Laparoscopic Use of a Hyaluronic Acid Carboxy cellulose Membrane Slurry in Gynecological Oncology

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ABSTRACT

Objectives: We evaluated the use of a hyaluronic acid-carboxycellulose membrane (HAC) slurry in complex laparoscopies.

Materials and Methods: A gel-like mixture of HAC was prepared and applied in 171 consecutive complex laparoscopies on a gynecologic oncology service. The HAC slurry was used to coat deperitonealized surfaces and surgical pedicles to prevent postoperative adhesions. The technique is described and the outcomes are prospectively evaluated for feasibility and safety.

Results: There were no postoperative bowel obstructions, 1 pelvic hematoma in a patient on clopidogrel (Plavix) immediately prior to surgery, 8 postoperative ileas, and 1 bowel perforation. The bowel perforation occurred in a patient with extensive adhesiolysis and intraoperative bowel suturing.

Conclusion: This report describes an easy approach to the laparoscopic application of HAC. Caution should be taken if HAC slurry is applied after significant bowel suturing because 1 of 9 patients with extensive adhesiolysis requiring suturing of the sigmoid colon developed sigmoid perforations.

Key Words: Seprafilm, Adhesion prevention, New technique, Gynecologic oncology surgery.

INTRODUCTION

Hyaluronic acid-carboxy cellulose (HAC) membrane has been FDA-approved, based on randomized trials, for prevention of postoperative adhesions due to surgical procedures performed via laparotomy. The use of HAC (Seprafilm) has demonstrated a reduction in both postoperative adhesions and early postoperative obstruction. In gynecologic surgeries, the application of HAC has also demonstrated improvements in postoperative pelvic pain.

It is well accepted that minimally invasive laparoscopic techniques have resulted in less postoperative adhesion formation. However, as the scope of laparoscopic surgeries has expanded to include more advanced intraperitoneal surgical procedures, the laparoscopic use of adhesion barriers has become a more important consideration. Several novel techniques for delivery of HAC sheets through laparoscopic trocars have been described primarily in patients undergoing laparoscopic myomectomies. Although effective in reducing postoperative pain, these techniques are cumbersome and time consuming.

Several institutions and gynecologic practices across the country have utilized a technique of mixing HAC in solution and injecting it laparoscopically for the purpose of adhesion prevention. However, very little data are available in the surgical or gynecologic literature describing its use. This study evaluates 171 consecutive laparoscopic applications of HAC slurry in patients referred to a gynecologic oncology practice. The purpose of this report is to evaluate the feasibility and safety of its use.

MATERIALS AND METHODS

Patient Selection

From May 1, 2007 to January 31, 2009, 171 consecutive laparoscopic surgeries utilized a single technique to apply HAC slurry. The patients were followed prospectively. A gynecologic oncologist performed each surgery. Patients were referred for new diagnoses of potential or previously diagnosed malignancies. In addition, occasional surgeries
were performed when intraoperative consultations were requested to repair injuries from benign gynecologic surgeries.

**Technique**

Three sheets of HAC are crumbled and mixed into 60cc of warm saline at least 5 minutes prior to the anticipated completion of surgery. Once a gel-like mixture (slurry) is established, it is poured into a catheter-tipped syringe. A sterile, 16 French red rubber catheter is attached to the syringe, and the tip of the catheter is cut off leaving a single opening through which the slurry can be injected. The catheter is placed through a trocar >5mm. By manually manipulating the trocar, the tip of the catheter is guided to precisely apply the slurry. If no trocars are >5mm, then the catheter is placed through a 5-mm trocar site after the trocar is removed. In this case, the tip of the catheter can be grasped by a laparoscopic instrument through another trocar and guided to precisely apply the slurry. The slurry is used to coat any deperitonealized areas and surgical pedicals.

**Outcomes**

Because it was not expected that many laparoscopic surgeries would be re-explored, the primary outcomes measured in this study were not related to adhesion prevention. The patient demographics, types of procedures, and untoward events following this technique for the laparoscopic use of HAC were prospectively monitored and recorded.

**RESULTS**

**Demographics**

The mean age of the patients was 55.2 (SD±15.3). The mean BMI was 32.7 (SD±8.1). The race distribution was as follows: Caucasian 71%, Hispanic 18%, and Black 11%.

