002). Hanson et al (1992) found that intestinal manipulation in horse lead to significant increase in RBCs numbers on the first post-operative day which significantly decreased after that. The total white blood cell count was significantly increased at the second and third day after induction of adhesion in DMSO treated group and

at the first, second and third day after induction of adhesion in SCMC treated donkeys. This may be due to the inflammation following induction of adhesion (Semrad, 1990; Mendes et al, 1999 and Cowell and Tyler, 2002). Hanson et al (1992) found that the total nucleated cells was significantly higher than normal on the first postoperative day after intestinal manipulation and had not returned to normal by the seventh postoperative day.

Regarding the peritoneal fluid differential leucocytic count, neutrophilia was noticed at the second and third day after induction of adhesion in DMSO treated group, and at the second day after induction of adhesion in SCMC treated donkeys. Hanson et al (1992) observed that intestinal manipulation in horse lead to neutophilia on the first postoperative day which remains unchanged by the seventh postoperative day. Neutrophils are the most common and important cell type in peritoneal effusions. They are attracted to the peritoneal cavity by chemostatic stimuli, and act in the primary cellular defense mechanisms against invading microorganisms (Steer and Lewis, 1983). Lymphopenia was observed at the first, second and third day after induction of adhesion in DMSO treated group and at the first, second and third day after induction of adhesion in lavasept treated donkeys. However, the percentage of macrophages, mast cells and mesothelial cells were significantly increased at the euthanization day in both DMSO and SCMC groups. Reactive mesothelial cells and macrophages are commonly increased in any peritoneal fluid transduate or exudate (Morris and Johnson, 1985). Similar results

were reported by Semard (1990); Cowell and Tyler (2002) and Mutsaers (2004).

The peritoneal fluid total protein was significantly increased at first day after adhesion induction in both DMSO and heparin treated donkeys. Peritoneal fluid fibrinogen was elevated significantly at the first day postoperation and significantly decreased at euthanization day in DMSO treated group. Peritoneal fluid total protein and fibrinogen concentration were significantly higher than normal, after intestinal manipulation, on the first postoperative day and remain unchanged by the seventh postoperative day (Hanson et al, 1992). The elevated peritoneal total protein and fibrinogen were previously reported in horses with peritonitis by Schneider et al (1988) and Cowell and Tyler (2002).

The changes in peritoneal fluid parameters indicated that surgical manipulation of abdominal viscera and/or peritoneal lavage creates a significant and rapid postoperative inflammatory reaction. This was in close agreement with the observations of Schneider et al (1988); Hanson et al (1992) and Lopes et al (1999).

In conclusion it can be said that, intra-abdominal adhesions are an important complication after abdominal surgery in equine. Several pharmacologic strategies have been devised to modulate the biochemical processes involved in inflammation and adhesion formation, but all have major limitations. Despite of general acceptance and widespread usage, the effectiveness of intraperitoneal lavage using dimethyl sulfoxide, heparin, lavasept

and sodium carboxymethylcellulose in the prevention of adhesions cannot be scientifically supported because the results were controversial and lacked any implication for clinical use. Failure of the used materials to prevent adhesions may be due to that stripping of the intestinal serosa in the examined donkeys may have created enough severe serosal damage that any form of pharmacologic interventions would not have prevented adhesions formation and equine being particularly susceptible to form fibrous adhesions. The efficacy of antiadhesion agents appears to be related to the agent's viscosity ability to coat the wound surface and residence time at the site of injury. Therefore, adequate prevention by pharmacologic intervention may require the development of an efficient vehicle or drug delivery system. Unfortunately, no method has gained wide acceptance and surgeons must rely on meticulous surgical technique which can minimize tissue trauma and reducing the risk of postsurgical adhesions formation.

