Vet.Med.J.,Giza. Vol.50, No.4. (2002):945-953.

EFFICACY OF SOME COMPOUNDS FOR PREVENTION OF EXPERIMENTALLY INDUCED PERITONEAL ADHESIONS IN DONKEYS

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Received: 21. 9. 2002

Accepted: 3. 10. 2002

SUMMARY

Twenty donkeys were subjeted to experimental induction of peritoneal adhesions. They were allocated into five equal groups including control (C), Saline treated (ST), heparin treated (HT), dimethyl sulfoxide treated (DT), and sodium carboxy methylcellulose treated (MT) groups. Group C did not receive any medicament . In the other groups saline, heparin, dimethyl sulfoxide, and sodium carboxy methylcellulose were intraperitonealy administered before closure of the abdomen to assess their efficacy for prevention of adhesions. In this respect, sodium carboxy methylcellulose proved the best drug preventing abdominal adhesions followed by heparin and dimethyl sulfoxide.

INTRODUCTION

Post-operative peritoneal adhesion is a potential complication of abdominal surgery in horses (Baxter et al, 1989; McDonald et al, 1989; Parker et al, 1989 and Baxter, 1992). Approximately twenty percent of horses that survived surgery for small intestinal lesions had required additional surgery because of intra abdominal adhesions (McDonald, et al, 1989; Parker et al, 1989; Baxter et al, 1989 and Baxter, 1991). Treatment of horses that suffer colic because of adhesions is difficult, therefor, preventing adhesion is important (Snyder, 1993). Numerous trials have been performed to determine methods of minimizing the formation of post-operative intra-abdominal adhesions. Use of corticosteroid (Khamis, 1964 and Elsayed, 1977), isonicotinic acid hydrazide, polyvinyl pyrolidone (Said et al, 1974 and Elsayed, 1977), povidone iodine (Abd El Mottaleb et al, 1981) broad spectrum antibiotics, non steroidal anti-inflammatory agents, dimethyl sulphoxide (Sulling et al, 1991 and White, 1992), have been tried for prevention of intra abdominal adhe-

sions. Heparin (Parker et al, 1987 and Sulling et al, 1991), intraperitoneal administration of high molecular weight solutions (Elkins et al, 1984; Moll et al, 1991; Yaacobi et al, 1993; Burns et al, 1995; Mueller et al, 1995; Wurster, 1995 and Hay et al, 2001), hyaluronate (Rodgers et al, 1997 and Kramer et al, 2002), halofuginone (Nagler et al., 1999), peritoneal lavage using either normal saline (Heidrick et al, 1994) or lactated Ringerís solution (Hague et al, 1998), omentectomy (Kuebelbeck et al, 1998) and the use of bioresorbable membrane (Mueller et al, 2000) have been also advocated to minimize intra abdominal adhesions.

The purpose of this study was to assess the efficacy of four compounds including normal saline, heparin, dimethyl sulfoxide (DMSO) and sodium carboxy methylcellulose (SCMC) in prevention of post-operative peritoneal adhesions in donkeys.

MATERIALS AND METHODS

Twenty clinically normal donkeys of both sexes aging 2-8 years and weighing 80-150kg were used in this study. The animals were randomly allocated into five equal groups, control (C), saline treated (ST), DMSO treated (DT), heparin treated (HT) and SCMC treated (MT) groups. Celiotomy and serosal abrasion in the jejunum were made to induce adhesions then one of the aforementioned drugs was applied.

The animals were prepared for surgery by withholding food overnight prior to surgery. Narcosis was performed using chloral hydrate 5 gm /50kg Bwt in 10 % solution injected intravenously. The donkeys were positioned in dorsal recumbence and prepared for aseptic abdominal surgery. A ventral median celiotomy incision and abdominal exploration were performed to examine the viscera. The jejunum was then exteriorized, examined and serosal abrasion was made in the antimesenteric border of a chosen area by stripping of the serosa using tooth-rat dissecting forceps after (Elsayed, 1977). This abrasion was made in an area of 50cm long and 2mm width (Fig. 1). Two chromic cat gut stitches were made in the periphery of the abraded length to delineate the abrased area. The Celiotomy incision was closed routinely using chromic catgut No.1 for peritoneum, linea alba and subcutaneous tissue and silk No 2 for skin.

