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Original Research Paper



THE ROLE OF HEPARIN IN TREATMENT OF EXPERIMENTAL PERITONITIS

Surgery

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ABSTRACT

Background: To produce peritonitis experimentally in albino rats by creation of a necrotic loop of terminal Ileum. Study of peritonitis and gross changes in peritoniteal cavity and to study the effect of single dose heparin (Anticoagulant) in experimentally produced peritonitis. Also to study and compare the effect of repeated

small dosage of heparin in peritonitis.

Material and Methods The rats were divided into 6 groups, under the 2 experiments. So each group comprised of 8 rats. The peritonitis was proceduced by Rasto's method, in which the peritonitis was caused by a gangrenous loop of small intestine. two types of experiment were carried out:

1. Experiment 1 : The gangrenous loop which produced peritonitis was excised after 24 hours, normal saline was given in control group, whereas heparin as a single dose and heparin in small repeated dose were given by sub-cutaneous or intraperitoneal route for 3 days. No abdominal toilet or antibiotics were given during the time. The surviving as well as the dead rats during observation period were subjected to laparotomy and detailed pathology of peritoneum was studied.

2. Experiment 2 : In this group the gangrenous loop was not resected after 24 hours and normal saline was given in control group 0.2 ml., or heparin in a single dose 50 I.U. or heparin in small repeated dose 20 I.U. twice a day for three days. All the rats were continuously observed during the post-operative period for evidence of any complications.

Results: The peritonitis produced by a necrotic bowel loop was severe & fibrino-purulent. The formation of inter-mesentric abscess in control group was much more evident than the heparinised rats. The size of inter-mesentric abscess was smaller in treated group of albino rats than in control. The incidence of adhesion formation was much more in control group, than in the heparin group, the adhesion were very less friable and easily breakable. The survival rate in heparin treatment group was 75% to 87.5% as compared to the control group, where the survival rate was 50% only. The mortality in the control group, where the necrotic loop, was not resected was as high as 87.5% and rats died within 8 days after operation whereas the mortality rate in treatment group was low that is, from 50% to 60% only.

Conclusion: By comparison and contrast of the results of the difference treatment group, it become evident that survival in the treated group was significantly better than control group. About the evidence of intra-peritoneal infection, it shows that in treated group clearance of peritonitis was much faster than the control group of albino rats: The number and size of intramesentric abscesses were also smaller in treated group. There was also a little beneficial effect on adhesion in heparinised albino rats as compared to control group. So heparin in small repeated doses has definitely a significant effect on secondary bacterial peritonitis and its subsequent results.

KEYWORDS : Peritonitis , Albino Rats , Necrotic Loop ,Heparin (Anticoagulant)

INTRODUCTION

Prior to work of Pasteur and Lister in the mid nineteenth century, nearly every surgical trespass in abdominal cavity resulted fatally with peritonitis. The development of rigid aseptic surgical technique has rendered abdominal surgery safer. However, peritonitis continue to be a dressed complication.

Virtually every bacterial organism has been implicated as a causative of peritonitis, most commonly E. Coli, alpha haemolytic and beta haemolytic streptococci, staphylococcus aureus, enterococci, "gram negative rods" and claustridium welchii, Gonococci and tuberculous peritonitis are not so frequent, as in the past.Peritonitis has been studied and managed by number of workers from various aspects in the last over hundred years, but still, it continues as most common cause of death following abdominal surgical treatment. In 5 to 7% of all autopsies, peritonitis is either a primary or contributory cause of death. (Edwards H. Storer, 1960).

Despite the use of Antibiotics, Blood transfusion and modern anaesthesia peritonitis is still a serious disease especially in the elderly, or in patients whose antibacterial and immunologic defenses have been compromised, that is the aged patient with cancer, uremia, hepatic insufficiency, nephrotoxic syndrome and patients under administration of Immunosuppressive drugs. The source of peritoneal contamination, its extent and the organism involved and prior condition of peritoneal cavity are all factors which help to

determine the severity of infection, localization and its spontaneous resolution and the response to treatment.

