تأثير الهيبارين فى علاج الالتهاب البريتونى

ع • ع • بلبـــل ، ع • حسنى ، م • طنطاوى ، ع • عبد المطلب ، م • ع • العسيلى

أجريت تجربة لمعرفة تأثير الهيبارين على الالتهاب البريتونى الصديدى فى الكـــلاب تم أحداث الالتهاب بالبريتونى فى ٣٠ كلب وذلك بفصل خمسة بوصات من الجزء الآخـــر من الأمعاء الدقيقة مع ترك الجزء المساريقى بدون ازاله •

قسمت الكلاب الى مجموعتين احداهما عولجت بواسطة الهيبارين تحت الجلد بمعدل خمسين وحده لكل كيلو جرام والأخرى بدون عـــلاج •

فى المجموعه المقارنة عاش كلها ن فقط من الخمسة عشر كلب خلال فترة المراقبة (١٤ يومـــا) بينما عاش أحد عشر كلبا فى المجموعه التى عولجت بالهيبارين • فى كل الكلاب المستخدمه فـــى هذه التجربة وجد بقايا التهاب بريتونى صديدى •

من هذه التجربة وجد أن الهيبارين ذو فعاليه فى منع الالتهاب البريتونى الصديدى وكذلك الالتصاقات داخل التجويف البريتونـــى •

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EFFECT OF HEPARIN IN THE TREATMENT OF EXPERIMENTAL PERITONITIS

(With 2 Figures)

By

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SUMMARY

An experiment was performed to determine the effect of heparin on experimental fibrinopurulent peritonits in dogs. Peritonitis was induced in 30 dogs by the creation of a five inches long isolated loop of terminal ileum. The mesenteric loop was not removed.

The dogs were divided into a control group with no therapy, and a treatment group receiving heparin 50 U/kg subcutaneously.

Only 2 out of 15 dogs of the control group survived the observation time of 14 days; compared with 11 out of 15 of the heparin treated group. However, in all dogs in this experiment residual intraperitoneal sepsis was found.

From this experiment, it was concluded that heparin is effective in preventing peritoneal sepsis and adhesions, as it will prevent any formation of fibrin rendering the bacteria more susceptible to cellular and non-clearing mechanisms.

INTRODUCTION

Peritonitis remain a serious disease especially in patients whose antibacterial and immunological defence have been compromised (i.e., the aged, patients with cancer, uraemia,

hepatic insufficiency, nephrotic syndrome, and patients receiving immuno-suppressive drugs). The source of peritoneal contamination, its quantity, the organisms involved and the prior condition of the peritoneal cavity are all factors which help to determine the severity of infection, its localization, its spontaneous resolution and its response to treatment.Mortality rate reaches about 20% with large bowel perforation and exceeds 50% in patients with old ages (DAWSON, 1963 and WELCH and DONALDSON, 1974).

Curative attempts beyond surgery and antibiotics are necessary for treatment of peritonitis. Some authors favour the use of anticoagulation as an adjunct for treatment of peritonitis (MIKI and SATANI, 1935, BOGART, 1937 and LEHMAN and BOYS, 1940). ZINSSER and PRYDE (1952) have shown that bacteria are more rapidly cleared from the peritoneal cavity in the heparinzed animals, and survival in acute experimental peritonitis have been shown to depend on the rapid clearing of bacteria.

The present work is an attempt to influence the outcome of experimental peritonitis in dogs by anticoagulation with heparin.

MATERIALS AND METHODS

The present investigation was carried out on 30 clinically healthy dogs of different age, sex and body weight.

The dogs were injected s.c. with Combelen (Bayer) at a dose rates of 0.05 ml/Kg b wt. General anaesthesia was induced by i.v. injection of Pentothal Sodium in a dose of 20 mg/Kg b wt.

The laparotomy incision about 10-12 cm long was performed through the midline. A segment of about five inches from the terminal ileum ending 10 cm. proximal to the ileo-caecal valve was freed up, keeping the mesenteric attachement intact. The continuity of the bowal was then re-established by one layer end-to-end anastomosis, using 4/0 silk.

The defect of the mesentry was then closed with interrupted 4/0 silk sutures. The ends of the isolated loop were closed with purse string suture and the blood supply of the isolated loop was ligated and left in place (Fig. 1). The abdominal wound was closed in the usual manner. During the operation the dogs received 500 ml of Ringer's Lactate solution but no antibiotics were given by any route.

