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Evaluation of sodium carboxymethylcellulose for prevention of adhesion in intestinal anastomosis in dogs

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Abstract : Adhesions are the most common postoperative complication in intestinal surgery in dogs. This study was aimed at verify to the efficacy of sodium carboxymethylcellulose (SCMC) in the adhesion prevention during healing of intestinal anastomosis. Twenty three healthy dogs were taken with average 4.17 years and weight was 5.68 kg and divided into 4 groups. The dogs of group III and IV, a pedicle of greater omentum was wrapped around the suture line. In the animals of group II and IV, 1% SCMC was infused (5 ml/kg, IP) at just before closure of the abdominal cavity. Two weeks after surgery, animals were reoperated and the adhesions were evaluated and graded. We found various degrees of intra-abdominal adhesions in animals of all the groups. The significantly ($P<0.05$) lower adhesion score was observed in group IV than that of other groups. Nevertheless, varying intra-peritoneal adhesions, healing of anastomotic site was normal in all groups. It could be concluded that intra-peritoneal administration of SCMC solution reduces postoperative adhesions without any adverse effects on healing, and a synergistic beneficial effect can be obtained by supplementation with omental graft for intestinal anastomosis.

Key words : adhesions, dog, intestinal anastomosis, sodium carboxymethylcellulose

Introduction

Intestinal anastomosis is one of the most common surgical procedures performed in abdominal affection; removing ischemic, necrotic, neoplastic, irreducible intussusceptions and fungal-infected segments of intestine. The primary goal of the intestinal anastomosis is to produce a rapid return to normal function of intestine, to maintain proper tissue alignment, optimal tissue healing and adequate stomal diameter [1-4, 8-13, 22, 29, 32]. Intra-abdominal adhesion is the detering factor in the normal activity of the bowel. Fibrous adhesions following previous surgical intervention is a major cause of intestinal obstruction and intra-peritoneal adhesions in human. Indeed an autopsy study of 752 patients who had undergone previous abdominal surgery revealed an adhesion rate of 67% [29]. Menzies and Ellis reported that intra-abdominal adhesions occur in 93% of previously operated patients. Also, it can be considered in small animal surgery [11, 32]. Various attempts have been made to prevent or reduce adhesion formation following abdominal surgery. Antibiotics, progestins, antihistamines, corticosteroids, anticoagulants, Dextran 70, anti-inflammatory drugs and fibrinolytic agents have been used in attempts to prevent postoperative adhesion formation, but none of them has been found to be consistently efficacious [5, 7, 17, 20, 21, 23, 26, 30, 31, 33]. More recently, promising results have been obtained with the use of sodium carboxymethylcellulose (SCMC), that may create a flotation bath, thus separating the serosal and peritoneal surfaces, that blocks formation of adhesions during the period of epithelial regeneration, also reducing fibroblast activities or proliferation and preventing fibrin deposition on the serosal surfaces of the injury [6, 14-16, 18, 24, 25, 27, 28]. The purpose of this study was to assess the efficacy of SCMC in

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intestinal anastomosis in reducing postoperative adhesions in dogs.

Materials and Methods

Preparation of SCMC

A 1% solution of SCMC was prepared by boiling 200 m*l* of sterile water and adding 10 g of SCMC powder while stirring. After the SCMC was in solution, additional sterile water was added, to make the total volume 1 L. The SCMC solution was then transferred into 500 m*l* glass bottles and autoclaved at 121°C for 20 minutes.

Experimental animals

Twenty-three healthy mongrel adult dogs of both sexes, weighing between 3-10 kg were used. The dogs were confirmed healthy through physical, hemato-biochemical and radiographic examinations. The dogs were randomly divided into 4 groups; group I, II and III comprised of 5 dogs whereas group-IV comprised of 8 dogs. The dogs were maintained in the cases with adequate food and water ad libitum. But food was withheld for 24 hours before surgery. Rectal temperature, heart rate, respiratory rate and viability were monitored in all the dogs one hour before surgery.

Premedication and anesthesia

Each animal received butorphanol as analgesics (Butophan; Myungmoon Pharm, Korea, 0.4 mg/kg, IV) and atrophine sulfate (Atrophine sulfate; Jeil Pharm, 0.05 mg/kg, IM). For the induction, thiopental sodium (Thionyl; Daehan Pharm, Korea, 12 mg/kg, IV) was administered and surgical anesthesia was maintained with isoflurane in 100% oxygen. Prophylactic antibiotics (Cephradine; Schnell Pharm, Korea, 20 mg/kg, IV) was infused. Lactated Ringer's solution (Hartmann's Dex. Inj; Daehan Pharm, Korea, 10 m*l*/kg/hr, IV) was administered during the surgical procedure.

