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الوقاية من التصاقات الأحشاء باستخدام بعض الأنزيمات المذبحة للفيبرين

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أجريت دراسة تجريبية على الكلاب بهدف الوقاية من التصاقات الأحشاء الداخلية التي تحدث عقب جراحات الجهاز الهضمي. ولقد تم استخدام الأنزيمات المذبحة للفيبرين موضعياً في التجريف البطني. ووجد أن أنزيم الهيالورونيد يزدوجافعية مؤثرة في منع هذه التصاقات.
PROPHYLAXIS OF ABDOMINAL ADHESIONS USING SOME FIBRINOLYTIC DRUGS
(With 4 Figures)

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SUMMARY

An experimental study was performed as a trial to prevent the post-operative abdominal adhesions by intraperitoneal topical application of hyaluronidase and alfa-chymotrypsin enzymes.

Hyaluronidase was found to be more effective in prevention of adhesions formation.

INTRODUCTION

Since the beginning of this century, enormous amount of work has been carried for prevention of peritoneal adhesions. Adhesions mostly develop following abdominal operations resulting in intestinal obstructions (ELLIS, 1971).

The destruction of serosa and anything which damages the endothelium whether it is rough handling, retraction, firm gauze swabbing or surgical denudation must necessarily be followed by persistent adhesions (LODWIG, 1926 and ELLIS, 1971).

Prophylaxis against adhesions has been approached from a number of aspects. Prevention of the deposition of fibrin in peritoneal exudate has involved the use of anticoagulant agents as citrate solution (PAPE, 1916) and heparin (BOLBOL et al., 1979). For the removal of the fibrin which has already formed, such enzymes as trypsin, pepsin and other fibrinolytic agents were used (BUCKMAN et al., 1975 and BOLBOL & MOSTAFA, 1984). Other drugs have also been attempted in order to prevent these adhesions such as Noxythiolan and aprotinin (RAFTERY, 1979 and BOLBOL & MOSTAFA, 1984), glucocorticoids (HOUWISH, 1963) and polyvenlypyridoline (ELLIS et al., 1955).

The aim of this study is to evaluate the use of some fibrinolytic enzymes in order to determine their efficacy in preventing the postoperative intraperitoneal adhesions.

MATERIAL and METHODS

This work was carried out on 24 adult clinically healthy dogs of different ages and sexes with very small differences in weight. The animals were kept under the same conditions and nutrition. They were divided into three equal groups.

The dogs were injected i.m. with Combelen (Bayer) in a dose of 0.05 ml/kg.b.wt. General anaesthesia was induced by i.v. injection of pentothal sodium (Nesdonal, Specia).

Laparotomy was performed through a midline incision. Adhesions were created by stripping the intestinal serosa in a length of 10 cm and 1.5 cm width. (Fig. 1).

In the first group, alfa-chymotrypsin (Alfaspin, choya), in a dose of 2.5 mg/10 kg.b.wt. was applied on the serosal defect before closure of the abdominal wall. The second group

received topically hyaluronidase enzyme in a dose of 600 U/10 kg.b.wt. (600 U/ml). The third control group was left without treatment. The abdominal wall was closed as usual.

All animals were sacrificed 21 days following surgery for postmortem examination (through a U-shaped incision extending from the costal margin to the pubis). The degree and the site of adhesions were then determined.

RESULTS

Animals of the control group showed severe degree of adhesions at the site of stripping on the free border of the intestine and omentum (Fig. 2). In one case the adhesion includes omentum and pancreas.

Two animals in the group treated with alfa-chymotrypsin showed severe degree of adhesions between the jejunum, omentum and abdominal wall. Two animals were free from adhesions. The others had slight degree.

The dogs received hyaluronidase enzyme gave the best results in which all animals showed no adhesions at the site of the operation (Fig. 4) except two of them which had slight to moderate degree of adhesions.

DISCUSSION

Although peritoneal adhesions are a protective process for covering the serosal defects yet they are not always beneficial for the body (HOUWISHI, 1963). The simple relationship that adhesions may develop after abdominal operation and produce intestinal obstruction has led surgeons to the concept that adhesions are necessarily malignant and its formation must be avoided at all costs (ELLIS, 1971).

The normal peritoneum has an inherent fibrinolytic activity, and the fibrinous adhesions are normally removed from the peritoneal cavity by fibrinolysis and absorption (JACKSON, 1958 and OPIE, 1964). GREGG et al. (1973) and BUCKMAN (1975) demonstrated that this fibrinolytic activity is depressed by injury or crushing to the peritoneum. Such depression may permit the persistence of fibrinous adhesions until fibroblasts can lay down leading to fibrous adhesion.

Only two dogs out of eight received intraperitoneal hyaluronidase enzyme following serosal stripping, showed slight to moderate form of abdominal adhesions, while the rest of animals showed no signs of adhesion formation.

It is well known that hyaluronidase enzyme has the property of hydrolyzing hyaluronic acid, one of the polypeptide (ELLIS, 1971).

The finding was confirmed by the results of CONNOLLY and RICHARDS (1952). They found that hyaluronidase which was administered intraperitoneally at the time of the insult was placed within the peritoneal cavity of dogs, inhibit adhesion formation. The results of this work denoted that the enzyme not only act to hydrolyse the fibrin but also prevent its formation. As well hyaluronidase, occurring naturally in certain tissues, which is mucolytic in action. It breaks down the linkages of large polysaccharide molecules, mainly hyaluronic acid, which is an important constituent of intercellular ground substance (DOUTHWAITE, 1952 and ELLIS, 1971). Therefore, the natural body hyaluronidase initiate the prevention of fibrin formation and thus is more helpful when another dose of enzyme was administered.

PROPHYLAXIS OF ABDOMINAL ADHESIONS

The results in the first group in which the animals received alfa-chymotrypsin intraperitoneally indicated that chymotrypsin may reduce adhesion formation. At the same time the enzyme can hydrolyse the fibrin clot but had no effect on prevention of fibrin formation.

In dogs injected with proteolytic enzymes (trypsin and chymotrypsin), it was shown by BOLBOL and MOSTAFA (1984) that single intraperitoneal injection of the preparation moderately reduce adhesion formation, while it was almost ineffective when intramuscularly injected 15 days postoperatively. These findings concluded that many preparations can be used successfully for prevention of intraperitoneal adhesion formation, where they interfere with the formation of fibrin. If the fibrin began to organise by connective tissue, most of the agents used became effective in reduction of these adhesions.

As a conclusion, it was found that hyaluronidase gave the best results in prevention of adhesion formation by either interfering with the fibrin formation or hydrolysis the well formed fibrin. Alfa-chymotrypsin gave a lower effect which reduces fibrin formation and digest the fibrin clot.

REFERENCES


Fig. 1 - Showing the Method of serosal stripping

Fig. 2 - Severe degree of adhesion between the omentum and the site of serosal stripping in control group.
Fig. 3—Slight adhesions after topical application of alfachymotrypsin.

Fig. 4—No adhesions were observed after topical application of hyaluronidase enzyme.