REFERENCES

- Bancroft, J. and Cook, H. (1994): Manual of histopathological technique. 3 rd Ed. Churchill, Livingstone, London and New York.
- Basbug, M.; Aygen, E.; Tayyar, M.; Kaya, E.; Narin, F. and Oktem, O. (1998): Hyaluronic acid plus heparin for improved efficacy in prevention of adhesion formation in rat uterine horn model. Eur. J. Obstet. Gynecol. Reprod. Biol., 78:109-112.
- Baxter, G. (1991): Intrabdominal adhesions in horses. Comp. Contin. Educ. Pract. Vet., 13:1587-1598.
- Baxter, G. (1992): Serosal adhesions-the next hurdle in col-

- ic surgery. Equine Vet. J. Suppl., 13:38-41.
- Baxter, G.; Broome, T. and Moore, J. (1989): Abdominal adhesions after small intestinal surgery in the horse. Vet. Surg., 18:409-414.
- Baxter, G.; Jackman, B.; Tyler, D. and Clark, E. (1991b): The use of calcium channel blockade for intraabdominal adhesion prophylaxis in ponies. Vet. Surg., 20:329-330.
- Baxter, G, Jackman, B, Eades, S. and Tyler D. (1993): Failure of calcium channel blockade to prevent intraabdominal adhesions in ponies. Vet Surg Nov-Dec; 22 (6):496-500
- Bhatia, D. and Allen, J. (1997): The prevention of experimentally induced postoperative adhesions. Am Surg Sep;63(9):775-7
- Boland, G. and Weigel, R. (2006): Formation and Prevention of Postoperative Abdominal Adhesions. J Surg Res. Jan 31.
- Bulbuloglu, E., Ezberci, F., Gul, M., Kurutas, E., Bozkurt, S., Kale, I. and Ciragil, P. (2005): Effects of the intraperitoneal lornoxicam on the formation of intraperitoneal adhesions in rat peritonitis model. ANZ J Surg.;75 (12):1115-9.
- Carlson, G. (2002): Clinical chemistry tests. In: Smith, B (ed): Large animal internal medicine, 3 rd ed., Philadelphia, mosby pp: 389-412.
- Cetin, M., Duran, B., Demirkoprulu, N., Guvenal, T., Erden, O. and Cetin, A. (2004): Effects of Diazeniumdio-lates (NONOates) and Methylene Blue on the Reduction of Postoperative Adhesion in Rats. Gynecol Obstet Invest.; 57(4):186-190.
- Chan, K., Marino, T., Qu W. and Tulandi, T. (1995): Effects of intraperitoneal Ringer's lactate instillation and infusion on postsurgical adhesion formation. J Gynecol Surg Winter; 11(4):241-3
- Coffman, J. (1980): Peritoneal fluid in horses. Vet. Med.

- Small Animal Clinician, August: 1285-1288.
- Cowell, R. and Tyler, R. (2002): Diagnostic cytology and hematology of the horse. 2nd ed., Mosby, st. louis, USA, pp: 127-162.
- Dabareiner, R. (2002): Peritonitis in horses. In: Smith, B (cd): Large animal internal medicine, 3 rd ed., Philadelphia, mosby pp:668-674.
- Diamond, MP (2001): Prevention of adhesions. In: Operative gynecology, 2nd ed, Philadelphia: W.B. Saunders; 211-222.
- Diamond MP, Daniell JF, Feste J. (1987): Adhesion formation and de novo adhesion formation after reproductive pelvic surgery. Fertil Steril.; 47:864-866.
- Diamond, M.; Linsky, C.; Cunningham, T.; Kamp, L.; Pines, E.; DeCherney, A. and Di Zerega, G.(1991): Synergistic effects of INTERCEED (TC7) and heparin in reducing adhesion formation in the rabbit uterine horn model. Fertil Steril Feb; 55(2):389-94
- Dijkstra, F.; Nieuwenhuijzen, M.; Reijnen, M. and Goor, H. (2000): Recent clinical developments in pathophysiology, epidemiology, diagnosis and treatment of intraabdominal adhesions. Scand J Gastroenterol Suppl; (232):52-9
- DiZerega, G. (1997): Biochemical events in peritoneal tissue repair. Eur J Surg Suppl;(577):10-6
- Duncan, J.; Prasse, K. and Mahaffey, E. (1994): Veterinary laboratory medicine: clinical pathology. 3rd ed., Iowa state university press, Ames, Iowa, USA.
- Eggleston, R.; Mueller, P.; Parviainen, A. and Groover, E. (2004): Effect of carboxymethylcellulose and hyaluronate solutions on jejunal healing in horses. Am J Vet Res.;65(5):637-43.
- EL-Ghoul, W. (2005): The effects of combined liquid and membrane barriers in prevention of post-operative intraabdominal adhesions after experimental jejunal anastomosis in dogs. Dtsch. Tierärztl. Wschr.112:3-10.

