

# Comparison of the resorbable barrier Interceed (TC7) and preoperative use of medroxyprogesterone acetate in postoperative adhesion prevention

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## Summary

**Purpose:** The purpose of this study was to compare the effectiveness of barrier agent Interceed (TC7) (Johnson & Johnson Medical, Inc) and preoperative use of commonly used progesterone, medroxyprogesterone acetate.

**Methods:** Forty-five Sprague-Dawley white rats of reproductive age (225-250 g) were employed as a model for postsurgical adhesion formation. Group 1 consisted of control rats, Group 2 consisted only of rats with Interceed applied to the denuded areas, Group 3 consisted of rats where preoperative MPA was used. Fifteen rats were exposed to daily IM injections of 15 mg medroxyprogesterone acetate (MPA) two weeks before the surgery.

**Results:** The total adhesion score of the MPA group was significantly less than the control and Interceed group respectively ( $\chi^2=10.15$ ) ( $p<0.001$ ), ( $\chi^2=4.67$ ) ( $p<0.03$ ). There was no significant difference between the Interceed and the control group ( $p>0.05$ ).

**Conclusion:** Preoperative long-term MPA treatment significantly decreases primary adhesion formation. It seems that there are some other mechanisms responsible for this effect rather than anti-inflammation and/or immunosuppression. It may be that the hypoeostrogenic milieu depends on the use of progesterone.

**Key words:** Adhesion prevention; Medroxyprogesterone acetate; Interceed TC7.

## Introduction

Postoperative adhesion formation is still one of the most frequent causes of pelvic pain and infertility. The increased morbidity and economic burden of abdominal adhesion disease yield more investigations and new approaches to the prevention of adhesion formation. It has been demonstrated that microsurgical techniques alone will not prevent adhesion formation [1-3]. A great deal of effort has been dedicated and several substances have been used in the attempt to reduce adhesion formation. Despite this precaution and elaborative attempts, adhesion development remains a frequent occurrence after reproductive pelvic surgery. So far, there are no proven agents that are unequivocally effective. The agents tested may be aimed at promoting fibrinolysis, reducing the inflammatory response, inhibiting coagulation or separating injured surfaces. Resorbable barrier materials have received attention, however the results have been contradictory and difficult to interpret. Some research affirmed its efficacy while others did not [4-6]. Montanino *et al.*, reported that systemic use of medroxyprogesterone acetate significantly reduced postoperative adhesions [7].

In our study, we used an effective adhesion model and a numeric adhesion grading system that helps to compare the results. We used a systemic agent which is a commonly used progesterone, medroxyprogesterone acetate (MPA) and a barrier agent, Interceed (TC7) (Johnson & Johnson Medical, Inc). The purpose of this study was to

compare the effectiveness of these two methods in an animal model.

## Materials and Methods

Forty-five Sprague-Dawley white rats of reproductive age (225-250 g) were employed as a model for postsurgical adhesion formation. The study was approved by the Experimental Medicine and Research Centre (DETAM), Istanbul University, Istanbul Medical School. The Helsinki agreement for the care and experimental use of animals was instituted by the investigators. Group 1 consisted of control rats, in Group 2 only Interceed covered the denuded areas, and in Group 3 preoperative MPA was used. Fifteen rats were exposed to IM injections of 15 mg medroxyprogesterone acetate (MPA) daily two weeks before the surgery.

**Adhesion model:** General anesthesia was induced and the abdomen was shaved and prepped with a solution of 70% alcohol. Laparotomy was then performed under clean but not sterile techniques through a midline incision. A superficial excision of 1 cm<sup>2</sup> of the peritoneal area was performed on the lower right side of the anterior parietal peritoneum. On the left side of the parietal peritoneum, a 2x1 cm<sup>2</sup> area was denuded by a scalpel until petechial bleeding was seen. The left uterine horn of each rat was subjected to a standardized lesion by crushing the serosa with a haemostatic clamp at three different sites. Interceed (TC7), which is an oxidized regenerated cellulose, was molded to both sides of the peritoneal defects. The parietal peritoneum was closed with a 4/0 polypropylene suture as a running stitch. The abdominal skin was closed with 3/0 silk suture material, separately. The animals were bandaged with sterile gauze.