Surgical technique

Through ventral midline celiotomy the intestine was brought out from the abdominal cavity. The viability of the intestine was examined by observing the color and peristaltic movement, and mesentery artery pulse. Intestinal segment of 10 cm proximal to ileocecal orifice was exteriorized and it's inner content was squeezed out by second and third fingers. The bowel was held by two Doyen intestinal forceps at a distance of 4 to 5 cm from the proposed resection site. Mesenteric and arcadial vessels were double ligated at the area of intestinal resection. The bowel was transected outside of the clamps and the mesentery was incised. End-to-end intestinal anastomosis was performed in all the dogs. In addition, a pedicle of greater omentum was wrapped around the anastomotic site and fixed by interrupted sutures on each side of the bowel in group III and IV. Abdominal lavage was performed with warm saline solution in all the animal. Additionally the animals of group II and IV received an intraperitoneal infusion of 1% SCMC at the dose rate of 5 m*l*/kg. The peritoneum, muscles and subcutaneous tissues were closed with 3-0 polyglycolic acid and the skin was closed with 3-0 nylon. Two weeks later the same surgical means were also employed to observed any adhesion at the anastomosis sites.

Postoperative management

Food was withheld and lactated Ringer's solution was administered (3 m*l*/kg/hr, IV) for 3 days. After recovery, dogs were allowed water ad libitum and food and they returned to full feed over the next 3 days. Antibiotics (Cephradine 20 mg/kg, IV) was administered for 7 days. All the animals were monitored incisional swelling, appetite, activity, defecation, micturation and rectal temperature during the period of experiment.

The evaluation of adhesions

Results indicating status of adhesion were measured by scoring. The adhesion scores were graded as shown in Table 1.

Statistical analysis

The data obtained from the present study were

Table 1. Grading of adhesion formation

Postoperative adhesion score	Description of adhesions
0	Complete absence of adhesions
1	Firmly, fibrin adhesions, easily removed by blunt dissection
2	Fibrous adhesions, easily dissectable
3	Thick fibrous adhesions, dissectable
4	Thick fibrous adhesions, not dissectable without damage to the adherent tissue

analyzed using ANOVA-test and the differences were considered significant when $P<0.05$.

Results

Intraoperative findings

Multiple adhesions between intestinal serosal surfaces and mesentry-intestinal serosal surfaces were observed in group I (Table 2). There was no significant difference between group I and group II. Moreover, adhesions created between intestinal serosa in group I and II had raised the potential risk that compress or anatomically distort the intestine. Table 3 summarized the length of adhesions of anastomotic sites with various structures.

SCMC intraperitoneal instillation resulted in significantly ($p<0.05$) fewer adhesions in group IV than the other groups. Mean adhesion score is highest in group I and lowest in group IV. The presence of SCMC combined with application of omental graft technique reduces peritoneal adhesion formation and increases anastomotic resistance. Abdominal adhesion severity score was assigned on the basis of number and severity of the adhesions (Table 4).

Table 2. Location of adhesion in intestinal anastomotic site at 14th day after operation

Group	Location of adhesion						
	AS-OG	IS-IS	IS-VP	IS-ME	ME-O	O-VP	ME-VP
I (n=5)	-	3	-	3	-	1	-
II (n=5)	-	4	-	2	-	-	-
III (n=5)	5	2	-	1	1	1	1
IV (n=8)	8	2	-	-	-	-	-

AS - OG; anastomotic site - omental graft, IS - IS; intestinal serosa - intestinal serosa, IS - VP; intestinal serosa - visceral peritoneum, IS - ME; intestinal serosa - mesentery, ME - O; mesentery - omentum, O - VP; omentum - visceral peritoneum, ME - VP; mesentery - visceral peritoneum, Group I; end-to-end intestinal anastomosis with saline lavage, Group II; end-to-end intestinal anastomosis with SCMC, Group III; end-to-end intestinal anastomosis with omental graft, Group IV; end-to-end intestinal anastomosis with omental graft and SCMC

Table 4. Postoperative adhesion scores and number of dogs with adhesions

Group	Adhesion site						Adhesion Score (mean±SE)
	AS-OG	IS-IS	IS-ME	ME-O	O-VP	ME-VP	
I	0	3	3	0	1	0	3±0.77
II	0	4	1	0	0	0	2.6±0.68
III	5	2	1	1	1	1	2.8±0.58
IV	8	2	0	0	0	0	1.25±0.16*

AS - OG; anastomotic site - omental graft, IS - IS; intestinal serosa - intestinal serosa, IS - ME; intestinal serosa - mesentery, ME - O; mesentery - omentum, O - VP; omentum - visceral peritoneum, ME - VP; mesentery - visceral peritoneum, Group I; end-to-end intestinal anastomosis with saline lavage, Group II; end-to-end intestinal anastomosis with SCMC, Group III; end-to-end intestinal anastomosis with omental graft, Group IV; end-to-end intestinal anastomosis with omental graft and SCMC, *There was significantly difference ($p<0.05$) compared with other groups in adhesion scores.