- Ellis, H. (1971): The cause and prevention of postoperative intraperitoneal adhesions. Surg Gynecol Obstet.;1 33:497-51 1.
- Ellis, H. (1980): Internal overhealing: the problem of intraperitoneal adhesions. World J. Surg., 4:303-306
- Ellis, H. (1982): The causes and prevention of intestinal adhesions. Br J. Surg May; 69 (5):241-3
- El-Sayed, A. (1977): Peritoneal adhesions its aetiology and prevention. Ph.D. Vet. Thesis, CairoUuniversity.
- Gehlbach, D.; O'Hair, K.,; Parks, A. and Rosa, C. (1994):
 Combined effects of tissue plasminogen activator and carboxymethylcellulose on adhesion reformation in rabbits. Int J Fertil Menopausal Stud May-Jun; 39 (3):172-6Related
- Gupta, S. and Jain, P. (1985): Low-dose heparin in experimental peritonitis. Eur Surg Res; 17(3):167-72
- Haney, A. and Doty, E. (1994): The formation of coalescing peritoneal adhesions requires injury to both contacting peritoneal surfaces. Fertil Steril Apr; 61(4):767-75
- Hague, B.; Honnas, C.; Berridge, B. and Easter, J. (1998): Evaluation of postoperative peritoneal lavage in standing horses for prevention of experimentally induced abdominal adhesions. Vet Surg Mar-Apr;27(2):122-6
- Hanson, R.; Nixon, A.; Gronwall, R.; Meyer, D and Pendergast, J. (1992): Evaluation of peritoneal fluid following intestinal resection and anastomosis in horses.
 Am.J.Vet.Res., 53:216-221.
- Hay, W.; Mueller, E.; Harmon, B. and Amoroso, L. (2001): One percent sodium carboxymethylcellulose prevents experimentally induced abdominal adhesions in horses. Vet. Surgery, 30:223-227.
- Heidrick, G.; Pippitt, C.; Morgan, M. and Thurnau, G. (1994): Efficacy of intraperitoneal sodium carboxymethylcellulose in preventing postoperative adhesion formation. J Reprod Med Aug; 39(8):575-578

- Hoogmoed, L.; Rodger, L.; Spier, S.; Gardner, I.; Yarbrough, T. and Snyder, J. (1999): Evaluation of peritoncal fluid pH, glucose concentration and lactate dehydrogenase activity for detection of septic peritonitis in horses. JAVMA, 214:1032-.
- Ivarsson, M.; Holmdahl, L; Franzen, G. and Risberg, B. (1997): Costs of bowel obstruction from adhesions. Eur. J. Surg., 163:679-84.
- Jansen, R. (1988): Failure of peritoneal irrigation with heparin during pelvic operations upon young women to reduce adhesions. Surg Gynecol Obstet.;166:154-160.
- Johnston, J. and Morris, D. (2002): Alterations in blood proteins. In: Smith, B (ed): Large animal internal medicine, 3 rd ed., philadelphia, mosby pp:
- Kramer, A; Adrian, V; Rudolph, P; Wurster, S. and Lippert H. (1998): Explantationstest mit Haut und Peritoneum der neonatalen Ratte als Voraussagetest zur Vertraegmoglichkeit lokaler Antiinfektiva für Wunden und Koerperhoelen. Chirurg 69: 840-845.
- Kuehl, R. (1994): Statistical Principles of Research Design and Analysis. Belmont, CA: Duxbury Press.
- Lopes, M.; Oliveira D.; Iamaguti, P.; Thamassian, A. and Figueiredo, L. (1998): Peritoneal adhesions in horses: prophylactic treatment with carboxymethylcellulose. Ciencia Rural, 28:423-430.
- Lopes, M.; Oliveira D.; Biondo, A.; Godin, L.; Iamaguti, P.; Thamassian, A. and Kohayagawa, A. (1999): Examination of peritoneal fluid and the hemogram of horses submitted to labarotomy with intraperitoneal infusion of carboxymethylcellulose. Ciencia Rural, 29:79-85.
- MacDonald, M.; Pascoe, J.; Stover, S. and Meagher, D. (1989): Survival after small intestinal surgery in the horse. Vet. Surg., 18:415-423.

