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A STUDY ON PREVENTION OF ABDOMINAL ADHESIONS BY INTRA-OPERATIVE HEPARIN ADMINISTRATION IN DOGS

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Adhesions are the fibrinous or fibrous bands that form abnormal unions between serosal surfaces. The fibrinolytic mechanism is stimulated by plasminogen activating substances that are present in mesothelial cells and submesothelial blood vessels. Fibrinolytic activity must be present continuously for several days after the onset of inflammation to prevent adhesion (Slatter, 1993). On the other hand, plasminogen activation is depressed by peritoneal injury.

Many studies have been conducted to find a reliable method for preventing post-operative abdominal adhesions. Several workers (Ellis, 1971 and 1982; Luciano *et al.*, 1989) have reviewed the causes and preventive modalities of abdominal adhesions in humans and stated that, in some situations such as localized peritonitis or abscessation following gastrointestinal perforation, adhesion formation is benefical for survival because they can prevent spread of infection and may also seal the perforated viscera. In such situations, absorption of the adhesion can cause a determined bactereamia and ultimate death. On the other hand, severe omental adhesions can cause gastrointestinal stasis, intestinal obstruction and/or strangulation and many other abdominal and pelvic crises (Slatter, *loc. cit.*; Thomson, 1984). There are many reports in Veterinary literature upon the importance of and economical losses due to post-operative adhesions, especially in horses. Baxter *et al.* (1989) have reported at 15.4% incidence of post-operative adhesions in 156 horses and 22.1% incidence of clinical signs following formation of the mentioned adhesions (Baxter *et al., loc. cit.*). Dogs and cats have active fibrinolytic mechanisms within their peritoneal cavities. This often prevents the development of serious fibrous adhesions by decreasing the amount of fibrin adhering to various visceral surfaces. But even in these animals, adhesions may follow abdominal exploration (Slatter, *loc. cit.*). It has been shown that 24-48 hours after peritoneal injury, fibrinous adhesions are observable. If a loose adhesion forms and disappears in 48-72 hours, it is called "reversible adhesion". But if the inflammatory process persists, the fibrin network will be organized by fibroplasia and capillary formation, such adhesions are called "irreversible forms" (Slatter, *loc.cit.*).

Many etiological factors, which are supposed to affect the abdominal adhesion formation, have been classified in three groups; tissue anoxic agents, serosal surface injuring factors and foreign materials (Ellis, 1971; Rappaport *et al.*, 1989; Slatter, *loc. cit.*). Accordingly many preventive aproaches have also been suggested. The

important ones are prevention of the fibrin deposition, removing fibrin exudate, separating adhesive surfaces and preventing fibroblastic proliferation (Ellis, *loc. cit.*; Tuchmann *et al.*, 1990). The purpose of this study was to identify the effectiveness and probable side effect(s) of direct abdominal content lavage by a known anticoagulant substance in preventing abdominal adhesions by means of preventing clot formation and subsequent fibrin deposition.

Materials and Methods

Twelve healthy mongrel dogs of both sexes were divided into two equal groups (test and control) and subjected to the followings.

On the pre-operative day : Hematocrit, erythrocytic sedimentation rate, fibrinogen concentration and total and differential leukocytic counts, for all animals were determined before they are pre-medicated by intramascular injection of 0-1 mg/kg acepromazine. (Acepromazine maleate, 2%, Belgium). A peritoneal fluid sample was also taken and studied microbiologically to detect the presence of any probable infective agent in the abdominal cavity which could be a potential cause of adhesion in due course. After proper aseptic preparation of the surgical site, general anesthesia was induced by 10 mg/kg intravenous injection of sodium thiopental (Nesdonal®, Specia, France) 2.5% and maintained by a mixture of halothane/O_2 and N_2O. A 20 cm midline abdominal incision was made anterior and posterior to the umbilicus. After exposing the abdominal contents, the ventral surface of the stomach, pancreas, duodenum, left and right kidneys, urinary bladder and the small intestinal mass were rubbed with a 4 x 4 gauze sponge (with 2 x 2 mm pores) by applying a constant and uniform pressure, for 3 minutes. The aim of this process was to initiate and promote the inflammatory response of these serosal structures. Thereafter, the abdominal cavity was rinsed with 30 ml/kg of heparinized saline solution (15 IU/ml) in the animals of test group and with sterile saline solution in the control group. After 5 minutes, one third of the mentioned lavaging fluid was sucked out and the abdominal wall was closed in a routine manner in three layers. After completion of the procedure, a peritoneal fluid sample was taken from each of the animals in order to determine any contamination of the abdominal cavity during the operation. Post-operative care in all animals consisted of administration of penicillin procaine G (10000 IU/kg), streptomycin (10 mg/kg) and morphine (1 mg/kg) intramuscularly every 12 hours for 4 days. Clotting time (CT) was determined in the animals of test group pre-operatively and every 12 hours after operation until 96 hours. Immediately after completion of the surgery and on the day 1, 3, 5, 7, 15 and 30 after the operation, blood samples were taken to determine the haematocrite, erythrocyte sedimentation rate, fibrinogen concentration and total and differential leukocytic counts.

