Comparison of the Effects of Different Concentrations of Sodium Carboxymethylcellulose on Prevention of Intraabdominal Adhesions in Rats

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SUMMARY

This experiment was conducted to compare the effects of different concentrations of sodium carboxymethylcellulose (SCMC) on prevention of experimentally induced intraabdominal adhesions in rats. Sixty male Wistar albino rats were divided into four equal groups. An adhesion model was constituted in the caecum and most caudal segment of the ileum of all rats. The lesion areas of rats from the first, second and third groups were coated with a 1 %, 2 % and 3 % SCMC solutions, respectively. Additionally, 7 ml/kg of body weight of a 1 %, 2 % and 3 % SCMC solution were instilled in the peritoneal cavity of animals of the first, second and third group respectively. For the fourth group (control group), a 0.9 % saline solution was used to coat the lesion area and 7 ml/kg of body weight of the same solution was instilled in the peritoneal cavity of each animal. Fourteen days later the rats were sacrificed and the adhesions were graded according to degree of severity. In conclusion, intra-peritoneal administration of SCMC is significantly effective in preventing intraabdominal adhesion formation in rat model.

Keywords: sodium carboxymethylcellulose (SCMC), intraabdominal adhesions, rat

Introduction

Surgical procedures are the most common causes of intraabdominal adhesions [19]. Adhesions are caused by a series of cellular and endogenous chemical inflammatory responses secondary to the injuries to serosal tissues. Various therapeutic modalities have been designed to prevent or reduce adhesions either by reducing the magnitude of the inflammatory response of damaged peritoneal surfaces or by separating the injured surfaces long enough to allow mesothelial repair without adhesion formation [2,6,7,13,14,25]. These include the use of corticosteroids, nonsteroidal antiinflammatory drugs, dextran, anticoagulants, tissue plasminogen activators and physical barriers [12,15]. However, in most instances initial enthusiasm faded when clinical use and further experimental studies failed to show the efficacy of these agents [1,25].

It is believed that viscous solutions reduce serosal trauma by coating the peritoneal surfaces, which become damaged during abdominal surgery. As a consequence, the coated peritoneal surfaces do not adhere to each other by fibrinous deposits and thus may heal without adhesion formation [21].

SCMC is an anionic polysaccharide that is available in different molecular weight ranges and degrees of substitution. The SCMC has been evaluated for adhesion prevention in the form of films, gels and sponges by various investigators [12,22,23].

The amount of fluid and the concentration of polysaccharides both might affect the adhesion reducing capacity of the SCMC solutions. Sufficient fluid should be instilled in the abdominal cavity to cause flotation of the viscera. Instillation of a fluid with a too-low viscosity will most likely be ineffective, due to rapid absorption by the peritoneum and through...
the diaphragmatic stomata. In contrast, fluids with a very high viscosity might partition in the peritoneal cavity longer than those with a lower viscosity and could adversely affect bacterial uptake. This might even cause an increased tendency of the peritoneal surfaces to adhere [21].

The purpose of this study was to investigate the effect of various concentrations of SCMC on prevention of intraabdominal adhesion formation in a rat model.

Material and Methods

MATERIALS

The experiment was conducted in the Animal Hospital of Veterinary Faculty of the First University of Turkey in accordance with usual guidelines.

Solutions of SCMC were prepared as reported by KOC et al. [13,14]. In brief, a 1 %, 2 % and 3 % solutions of SCMC were prepared by boiling 200 ml of sterile water and adding 5 g, 10 g and 15 g of SCMC powder (Sigma No, C-5013, Chemical Company, U.S.A) respectively while stirring. After the SCMC was in the solution, additional sterile water was added while stirring to bring the total volume to 500 ml. The SCMC solutions were autoclaved at 121 C for 20 minutes.

EXPERIMENTATION

Experiment was carried out in 60 male Wistar albino rats weighing between 250 and 300 g. The rats were obtained from the Veterinary Control and Research Institute in Elazig, Turkey. Animals were housed at 21°C with a day/night cycle of 12 h. They had free access to water and standard rodent feed.

Rats were divided randomly into four equal groups and anaesthetized with single intramuscular injection of ketamine (85 mg/kg) and xylazine (6 mg/kg). The abdomens of the rats were shaved and prepared with 1 % antiseptic povidone-iodine solution and a 2 cm midline laparotomy was made. The most lower caudal ileum and caecum of all animals mobilized and placed onto a wet gauze. Both sides of the ileum, just proximal to the caecum, and caecum were scraped superficially until there were serosal haemorrhages on their surfaces. Additionally all animals received standard surgical interventions and in 3 % of all laparotomies [3,20].

The understanding of the pathogenesis especially at the cellular and molecular level can help to further develop more effective treatments for prevention of adhesion formation and reformation [4]. Adhesion formation is related to a reduced fibrinolytic capacity [10]. Following an injury to the peritoneum, fibrinolytic activity over the peritoneal surface decreases, leading to changes in the expression and synthesis of various cellular mediators and in the remodelling of the connective tissue [4]. On the other hand, strong increase in the fibrinolytic capacity was found to be associated with the persistence of adhesions; the extent of adhesions was almost constant throughout all observation periods from day 1 up to 1 year postoperatively [10].

