An experimental study evaluating the effect of sodium carboxymethylcellulose on the prevention of postoperative intraabdominal adhesions

Y. KOÇ, F. ALKAN and M. EROL

SUMMARY

Sixty rabbits were used to evaluate the effect of 1 % sodium carboxymethylcellulose (SCMC) on prevention of experimentally induced postoperative intraabdominal adhesions. Thirty rabbits were assigned to each of two groups. In all rabbits in both two groups, a ventral midline celiotomy, a cecotomy and a serosal peritoneal on caecal serosa abrasion were performed. In treatment rabbits (n = 30), 1 % solution of SCMC (7 ml/kg of body weight) and in control rabbits (n = 30), 0.9 % NaCl solution (7 ml/kg of body weight) were infused in to the abdominal cavity before and after manipulations. Two weeks later all rabbits again underwent celiotomy via a paramedian incision were evaluated for adhesions. Twenty six rabbits in the control group, and six rabbits in the treatment group had intraabdominal adhesions. The adhesions were graded in a blinded fashion utilizing the classification system described by NAIR et al. Statistically significantly more rabbits of the control group had adhesions when compared to treatment group (P < 0.001). In conclusion, this study reveals that intra peritoneal administration of 1 % SCMC to serosal abrasions and cecotomies in rabbits were effective in preventing intraabdominal adhesion formation before and after surgical manipulations. We have suggested that this beneficial effects may be attributable to lubrication and hydroflotation properties of SCMC.

KEY-WORDS : adhesions - sodium carboxymethylcellulose (SCMC) - rabbit.

1. Introduction

Intraabdominal adhesions may be acquired or congenital. Most are acquired as a result of peritoneal injury caused by abdominal surgery. They are induced by the inadvertible dissection and retraction of tissues and organs during the course of operation [4, 6, 14]. Injury or inflammation of the peritoneum results in production of a protein-rich serosanguineous exudate. Coagulation of this exudate results in the adhesion of injured peritoneal surfaces within three hours [21]. Under normal circumstances, the majority of early fibrinoid adhesions are lysed and absorbed within 48 to 72 hours. This adhesions are termed reversible adhesions. However, in some cases, fibrin may remain and become invaded by fibroblasts,
resulting in irreversible fibrous adhesions [3, 15, 21]. When two damaged peritoneal surfaces come into apposition, fibrous adhesions form between the surfaces. In the present of sufficient fibrinolytic activity (fibrinolysis) there is a resolution of fibrin strands. However, if there is insufficient fibrinolytic activity, organization of the fibrin matrix and fibroblasts and capillaries ingrowth ensues, leading to fibrous bands between the structures [4].

The causes of adhesion formation have been divided into four main types; tissue anoxia, serosal injury, infection and presence of foreign materials. Contaminated suture materials may also cause intraabdominal adhesions. These adhesions may lead to intestinal constriction, incarceration and obstruction as well as secondary intestinal volvulus [3, 6, 7, 8, 21].

Until recently, progress in clinical adhesion prevention has barely been made despite numerous animal studies showing favourable results of various drugs and intraabdominal liquids [4, 11, 12]. The introduction of barrier membranes and gels, separating damaged surfaces to heal adhesion-free, held promise of successfully preventing adhesion in patients [5, 7, 11, 12, 17].

High-molecular weight solutions infused into the abdominal cavity of rats and rabbits have been used to prevent adhesion formation after surgical trauma [7, 8]. Such agents are believed to provide a mechanical lubricating barrier between adjacent serosal surfaces, thereby preventing formation of adhesions [10, 11, 12].

Sodium carboxymethylcellulose (SCMC) has been used successfully in models to prevent adhesions in laboratory animals [9, 22, 24], ewes [16], ponies [15], horses [10, 18]. SCMC is a high-molecular-weight substituted polysaccharide that is prepared by reacting sodium monochloracetate with cellulose [9, 10, 16, 18]. The beneficial effects of SCMC are derived from the creation of a ‘hydroflotation effects’ that mechanically separates serosal and peritoneal surfaces, thus preventing adhesion formation [10, 16, 24].