Table 3. Adhesion length in intestinal anastomotic site at 14th day after operation

Group	Adhesion formation (mm / mean±SE)					
	AS-OG	IS-IS	IS-ME	ME-O	O-VP	ME-VP
I	0	19.6±8.64	8.6±4.12	0	0.4±0.39	0
II	0	14.4±6.49	1.7±0.8	0	0	0
III	22±3.73	1.8±1.11	1.4±1.39	1.2±1.2	0.4±0.4	0.6±0.6
IV	13.13±4.97*	2.38±1.58	0	0	0	0

AS - OG; anastomotic site - omental graft, IS - IS; intestinal serosa - intestinal serosa, IS - ME; intestinal serosa - mesentery, ME - O; mesentery - omentum, O - VP; omentum - visceral peritoneum, ME - VP; mesentery - visceral peritoneum, Group I; end-to-end intestinal anastomosis with saline lavage, Group II; end-to-end intestinal anastomosis with SCMC, Group III; end-to-end intestinal anastomosis with omental graft, Group IV; end-to-end intestinal anastomosis with omental graft and SCMC, *There was significantly difference ($p<0.05$) compared with other groups in adhesion scores.

Postoperative clinical findings

All the dogs recovered from surgery without complications. Postoperative fever, depression and anorexia were not observed. All dogs were active and had good appetite after surgery. Various degrees of defecation had been showed in dogs of each group but evacuation improved to normal status 5 days after surgery in the all dogs except one dog in group II that showed between soft feces to diarrhea repeatedly until 1 week.

Discussion

Intra-peritoneal administration of SCMC, a high molecular weight, substituted polysaccharide, has been used successfully to prevent adhesions in intestinal anastomosis in laboratory animals and horses [19, 27]. This solution provides a mechanical lubricating barrier between serosal and peritoneal surfaces, preventing the formation of adhesions in the early postoperative healing period [27, 28, 29].

In this study, intra-peritoneal administration of 1% SCMC and application of omental pedicle graft to anastomotic sites in the small intestine of dogs significantly ($p<0.05$) reduced adhesion formation and did not adversely affect healing. There were no significant differences in anastomosis between SCMC treated group with omental pedicle graft application and SCMC. Many previous studies have demonstrated that omental wrapping around suture line can be helpful to prevent adhesion formation for providing a valuable alternative blood supply to ischemic tissues and encouraging healing [2, 7, 23]. However, in our study we observed that instillation of SCMC is more effective than application of omental pedicle graft alone. Only SCMC application showed less adhesions than with abdominal lavage. Therefore, SCMC has shown the efficacy of reducing peritoneal adhesions.

All dogs were survived and recovered without complication such as dehiscence, intussusception and ileus except one dog of group II in which intestinal perforation occurred when attempted to separate adhesions during the evaluation of adhesions. After operation, all dogs were monitored everyday for signs of pain, incisional swelling or drainage, food consumption, pulse and respiratory rates, and rectal temperature and there was no obvious differences among four groups. Postoperative complications such as fever, depression and anorexia were not seen. Accordingly, intra-peritoneal administration of SCMC did not affect postoperative recovery and intestinal or abdominal wound healing.

The result of in this study has shown intra-peritoneal SCMC has efficacy in the prevention of postoperative adhesions and do not interfere with the normal process of bowel anastomotic healing. Though effect of SCMC in reducing postoperative adhesion was demonstrated, intra-peritoneal administration of SCMC will never be an answer in itself to the adhesion problem also, as with many aspects of clinical medicine, there is yet to be a single or definitive cure for postoperative adhesion formation. Because treatment of adhesions after they have formed is unrewarding, costly and associated with high patient morbidity and mortality, an emphasis should be placed on prevention of adhesion formation accordingly the aggressive use of adhesion reducing techniques appears warranted. Meticulous surgical technique, avoidance of infection, use of anti-inflammatory agents and solutions like SCMC may all be necessary adjuncts in the successful prevention of adhesions [29].

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