**Type of Surgical Procedures**

The most common procedures performed were total laparoscopic hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic and paraaortic lymphadenectomy, which was performed in 56 (32%) of the patients. In patients who underwent 98 procedures for benign anomalies, 79 (80%) had the preoperative diagnosis of a complex ovarian mass. The variety of cases performed can be seen in Table 1. In 41 (24%) of the surgeries extensive adhesiolysis was required (defined as adhesiolysis requiring more than 60 minutes) as a part of the procedure, and 9 (5.3%) required laparoscopic suturing of the sigmoid colon.

**Postoperative Outcomes**

The median length of stay was 1 day (range, 0 to 8). Untoward events included the following. There have been no postoperative bowel obstructions, 1 left obturator space hematoma that was observed in a patient on clopidogrel (Plavix) immediately prior to surgery for medical indications, 8 cases of postoperative ileus, and 1 bowel perforation recognized postoperatively. The bowel perforation occurred in 1 of 9 (11%) patients with extensive adhesiolysis and laparoscopic suturing of the sigmoid colon.

The median length of time of surgery among the 8 patients who developed a postoperative ileus was 165 minutes (range, 120 to 210). Part of each of the surgical procedures included extensive adhesiolysis using hydrodissection and Endoshear sharp dissection. Electrocautery was not used to separate adhesions in any cases presented in this report. Three of the cases also required suturing of the sigmoid colon. Ileus was diagnosed on postoperative day 1 in each of these patients when they demonstrated intolerance of oral intake, and abdominal x-rays described dilated loops of small and large bowel. Conservative management with bowel rest until flatus was undertaken. Five patients were discharged home on postoperative day #3.

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**Table 1.**

List of 171 Laparoscopic Procedures

| Procedures†‡ | Number |
|--------------|--------|
| Salpingo-oophorectomy ± hysterectomy | 109 |
| Total hysterectomy ± salpingo-oophorectomy | 102 |
| Lymph node dissection | 63 |
| Tracheectomy | 5 |
| Staging biopsy | 5 |
| Partial omentectomy | 5 |
| Cystotomy repair | 2 |
| Ureteronecystostomy | 2 |
| Myomectomy | 2 |
| Sacrocolpopexy | 1 |

*Laparoscopic surgeries included several of the above-listed procedures concomitantly.
†Final pathology was benign for 98 procedures performed and malignant for 73 procedures performed.
2 on day #4, and 1 on day #8 after spontaneous resolution of their ileus.

In the case that was complicated by a postoperative bowel perforation after laparoscopic suturing of the sigmoid, the patient was discharged home on postoperative day #2 after demonstrating tolerance of a regular diet for both breakfast and lunch. On postoperative day #4, she returned to the emergency department after having a sudden onset of severe abdominal pain. A computed tomographic scan demonstrated free air in the abdomen and a collection of fluid in the pelvis. She was taken to the operating room where she underwent exploratory laparotomy, peritoneal washout, and suture repair of a sigmoid perforation at the site of her previous laparoscopic suture repair. At laparotomy, the sigmoid colon defect was sutured in a single layer using 3–0 PDS suture. The patient tolerated liquids on postoperative day #2 and advanced to a regular diet after passage of flatus on day #4. She was discharged home on day #5.

CONCLUSION

Historically, HAC was FDA approved for adhesion prevention during laparotomy. With proven efficacy at laparotomy and the trend toward increasing radicality of laparoscopic surgeries, there is a growing interest in identifying an easy method to incorporate the use of HAC during laparoscopic surgical procedures. Several novel techniques of delivery of the HAC sheet through trocar incisions have been described. The laparoscopic placement of HAC sheets has shown benefits in reduction of pelvic pain in gynecologic surgery; however, these techniques are not widely used due to technical difficulty. Previous reports of HAC in gynecologic laparoscopy have been predominantly limited to application during laparoscopic myomectomy.8–10

This report is among the first to demonstrate the use of HAC slurry in a large cohort of gynecologic patients undergoing laparoscopic surgeries. It is the first to describe its use in a cohort largely made up of gynecologic cancer patients and complex pelvic surgeries. Although 8 postoperative ilea in 171 routine laparoscopic cases would be more than expected, it is easily justified in a series of patients who undergo laparoscopic procedures with this degree of complexity. In a single patient with extensive pelvic adhesiolysis and suturing of the sigmoid colon, we encountered a postoperative perforation at the site of suture repair. It should be noted that in 9 total suture repairs of the sigmoid after extensive adhesiolysis, only 1 perforation occurred. Though this anecdotal incident may not represent a complication related to the HAC slurry application, it may be prudent to avoid its use over areas of significant suturing of the intestinal tract. This is relatively consistent with established recommendations not to coat bowel anastomoses with HAC sheets at the time of laparotomy.