In group C, none of the tested solutions was used before closure of the abdomen. In group ST, the jejunum was washed with 350ml saline and other 150 ml were poured into the abdominal cavity after reposition of the jejunum. The same protocol was adopted in HT, DT and MT groups using heparin 10U/ml in saline, DMSO 20 % and SCMC 1% respectively.

After recovery, water was allowed ad labitum and the animals gradually returned to full feed over the next 24 hours. All animals did not receive antibiotics or anti-inflammatory drugs and moni-

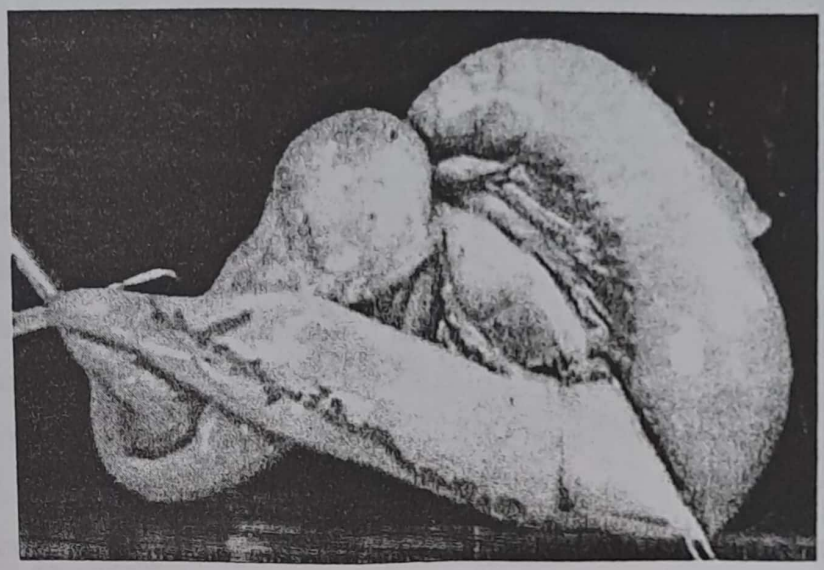

Fig. 1: Serosal abrasion in the antimesenteric border of jejunum.

tored daily for signs of pain, swelling or discharge and pulse, respiratory rate, and rectal temperature. Animals in all groups were euthanatized 15 days post-surgery and the site of abdominal incision, peritoneal cavity and the abdominal organs were examined for presence of adhesions.

RESULTS

All donkeys tolerated surgery well and without complications up to the time of necropsy.

In group C, the post mortum examination revealed that the jejunum was thickened with focal areas of serosal hemorrhage at the site of abrasion. Fibrous adhesions were not present at the abrasion site and developed in all donkeys between cecum and peritoneum at the celiotomy incision (Fig.2 A&B).

In group ST, the jejunum at the abrasion area was similar to that of group C. Out of the four operated donkeys, three developed adhesions between cecum and peritoneum at the site of laparotomy incision. The other one had adhesion between the abraded part and other parts, of jejunum cecum and omentum in addition to adhesions between cecum and the site of abdominal incision (Fig.3). In HT and DT groups, the jejunum at the abraded area was similar to that of C and ST groups. Adhesions were detected between cecum and peritoneum at the site of abdominal incisions in three donkeys of each group. The last donkey from both the two groups did not show any adhesions with minimal areas of thickening in the serosal abraded parts of the jejunum. In group MT, no adhesions was formed in all animals. Areas of thickening and serosal hemorrhage were seen opposite to some areas in the serosal abrasion surface.

