قسم : الجراحـــــــــة .
كليـة : الطب البيطرى ـ جامعة أسيوط .
رئيس القسم : أ . د . ٪ نبيل أحمد على مسك .

الوقاية من التصاقات الاحشاء باستخدام بعض الانزيمات المذيبه للفيبرين

محمد عـادل ، هارون يوســف ، عاطف بلبــل

أجريت دراسة تجريبية على الكلاب بهدف الوقاية من التصاقات الأحشـــاء الداخلية التي تحدث عقب جراحات الجهاز الهضمي . ولقد تم اســـتخدام الأنزيمات المذيبه للفيبرين موضعيا في التجويف البطني . ووجد أن أنزيـم الهيالورونيدز ذو فاعلية مؤثرة في منع هذه الالتصاقات .

Dept. of Surgery,
Faculty of Vet. Med., Assiut University
Head of Dept. prof. Dr. N.A. Misk.

PROPHYLAXIS OF ABDOMINAL ADHESIONS USING SOME FIBRINOLYTIC DRUGS

(With 4 Figures)

By
M.A. ALY; H.A. YOUSSEF and A.E. BOLBOL
(Received at 10/2/1985)

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 necessrily be followed by persistent adhesions (LODWIG, 1928 and ELLIS, 1971).

Prophylaxis against adhesions has been approached from a number of aspects. Prevention of the depostion 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 been 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 Noxythiolin and aprotinin (RAFTERY, 1979 and BOLBOL & MOSTAFA, 1984), glucocticoids (HOUWISHI, 1963) and polyvenylpyrolidine (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 intrapertioneal 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 (Alfapsin, choay), 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

recieved 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 postmortum 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 deudenum, omentum and abdominal wall. Two animals were free from adhesions. The others had slight degree.

The dogs received hyaluronidase enzyme gave the best resuls 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 preocess 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). GREVIN 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 persistance 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 formtion.

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

The finding was confirmed by the results of CONNOLLY and RICHARDS (1952). They found that hyaluronidase which was adminestered intraperitoneally at the time talc 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 adminstered.

The results in the first group in which the animals recieved 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 intrmuscularly injected 15 days postoperatively. These findings concluded that many preparations can be used succesfully for prevention of intraperitoneal adhesion formation, where they interfere with the formation of fibrin. If the fibrin began to organize by connective tissue, most of the agents used became in 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 interferring 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

Bolbol, A.E; Hosny, A., Tantawy, M., Abdel-Mottelib, A and El-Oseely, M.A. (1979): Effect of heparin in the treatment of experimental peritonitis. Assiut Vet. Med. J. 6: 209 - 218.

Bolbol, A.E. and Mostafa, F.M. (1984): Prevention of peritoneal adhesions. Assiut Med. J. 7: 178 - 186.

Buckman, R.F., Bordos, D., Bell, W.R. and Cameron, J.L. (1975): Prevention of experimental postoperative adhesions by Ancord defibrinogination. J. Surg. Res., 18: 377.

Connolly, J.E. and Richards, V. (1952): Experimental use of hyaluronidase in prevention of intestinal adhesions. Surg. Forum. 2 : 85.

Douthwaite, A.H. (1952): Pharmacology and therapeutics. J. & A. Churchil LTD, London.

Ellis, H., Harrison, W. and Hugh, T.B. (1955): The healing of peritonuem under normal and abnormal conditions. Br. J. Surg., 52: 471.

Ellis, H. (1971): The cause and prevention of postoperative intraperitoneal adhesions. Surg., Gynae & Obst. 133: 497 - 510.

Griven, A.S., Puket, C.L. and Silver, D. (1973): Serosal hypofibrinolysis, a cause of postoperative adhesions. Am. J. Surg., 128: 80 - 88.

Houwishi, Y.K. (1963): Experimental investigations in rabbits for the prevention of peritoneal adhesions using different glucocorticoids. Egypt Vet. Med. J., Giza, 9 : 167 - 188.

Jackson, B.B. (1958): Observations on intraperitoneal adhesions; an experimental study. surgery, 44 : 507.

Lodwig, A. (1928): Beitrage zur morphologie intraperitoneal adhesionen. Arch.Klin. Chr.,151:1.

Opie, E.L. (1964): inflammation in serous cavities, definiton and measurements. Arch. Path., 78: 1.

Pape, S. (1916): Prevention of peritoneal adhesions by the use of citrate solution. Ann. Surg., 63: 205 - 206.

Raftery, A.T (1979): Noxythiolin (Noxyflex), aportinin (Trasylol) and peritoneal adhesion Formation: An experimental study in the rat. Br. J. Surg. 166: 654 - 656.

