

EFFECTS OF RINGER'S LACTATE AND ASPIRIN ON POSTSURGICAL ADHESION FORMATION

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- ✓ This research was planned to evaluate the effects of Aspirin (acetyl salicylic acid-ASA) and Ringer's lactate solution (RL) on postoperative pelvic adhesion formation. After creating a standard lesion over the uterus, thirty adult female rats were randomly divided into 3 groups. In group II, Aspirin, 0.35 mg every 6 hours for 96 hours im; and in group III, intraperitoneal RL were applied. Group I was the control group. Relaparotomy was performed 15 days later to score the adhesion formation. Mean adhesion scores were 2.90 ± 0.31 (mean \pm SEM), 2.00 ± 0.26 and 1.00 ± 0.30 in group I (control), group II (Aspirin) and group III (RL) respectively. Group III had significantly lower adhesion scores than group I and II ($p < 0.05$). The scores of group I and II did not show significant difference ($p > 0.05$).

In this study, although Aspirin decreased postoperative adhesion formation, there was no statistically significant difference between the control group and the Aspirin-treated group. RL solution was significantly superior to Aspirin in preventing the adhesion formation.

Key words: Aspirin, Ringer's Lactate, adhesion formation.

- ✓ **Ringer Laktat ve Aspirin'in Cerrahi Sonrası Yapışıklıklar Üzerine Etkisi**
Bu çalışma, Aspirin (asetil salisilik asit) ve Ringer laktat (RL) solusyonunun postoperatif pelvik adezyon formasyonu üzerine etkilerini araştırmak amacıyla yapıldı. Otuz dişi rat, uterus üzerinde standart bir lezyon oluşturulduktan sonra randomize olarak 3 gruba ayrıldı. Grup II'ye 96 saat süreyle ve 6'şar saat aralarla 0,35 mg Aspirin im; grup III'e de intraperitoneal RL uygulandı. Grup I kontrol grubu kabul edildi. Adezyon formasyonunu skorlamak amacıyla 15 gün sonra relaparotomi yapıldı. Ortalama adezyon skorları, grup I (kontrol), grup II (Aspirin) ve grup III (RL)'te sırasıyla 2.90 ± 0.31 (mean \pm SEM), 2.00 ± 0.26 ve 1.00 ± 0.30 olarak tespit edildi. Grup III'te adezyon skorları grup I ve II'ye göre anlamlı olarak daha düşüktü ($p < 0.05$).

Bu çalışmada Aspirin postoperatif adezyon formasyonunu azalttıysa da, kontrol grubu ve Aspirin uygulanan grup arasında istatistiksel olarak anlamlı bir fark tespit edilemedi. Adezyon oluşumunu önlemede, Ringer laktat Aspirine göre daha üstün bulundu.

Anahtar kelimeler: Aspirin, Ringer laktat, adezyon formasyonu.

INTRODUCTION

Intraperitoneal adhesions after surgery continue to be a significant source of longterm morbidity. A special case is pelvic surgery in which tuboovarian adhesions may impair future fertility. By some estimates 25% of infertility is caused by adhesive disease, either secondary to operations or infections⁽¹⁾.

Although the precise pathophysiological

mechanism of adhesion formation is not clearly outlined, it is widely accepted that inflammation, ischemia, or trauma to the serosal surface of the abdominal organs are the initiatory of the inflammatory reaction, followed by an increase in vascular permeability and the release of a fibrin-rich exudate^(2,3). If fibrinolysis is not completed through the plasminogen-plasmin cascade, adhesions may form through collagen

deposits on a framework of proteoglycan and fibronectin⁽⁴⁾. Since inflammation, as shown by the focal infiltration of white cells, edema and neovascularization, is an integral part of postsurgical healing, a major challenge would be the identification of drugs that would not affect the natural healing process, but rather would significantly reduce post-surgical adhesion formation⁽⁵⁾.

Aspirin (acetylsalicylic acid) is the most widely known non-steroidal anti-inflammatory drug which acts through the irreversible inactivation of the enzyme cyclo-4 oxygenase and is believed to have the potential of inhibiting post-traumatic adhesion formation^(2,6).

In the present study, we investigated the effects of systemically administered Aspirin (0.35 mg every 6h for 96 h in addition to the pre-operative dose of 0.70 mg, as proposed by Golan A. et.al.) and intraperitoneal RL solution on the prevention of adhesion formation in rats⁽⁵⁾.

