

Strategies to Minimize Adhesion Formation After Surgery

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ABSTRACT

Objectives: To compare the potential for postoperative laparoscopic adhesion formation utilizing either monopolar cautery or ultrasonic energy and to determine whether there is added benefit with the addition of a suspension of hyaluronate/carboxymethylcellulose in saline versus saline alone.

Methods: Injuries were induced in rabbits by using monopolar cautery on 1 uterine horn and adjacent sidewall and ultrasonic energy on the opposite. Hyaluronate/carboxymethylcellulose or saline was added to every other animal. Autopsies were performed after 3 weeks. Clinical and pathologic scoring of adhesions was performed by blinded investigators.

Results: A very significant difference occurred in pathologic adhesion scores favoring the ultrasonic scalpel when the animals were treated with saline. However, a borderline significant difference was found in pathologic scores favoring the ultrasonic scalpel compared to the monopolar cautery. There was no significant difference in clinical adhesion scores between the 2 modalities. No significant difference in either score was found with the addition of

hyaluronate/carboxymethylcellulose or saline with either instrument.

Conclusion: No benefit was found for adhesion prevention with hyaluronate/carboxymethylcellulose. Although no reduction was achieved in clinical adhesions, the ultrasonic scalpel resulted in fewer histologic signs of tissue inflammation in the early postoperative period, suggesting that further clinical adhesions might develop over time with cautery.

Key Words: Laparoscopy, Energy Sources, Hyaluronate/carboxymethylcellulose, Adhesions.

INTRODUCTION

Adhesion formation after pelvic surgery is common and may be associated with significant morbidity, including infertility, chronic pelvic pain, bowel obstruction, and difficult repeat operations. A significant number of these repeat laparoscopies may result in inadvertent enterotomies and/or need to convert to laparotomy. In fact, the major cause of bowel obstruction in the female is adhesion formation following abdominal hysterectomy.^{1,2} Many strategies have been developed to minimize or prevent postoperative adhesions in pelvic and abdominal surgery. These include numerous modifications of surgical technique and instrumentation as well as the use of pharmacologic adjuvants and/or barrier agents. Currently, 2 of the most commonly used instruments for dissection during complex laparoscopic surgery are the monopolar electro-surgical scissors and the Harmonic Ace Scalpel. The purpose of this study is 2-fold. The primary goal is to compare the potential for postoperative adhesion formation when using either one of these energy sources. The secondary goal is to evaluate whether an additional benefit in prevention of postoperative adhesion formation can be achieved by the addition of a suspension of sodium hyaluronate/carboxymethylcellulose (Seprafilm) in saline. This material has demonstrated benefit in open abdominal and pelvic surgery when applied as a dry sheet to all denuded peritoneal and/or serosal surfaces.³⁻⁵ Although the laparoscopic preparation of this product (Sepracot)

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was removed from the market by the FDA for failure to demonstrate sufficient efficacy, some surgeons continue to use a modified version off label. This is prepared in the OR by crumbling a sheet of Seprafilm in 30mL to 60mL of normal saline to produce a suspension or “slurry” that is then placed through a laparoscopic port at the conclusion of the procedure.

MATERIALS AND METHODS

The Winthrop University Hospital Institutional Animal Care and Utilization Committee approved this study. Thirty-two sexually mature New Zealand albino rabbits (*Oryctolabius cuniculus*) weighing between 2500g and 3500g were admitted to the animal care facility one week prior to surgery for observation and adjustment. They were fed a standard scientific diet supplemented with additional fresh vegetables and given water ad libitum. The rabbits were premedicated with Ketamine 35mg per kilogram, xylazine 5mg per kilogram, and butorphanol 0.1mg per kilogram subcutaneously before augmentation of anesthesia with isoflurane at 1% to 3% by mask. A single dose of gentamicin 5mg per kilogram was given 1 hour before surgery and continued once daily for 5 days postoperatively.

Operative Procedure

The animals were placed supine on the operating table, and their abdomens were prepped with an alcohol/chlorhexidine scrub. An open laparoscopic technique was used by making a 12-mm to 14-mm midline vertical skin incision above the umbilicus with a scalpel and carrying it down to and through the peritoneum. The sleeve of a standard 11-mm trocar was then placed into the abdomen through the wound. The trocar was secured with a curved hemostat. After insufflating the abdomen to a pressure of 8mm Hg to 10mm Hg, two 5-mm accessory trocars were placed under direct visualization, one in each lower quadrant.