Two weeks after the initial surgery, the rats were sacrificed and the degree of adhesions was scored using an adhesion scoring

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Table 1. — Adhesion scores of the sacrificed rats two weeks after the initial surgery. Total adhesion scores are means  $\pm$  SEM.

	Adhesions/sites (n/n)	Total scores (mean)
Control (Group 1)	19/20	5.6 $\pm$ 0.20
Interceed (Group 2)	16/20	5.1 $\pm$ 0.23
MPA (Group 3)	10/20	4.2 $\pm$ 0.21*

\*The MPA group is significantly different from the control and Interceed group ( $\chi^2=10.15$ ) ( $p<0.001$ ), ( $\chi^2=4.67$ ) ( $p<0.03$ ).

scale as previously described by Linsky *et al.* [4]. The adhesion scores were based on the extent of peritoneal defects and thickness. Statistical analysis was performed using the Kruskal-Wallis one-way ANOVA. All data were expressed as means  $\pm$  SEM.

## Results

The postoperative period was uneventful. Adhesions were found in all rats. In the control group adhesions were more dense and extensive. In the control group, adhesions were found in 19 of 20 denuded peritoneal areas. The adhesion scores of the 3 groups are shown in the Table. The total adhesion score of the MPA group was significantly lower than the control and Interceed group, respectively ( $\chi^2=10.15$ ) ( $p<0.001$ ), ( $\chi^2=4.67$ ) ( $p<0.03$ ). There was no significant difference between the Interceed and the control group ( $p>0.05$ ). It seems that MPA is more effective than Interceed (TC7) in reducing adhesion formation. Although the comparison of Interceed and the control group revealed that the Interceed application caused fewer adhesion formations, the result was not statistically significant ( $p>0.05$ ).

## Discussion

The methods or agents tested may be aimed at promoting fibrinolysis, reducing the inflammatory response, inhibiting coagulation, or separating injured surfaces [8]. It is commonly believed that a resorbable barrier may prevent adhesion formation by preventing contact of injured tissues. Interceed (TC7) is a oxidized regenerated cellulose and it maintains its position within the peritoneum without the use of sutures. However, the studies investigating its efficacy are divergent. In a rat model Pagidas *et al.* have concluded that the use of Interceed (TC7) is non-efficacious [6]. This finding concluded that it may depend on the foreign body reaction to Interceed (TC7). Contrary to this report, some studies claim that it is an effective way of adhesion prevention [4, 5]. This difference may depend on the species difference. According to the findings of our study, we did not find its use effective in adhesion prevention. The result of our study has

shown that the preoperative use of MPA significantly reduced adhesion formation in an animal model. This result is consistent with the study by Montanino *et al.* where they claim that MPA significantly reduced postoperative adhesions with its immunosuppressive and anti-inflammatory properties [7]. This is the first report comparing the systemic preoperative use of MPA and a barrier agent, Interceed (TC7). The adhesion model used in our study is an effective animal model. Most of the denuded peritoneal areas (19/20) in the control group were found to have dense adhesions.

In conclusion, controversies still exist about the drugs and materials used in the prevention of adhesion formation. Preoperative long-term MPA treatment significantly decreases primary adhesion formation. It is inexpensive and definitely cost-effective when compared with the resorbable barrier methods. It seems that there are some other mechanisms responsible for this effect rather than anti-inflammation and/or immunosuppression. It may be that the hypoestrogenic milieu depends on the use of progesterone. We still need more experimental studies and clinical trials to clarify the role of MPA in preventing adhesion formation and to understand the molecular mechanism of adhesion formation.

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