

Novel Carboxymethylcellulose-Derived Hydrogel Prevents Postoperative Adhesions in an Objective Rat Model

Masaya Ito, Nobuyuki Endo, Hiroaki Kaneko

Innovation Research Institute, Teijin Ltd., Hino, Tokyo, Japan

Statement of Purpose: Postoperative adhesion formation is a significant clinical problem within every surgical specialism. Due to the problems that adhesions cause, a wide variety of adjunctive treatments to prevent the formation of adhesions have been proposed. One of the modalities that has been studied extensively, and that has been showing the most promising results is the so-called barrier method. Novel carboxymethylcellulose (CMC)-derived hydrogels in which phosphatidylethanolamine (PE) was introduced into the carboxyl groups of sodium CMC was newly developed.

The objective of the present study is to evaluate the efficacy of the CMC-PE hydrogel in the prevention of postoperative adhesion formation in a standardized rat intraperitoneal adhesion model and compare with Seprafilm™.

Methods: In total thirty male Sprague-Dawley rats were divided into three groups, each consisting of 10 rats, which underwent standard cecal abrasion preceding midline laparotomy. The cecum was mobilized into the surgical field, placed on a gauze pad, then abraded with a gauze until petechial hemorrhages were present. The cecum was returned to the abdomen, and a 1.6 × 0.8-cm parietal peritoneal defect was created using an 8-mm punch biopsy. The abraded cecum was placed in apposition to the peritoneal wall defect and abdominal was closed. In the preventive groups, 1 mL of 1 wt% CMC-PE hydrogel or Seprafilm™ (2.5 × 2.5-cm) were applied to the peritoneal defect before abdominal closure. The control group received no treatment. At four weeks after surgery, all rats were euthanized with overdose of pentobarbital, and adhesions were scored macroscopically according to their extent in a blinded manner. The degree of adhesions was graded from 0 to 3 using an adhesion scoring scale as follows: grade 0 represents complete absence of adhesions, grade 1 represents thin and easily separated adhesions, grade 2 represents moderate adhesions, and grade 3 severe adhesions.

Moreover, the adhesion strength of cecum/abdominal wall adhesion was measured as previously described (1).

Briefly, a document clip was attached to the cecum and secured with 3-0 silk suture. Then the clip containing the cecum was pulled from the peritoneal wall defect using a 1-kg mechanical force gauge, generating an objective measurement of adhesion strength in grams. Rats that failed to produce an adhesion between the cecum and the abdominal wall were measured as 0 g.

All evaluations were made by investigators blinded to the treatments.

For statistical analysis, ANOVA was used. All data were expressed as mean ± standard errors (S.E.). Adhesion score and strength data were compared across groups with Steel-Dwass's test and Tukey's test, respectively, and a *P* value less than 0.05 was considered significant.

This study was approved by our institutional review board.

Results: The adhesion score of control rats was 2.1 ± 0.3. The CMC-PE hydrogel-treated group showed a significant decrease of the adhesion score (0.3 ± 0.7), which was lower than that of the Seprafilm™-treated group (0.8 ± 0.9) (Figure 1).

Similarly, the control rats showed the significant adhesion strength (473.3 ± 74.5 g). The CMC-PE hydrogel-treated group showed a significant decrease of the adhesion strength (47.0 ± 32.6 g), which was lower than that of the Seprafilm™-treated group (175.5 ± 75.7 g) (Figure 2). The CMC-PE hydrogel did not induce excess inflammation at the applied sites.

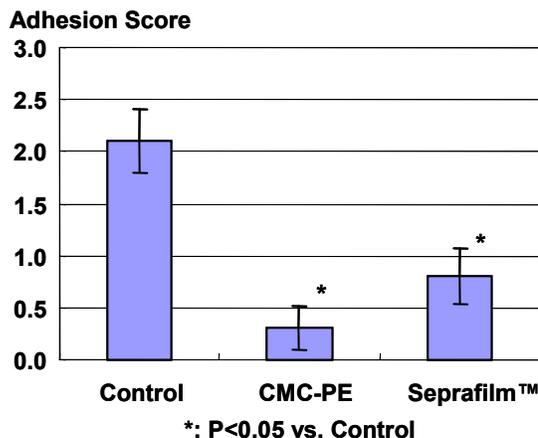


Figure 1. Comparisons of Adhesion Score

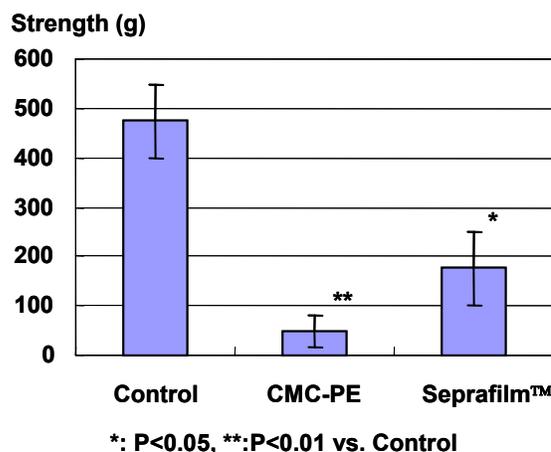


Figure 2. Comparisons of Adhesion Strength

Conclusions: The novel CMC-PE hydrogel was highly effective in reducing postoperative adhesions in the model used. The hydrogel may be appropriate for human clinical trials in open and laparoscopic surgical procedures.

References:

1. Buckenmaier CC 3rd. Am Surg. 1999;65:274-282.