Still the morbidity and mortality rate is quite high in peritonitis. So it appears desirable to develop additional modalities in treatment of peritonitis beyond the scope of Antibiotics therapy and surgical intervention. Several new therapeutic measures which are still under experimental scrutiny may come up in future including platelet rich plasma, granulocyte infusion, chemotactic factors and heparin.

A number of lines of evidences favour the use of Anticoagulation as an adjuvant for treatment of peritonitis. Zinner and Pryde (1952) have show that bacteria are more rapidly cleared from peritoneal cavity in heprinised animals and survival in acute experimental peritonitis has shown to be depend on early and rapid clearance of bacteria. Toni Hau and Simmons (1978) has reported that a single dose of 100 units of Heparin administered intraperitoneally or subcutaneously is able to prevents the formation of intraperitoneally or subcutaneously abscesses and adhesions along with an increase in survival in experimental peritonitis significantly.

It has also been concluded from the present experimental studies that Heparin has certainly a significantly beneficial effect in early clearance of bacteria, prevention of abscess formation and adhesions when the source of bacterial

peritonitis, in the cases studies like ischaemic segment of lleum is resected. The most likely mechanism of action of Heparin that it acts as an anticoagulant to prevent the fibrin deposition and the entrapment of bacteria within this fibrin thus rendering the bacterial organism more susceptible to both non-phagocytic absorption from peritoneal cavity and phagocytic destruction.

MATERIALS AND METHODS

Study design/Type of study - The present experimental study was conducted on 48 (fourty Eight) normal, healthy Albino rates in the Department of Surgery, (Experimental laboratory), Pharmacology and Pathology, Gandhi Medical College, Bhopal.

Sample size & Duration of study- The present study was undertaken in the Experimental Laboratory of Gandhi Medical College, Bhopal, on fifty albino rats. The rats were healthy, weighing from 150-300 grams. Half of them were male and half female. One rat died during induction of anaesthesia and one died while operating probably due to excess of other inhalation. These two have been not included from the present study.

Data collection procedure : All the animals started moving immediately after subsequent to completed. A slight abdominal rigidity and distension was observed in all rats during the post-operative period. Both distention and rigidity disappeared in 1 to 5 days time. No antibiotics or drugs were given post-operative except heparin in the Experimental group and normal saline in the control group.

Surgical Proceedures done: The study was completed in 6 groups. The animals were anaesthetized by Ether-Jar technique. And submitted to Laparotomy twice and on the third occasion an autopsy was performed by killing the animal by Ether-Jar technique on 14^{th} Post-operative day.Skin stitches were removed on 7^{th} day after 2nd operation. Continuous post-operative observations were carried out on animals to note the occurrence of any complications due to anaesthesia or surgery or Heparin.

Follow-up: One rat developed stitch abscess which was drained and dressed, no wound sepsis was noted during the period of study. All the surviving rats were put on oral liquid feeds from the 2nd post-operative day and soft diet from the 3rd post-operative days. The evacuation of bowel, varied in different rats but all of them started passing stools from 2nd to 3rd post-operative day. The intestinal anaestomoses of all rats in control as well as treated group did not show any evidence of disruption and the wound got healed by the time of sacrifice.

Ethical approval : Taken

Experiment No. 1: (Single dose heparin in peritonitis, with and without presence of necrotic loop after 1st post-operative day). Twenty four albino rats of either sex weighing about 150-300 gms. Were used. The ether jar technique was used to anaesthetised, and animla was fixed on dissection table. After painting the abdomen with savlon, draping of part done by a hole-towel. Under all aseptic precautions the abdomen was opened by a mid-line incision, and different layers were opened in same line.

Peritonitis is produced by the method described by Rasato (1972) in which a segment of terminal ileum about 2 cms. In length about 6-8 cms. Proximal to ileocaecal valve is mobilized and resected, leaving its mesenteric attachment intact. The continuity of bowel was maintained by end to end anaestmosis of the gut in a single layer by continuous inverted suture. Suture material used was 4-0 silk (Plain). The both ends of the isolated loop were closed in one layer using the same 4-

0 plain silk and finally the blood supply of isolated loop was ligated. The defect in mesentery of ileum was closed by 4-0 silk with interrupted sutures.