The data obtained were studied by ANOVA and Duncan tests in SPSS computer program (release 5, SPSS Inc., Chicago, IL, USA). The skin sutures were removed ten days after surgery. The animals were euthenized on the 30th post-operative day. At necropsy, the abdominal cavity was examined in order to determine the gross and microscopic characteristics of probable adhesions in both groups.

Results and Discussion

Though there was a post-operative increase in the total number of leukocytes and neutrophils from day 1 to 7 in both groups, fibrinogen concentration from day 1 to 5 in the test group and on day 5 in the control group, there was no significant difference in other haematological parameters between the test and control groups and the changes were identical in the both of them. The differences between pre and post-operative clotting time were also insiginificant and the results of microbiological examination of the peritoneal fluids were negative in all animals.

Significant differences were observed in gross and microscopic findings between two groups. The incidence and severity of fibrinous adhesions were moderate to mild in two dogs in the heparin group; but in the same group, the incidence of subserosal and parenchymal haemorrhages were moderate in three dogs. In control groups fibrinous adhesion was severe to moderate in three dogs. Unlike in treated dogs subserosal and parenchymal haemorrhages were very mild.

Ryan *et al.* (1971) showed that serosal bleeding and clot formation have a very distinct role in experimental adhesion formation. In their study, manipulation of serosal surfaces, use of suture materials and other interfering factors causing an inflammation in the abdominal cavity, which could induce noticeable adhesions. Heparin is an anionic polysaccharide with a straight strand, which activates prothrombin III and accelerates neutralization of serine proteases in the coagulation cascade. Heparin also binds to the thrombin and inhibits its action on fibrinogen. Heparin directly decreases platelet aggregation and indirectly inhibits release of platelet aggregating factors via inhibition of thrombin formation (MacHarg *et al.*, 1983). In our study, although paraclinical investigations showed that the severity of the inflammatory process in the test group was fairly similar to the control group, the pathological findings showed that the incidence and severity of adhesions in the test group was lower than the control. However, the incidences of pancreatic and serosal haemorrhagic lesions were greater in the test group. One explanation may be that heparin impairs the normal coagulation cascade in the studied animals and was responsible for causing such haemorrhages. But on the other hand, table 1 shows that there were even more splenic and hepatic haemorrhages in the control group. Therefore, it can be possible that severity of the inflammatory response was responsible for the occurrence of haemorrhages and they may not be directly due to coagulation impairment following heparin administration. Meanwhile, it may be emphasized that no abnormality in coagulation time was observed 48 hours after operation. These results are comparable with those reported by Turkcaper *et al.* (1995), who compared intra-peritoneal and subcutaneous use of heparin-saline solution in preventing peritoneal adhesions in rats and proved that intra-peritoneal route gave better results. But the results of our study are in contrast with few others, including Lundin *et al.* (1989) who compared the effectiveness of flunixin meglumine, penicillin G, heparin, dimethyl sulfoxide and carboxy methyl cellulose in prevention of peritoneal adhesion in foals. They reported most prominent adhesions in heparin and carboxy methyl cellulose groups.

Summary

During exploratory laparotomy on twelve healthy dogs a few definite abdominal viscerae were manipulated with a gauze sponge in order to promote an inflammatory response. Then the abdominal cavity was lavaged either with or without heparinized saline solution in test and control groups respectively. Haematological parameters did not exhibit any significant difference between the control and test groups but gross and microscopic pathological examinations at necropsy revealed that the incidence and severity of the adhesions were more noticeable in the control animals. It was concluded that heparin solution as a lavaging fluid may prevent some kind of post-operative abdominal adhesions due to its anticoagulant properties.

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