The dogs were randomized into a control group and a treatment group reciving heparin 50 U/Kg. b wt, s.c. every 8 hrs.

All animals dying of any cause were autopsied; surviving animals were sacrificed 14 days after surgery and autopsy was performed with special reference to remaining intraperitoneal infection.

RESULTS

The survival rate of the dogs treated with s.c. heparin triple daily is shown in fig. 2. Of the 15 dogs in the control group, eleven dogs died of peritonitis within four days after surgery.

Eleven of the 15 dogs treated with s.c. heparin, survived the 14 days observation period without any evidence of remaining peritonitis or intraperitoneal abscesses at the time of sacrifice. Post mortum examination of all died dogs in both

groups showed fibrinopurulent peritonitis extending over the entire abdomen as well as intramesenteric abscesses walled by mesentery, bowel loops and omentum.

Only one survived dog of the treated group and the two survived control dogs showed presence of minimal adhesions and an intra-mesenteric abscess. The intestinal anastomosis of all dogs in both control and treated groups showed no evidence of disruption and the healing is good at the time of sacrifice.

DISCUSSION

Clinical peritonitis is frequently characterized by a fibrinous or fibrinopurulent exudate. The helaing of wounds depends on the fibrin formation, especially wound of the intestinal tract which are closed by serosa-serosal anastomosis, so that fibrin sealing will take palce and considered a peritoneal defence (HAU and SIMMONS, 1978). The presence of injury in the peritoneal serosa respond the release of histamine and other permeability factors. These substances cause an increase in vascular permeability mainly in the small venules and a protein rich, fibrinogen containing plasma is exuded into the peritoneal cavity (MANZO and PALADE, 1961). The formation of peritoneal adhesions is the final result of an exudate on the peritoneal surface. This exudate,at first serous or seropurulent, becomes fibrinous, and the fibrin, in turn is organized by the connective tissue, and the blood vessel elements of the subserosa. The process of organization always takes place in fibrin and cannot take place without fibrin (LEHMAN and BOYS, 1940).

The normal peritoneum has an inherent fibrinolytic activity, and the fibrinous adhesions are normally removed from

the peritoneul cavity by fibrinolysis and absorption (JACKSON, 1958 and OPIE, 1964). GREVIN et al. (1973) and BUCKMAN (1975) demonstrated that this fibrinolytic activity was 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 adhesions.

It seems logic, therefore, to expect that the prevention of the formation of fibrin will prevent the organization that is the essential element of a permanent pathologic nature. One cannot prevent exudation, but it may be possible to prevent the coagulation of the exudate.

It is known that heparin will prevent the formation of fibrin in the blood. The possibility suggests itself that heparin might also prove effective in preventing this reaction in an exudate; and consequently may constitute a physiologic prevention of peritoneal adhesions. MIKI and SATANI, in 1932, had experimented with heparin in the peritoneum of rabbit with some success, using the old, crude product. They found heparin saline solution much superior to sodium citrate, and did not observe any toxic effects of heparin in their animals. LEHMAN and BOYS (1940) reported that heparin introduced into the peritoneal cavity of the dog and rabbits is effective in preventing the formation and reformation of adhesions.More recently. KNIGHTLY (1962) has reported that heparin alone, and in combination with fibrinolysin, was effective in the prevention of adhesions after peritoneal irritation in the rat.

Many studies to prevent the peritoneal adhesions were concentrated to destroy fibrin and to prevent its formation. In order to destroy or digest fibrin,the use of amniotic fluid

(JOHNSON, 1928 and LACEY, 1930) and PAPIN (WALTON; 1931 and DONALDSON, 1938) as a direct digestant of fibrin,have been the first trials. The use of anticoagulants in preventing the peritoneal adhesions takes a considerable attention. It should be noted that other anticoagulants than heparin have been unsuccessfully tried for the prevention of coagulation of exudates in the serous cavities such as hirudin (VOGEL, 1902), citrate and oxalate (GELLHORN, 1901 and POPE, 1916). Recently, the use of fibrinolysis have been widely used with success which was able to prevent adhesion formation after creation of an avascular peritoneal patch.The most fibrinolytics used were anarod, a proteolytic enzyme (BUCKMAN, 1976), streptokinase and urokinase (GREVIN et al., 1973).

It was apparent from our experiment that the high mortaity rate from peritonitis (87%) was exhibited during the first four to five days following surgery. After this period the risk of peritonitis, due to the action of heparin, was highly decreased (26%),but was not able to prevent abscess formation, if the source of infection is not removed.This view was nearly similar with the observations of HAU and SIMMONS (1978).