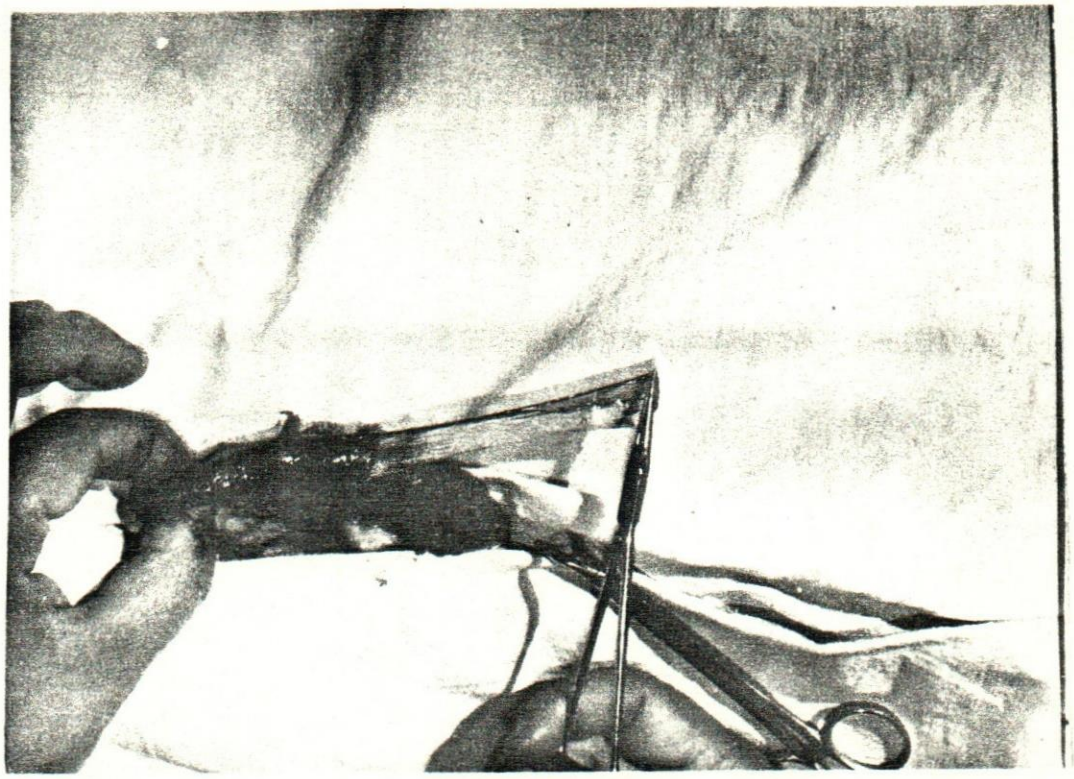

Fig. 1- Showing the Method of serosal stripping

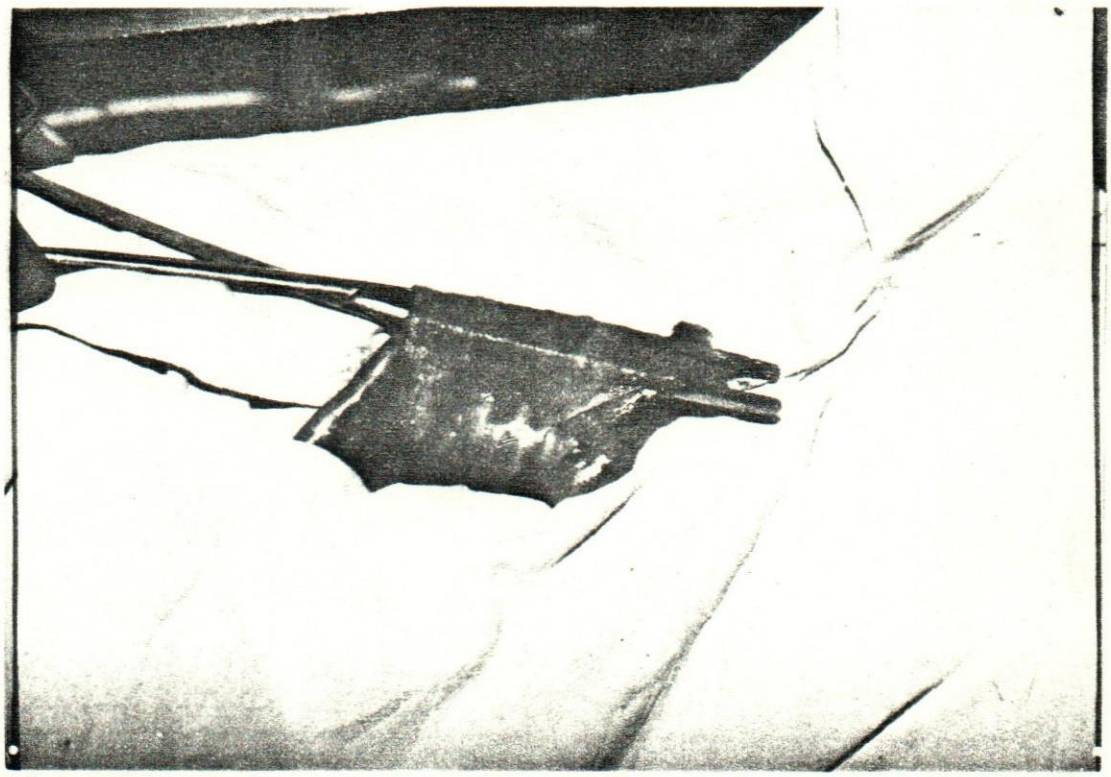

Fig. 2- Severe degree of adhesion between the omentum and the site of serosal stripping in control group.