MATERIAL AND METHODS

This single blind study was made on a

total of 30 adult female rats, weighing 200-250 gr, in Ondokuzmayis University, Medical Faculty, Surgical Research Center. General anesthesia was induced via intraperitoneal injection of ketamine hydrochloride (60 mg/kg of body weight). The abdomen was shaved and prepared with povidine-iodine solution. Preoperatively each animal received 0.1 mg of ampicillin subcutaneously for prophylaxis. Laparotomy was then performed under clean but not sterile techniques, using a 4 cm midline incision. After exposing the bicornuate uterus (Fig. 1), the right uterine horn of each rat was subjected to a standardized lesion by denuding a 3 cm segment of the serosa on the proximal antimesometric area with a scalpel until macroscopic punctate bleeding was seen and by electrocauterization of that segment (Fig. 2). The rats were randomized into 3 groups (10 rats/group): Group I (control) had no treatment; Group II received Aspirin in doses of 0.35 mg every 6h for 96h intramuscularly in addition to the preoperative dose of 0.70

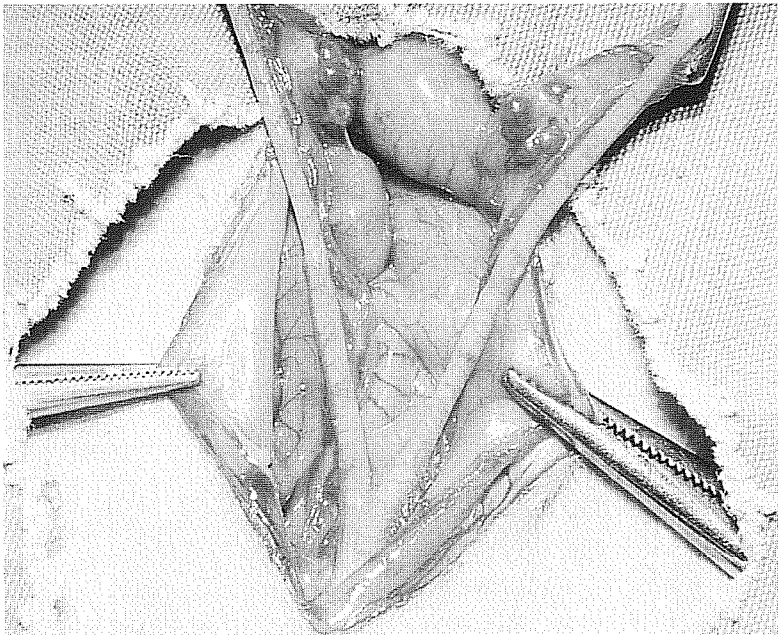


Figure 1.
Normal uterine horns of rat

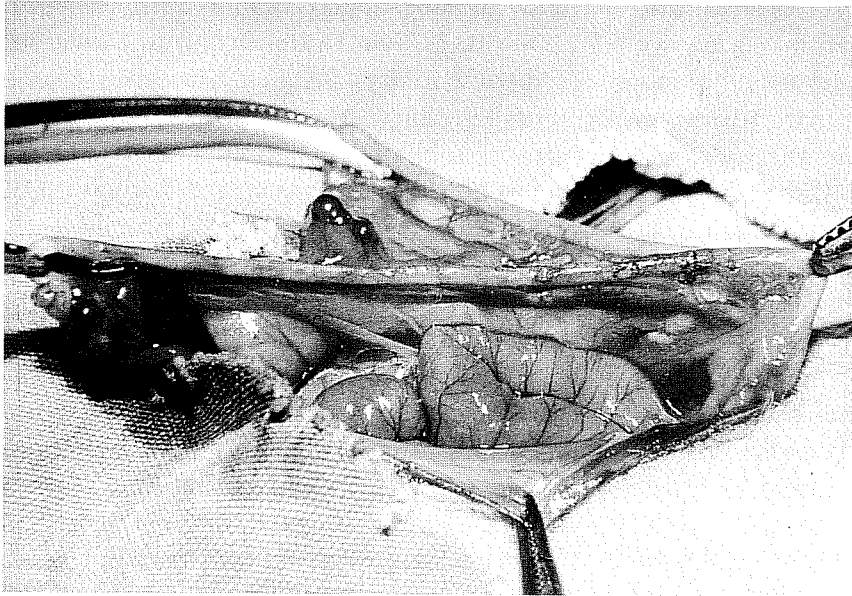


Figure 2.
The standard lesion over
the right uterine horn

mg. In Group III, Ringer's Lactate solution (6 ml) was instilled into the peritoneal cavity before abdominal closure.