The use of therapeutic agents that effectively reduce post-operative adhesion formation without adversely affecting normal peritoneal and serosal healing may be beneficial in reducing the morbidity and mortality associated with abdominal surgical disease in animals. The purpose of the study was to evaluate the effect of 1% SCMC on prevention of experimentally induced intraabdominal adhesions in rabbits before and after surgical manipulations.

1. Materials and methods

Experimental procedures and animal care were approved by the Selcuk University animal care and committee.

A) ANIMALS

A total 60 adult New Zealand White rabbits (23 males and nonpregnant 37 females, mean age, 2 years ranging from 1.5 to 3 years old and mean body weight 2.9 kg, ranging from 2 to 3.5 kg) were used in this study. Rabbits were randomly assigned to either a control (n : 30) or a treatment (n : 30) group. The animals were given a standard diet and water before and after surgery.

B) PREPARATION AND ANESTHESIA

Food was withheld from the rabbits for 12 hours before surgery. General anesthesia was induced with an intramuscular injection of xylazine hydrochloride (Rompun, Bayer, 4 mg/kg) and ketamine hydrochloride (Ketalar, Parke-Davis, 30 mg/kg).

C) PREPARATION OF SODIUM CARBOXYMETHYLCELLULOSE (SCMC)

A 1% solution of SCMC was prepared by boiling 200 ml of sterile water and adding 10 g of SCMC powder (Sigma No.C-5013, Chemical company, U.S.A) while stirring. After the SCMC was in the solution, additional sterile water was added while stirring to bring the total volume to 1 L. The SCMC solution was then transferred in to 500 ml glass bottles and autoclaved at 121 °C for 20 minutes.

D) SURGICAL PROTOCOL

The effects of SCMC on postoperative adhesion formation were evaluated using an established model of serosal trauma and caecotomy to induce intraabdominal adhesions. Rabbits were positioned in dorsal recumbency and prepared for aseptic abdominal surgery. After a ventral midline celiotomy, 6 cm in length, SCMC (1%, 7 ml/kg) was used to lubricate the intestines during manipulation in the treatment group whereas an equal volume of sterile saline (0.9% NaCl) solution was used to lubricate the intestines in the control group, the caecum and appendix vermiformis were exteriorized. The antimesenteric border of the proximal end of the caecum was used for caecotomy. In each rabbit, the caecotomy approximately 5 cm length on antimesenteric border of the caecum was performed. The caecotomies were closed in two layers: a simple continuous pattern in the mucosal layers, (using 2-0 chromic gut suture) followed by a cusching pattern in the seromuscular layers, using 2-0 chromic gut suture. In each rabbit; a 4-5 cm area on the appendix vermiformis was rubbed 20 times using a sterile dry gauze, until the serosal layer was petechial hemorrhages developed. The caecum and appendix vermiformis were subsequently returned to the peritoneal cavity. Before abdominal closure, in the treatment group same volume of 1% SCMC was applied to the intestines at the completion of surgical manipulation. An equal volume of sterile saline was applied to the intestines in the control group. In closing of the abdominal wall was performed in two layers. The linea alba and subcutaneous tissue were closed with 2-0 chromic gut in a simple continuous pattern. The skin was closed with 2-0 silk in a simple interrupted pattern.
E) EVALUATION

Two weeks later, all rabbits again underwent receliotomy via a paramedian incision with same anesthesia procedure and the abdominal cavity was evaluated for adhesion formation. The adhesions were graded in a blinded fashion utilizing the classification system described by NAIR et al [20]. (Table I)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>Complete absence of adhesions</td>
</tr>
<tr>
<td>1</td>
<td>Single band of adhesion between viscera or from one viscus to the abdominal wall</td>
</tr>
<tr>
<td>2</td>
<td>Two bands, either between viscera or from viscera to the abdominal wall</td>
</tr>
<tr>
<td>3</td>
<td>More than two bands between viscera or from viscera to the abdominal wall</td>
</tr>
<tr>
<td>4</td>
<td>Multiple dense adhesions, or viscera directly adherent to the abdominal wall and extent of adhesive bands</td>
</tr>
</tbody>
</table>

TABLE I. — Grading of Postoperative Adhesions.