No antibiotics or saline lavage was carried out. The abdomen was closed in two layers. No antibiotics were given post operatively. After 24 hours of operation rats were reopened by right para median incision and details of peritoneal cavity were noted down. The cavity showed signs of severe fibrino purulent peritonitis alongwith excess peritoneal fluid originating from necrotic loop and extending over the entire of abdominal cavity. The smear of pus was prepared on an slide and the pus collected for culture and antibiotics sensitivity.

The rats were blindly randomized into:

Control groups: in this groups the Ischaemic bowel was resected and normal saline 0.2 ml. administered subcutaneously or intra peritoneally.

a. Group of 8 animals in which the ischaemic bowel loop was excised and heparin given in single dose of 50 I.U.

b. Group of 8 animals in which the ischaemic bowel loop was resected and heparin given in repeated dose of 20 I.U. B.D. for 3 days.

During this operation ischaemic loop of ileum is excised and abdomen was closed without any debridement irrigation and rats did not receive any antibiotics during the post-operative periods.

All the animals dying of any cause were autopsied and the surviving animals were scarified on the $14^{\rm th}$ post-operative day. Autopsy was carried out with special attention to intraperitoneal sepsis, abscess and adhesions.

Experiment No. 2: (Single and repeated small dose of heparin in peritonitis, with the presence of necrotic bowel loop after 1st post-operative day)

In this experiment 24 albino rats of either sex (male, female) weighing 150-300 Gms. Were used. The peritonitis was induced in same manner as in previous experiment by ischaemic bowel loop. However, after second laparotomy the animals are again divided into three groups:

- a. The resection of necrotic loop were not carried out in 8 rats and normal saline 0.2 ml. is given subcutaneously.
- b. The resection of necrotic loop was not carried in another 8 rats of this group and a single dose 50 I.U. of heparin was given subcutaneously or intra-peritoneally.
- c. In the group of 8 animals the necrotic bowel loop was not resected and repeated small dosage of heparin (i.e. 20 I.U.B.D.) was given for 3 days.
- d. Animals dying during the post-operative period had to undergo the post-mortem. All surviving animals were killed after 14 days and autopsy was carried out.

OBSERVATIONS

Experiment No. 1

Effect of heparin in peritonitis in absence of necrotic bowel.In the control group only eight rats were used, remaining 16 rats were used for treatment group in which heparin was given as a single dose or as repeated small dose.

Table:1 Different Groups of albino rats used for study.

S. No.	Group	Number of
		Animal used
1.	Control Group	8
2.	Single dose heparin therapy	8
3.	Repeated small dose Heparin therapy.	8

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TABLE: 2 SURVIVAL RATE

Group	No. of	Number of	No. of
	Rats used	Rats survived	Rats died
Control	8	4	4
Heparin in single dose	8	6	2
Heparin in repeated small doses.	8	7	1

The results of study were recorded and mortality and survival has been recorded in Table no. 2, which shows 50% survival in control group, while the rest 50% died due to peritonitis; whereas in treated group mortality was 25% and 12.5% Second laparotomy was done 24 hours after the first and following details were noted:

TABLE:3 EVIDENCE OF INFECTION, ABSCESS AND ADHESIONS FORMATION IN CONTROL AND TREATMENT GROUP.

Group	Total animal	Intra peritoneal infection	Intra peritoneal abscess	Intra peritoneal adhesions
Control	8	4	2	4
Single dose heparin group	8	-	3	3
Repeated small dose heparin group	8	-	1	2

 2^{nd} Experiment : Effect of heparin on peritonitis in prescience of necrotic bowel.

In this group the necrotic loop of Intestine which was created at the first laparotomy was not excised during the 2^{nd} laparotomy, and normal saline 0.02ml. was administered sub-cutaneously in control group and single dose subcutaneous heparin 50 I.U. given in 8 rats and in other 8 rats 20 I.U. heparin given twice a day for three days.