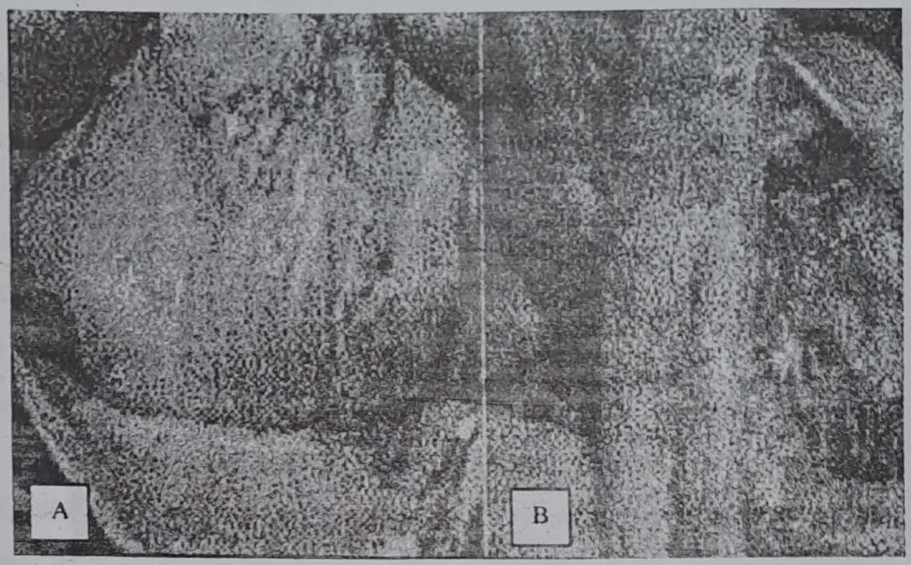

Fig. (2): Adhesions between cecum and abdominal wall (A) and healing of serosal abrasion (B).

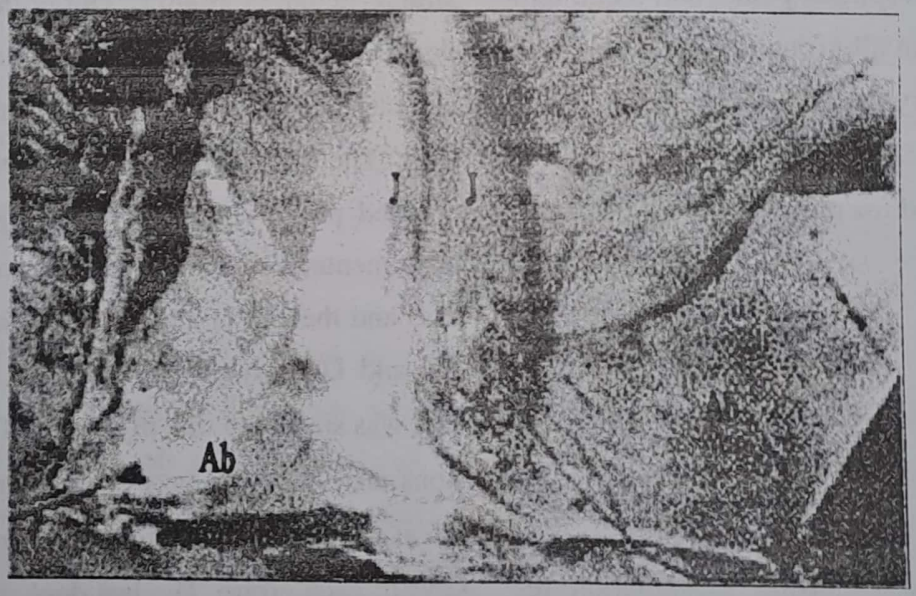

Fig. (3): Adhesions between jejunum, cecum and abdominal wall.
J. Jejunum C: Cecum Ab; Abdominal wall

DISCUSSION

All animals of both group C and ST and three donkeys from both of group HT and DT showed peritoneal adhesions. On the contrary, none of those animals belonging to group MT developed adhesions. The known three types of intra abdominal adhesions (omental, bowl-bowl and bowl-abdominal wall) were detected only in one donkey of group ST, where as bowl-abdominal wall adhesions were seen in all other animals.