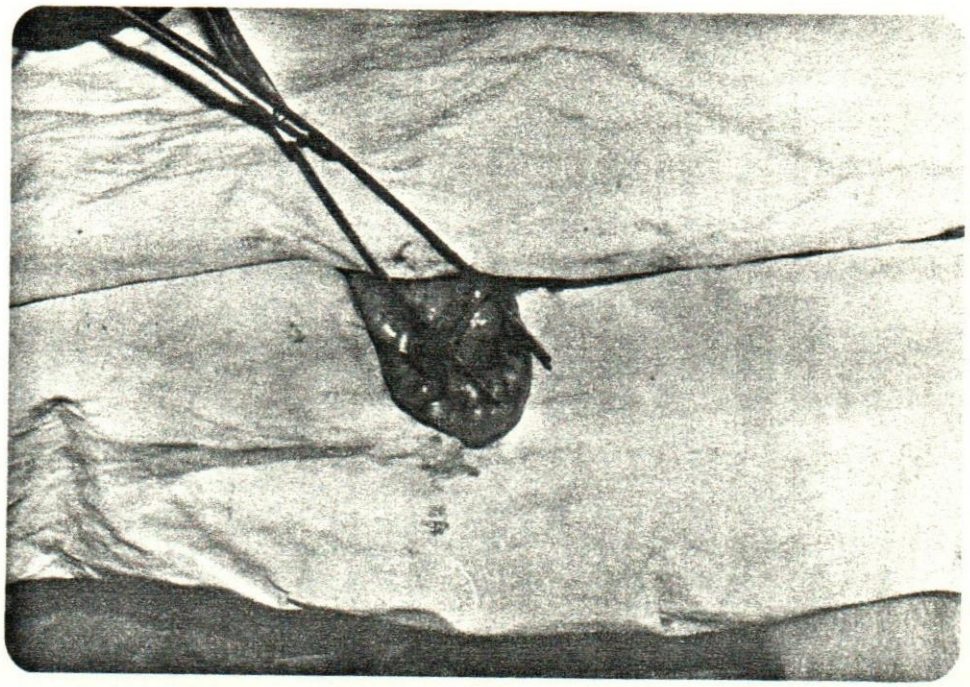

Fig. 3- Slight adhesions after Topical application of alfachymotrypsin.

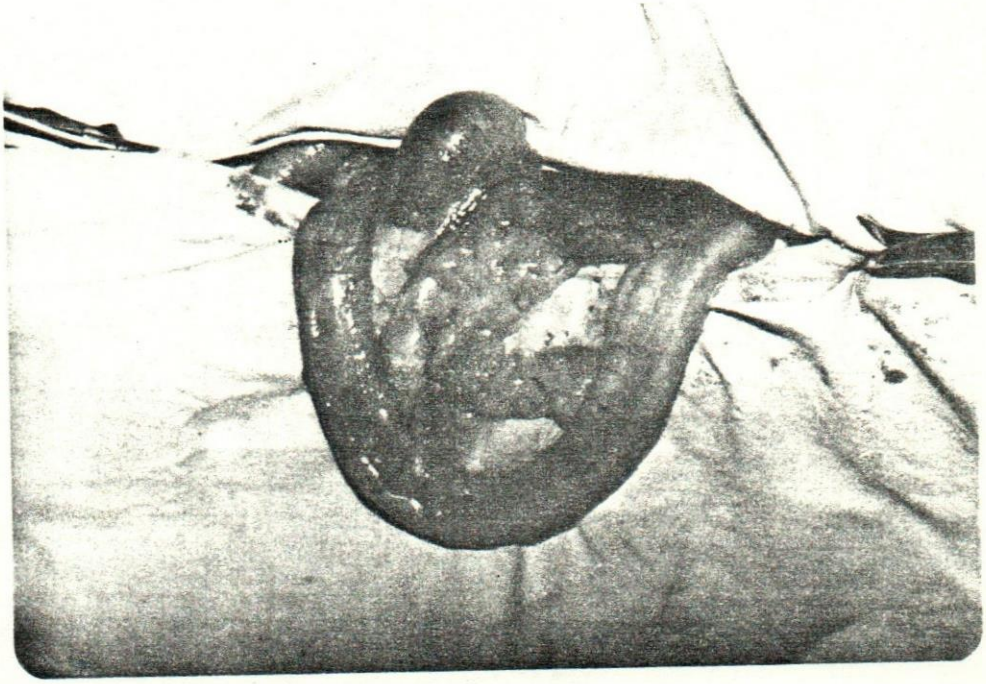

Fig. 4- No adhesions were observed after topical application of hyaluronidase enzyme.