As a conclusion, heparin when injected subcutaneously in a repeated small doses appear to be effective in preventing severe intraperitoneal sepsis and adhesions in about 74% of the animals.

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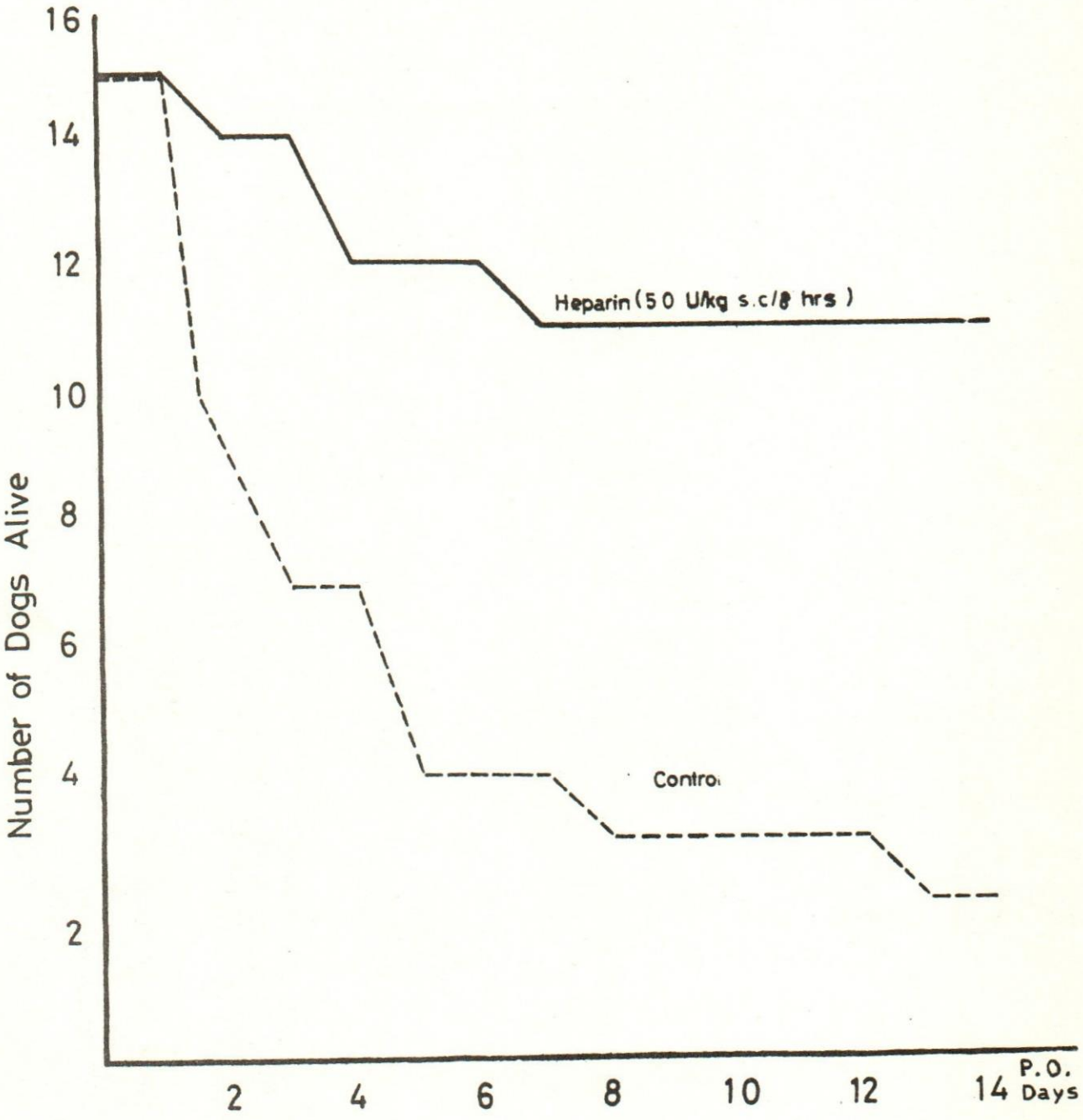

FIG. 2. Survival curve of dogs treated with heparin (50 units /kg subcutaneously every 8 hours).

Fig. 1: A necrotic loop about 10 cm (a) was freed from the terminal ileum. The loop was left in situ.