It is recognized that the weakness of this report lies in the fact that it is observational and lacks a comparison group. Despite this, the information gleaned from this report adds to the documented knowledge about the safety and feasibility of the HAC slurry to attempt to prevent adhesions in the postoperative setting following laparoscopic surgical procedures with a high degree of complexity. While many believe that adhesion prevention with this technique should be similar to the use of HAC sheets, this has not been proven in clinical evaluations, nor was this the intent of the current report. However, in preclinical animal models, the HAC slurry demonstrated marked adhesion prevention.12 Therefore, it is not unreasonable to assume that mixing HAC in physiologic solution should change its composition or function significantly more than allowing it to mix into physiologic body fluids after it is placed as a sheet.

The report describes an easy approach to the laparoscopic application of HAC slurry to pelvic surfaces following a variety of gynecologic surgical procedures. Definitive statements on the effectiveness of the technique cannot be drawn from this experience, because second-look procedures were not used to evaluate the formation of postoperative adhesions. However, it is notable that no bowel obstructions have occurred in 171 complex pelvic laparoscopies. The data demonstrate that HAC slurry can be applied safely at the completion of laparoscopic gynecologic procedures. With greater use of this technique and future clinical investigation including second-look procedures, the efficacy of the HAC slurry may be better elucidated. Furthermore, with industry innovations, other means of laparoscopic application of HAC may become more widely available.

References:

1. Kling J. Genzyme’s Seprafilm gets FDA marketing nod. Nat Biotechnol. 1996;14(5):572.
2. Diamond MP. Reduction of adhesions after uterine myomectomy by Seprafilm membrane (HAL-F): a blinded, prospective, randomized, multicenter clinical study. Seprafilm Adhesion Study Group. Fertil Steril. 1996 Dec;66(6):904–910.
3. Beck DE, Cohen Z, Fleshman JW, Kaufman HS, van Goor H, Wolff BG; Adhesion Study Group Steering Committee. A pro-
spective, randomized, multicenter, controlled study of the safety of Seprafilm adhesion barrier in abdominopelvic surgery of the intestine. *Dis Colon Rectum.* 2003;46(10):1310–1319.

4. Cohen Z, Senagore AJ, Dayton MT, et al. Prevention of postoperative abdominal adhesions by a novel, glycerol/sodium hyaluronate/carboxymethylcellulose-based bioresorbable membrane: a prospective, randomized, evaluator-blinded multicenter study. *Dis Colon Rectum.* 2005;48(6):1130–1139.

5. Mohri Y, Uchida K, Araki T, et al. Hyaluronic acid-carboxycellulose membrane (Seprafilm) reduces early postoperative small bowel obstruction in gastrointestinal surgery. *Am Surg.* 2005;71(10):861–863.

6. Fuazio VW, Cohen Z, Fleshman WU, et al. Reduction in adhesive small-bowel obstruction by Seprafilm adhesion barrier after intestinal resection. *Dis Colon Rectum.* 2006;49(1):1–11.

7. Khaitan L, Scholz S, Houston HL, Richards WO. Results after laparoscopic lysis of adhesions and placement of Seprafilm for intractable abdominal pain. *Surg Endosc.* 2003;17(2):247–55.

8. Chuang YC, Fan CN, Cho FN, Kan YY, Chang YH, Kang HY. A novel technique to apply a Seprafilm (hyaluronate-carboxymethylcellulose) barrier following laparoscopic surgeries. *Fertil Steril.* 2008;90(5):1959–1963.

9. Khaitan E, Scholz S, Richards WO. Laparoscopic adhesiolysis and placement of Seprafilm: a new technique and novel approach to patients with intractable abdominal pain. *J Laparoendosc Adv Surg Tech A.* 2002;12(4):241–247.

10. Takeuchi H, Kitade M, Kikuchi I, Shimanuki H, Kinoshita K. A novel instrument and technique for using seprafilm hyaluronic acid/carboxymethylcellulose membrane during laparoscopic myomectomy. *J Laparoendosc Adv Surg Tech A.* 2006;16(5):497–502.

11. Fenton BW, Fanning J. Laparoscopic application of hyaluronate/ carboxymethylcellulose slurry: An adhesion barrier in a slurry formation goes where the available sheets cannot. *Am J Obstet Gynecol* 2008;199(3):325.

12. Greenawalt K, Colt J, Corazzini R, Krauth M, Holmdahl L. An evaluation of the adhesion reduction efficiency of Seprafilm bioresorbable membrane applied as a slurry in two preclinical models. *J Min Invas Gynecol.* 2008;15:98.