TABLE:4 ALBINO RATS WITH NECROTIC LOOP

Group	No. of rats
Control group	8
Single dose heparin group	8
Repeated small dose heparin group	8

On second laprotomy abdomen was opened and it was observed that all the rats shows severe fibrino-purulent peritonitis along with wide-spread exudates all over the peritoneal cavity. All rats were observed closely for any complication. Nine out of sixteen rats treated with heparin survived the observation period while only one rat survived the fourteenth (14^{th}) day observation period in control group.

TABLE:-5 SURVIVAL RATE IN EXPERIMENT II

Group	No. of Rats survived	No. of Rats dead
Control Group	1	7
Single dose heparin group	4	4
Small repeated dose group	5	3

The rats which died during observation period were subjected to autopsy and detail were observed are as follows:

TABLE:6 POST OPERATIVE RESULTS

Group of Rats	No. of	Intra	Intra	Intra
	Total	peritoneal	peritoneal	peritoneal
	Rats	infection	abscess	adhesions
Control group	8	8	5	6
Single dose heparin therapy Group	8	8	6	7
Repeated small dose Heparin Therapy Group	8	8	4	2

RESULTS

- 1. The peritonitis produced by a necrotic bowel loop was severe & fibrino-purulent.
- 2. The formation of inter-mesentric abscess in control group was much more evident than the heparinised rats.
- 3. The size of inter-mesentric abscess was smaller in treated group of albino rats than in control.
- 4. The incidence of adhesion formation was much more in control group, than in the treatment group, the adhesion were very less friable and easily breakable.
- 5. The survival rate in heparin treatment group was 75% to 87.5% as compared to the control group, where the survival rate was 50% only.
- 6. The mortality in the control group, where the necrotic loop, was not resected was as high as 87.5% and rats died within 8 days after operation whereas the mortality rate in treatment group was low that is, from 50% to 60% only.

STATISTICAL ANALYSIS

After getting the required information, the collected data were coded, tabulated and analysed. The various statistical techniques i.e. the mean, standard deviation and test of significance (t-test and chi-square-test) were used for drawing valid conclusions. Statistical analysis done using student t-test. SPSS 13.0 software was used to calculate p value.P<0.05 was taken as statistically A descriptive analysis was done on all variables to obtain a frequency distribution. The mean + SD and ranges were calculated for quantitative variables. Continuous variables were compared by the Student t test. Proportions were analyzed with the chi-square test

DISCUSSION

Peritonitis continues to be one of the major infectious problems confronting surgeons. Despite the many advances in antimicrobial agents and supportive care, mortality from diffuse suppurative peritonitis remains unacceptably high. Maddaus MA et al review the anatomy and defense capabilities of the peritoneal cavity and then focus on the polymicrobial nature of peritonitis, microbial interactions with host defenses, there is either resolution or persistent infection. They also consider possible infection-potentiating agents in the peritoneal cavity and experimental modes of therapy.[1]

Fibrin deposition during secondary peritonitis predisposes to abscess formation by protecting bacteria from host-defence mechanisms. To test the hypothesis that local fibrinolytic therapy can prevent the formation of intra-abdominal abscess, Rosenthal GA et al studied prevention of intra-abdominal abscesses with fibrinolytic agents. Daily injections of the fibrinolytic enzymes trypsin and tissue plasminogen activator (t-PA) were administered intraperitoneally to rats inoculated intraperitoneally with infected fibrin clots . In-vitro studies demonstrated that trypsin had no bactericidal effect on B. fragilis, suggesting enhanced clearance of bacteria. From these studies it appears that controlled fibrinolysis at operation may be a useful adjunct to surgery and systemic antibiotics in preventing abscess formation postoperatively. [2]