Serosal abrasion model have been previously used to evaluate methods of preventing adhesions formation in horses (Parker et al, 1987; Moll et al, 1991; Baxter et al, 1993 and Hague et al, 1998), whatever the model used it should not influence the results of therapeutic studies as the pathogenesis of adhesion formation is similar regardless of the inciting cause (Ellis, 1980 and Gervin et al, 1973). Kuebelbeck et al, 1998, added that adhesion models mainly performed in the small intestines because it always show higher incidence of adhesions than the large intestines.

Formation of adhesions begins during the early inflammatory stage of healing and become well formed by five to seven days after injury (Aurora et al, 1974; Buckman et al, 1976; Henderson, 1982 and Holmdahl et al, 1997). Adhesions formation begin with coagulation, which initiates a cascade of events resulting in the build up of fibrin gel matrix that serves as the progenitor to adhesion (Holmdahl et al, 1997). Protector fibrinolytic enzyme systems of the peritoneum such as plasminogen system can remove this fibrin gel matrix, however, surgery dramatically diminishes the fibrinolytic activity (Baxter, 1991 and Holmdahl, 1996). The use of peritoneal lavage aimed on removal of inflammatory byproduct that might decrease fibrin deposition and subsequently prevent adhesion formation (Baxter et al, 1989 and Baxter, 1992). In the present study, the entire ST group had developed adhesions, reflecting the insufficient role of saline in preventing adhesions properly. Moreover, peritoneal lavage with saline solution produced mild transient inflammatory reaction (Schneider et al, 1988). On the other hand, use of postoperative lavage may be more beneficial than intraoperative lavage because it allows for removal of fibrin that forms after surgery (Heidrick et al, 1994 and Hague et al, 1998).

The use of heparin reduced adhesions formation in one animal in HT group. In addition to its anticoagulant properties, heparin also promotes fibrinolysis by increasing tissue plasminogen activator activity (Marsh, 1990). Although, heparin reduced adhesion by either systemic or intraperitoneal administration, the reported results were greatly varied (Parker et al, 1989; Marsh, 1999; Florencio et al, 1991 and Sullins et al, 1991). In this study, ad-

ministration of 5000 U heparin intraperitoneally was not enough to prevent adhesion.

In the DT group, adhesion was also prevented in one of the group members. Despite its antifibrotic properties (Douwes and Van der Kolky, 1998), DMSO showed a little effect in preventing adhesions. In the present study the effect of heparin and DMSO were equal in preventing adhesions, however, Sullins et al, 1991 reported that DMSO was superior to heparin in preventing adhesions.

In the MT group, all donkeys developed no adhesions to a distant site in the abdominal cavity. Intra-abdominal administration of SCMC successfully prevented adhesions of the experimental models (Elkins, 1984; Friedricks et al, 1986; Moll et al, 1991 and Hay et al, 2001). A result that drew our attention was that mentioned by Yaacobi et al, 1993, who concluded that precoating the intestines before manipulation in laboratory animals minimized adhesions formation. The beneficial effect of SCMC was derived from the creation of a hydrofloatation effect that mechanically prevents apposition of serosal and peritoneal surfaces and thus preventing adhesion formation (Elkins et al, 1984 and Moll et al, 1991). Large volume of SCMC (two liters) might be used to achieve the hydrofloatation in the equine abdomen (Moll et al, 1991 and Hay et al, 2001). As a drawback of such material, Burkhard and Baxter, 1996 emphasized that systemic absorption after intraperitoneal administration of large amounts to horses resulted in postoperative pyrexia, depression and anorexia. However, other studies on ponies and horses did not result in such complications (Moll et al, 1991; Mueller et al, 1995 and Hay et al, 2001). In this respect, the use of small amount of SCMC for donkeys in the present study produced neither adhesions nor systemic reactions. However, one can not neglect the fact that good surgical technique designed to minimize trauma is a crucial part of adhesion prevention, moreover, technique alone can not effectively eliminate adhesions formation (Gomel et al, 1996).

IN CONCLUSION

Sodium carboxy methylcellulose proved the best solution in preventing intra abdominal adhesions. Moreover, it can be used safely and effectively to prevent adhesion. The use of meticulous surgical technique together with SCMC intra-peritoneally during surgery might reduce intra abdominal adhesions.

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