- Mair, T. and Smith, L. (2005): Survival and complication rates in 300 horses undergoing surgical treatment of colic. Part 3: Long-term complications and survival. Equine Vet J. 2005 Jul;37(4):310-4.
- Mansour, M.; Senna, N. and Abdo, G. (1999): Adhesions prevention following repeated superovulation and surgical embryo recovery in balady goats. Vet. Med. J, Giza; 47:137-148.
- Mendes, L.; Marques, L.; Bechara, G. and Peiro, J. (1999): Experimental peritonitis in horses: Peritoneal fluid composition. Arquivo Veterinaria e Zootecnia, 51: 217-221.
- Menzies D. and Ellis H. (1990): Intestinal obstruction from adhesions-how big is the problem? Ann R Coll Surg Engl.; 72:60-63.
- Moll, H.; Schumacher, J.; Wright, J. and Spano J. (1991): Evaluation of sodium carboxymethylcellulose for prevention of experimentally induced abdominal adhesions in ponies. Am J Vet Res Jan; 52(1):88-91
- Moll, H.; Wolfe, D.; Schumacher, J and Wright, J. (1992): Evaluation of sodium carboxymethylcellulose for prevention of adhesions after uterine trauma in ewes. Am J Vet Res Aug; 53(8):1454-6.
- Morris, D. and Johnson, J. (1985): Peritoneal fluid constituents in horses with colic due to small intestinal disease.

 Second equine colic research symposium, 134-141.
- Morris, D. (2002): Alterations in the erythron. In: Smith, B (ed): Large animal internal medicine, 3 rd ed., Philadelphia, mosby pp: 415-419.
- Morris, D. (2002): Alterations in the leukogram. In: Smith, B (ed): Large animal internal medicine, 3 rd ed., Philadelphia, mosby pp: 420-426
- Mueller, P.; Hunt, R.; Allen, D.; Parks, A. and Hay, W. (1995): Intraperitoneal use of sodium carboxymethylcellulose in horses undergoing exploratory celiotomy. Vet Surg Mar-Apr; 24(2):112-7
- Mueller, E.; William, P.; Harmon, B. and Amoroso, L.

- (2000): Evaluation of a bioresorbable hyaluronate-carboxymethylcellulose membrane for prevention of experimentally induced abdominal adhesions in horses. Vct. Surgery; 29:48-53.
- Mueller, S.; Treutner, K.; Haase, G.; Kinzel, S.; Tietze, L. and Schumpelick V. (2003): Effect of intraperitoneal antiadhesive fluids in a rat peritonitis model. Arch Surg 2003 Mar; 138(3):286-90
- Murphy, D.; Peck, L.; Widenhouse, C. and Goldberg, E. (2000): Efficacy of carboxymethylcellulose for the prevention of post-operative adhesions in a modified equine bowel adhesion model. Tenth Annual American College of Veterinary Surgeons Symposium, Arlington, VA.
- Mutsaers, S. (2004): The mesothelial cell. Int J Biochem Cell Biol. Jan; 36(1):9-16.
- Otcu, S.; Ozturk, H.; Aldemir, M.; Kilinc, N. and Dokucu, A.(2003): Influence of the Platelet-Activating Factor Recep tor Antagonist BB-882 on Intra-Abdominal Adhesion Formation in Rats. Eur Surg Res 2003; 35(1):41-5
- Ozel, H.; Avsar, F.; Topaloglu, S. and Sahin, M. (2005): Induction and assessment methods used in experimental adhesion studies. Wound Repair Regen.;13(4):358-64.
- Parker, J.; Fubini, S.; Carr, B. and Erb, H. (1987): Prevention of intra-abdominal adhesions in ponies by low dose heparin therapy. Vet. Surg., 16:459-462.
- Parker, J.; Fubini, L. and Todhunter, R. (1989): Retrospective evaluation of repeat celiotomy in 53 horses with acute gastrointestinal disease. Vet. Surg., 18:424-431.
- Prasse, K.; Topper, M.; Moore, J. and Welles, E. (1993): Analysis of hemostasis in horses with colic. JAVMA, 203:685-693.
- Risberg, B. (1997): Adhesions: preventive strategies. Eur J Surg Suppl;(577):32-9.
- Rodgers, K.; Girgis, W.; Campeau, J. and DiZerega, G. (1996): Reduction of adhesion formation by intraperitoneal administration of a recombinant Hirudin analog. J.