Relaparotomy was performed 2 weeks after the initial surgery. With a magnifying lens, the degree of adhesions was scored according to the modified scoring scale based on the number, thickness and vascularity of the adhesion strings (Table I). The adhesion scores of the 3 groups were compared using nonparametric statistics (Kruskal-Wallis test, Mann-Whitney U test). All values are expressed as the mean \pm standard error of the mean (SEM).

RESULTS

The average adhesion scores assessed at relaparotomy are shown in figure 3. Mean adhesion scores were 2.90 ± 0.31 , 2.00 ± 0.26 and 1.00 ± 0.30 in group I (control), group II (Aspirin) and group III (RL) respectively. Group III had significantly lower adhesion scores than group I and II ($p < 0.05$). Although group II had lower adhesion scores than the control group, this difference was not statistically significant ($p > 0.05$).

Table II shows the adhesion scores with respect to the groups. All the rats in group I and II had adhesions over the right uterine horn whereas there weren't any adhesions in

Table I. Modified Adhesion Scoring Scale.

Scores:	Number of adhesions:
0	No visible adhesion
1	1 thin, easily separable, avascular adhesion
2	2 thin, easily separable, avascular adhesions
3	3 thin, easily separable, avascular adhesions
4	> 3 thin, easily separable, avascular adhesions or vascularized or diffuse adhesions

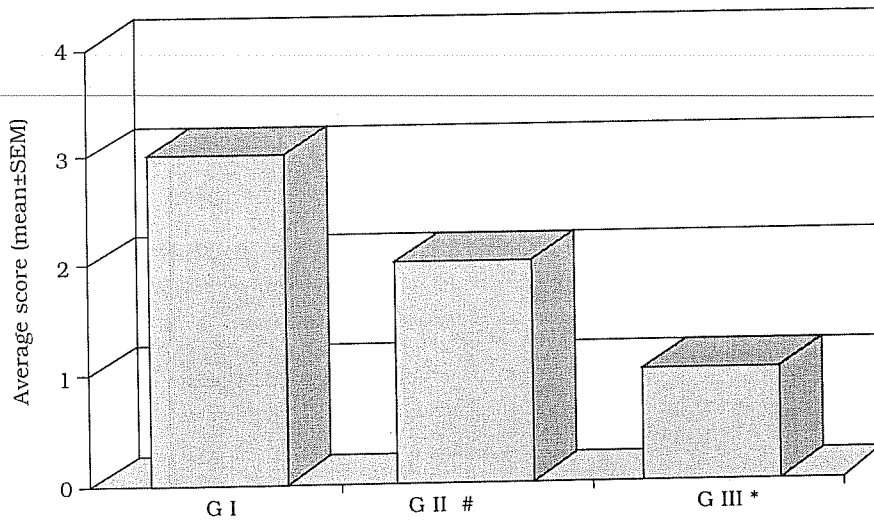


Figure 3.
Average adhesion scores for each group

* : p<0.05 versus Group I and Group II
#: p>0.05 versus Group I

Table II. Distribution of Adhesion Scores Among Groups.

Adhesion Score	Group I (n)	Group II (n)	Group III (n)
0	-	-	3
1	-	3	5
2	5	4	1
3	1	3	1
4	4	-	-

3 cases of group III. Five cases of group I had adhesion scores of 3 and 4 (Fig. 4), although there were 3 cases in group II and 1 case in group III with the adhesion score of 3. There were no cases with the score of 4 (having diffuse vascular adhesions) among the Ringer lactate or Aspirin treated rats.

DISCUSSION

A great number of solutions, chemical agents, natural and synthetic graft materials have been tried to reduce adhesion formation. Saline solution, Ringer's lactate, Dextran 70, promethazine, heparin, glucocorticoids, progesteron, nonsterodial anti-inflammatory

drugs, calcium channel blockers are examples for the solutions and chemical agents used (7-9). Natural graft materials have included peritoneum, omentum, fat and amnion (10-12). Synthetic materials, including polyvinyl alcohol film and tantalum foil were used in the past and more recently barriers consisting of Gelfilm and Gelfoam paste, Surgicel, Silastic, meshes of Gore-tex and Interceed have been employed(10,12-18).

In spite of these studies, adhesion formation and reformation are still the major problems of infertility surgery.