Beginning first with the Harmonic scalpel (Ethicon Endo-Surgery, Inc., Johnson & Johnson Medical SPA, Somerville, NJ) set at power level 3, energy was applied for 5 seconds with the tip of the active blade to successive points along the antimesenteric serosal surface of 1 of the 2 uterine horns. This power level and application time were chosen, because they equal the time and energy required to occlude a 5-mm vessel. In this manner, ultrasonic energy was applied to the entire serosal surface from the uterotubal junction to the uterine bifurcation. An additional 2-cm x 2-cm area of adjacent pelvic sidewall

peritoneum was treated in a similar manner with the Harmonic scalpel. Next, by using monopolar cautery set at 35 watts of energy, a similar procedure was carried out on the opposite tube and pelvic sidewall. Application of monopolar energy with the tips of scissors (Endoshears, Ethicon Endo-Surgery, Inc) required only 1 to 2 seconds of serosal exposure to rapidly produce visible blanching and contraction of the treated tissue.

Each animal had all treated surfaces covered with approximately 5mL to 10mL of sterile saline or a freshly prepared suspension of Seprafilm (Genzyme Corporation) in sterile saline. The Seprafilm was prepared by crumbling a standard 13-cm x 15-cm sheet of the material in 30mL of sterile normal saline introduced through 1 of the 5-mm trocars. All trocar sites were closed with interrupted sutures of 2-0 Vicryl.

Surgeons

The senior author performed or assisted at all surgical procedures in conjunction with either a laboratory animal technician or 1 of 2 senior obstetric and gynecologic residents.

Postoperative Course

The animals were allowed to recover for 3 weeks after which they were euthanized by injection of pentobarbital. They were subsequently autopsied through midline vertical abdominal incisions. Clinical grading of the adhesions was from 0 to 4 as noted in **Table 1**.⁶ Investigators performing the autopsies were blinded to the specifics of the surgical procedures and specific adjuvants used in the animals. Biopsies taken by removing each horn and adjacent sidewall peritoneum with underlying muscle were examined by pathologists and graded for degrees of inflammation and necrosis as shown in **Table 2**.⁷

Table 1.
Clinical Adhesion Scoring System

Grade	Description
0	No adhesions
1	Thin or narrow, easily separable adhesions
2	Thick adhesions limited to one area
3	Thick and widespread adhesions
4	Thick and widespread adhesions plus adhesions of viscera to anterior and/or posterior abdominal wall

Table 2.
Pathologic Adhesion Scoring System

Score	Polymorphonuclear Cells or Lymphocytes	Giant Cells	Collagen Necrosis
1	None	None	None
2	1 to 5 per section	Difficult to find	Mild
3	6 to 10 per section	Easy to find	Moderate
4	>10 per section	Many	Severe

Operative and Postoperative Complications

Thirty of 32 animals undergoing the laparoscopic procedures survived the study period to be included in the statistical analysis. There were 3 major surgical complications with 2 fatalities. The first fatality occurred in the first animal operated on. The animal expired 42 minutes post-operatively. Autopsy revealed laceration of both epigastric vessels, most likely due to insertion of a 10-mm-bladed trocar at the level of the umbilicus after insufflation by a Veress needle. Large, bilateral hematomas were noted below the rectus muscles. This resulted in a change in surgical technique to an open laparoscopic approach via a 12-mm vertical supraumbilical incision noted in the Methods section above.

Two rabbits suffered wound eviscerations by escaping from their protective cervical collars and gnawing open their umbilical incisions. Rabbit number 14 was found on postoperative day number 1 with omentum protruding from its open incision. The animal was reoperated on and survived the subsequent 3-week study period. Animal number 28 was found dead in its cage on postoperative day number 3 with eviscerated small bowel in a pool of blood most likely due to mesenteric vessel trauma.

Surgical procedures lasted approximately 25 minutes (range, 16 to 83). Only 4 procedures lasted over 39 minutes, all occurring in the first 6 animals operated on.

Statistical Analysis

Statistical analysis was performed using the Wilcoxon matched-pairs signed-ranks and Mann-Whitney tests.

RESULTS

Analysis of the data obtained demonstrated a very significant difference in pathologic adhesion scores favoring the Harmonic scalpel when the animals were treated with saline alone. In this case, the mean pathologic score for Harmonic was 3.8 vs 5.3 for cautery with

Table 3.
Predisposing Factors for Adhesions

Ischemia
Drying of serosal surfaces
Excessive suturing
Omental patches
Traction on peritoneum
Blood clots retained in peritoneal cavity
Prolonged operations
Adnexal trauma
Infection

a P value <.01. In addition, in the animals treated with Seprafilm, the difference between pathologic adhesion scores was borderline significant (P=.05) when comparing the Harmonic scalpel (mean score=4.2) with monopolar cautery (mean score=5.9). However, there was no significant difference in clinical adhesion scores when the animals were treated with Seprafilm or saline using either monopolar cautery or ultrasonic Harmonic scalpel (range, P=.22 to P=.57).