- Invest. Surg., 9:385-91.
- Ryan, C. and Sax, H. (1995): Evaluation of a carboxymethylcellulose sponge for prevention of postoperative adhesions. Am J Surg Jan; 169(1):154-9; 159-60
- Sahin, Y. and Saglam A. (1994): Synergistic effects of carboxymethylcellulose and low molecular weight heparin in reducing adhesion formation in the rat uterine horn model.Acta Obstet Gynecol Scand Jan; 73(1):70-3
- Sagol, S.; Ozsener, S.; Dincer, O.; Yilmaz, H. and Karada-das, N. (1999): The effect of medroxyprogesterone acetate and heparin in the prevention of postsurgical adhesion formation in the rat uterine model. J Obstet Gynaecol Res Aug; 25(4):287-93
- Schmit-Neuerburg, K.; Bettag, C.; Schlickewei, W.; Fabry, W. and Hanke, J. (2001): Effectiveness of an improved antiseptic in treatment of contaminated soft tissue wounds. Chirurg, 72:61-71.
- Schneider, R.; Meyer, D.; Embertson, R.; Gentile, D. and Buergelt, C. (1988): Response of pony peritoneum to four peritoneal lavage solutions. Am. J. Vet. Res., 49:889-894.
- Semard, S. (1990): Peritonitis in the horse. In: Smith, B (ed): Large animal internal medicine. Philadelphia, Mosby. pp: 674-679.
- Shirley, S.; Stewart, B. and Mirelman, S. (1978): Dimethyl sulfoxide in treatment of inflammatory genitourinary disorders. Urology, 11:215-220.
- Siegler, A.; Kontopoulos, V. and Wang, C. (1980): Prevention of postoperative adhesions in rabbits with ibuprofen, a nonsteroidal anti-inflammatory agent. Fertil Steril Jul; 34(1):46-49.
- Sikkink, C.; Reilingh, T.; Malyar, A.; Jansen, J.; Bleichrodt, R. and Goor, H. (2006): Adhesion formation and reherniation differ between meshes used for abdominal wall reconstruction. Hernia. Feb 16;
- Singer; Livesey; Hurtig; Barker and Conlon (1996): Utiliza-

- tion of the serosal scarification model of postoperative intestinal adhesion formation to investigate potential adhesion-preventing substances in the rabbit. Can.J.Vet.Res. 60:305-311.
- Smith, C.; Dowling, B. and Dart, A. (2005): Recent advances in equine abdominal surgery. Vet J.;170(1):41-51.
- Southwood, L. and Baxter, G. (1997): Current concepts in management of abdominal adhesions. Vet Clin North Am Equine Pract Aug; 13(2):415-35
- Southwood, L.; Baxter, G; Hutchison, J. and Shuster, R. (1997): Survey of diplomates of the American College of Veterinary Surgeons regarding postoperative intraabdominal adhesion formation in horses undergoing abdominal surgery. J Am Vet Med Assoc Dec 15; 211 (12):1573-6
- Steer, H. and Lewis, D. (1983): Peritoneal cell response to acute gastrointestinal inflammation. Pathology; 140:237-253.
- Sullins, K.; White, N.; Lundin, C.; Gaulin, G. and Dabareiner, R. (1991): Treatment of ischemia -induced peritoneal adhesions in foals. Vet. Surg., 20:348.Sullins, K.; White, N.; Lundin, C.; Dabareiner, R. and Gaulin, G. (2004): Prevention of ischaemia-induced small intestinal adhesions in foals. Equine Vet J.;36(5):370-5.
- Tayyar, M. and Basbug, M. (1999): The effects of intraperitoneal piroxicam and low molecular weight heparin in prevention of adhesion reformation in rat uterine horn. Res. Exp. Med (Berl), 198:269-275.
- Treutner, K. and Schumpelick, V. (2000): Prevention of adhesions. Wish and reality Chirurg May; 71(5):510-7
- Tsimoyiannis, E.; Tsimoyiannis, J.; Sarros, C.; Akalestos, G.; Moutesidou, K.; Lekkas, E. and Kotoulas, O. (1989): The role of oxygen-derived free radicals in peritoneal adhesion formation induced by ileal ischaemia/reperfusion. Acta.Chir.Scand., 155:171-174.

