Evaluation of a Bioresorbable Hyaluronate Membrane for Prevention of Experimentally Induced Abdominal Adhesions in Horses

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The use of a bioresorbable, hyaluronate membrane during exploratory celiotomy in horses minimizes postoperative intra-abdominal adhesion formation. In horses at an increased risk of intra-abdominal adhesion formation, the application of hyaluronate membranes during exploratory celiotomy may reduce the morbidity and mortality associated with abdominal surgery. Authors' address: Depts. of Pathology (Harmon) and Large Animal Medicine (all other authors), College of Veterinary Medicine, University of Georgia, Athens, GA 30602. © 1998 AAEP.

1. Introduction

Intra-abdominal adhesions are a common cause of postoperative intestinal obstruction and mortality in horses. Adhesions that cause signs of abdominal pain and intestinal obstruction reportedly occur in 22% of adult horses that survive surgery for small intestinal lesions. Intra-abdominal adhesions are the second most common cause for repeated celiotomy in horses with gastrointestinal disease; intestinal ischemic necrosis is the most common. In these studies, horses with intra-abdominal adhesions had a high incidence of recurrence of adhesions and a poor prognosis for survival.

Adhesions become a clinical problem when they compress or anatomically distort the intestine. This may lead to intestinal constriction, incarceration, or volvulus, predisposing the patient to intestinal obstruction and signs of abdominal pain. Numerous clinical trials and laboratory investigations have been devoted to an evaluation of methods to minimize the formation of postoperative intra-abdominal adhesions. Broad-spectrum antibiotics, nonsteroidal anti-inflammatory agents, dimethyl sulfoxide, heparin, the intraperitoneal administration of high molecular weight solutions, omentectomy, and postoperative peritoneal lavage have all been advocated to minimize adhesion formation.

A bioresorbable hyaluronate membrane (HA membrane) has been developed to reduce postoperative adhesion formation in people. The HA membrane is placed on the serosal surface of the intestine or parietal peritoneum, thereby temporarily preventing serosal-serosal or serosal-peritoneal apposition during the early postoperative healing period. In experimental studies, the HA membrane reduced the frequency and severity of postsurgical adhesions to parietal and visceral peritoneal surfaces and the pericardium. In a prospective multicenter study, the use of the HA membrane decreased the incidence of postoperative adhesions from 94% to 51% in...
people undergoing abdominal surgery for a colectomy and diverting-loop ileostomy.5 The identification of therapeutic agents that effectively reduce adhesion formation without adversely effecting normal peritoneal and serosal healing may be beneficial in reducing the morbidity and mortality associated with abdominal surgery in horses. The purpose of this study was to evaluate the efficacy of a biodegradable HA membrane for the prevention of experimentally induced abdominal adhesions in horses.

2. Methods
In the proposed study, the effect of a bioresorbable HA membrane on postoperative adhesion formation was evaluated by using an established model of serosal trauma to induce intra-abdominal adhesions.4 Twelve healthy adult horses were utilized in the study. Experimental procedures and animal care were approved by the University Animal Care and Use Committee. Horses were randomly assigned to one of two groups. Whole blood and serum samples were obtained from each horse for hematologic and biochemical evaluation. Group 1 horses (n = 6) served as controls and group 2 horses (n = 6) were treated with HA membranes.

Food was withheld for 12 h before surgery. One hour before the induction of anesthesia, potassium penicillin G (22,000 IU/kg IV), gentamicin sulfate (6.6 mg/kg IV), and flunixin meglumine (1.1 mg/kg IV) were administered. Each horse was sedated with xylazine hydrochloride (1.1 mg/kg of body weight IV). Anesthesia was induced with ketamine hydrochloride (2.2 mg/kg of body weight IV) and maintained with halothane in oxygen in a semi-closed system. Lactated Ringer’s solution [10 (ml/kg)/h IV] was administered during the surgical procedure. The horses were positioned in dorsal recumbency, and the ventral midline was prepared for aseptic surgery.

A ventral midline celiotomy and systematic abdominal exploratory were performed to examine the viscera. If adhesions or anatomic abnormalities were identified, the horses were excluded from the study. The jejunum was exteriorized and examined from the ileocecal orifice to the duodenocolic ligament. Sterile saline was used to lubricate the intestine during this manipulation. Two jejunal resections and end-to-end jejunal anastomoses were performed, 7 and 12 m proximal to the ileocecal orifice. The anastomoses were closed in two layers: a simple continuous pattern was used in the mucosal layer, with 2-0 polydioxanone,4 and then a Cushing suture pattern was used in the seromuscular layer, with 3-0 polydioxanone. Two 6 cm × 4 cm areas of the antimesenteric border of the jejunum, 4 and 10 m proximal to the ileocecal junction, were briskly rubbed 100 times with a sterile dry gauze, and then three simple interrupted 2-0 chromic gut sutures that did not penetrate the intestinal lumen were placed in the abraded area. In the horses treated with the HA membrane (group 2), 7 cm × 6 cm sheets of HA membrane6 were applied to the jejunum to cover completely each of the anastomoses and abraded areas of the jejunum. Horses in group 1 served as nontreated controls. The linea alba was closed with #8 polyglactin 910 in a simple continuous pattern, and the subcutaneous tissues were closed with 2-0 polydioxanone in a continuous horizontal mattress pattern. The skin edges were apposed with skin staples.