F) STATISTICAL ANALYSIS

The frequency of intraabdominal adhesion formation between control and treatment groups was compared using a contingency table analysis of coded raw data. The effect of treatment (SCMC) was evaluated using a χ² test for independence. Statistical significance was established of $P < 0.05$.

2. Results

A) CLINICAL EVALUATION

All rabbits recovered from anesthesia without complications. Some of the rabbits in each group developed transient incisional swelling that appeared to be nonpainful and all celiotomy wound healed well. In the treatment group (SCMC) three rabbits died after 24 hours from operation. Two rabbits died after 72 hours from operation in the other group. Surviving rabbits showed no evidence of the complications.

B) RECELIOTOMIC EVALUATION

At receliotomy two week after operation, 26 rabbits in the control group and 6 rabbits in the treatment group had intraabdominal adhesions (Table II). Statistically significantly more rabbits of the control group had adhesions when compared to treatment group ($P < 0.001$).

The most of fibrinous and fibrous adhesions in the control group developed between the caecotomy sites and the midline incised abdominal wall (Figure 1), and between viscera.

Two rabbits in the control group did not develop adhesion. Four rabbits in the treatment group had fibrous adhesions between caecotomies sites and abdominal wall. Two rabbits in the treatment group had two bands between viscera (Figure 2). The other rabbits in the treatment group had no adhesion. Three rabbits in the treatment group showed pericaciotic abscess formation. Signs of diffuse peritonitis (such as diffusely inflammed serosa or abundant amount of peritoneal fluid), stricture at the caecotomic site, fever or depression were not seen in the rabbits of either group. The adhesions between viscera resulted band of the caecum. None of the adhesion resulted in obstruction or stricture of the caecum lumen and appendix vermiformis.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Treatment Group (1 % SCMC)</th>
<th>Control Group (0.9 % NaCl)</th>
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<tbody>
<tr>
<td></td>
<td>(n = 30)</td>
<td>(n = 30)</td>
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<tr>
<td>0</td>
<td>21</td>
<td>2</td>
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<tr>
<td>1</td>
<td>4</td>
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<td>2</td>
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<tr>
<td>3</td>
<td>0</td>
<td>12</td>
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<tr>
<td>4</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>died</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

TABLE II. — Distribution of rabbits with different grades of adhesions in the two groups ($P < 0.001$).

3. Discussion

Serosal abrasion and intestinal ischemia models have been used to evaluate methods of preventing adhesion formation in horses [10, 17, 18, 19], ponies [15], ewes [16], rats [24, 25], rabbits [9] and cows [23]. All models cause an inflammatory response. The caecum appears to be a suitable intraabdominal organ for the study of surgical adhesions. Caecotomy on antimesenteric area of proximal caecum proved to be a satisfactory and convenient model used in the rabbits of this study for simulating surgical trauma. In addition to caecotomy we performed controlled manual gauze sponge serosal abrasion on appendix vermiformis. We attempted to evaluate the effect of sodium carboxymethylcellulose on prevention of experimentally induced intraabdominal adhesions in rabbits.