A Kruskal Wallis non-parametrical test was used to compare the adhesion scores between the groups SCMC 1 %-2 % - 3 % and control group. These analyses were accomplished by using statistical analysis system configured for computer (SPSS, Relase 12.0, SPSS. Inc).

Results

All animals recovered from anaesthesia with no evidence of complications.

The SCMC solution was easily applied and remained in place until closure of the peritoneum. At necropsy, there was no evidence of residual solution.

At relaparotomy 14 days after operation, all the rats in the control group, 11 rats in the 1 % in the SCMC group (p < 0.032), 8 rats in the 2 % SCMC group (p < 0.023) and 5 rats in the 3 % SCMC group (p < 0.012) had intraabdominal adhesions (Table II). The incidence of adhesion-free animals was significantly higher in rats treated with SCMC compared to controls.

Five rats in the 1 % SCMC group, 4 rats in the 2 % SCMC group and 3 rats in the 3 % SCMC group had fibrinous adhesions between scraped areas caudal ileum and caecum and abdominal wall (Grade 1 adhesion). Six rats in the 1 % SCMC group, 4 rats in the 2 % SCMC group and 2 rats in the 3 % SCMC group had two bands between viscera (Grade 2 adhesion). Ten rats had more than two bands between viscosa and abdominal wall in the control group (Grade 3 adhesion). Three rats had multiple dense adhesions between viscosa and abdominal wall in the control group (Grade 4 adhesion). None of the adhesion resulted in obstruction or stricture of the caecum. The other rats in the SCMC groups had no adhesion. As seen in Table II, increase of the concentration of SCMC resulted in a better score.

Discussion

Post-operative intraabdominal adhesion formation and reformation after surgery is a cause of significantly morbidity and mortality, resulting in infertility and pain [4,19]. Peritoneal adhesions (PA) developed in 90 % of all laparotomies; intestinal obstruction related to PA was seen in 1 % of all surgical interventions and in 3 % of all laparotomies [3,20].

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Theoretically, the removal of cellular debris, endotoxins, bacteria and other inflammatory derivatives, and the physical separation of bowel loops should aid in the reduction of adhesion formation [8].

SCMC is a high molecular weight water-soluble, absorbable polysaccharide polymer solution. SCMC is supplied as a powder, reconstituted with water to achieve a 1% solution, and autoclaved. It acts as a physical barrier, coating the viscera and preventing immediate bowel-to-bowel contact [9]. The other proposed mechanism of action of SCMC is through its effect on fibroblastic and cellular activities [11,24]. RYAN and SAX [24], have observed marked suppression of serosal fibroblast growth in SCMC-treated animals in a caecal abrasion model. However, in the in vitro component of their study they were unable to show significant changes in fibroblast growth and collagen formation [24]. The recommended volume ranges between 1 and 7 ml/kg body weight introduced into the abdomen prior to intestinal manipulation [13,14]. For that reason, we have chosen 7 ml/kg body weight SCMC in our study. The SCMC solution was easily applied and remained in place until closure of the peritoneum.

There are many experimental models for constituting peritoneal adhesions: the damaged uterine horn model, the ileal transection model, the large bowel anastomosis model, the peritoneal damage model, the bacterial peritonitis model and the scraping model [3,6,19,20]. The caecum appears to be a suitable intraabdominal organ for the study of surgical adhesions. The scraping model is very effective in constituting peritoneal adhesions because direct mechanical intestinal wall damage is created. As this model mimics abdominal surgery, we have chosen gauze scraping and applied it until petechial spots appeared.

The Nair model grades adhesions from 0 to 4 according to their severity [18]. We have applied this model because of its simplicity.

The most fibrinous and fibrous adhesions in the control group developed between the scraped areas of caecum and the abdominal incision, and between viscera as reported by KOÇ et al. [13]. The grade of adhesions in each group is summarised in Table II.

Comparison of the four groups indicated that post-surgical adhesion formation was significantly reduced in animals treated with SCMC solution when compared with controls. The hydroflotation effect of SCMC [16,17], may have helped to prevent intraperitoneal adhesions between serosal surfaces. Precoating the intestine with SCMC before manipulation decreased intraabdominal adhesion formation compared with application of SCMC after manipulation [9]. The results of this study showed that applications of SCMC before and after manipulation decreased adhesion formation as reported by Koç et al. [13].

Instillation of a too-low viscosity fluid will most likely be ineffective, due to rapid absorption [21], while fluids with a very high viscosity may partition within the peritoneal cavity. SCMC reduced primary adhesion formation in this study with adhesion scores directly correlated to concentrations of 1%, 2% and 3%. This results did not agree with those reported by Diamond et al. [5]. The adhesion preventive effect of SCMC is demonstrated by this experiment and is in full agreement with others [1,2,7,15,21,25].

Minimizing the risk of adhesions will continue to be of paramount interest and importance to veterinarians; the use of adjusted measures can decrease the incidence of this complication.

### References