After recovery, the horses were allowed to have water, free choice, and they were gradually returned to full feed over the next 36 h. Intravenous administrations of potassium penicillin (q 6 h), gentamicin (q 24 h) and flunixin meglumine (q 12 h) were repeated for 48 h. Any horse demonstrating clinical signs of abdominal pain after surgery was examined and treated appropriately. Each horse was monitored every 6 h for food consumption, pulse and respiratory rate, rectal temperature, and signs of pain, incisional swelling, or drainage.

Horses in both groups were euthanized with an overdose of pentobarbital sodium solution 10 days after surgery. The abdominal incision, peritoneal cavity, and all abdominal organs were evaluated for adhesions and any other abnormalities that could be related to HA membranes. Adhesions were designated as fibrinous if they could easily be pulled apart or fibrous if they could not be pulled apart without tearing the serosa.4 The number of intra-abdominal adhesions in the two groups were compared with a Wilcoxon signed rank test. Statistical significance was set at p < 0.05.

3. Results
Preoperative hematologic and biochemical values for all horses were within normal limits for our laboratory. All horses recovered from surgery without complications. Two control horses and one treatment horse experienced a single episode of postoperative abdominal pain that responded to medical treatment. At necropsy, the jejunum at the abrasion sites of the control horses was thickened with focal areas of serosal hemorrhage. Fibrous adhesions were associated with both abraded jejunal sites in all six control horses. In two control horses, fibrous adhesions occurred between the abraded jejunal site and a distant segment of jejunum. In the other four control horses, the adhesions were firm attachments of the jejunal serosa to the adjacent mesentery. Two of the control horses had fibrous adhesions from the anastomatic sites to the adjacent mesentery (three sites) and distant mesentery (one site). None of the adhesions resulted in stricture of the jejunal lumen.

There were no adhesions present at the jejunal abrasion or anastomatic sites in any of the HA-membrane-treated horses. Two horses had mild contracture of the mesentery adjacent to the anastomatic site. There were significantly fewer adhesions at the jejunal abrasion sites in the HA-membrane group compared to the control group.
than in the control group. There was no evidence of diffuse peritonitis, perianastomotic abscess formation, or stricture at the anastomotic site in any of the horses.

4. Discussion
The morbidity associated with postoperative adhesions has prompted extensive research efforts into potential preventative treatments. The most important factors in minimizing the formation of intra-abdominal adhesions are an aseptic surgical technique and the removal of all potentially ischemic bowel. The primary objectives in preventing adhesions are as follows: (1) to minimize serosal inflammation, (2) to minimize fibrin production, (3) to stimulate adequate intestinal motility, and (4) to mechanically separate fibrin-covered surfaces. The intravenous administration of penicillin and gentamicin, flunixin meglumine, dimethyl sulfoxide, heparin, and intestinal motility-enhancing agents have all been advocated to accomplish the first three objectives, and they have been associated with favorable results in individual experimental settings.

The intra-abdominal infusion of high molecular weight solutions is directed at accomplishing the fourth objective. The mechanical separation of serosal surfaces during the early postoperative period reduces intra-abdominal adhesions associated with exploratory celiotomy in several animal models. The intraperitoneal administration of sodium carboxymethylcellulose (SCMC), a high molecular weight substituted polysaccharide, has been used successfully in experimental models to prevent adhesions in ponies. The beneficial effects of SCMC are derived from a hydrofloation effect, which mechanically prevents the apposition of serosal or peritoneal surfaces, thus preventing adhesion formation. Large volumes of SCMC (2–4 L), however, must be used to achieve this effect in the equine abdomen. Recently, the systemic absorption of SCMC after the intraperitoneal administration of large volumes of the solution has been associated with postoperative pyrexia, depression, and anorexia in horses.

In the present study, the use of a bioresorbable HA membrane prevented the formation of experimentally induced intra-abdominal adhesions in six of six treatment horses. The adhesion model used in this study was selected because it has been established as a reliable means of adhesion formation with minimal morbidity in a variety of animal species. All of the control horses developed adhesions, thereby supporting the predictability of this adhesion model.

The HA membrane is composed of sodium hyaluronate and SCMC and has been developed to reduce postoperative adhesion formation in people. The HA membrane prevents adhesion formation by a mechanism similar to that of SCMC, i.e., the separation of serosal surfaces during the early postoperative healing period.

5. Conclusions
The ease of application, ability for accurate placement, and decreased potential for systemic absorption are advantages of HA membranes over the intraperitoneal administration of high molecular weight solutions. The results of this study suggest that in horses at an increased risk of intra-abdominal adhesion formation, the use of HA membranes during exploratory celiotomy may reduce the morbidity and mortality associated with abdominal surgery.

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References and Footnotes