Dunn RC, Steinleitner AJ et al studied synergistic effect of intraperitoneally administered calcium channel blockade and recombinant tissue plasminogen activator to prevent adhesion formation in an animal model. These agents were studied in a rabbit uterine horn model. Adhesion scores were evaluated after this time period by estimating the total uterine horn surface involved in adhesions at a terminal laparotomy and by clinically grading the response to determine whether minimal adhesions formed. Results show a synergistic benefit of verapamil and recombinant tissue plasminogen activator to prevent postsurgical adhesion formation when delivered via the intraperitoneal route .[3] The objective of the study done by Chalkiadakis GE et al was to determine the effect of pentoxifylline on the clinical and pathologic course of experimentally induced peritonitis in rats. This drug is a methyxanthine derivative that has vasodilating properties and may decrease platelet aggregation. Peritonitis was induced in 40 Wistar rats by creating a closed ileal loop 4 cm long 5 cm from the ileocecal valve. The animals were divided into two groups of 20 animals each. The first group served as controls, while each animal of the second group received 17 mg/kg/day of pentoxifylline intramuscularly from the day of operation until 30 days postoperatively. The survival rate was significantly Increased in the group receiving pentoxifylline and adhesion or abscess formation was considerably reduced. It was concluded that the administration of pentoxifylline prolongs significantly the survival of animals with experimental peritonitis and reduces the development of adhesions and abscesses in the peritoneal cavity. This beneficial effect may be attributed to decreased fibrinogen deposits and increased fibrinolytic activity within the peritoneal cavity, thus rendering the bacteria more susceptible to cellular and noncellular clearing mechanisms.[4]

Ferrara J et al studied effects of fibrinogen degradation fragments D and E on cell-mediated immunity. McRitchie DI et al emphasized effect of delayed administration of tissue plasminogen activator and its role in reduction of intraabdominal abscess formationThe efficacy of delayed administration of t-PA on intra-abdominal abscess formation was examined. A delay of 2,6, and 18 hours had no effect on the rate of abscess formation but did reduce abscess size, indicating partial fibrinolysis. Since fibrin clots dehydrate in vivo, we hypothesized that a higher concentration of t-PA might be necessary to effect complete abscess resolution. High-dose t-PA (0.1 mg/mL) prevented abscess formation following a 6-hour delay and reduced mean weight following an 18-hour delay. Since heparin sodium may prevent new fibrin deposition and enhance t-PA activity, it was combined with t-PA to investigate potential synergistic effects. It was concluded that delayed administration of t-PA is effective in preventing abscess formation and may have implications for the clinical setting where initial surgical intervention is usually delayed.[5,6]

Tayyar M, Başbuğ M et al did a study with our objective was to determine the effectiveness of intraperitoneal single dose piroxicam and low molecular weight heparin (LMWH) on prevention of adhesion reformation in the rat uterine horn. A standard lesion was created in 72 uterine horns of 36 female Wistar-Albino rats. After 2 weeks, adhesion formation scores were determined and adhesiolysis was performed in the second-look laparotomy. Animals were then randomly assigned into three groups. Each group contained 12 animals: group 1 was the control group where no adjuvant was given; in group 2, 1 ml 50 U Axa IC/ml solution LMWH was applied to the horns postoperatively, and in group 3, 1 ml 2 mg/ml piroxicam solution was applied to the horns after adhesiolysis. Two weeks later the rats were killed and adhesion reformation was evaluated. The number of horns with adhesion formation and the cumulative scores were not significantly different among the three groups in the second-look laparotomies, but after third-look laparotomies, the number of horns with adhesion reformation, after calculating the extent, severity and total scores of adhesion reformation, was found to be significantly less in LMWH and piroxicam groups than in the control group. Also, the effectiveness of piroxicam was significantly greater in all scores of adhesion reformation than LMWH was. In conclusion, both LMWH and piroxicam doses reduce adhesion reformation in the rat uterine horn, but the effectiveness of piroxicam is significantly greater than that of LMWH. [7]

The study by Vela AR et al on the effects of minidose heparin and low molecular weight heparin on peritonitis in the rat and similar study by Hau T et al in which heparin was used in the treatment of experimental peritonitis in dogs .In the latter study, two experiments were performed to determine the effect of heparin on experimental fibrinopurulent peritonitis in dogs. Peritonitis was induced by the creation of a 10 cm long isolated loop of terminal ileum. In a first experiment comprising 24 dogs the necrotic loop was removed 24 hours later without cleaning or irrigating the peritoneal cavity. All dogs showed fibrino-purulent peritonitis at that time. In a second experiment peritonitis was induced in 24 dogs as described above, but the necrotic loop was not removed. The dogs were blindly randomized to daily low dose heparin (50 u/kg s.c. b.i.d.) or no therapy. Only two out of 12 dogs of the control group survived the observation period of 14 days compared with eight out of 12 of the heparin treated group ($p \le 0.05$). However, in all dogs in this experiment residual i.p. sepsis was found. The authors concluded that heparin has a therapeutic effect in experimental canine peritonitis by preventing the additional apposition of fibrin and, thus, rendering the bacteria more susceptible to cellular and noncellular clearing mechanisms.[8,9]