DISCUSSION

It is generally accepted that laparoscopic surgery results in significantly fewer de novo postoperative adhesions than that performed by laparotomy; 75% to 95% with laparotomy versus 12% to 40% with laparoscopy. **Table 3** lists some of the pathophysiologic advantages of laparoscopy that could explain this benefit.^{1,2,8}

Several animal and human studies have supported this thesis.⁸⁻¹⁰ A study by Luciano et al⁹ in rabbits utilizing the CO₂ laser clearly showed a marked decrease in adhesions at 3 weeks postoperatively in the animals operated on by laparoscopy compared to the laparotomy group. When the adhesions formed in the laparotomy group underwent adhesiolysis by the laser, those re-operated on by laparoscopy demonstrated a significant decrease in adhesion scores. However, the laparotomy group did not demonstrate a significant reduction.

Tittel et al¹⁰ in their rabbit study were able to demonstrate a significant reduction in recurrent adhesions when adhesiolysis was accomplished by laparoscopy rather than laparotomy. However, they could not demonstrate any advantage of monopolar cautery dissection over sharp and blunt dissection in the laparoscopy group.

Diamond et al⁸ working in the Operative Laparoscopy Study Group studied a group of patients who underwent a second-look laparoscopy within 90 days of laparoscopic adhesiolysis. Adhesions were lysed using a number of techniques including electrocautery, sharp dissection, and CO₂, Argon, or KTP laser. No adjuvants or barriers were used. Ninety-seven percent of patients demonstrated a recurrence of approximately 66% of their adhesions. However, de novo adhesions occurred in only 12% of patients.

We could find no studies, either animal or human, that compared adhesion formation or re-formation between monopolar cautery and Harmonic scalpel utilizing laparotomy or laparoscopy. However, a recent metaanalysis by Sasi¹¹ did look at outcomes after laparoscopic cholecystectomy comparing monopolar cautery dissection to ultrasonic energy. The factors included postoperative pain, length of hospital stay, and time to return to work. All factors favored procedures utilizing ultrasonic energy and suggest less operative inflammatory reaction. One could speculate that less operative inflammation might result in lower postoperative adhesion rates.

Animal and human studies have fairly consistently demonstrated an advantage in the prevention of adhesions after laparotomy by hyaluronic acid-based preparations with or without the addition of carboxymethylcellulose, whether applied in a film or gel form.^{4,5,12-15} However, a notable exception to this view is found in a Cochrane review updated on December 20, 2007, which concluded that evidence demonstrating the effectiveness of Seprafilm in adhesion prevention was insufficient.¹⁶ Animal studies using this preparation during laparoscopic surgery have been conflicting. For example, the rabbit study by Detchev et al¹⁵ did not demonstrate any difference between hyaluronate gel, saline, and no adjuvant treatment after laparoscopic surgery followed by autopsy on postoperative day 10. On the other hand, a rabbit study by De Laco et al¹⁷ did reveal a significant reduction in severe adhesions both clinically and histologically in hyaluronate gel-treated animals compared to untreated controls and those treated with oxidized-regenerated cellulose 6 weeks postoperatively. In addition, the FDA has withdrawn approval for the laparoscopic preparation of this material due to lack of convincing human data demonstrating significant effectiveness.¹⁸

CONCLUSION

Based on the findings of this study, in laparoscopic surgeries, there appears to be little additional benefit in the

reduction of adhesions both by gross and microscopic inspection through the use of hyaluronate/carboxymethylcellulose (Seprafilm) suspended in normal saline compared to the use of saline alone. This is in contrast to benefits shown with the use of Seprafilm as overlapping sheets over surgically denuded surfaces in open procedures in both human and animal studies. Perhaps any benefit of this adjunct is obscured by the overwhelming advantage that laparoscopic surgery provides in prevention of postoperative adhesions compared to open surgery.

Although no clinical benefit could be demonstrated by performing surgical dissection with a monopolar scissors compared with an ultrasonic shears, there was a marked decrease in histologic indicators of tissue inflammation and necrosis in the early postoperative period with the ultrasonic shears. This suggests that a clinically apparent benefit might in fact become evident if the animals were examined in the late postoperative period.

Therefore, we are currently repeating this study with one major modification. The animals operated on will be allowed to survive for 8 rather than just the 3 weeks in the current study. Eight weeks should allow for full pathologic and clinical maturation of adhesions and, thus, more clearly demonstrate whether any benefit exists in the use of the Harmonic scalpel over monopolar cautery for prevention of postoperative adhesions after surgical dissection. We hope that our preliminary work will stimulate others to pursue further animal studies in their centers. We believe it may be prudent to minimize the use of monopolar energy during laparoscopic surgery while awaiting results of future studies in hopes of reducing postoperative adhesion formation.

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