In our study, the use of intraperitoneal administration of 1 % sodium carboxymethylcellulose, a high molecular weight substituted polysaccharide, significantly reduced postoperative intraabdominal adhesion formation in rabbits. The sodium carboxymethylcellulose is highly viscous and is thought to prevent adhesion by its lubricating, as well as hydroflotation effect [15, 16], that mechanically separates serosal and peritoneal surfaces [10, 15, 18]. It may act by separating the abdominal viscera during the inflammatory stage of healing of serosal abrasion and caecotomies sites.
In this study all control rabbits developed intraabdominal adhesions; 6 rabbits had abrasions at both adhesion sites, and 20 rabbits had adhesions at both caecotomy sites. In contrast to the control rabbits in this study, no treatment rabbits developed intraabdominal adhesions. In four rabbits in the treatment group fibrinous adhesions did form between caecotomies sites and abdominal wall. The hydro flotation effect of SCMC may have helped to prevent the intraperitoneal adhesion between serosal surfaces or abdominal wall to these sites. Morbidity associated with adhesions of surgery has prompted extensive research efforts into potential preventative treatments. Intraperitoneal infusion of high molecular-weight solutions and application of temporary barrier agents are directed at mechanically separating damaged peritoneal and serosal surfaces to heal adhesion-free, held promise of successfully preventing adhesions in patients [7, 10, 12].

In animals, precoating the intestine with SCMC before manipulation decreased intraabdominal adhesion formation compared with application of SCMC after manipulation [10, 25]. Lubrication of the intestine decreased friction associated with intestinal manipulation and thus minimizes serosal damage during surgery [10, 25]. In this study, 1% SCMC decreased the incidence of adhesions in response to serosal abrasions and caecotomies in rabbits. 7 ml/kg of 1% SCMC was sufficient to lubrication of the intestines and surgeons gloves that subjectively greatly reduced friction during manipulations. The second 7 ml/kg of 1% SCMC applied after manipulations, resulted in pooling of the SCMC in the abdominal cavity. The results of this study suggested that applications 7 ml/kg of 1% SCMC before and after manipulation decreased adhesion formation.

Postoperative intraabdominal adhesions begins during the early inflammatory stage of healing 24 to 48 hours after injury and depends on the functional ability of the fibrinolytic system within the peritoneal cavity and intestinal serosa [18, 19]. The adhesions usually are well formed by 5 to 7 days after injury [3, 6]. The fibrinolytic mechanism is stimulated naturally by plasminogen- activating substances, that are present in mesothelial cells and submesothelial blood vessels. Plasminogen activation is depressed by peritoneal injury only in the local areas of injury and inflammation [3]. Adhesions may be beneficial in their ability to provide an additional blood supply to ischemic serosa or intestine [2, 18]. Perianostomotic adhesions may prevent generalized peritonitis [2]. By pharmacologically altering the response of the peritoneal or serosal surfaces, the normal healing response of the abdominal cavity may be impaired. The use of intraperitoneal SCMC in rats increased the incidence of perianostomatic abscess formation, peritonitis and mortality [24]. However all serosal abrasions and jejunal anastomoses in horses that the use of intraperitoneal 1% SCMC, healed without complication had been reported by HAY and al [10]. In our study, three rabbits the use of intraperitoneal SCMC were observed pericaecotomic abscess formation. The other rabbits were no observed pericaecotomic abscess formation.

Postoperative adhesions can result in impaired intestinal motility and low obstruction and predispose the animal to inadvertent incision of abdominal organs during entry to the abdomen in subsequent surgical procedures. Therefore, prevention of adhesions is important, whereas proper aseptic, atraumatic surgical techniques, exacting hemostasis, minimization of spillage of abdominal contents moistening of tissues and deliberate nonsuturing of peritoneal incisions and defects are the most important factors in minimizing intraabdominal adhesion formation [6, 7, 8, 11, 12, 13].

4. Conclusion

In this study, intra peritoneal administration of 1% SCMC to serosal abrasions and caecotomies in rabbits were effective in preventing intraabdominal adhesion formation before and after surgical manipulations. This beneficial effects may be attributable to lubrication and hydro flotation properties of SCMC.

5. Acknowledgments

We wish to thank to Dr. Kemal KIRIKÇI and Dr. Aytekin GÜNLÜ to help for statistical analysis in the study.

References


Revue Méd. Vét., 2002, 153, 12, 803-807