The aim of investigaton done by Gupta S, Jain PK.et al was to study the beneficial role of low-dose heparin in peritonitis. Peritonitis was induced in 20 dogs ,10 of which received lowdose heparin subcutaneously for 5 days in a dose of 100 units/kg body weight. Decreased mortality as well as decrease in the formation of intra-abdominal abscesses and adhesions were observed in the heparin-treated dogs. Some of the possible underlying mechanisms for beneficial effects of heparin in peritonitis was seen .[10]

In a similar study like us ,Chalkiadakis G, Kostakis A et al studied the effect of heparin upon fibrinopurulent peritonitis in rats. Peritonitis was induced in 40 rats by creating a closed ileal loop 4 centimeters long at a distance of 5 centimeters from the ileocecal valve. The rats were divided into two groups of 20 each. The first group served as the control group while each rat of the second group received 30 units of heparin subcutaneously per day postoperatively. Survival was drastically increased in the group receiving heparin (p = 0.001). Adhesion or abscess formation was considerably reduced in this group. The results of peritoneal cultures showed decreased incidence of Escherichia coli and clostridia in the heparin-treated groupThis beneficial effect could be attributed to decreased fibrinogen deposits within the peritoneal cavity, thus rendering the bacteria more susceptible to cellular and noncellular clearing mechanisms. Davidson RK et al studied the effects of heparin and low molecular weight dextran on survival after fibrinopurulent peritonitis. Both these studies are in conjunction with our study.[11,12]

Inhibition of postsurgical adhesions in a standardized rabbit model with intraperitoneal treatment with heparin.was studied by Fukasawa M, Girgis W.The formation of adhesions after peritoneal trauma is thought to result from the deposition of fibrin and its subsequent organization by fibroblast ingrowth and, in some cases, neovascularization and reepithelialization. Since heparin is an effective anticoagulant, and clotting is a major contributor to postsurgical fibrin deposition, the authors studied the effects of heparin delivered locally into the peritoneal cavity at the site of the injury on the subsequent formation of postsurgical adhesions. Effective adhesion prevention occurred with only two days of treatment beginning the day of surgery.. These findings suggest that local intraperitoneal administration of low-dose heparin throughout the immediate postoperative interval may result in adhesion-free healing.[13]

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O'Leary JP et al studied the effects of a minidose of heparin on peritonitis in rats. Rats with peritonitis treated with either a subcutaneous or intraperitoneal minidose of heparin show a significant increase in survival time when compared with controls. In the treatment groups, adhesions and abscesses were less severe and localized to the area of gangrenous bowel. Heparin also significantly reduced the incidence of recovery of viable bacteria from the blood and peritoneal cavity. These findings may be related to a decreased deposition of fibrinogen within the abdomen or to the early mobilization of fibrin.[14]

CONCLUSION

The survival rate of treatment group shows that there is early and complete clearance of peritonitis as compared to control group where the rats either died of peritonitis, or if survived could not be clear up the peritonitis during the observation period. In heparin treated group, beneficial effects were better in small repeated doses than the group receiving single dose.

Small repeated dose therapy has no complication as far as the coagulation mechanisms concern involved, and have a beneficial effect in peritonitis as well as in sub-clinical case of intra-vascular coagulation and septic shock. It has been concluded from the present study that heparin in small repeated doses has an definite beneficial effect on peritonitis and its sequalae by preventing coagulation, firbin deposition in peritoneal cavity and sub-diaphragmatic and sub-peritoneal lymphatics, it helps in early clearance of bacteria from peritoneal cavity and renders the bacterial more prone to phagocytic and non-phagocytic destruction accelerating the resolution of the peritonitis. Judge from the results, or present study, it becomes apparent that trial of Heparin as an adjunct in clinical peritonitis may prove to have highly beneficial effects.