- Ustun, C.; Yanik, F.; Kocak, I.; Canbaz, M. and Cayli, R. (1998): Effects of Ringer's lactate, medroxyprogesterone acetate, gonadotropin-releasing hormone analogue and its diluent on the prevention of postsurgical adhesion formation in rat models. Gynecol Obstet Invest; 46 (3):202-5
- Vegad, J. (1995): Textbook of veterinary general pathology. ist ed. Nikas Publishing House, London, Philadelphia and New York.
- Vela, A.; Littleton, J. and O'Leary, J. (1999): The effects of minidose heparin and low molecular weight heparin on peritonitis in the rat. Am Surg May; 65(5):473-7
- Vural, B.; Mercan, R.; Corakci, A.; Ozeren, S.; Keskin, N.;
 Vural, S.; Yucesoy, I. and Erk, A. (1998): A trial of reducing adhesion formation in a uterine horn model.
 Gynecol. Obstet. Invest., 45:58-61.
- Willenegger, H. (1994): Local antiseptics in surgery-rebirth and advances. Unfallchirurgie, 20:94-110.
- Wurster, S., Bonet V., Mayberry A., Hoddinott, M., Williams, T. and Chaudry, I. (1995): Intraperitoneal sodium carboxymethylcellulose administration prevents reformation of peritoneal adhesions following surgical lysis.

 J Surg Res Jul; 59:97-102.
- Yaacobi, Y.; Israel, A. and Goldberg, E. (1993): Prevention of postoperative abdominal adhesions by tissue precoating with polymer solutions. Surg Res.; 55:4224-26.
- Yagmurlu, A.; Barlas, M.; Gursel, I. and Gokcora, I. (2003): Reduction of surgery-induced peritoneal adhesions by continuous release of streptokinase from a drug delivery system. Eur Surg Re s 2003; 35 (1):46-9.

كفاءة الغسيل البريتونى اثناء وبعد العمليات الجراحية في منع تكون التصاقات الغشاء البريتوني في بطن الحمير : دراسة تجريبية

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أجريت هذه الدراسة على ٢٢ من الحمير والتى تبدو إكلينيكيا سليمة حيث تعرضت جميع الحمير إلى نزع جزء من مصلية الصائم والمستقيم كطريقة الحث على تكون الإلتصاقات في التجويف البطني. وقسمت الحمير إلى خمس مجموعات ، في المجموعة الأولى الضابطة لم تتعرض الحمير إلى أي علاج بينما في المجموعات الأربع الأخرى تم عمل غسيل بريتوني لمكان نزع مصلية الصائم والمستقيم والتجويف البطني أثناء العملية وكذلك الغسيل البريتوني لمدة طائحة أيام متتالية من بعد العملية . وكانت المواد المستخدمة في الغسيل البريتوني في المجموعة الثانية هي -sodium chloride sterile solution وفي المجموعة الشائشة هي thyl sulfoxide 20% solution Ringc 's lactate sterile solution وفي المجموعة الرابعة هي containing 5000 IU heparin/iter . 1% sodium. من معموعة المحموعة الخامسة هي sodium chloride المحموعة والتحاليل الإكلينيكية وجود أوضحت نتائج الفحوصات التشريحية الكمية ونظام سجل الإلتصاقات الهيستوباثولوجية والتحاليل الإكلينيكية وجود فروق غير معنوية في سجل الإلتصاقات المتكونة بعد الجراحة بين مجموعات الحمير الأربع التي تم عمل الغسيل البريتوني لم وبين مجموعة الحمير الفابلة . ويمكن القول أن فاعلية المواد المستخدمة في الغسيل البريتوني أثناء وبعد العمليات الجراحية في منع تكون التصاقات الغشاء البريتوني لم يتم إثباتها علمياً في هذه الدراسة حيث أن الجراحية التي تقلل من درجة جرح الإنسجة في عمليات البطن في الحد من خطورة تكوين الإلتصاقات البريتونية بعد الجراحية التي تقلل من درجة جرح الإنسجة في عمليات البطن في الحد من خطورة تكوين الإلتصاقات البريتونية بعد العمليات المراحية التي العراحة .