The clinical benefit of aspirin is thought to stem from the inhibition of thromboxane A₂

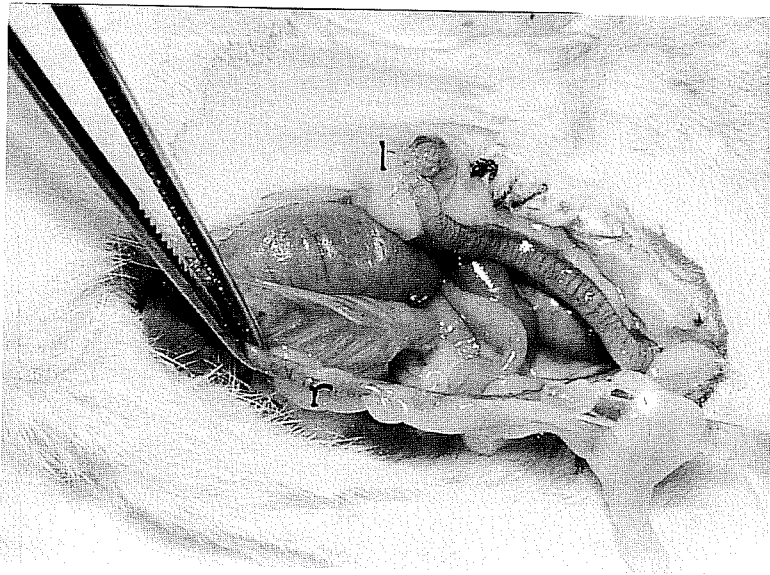


Figure 4.
Post-traumatic adhesion
formation over the right
uterine horn
r: right uterine horn
l: left uterine horn

production, a potent vasoconstrictor formed from arachidonic acid and known as a mediator in the process of inflammation^(19,20). However, it has been shown that aspirin's antithrombotic efficacy may be limited by the coincidental inhibition of prostacyclin, a major product of vascular endothelium, which affects platelet function and vascular tone in an opposite way to that of thromboxane A_2 ⁽²⁰⁾. Other known anti-inflammatory qualities of aspirin include its capacity to inhibit the kallikrein system and act as an antioxidant directly through its ability to absorb free radicals⁽²¹⁾. Several investigators have suggested that the enzyme release from both platelets and mast cells may promote the conversion of prothrombin to thrombin during the repair phase of adhesion formation^(22,23). The specific ability of aspirin to annihilate platelet enhancement and counteract thrombin formation in the process of adhesion formation is probably another quality which has been demonstrated⁽²²⁾.

Aspirin administration i.p. was able to inhibit prostaglandin $F_{2\alpha}$ and E_2 formation, thus suggesting that the anti-adhesive effect of aspirin might be related to its

anti-prostaglandin activity and could be the biochemical basis for its anti-adhesive effect⁽⁶⁾.

In the present study, it has been shown that systemic administration of low dose aspirin, during the first 96 h of the initial acute post-inflammatory reaction following surgery, demonstrates a beneficial effect in limiting the extent of tissue involvement in the adhesive process. Although the total adhesion scores are not significantly different from the control group, Aspirin treatment decreases the density and diffuseness of the postsurgical adhesions.

Similarly, several studies have demonstrated the beneficial effect of nonsteroidal anti inflammatory drugs such as oxyphenbutazone, ketorvolac, ibuprofen, meclofenamate as well as aspirin, in limiting the extent of adhesion formation^(1,5,20,24,25).

RL appears to be an effective solution for preventing adhesion formation and reformation⁽²⁶⁻²⁹⁾. The mechanism by which RL prevents adhesion formation remains unclear. The floatation effect, whereby contact between raw peritoneal surfaces is limited; and dilution of fibrin and fibrinous exudate

released from the injured surface, are the possible explanations. The fact that RL is still retained in the abdominal cavity in significant amount for upto 36 hours; substantiates this theory⁽²⁷⁾.

This study also shows that intraperitoneal RL is effective in decreasing the adhesion formation when compared to the control group. Besides this; classical intraperitoneal application of RL appears to be significantly more beneficial than systemic low-dose Aspirin treatment in preventing the adhesive process.

Caution is advised whenever inferences from animal studies are extended into human clinical practice. The use of aspirin during the intra or postoperative period is not advised, since it may induce bleeding due to its prolongation of bleeding time by inhibiting platelet aggregation⁽³⁰⁾. Thus, we believe further animal and human studies are required about Aspirin usage in the prophylaxis of postoperative adhesions.

We may conclude that, RL is still the most commonly used and preferable agent in the prophylaxis of postoperative adhesion formation, as it is cheap, readily found and easily applied.

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