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Conflict of interest: No conflict of interest Ethical approval: Taken

WHAT THIS STUDY ADD TO EXISTING KNOWLEDGE :

It has been concluded from the present study that heparin in small repeated doses has an definite beneficial effect on peritonitis and its sequalae by preventing coagulation, firbin deposition in peritoneal cavity and sub-diaphragmatic and sub-peritoneal lymphatics, it helps in early clearance of bacteria from peritoneal cavity and renders the bacterial more prone to phagocytic and non-phagocytic destruction accelerating the resolution of the peritonitis. Judge from the results, or present study, it becomes apparent that trial of Heparin as an adjunct in clinical peritonitis may prove to have highly beneficial effects.

LIMITATION OF OUR STUDY

- 1. Experimental study
- 2. Small sample size
- 3. Chances of bias
- 4. Single center trial

REFERENCES

- Maddaus MA, Ahrenholz D, Simmons RL. The biology of peritonitis and implications for treatment. Surgical Clinics of North America. 1988 Apr 1;68(2):431-43.
- Rosenthal GA, Quinto J, Kao J, Rotstein OD. Prevention of intra-abdominal abscesses with fibrinolytic agents. Canadian journal of surgery. Journal canadien de chirurgie. 1988 Mar;31(2):98-100.
- Dunn RC, Steinleitner AJ, Lambert H. Synergistic effect of intraperitoneally administered calcium channel blockade and recombinant tissue plasminogen activator to prevent adhesion formation in an animal model. American journal of obstetrics and gynecology. 1991 May 1;164(5):1327-30.
- Chalkiadakis GE, Kostakis A, Karayannacos PE, Chalkiadakis ME, Sgouromali S, Giamarellou H, Skalkeas GD. Pentoxifylline in the treatment of experimental peritonitis in rats. Archives of surgery. 1985 Oct 1;120(10):1141-4.
- Ferrara JJ, Kan C, Luterman A, Curreri PW. Effects of fibrinogen degradation fragments D and E on cell-mediated immunity. Journal of Surgical Research. 1989 Aug 1;47(2):134-7.

- McRitchie DI, Cummings D, Rotstein OD. Delayed administration of tissue plasminogen activator reduces intra-abdominal abscess formation. Archives of Surgery. 1989 Dec 1;124(12):1406-10.
- Tayyar M, Başbuğ M. The effects of intraperitoneal piroxicam and low molecular weight heparin in prevention of adhesion reformation in rat uterine horn. Research in experimental medicine. 1999 Sep 1;198(6):269-75.
- Vela AR, Littleton JC, O'Leary JP. The effects of minidose heparin and low molecular weight heparin on peritonitis in the rat. The American surgeon. 1999 May 1;65(5):473.
- Hau T, Simmons RL. Heparin in the Treatment of Experimental Peritoniitis. Annals of surgery. 1978 Mar; 187(3):294.
- Gupta S, Jain PK. Low-dose heparin in experimental peritonitis. European surgical research. 1985;17(3):167-72.
- Chalkiadakis G, Kostakis A, Karayannacos PE, Giamarellou H, Dontas I, Sakellariou I, Skalkeas GD. The effect of heparin upon fibrinopurulent peritonitis in rats. Surgery, gynecology & obstetrics. 1983 Sep;157(3):257-60.
- Davidson RK, Cardenas A, Buruttil RW. The effects of heparin and low molecular weight dextran on survival after fibrinopurulent peritonitis. Surgery, gynecology & obstetrics. 1981 Sep;153(3):327-31.
- Fukasawa M, Girgis W. Inhibition of postsurgical adhesions in a standardized rabbit model: II. Intraperitoneal treatment with heparin. International journal of fertility. 1991;36(5):296-301.
- O'Leary JP, Malik FS, Donahoe RR, Johnston AD. The effects of a minidose of heparin on peritonitis in rats. Surgery, gynecology & obstetrics. 1979 Apr;148(4):571-5.