COMPARATIVE EFFECTS OF VARIOUS DRUGS IN THE PREVENTION OF EXPERIMENTAL PERITONEAL ADHESIONS IN DOGS.

A THESIS

Presented to

The Faculty of Veterinary and Animal Science

MOHAN LAL SUKHADIA UNIVERSITY

UDAIPUR

In partial fulfilment of

the requirements for the degree

MASTER OF VETERINARY SCIENCE

(SURGERY)

By

SURENDRA KUMAR

B. V. Sc. & A. H.

JANUARY, 1983

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CERTIFICATE I

Dated 15-1-, 1983.

This is to certify that SURENDRA KUMAR has successfully completed the COMPREHENSIVE EXAMINATION held on 21.12.1982 as required under the regulations for the Degree of MASTER OF VETERINARY SCIENCE.

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CERTIFICATE II

Dated 15 - 1 - 1983.

This is to certify that Thesis entitled, "COMPARATIVE EFFECTS OF VARIOUS DRUGS IN PREVENTION OF EXPERIMENTAL PERITONEAL ADHESIONS IN DOGS" submitted for the Degree of MASTER OF VETERINARY SCIENCE in the subject of SURGERY of the Mohan Lal Sukhadia University, Udaipur is a bonafide research work carried out by SURENDRA KUMAR under my supervision and that no part of this thesis has been submitted for any other degree. The assistance and help received during the course of investigation have been fully acknowledged.

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CERTIFICATE III

Dated 6.12., 1983.

This is to certify that the Thesis entitled, "COMPARATIVE EFFECTS OF VARIOUS DRUGS IN THE PREVENTION OF EXPERIMENTAL ADHESIONS IN DOGS" submitted by SURENDRA KUMAR to the Mohan Lal Sukhadia University, Udaipur in partial fulfilment of the requirements for the Degree of MASTER OF VETERINARY SCIENCE in the subject of SURGERY has been approved by the Students, Advisory Committee after an oral examination on the same, in collaboration with an external examiner.

External Examiner

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Chairman, Faculty of Vety. & Anl. Sc.,
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BIKANER

DEDICATED

TO MY

WORTHY ADVISOR

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(SURENDRA KUMAR)

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INTRODUCTION

The peritoneal adhesions are the areas of fibrous connective tissue formation. Adhesions are an essential part of the healing process or offensive in areas where gross bands of fibrous connective tissue extend from structure to structure.

The post-operative peritoneal adhesions often result after the successful operations, because the peritoneum and other serous membranes are unique in their ability to form adhesions.

Physiologically the peritoneum functions by it's abilities of absorption, transudation and exudation. It has ability to form adhesions in the presence of inflammatory process (Douglas, 1981). The adhesion formation between injured serosal surfaces may be explained as they become inflammed and fibrinogen oozes out; a fibrin clot glues the injured area together. The fibrinous attachment becomes organised into a permanent adhesion (Ryan, 1971).

The other factors which may lead to formation of peritoneal adhesions are crushing of bowel, stripping or scrubbing the outer layer from long segments of bowel wall. Ischaemia plays a major role in formation of the adhesions. Ischaemic tissue is not only stimulous of an inflammatory vascular response in neighbouring structure, but drying, wiping or wetting with saline causes, some degree of injury to the mesothelium of the peritoneum. All of these insults

destroy the mesothelium and induce adhesions. The other irritating agents that enter the peritoneal cavity at the time of laparotomy may be responsible for the development of fibrous peritoneal adhesions are talcum powder, starch powder, antibiotic powder, gauge particles, large piece of skin and vast quantity of hair.

The mechanism of peritoneal adhesion formation still remains in doubt, after many years of experimental study. Several etiological factors have been suggested, but it is generally accepted that trauma is the important cause of adhesion formation. Trauma in the peritoneal cavity leaves it's imprints by formation of peritoneal adhesions.

The peritoneal adhesions have been given a least importance in the Veterinary field and little work on this issue has been done inspite of the problems, they may cause. Adhesions are of major importance in the production of vagus indigestion in cattle and may cause intestinal obstruction in horses as a sequelae to mesenteric verminous arteritis or perforation of a gastric ulcer (Blood et al., 1979); and can interfere with the natural functions of bowels and other abdominal organs in dogs (Banks, 1963).

Boys (1942) reviewed the problem in human and suggested the various methods for the prevention of peritoneal adhesions. In view of the magnitude of the problem and absence of any knowledge about the exact etiology, very

many agents and procedures have been tried for the prophylaxis and treatment of the peritoneal adhesions, but none has yet proved to be useful, because some of the procedures and agents have proved to be uneffective or partially effective, while some of the substances acts as foreign bodies. Amongst the most prominent agents proposed by various workers are heparin, sodium citrate, trypsin, pepsin, hyaluronidase, streptokinase, corticosteroids and cytotoxic agents.

A great deal of work has been carried out in this field but little success has been achieved. Accordingly a drug that can prevent or minimize the formation of the peritoneal adhesions, will be of great interest in veterinary field. Therefore, in the present work the action of the various drugs, viz., cortisone and non-steroid anti-inflammatory drugs for the prevention of the peritoneal adhesion has been investigated in the dogs, considering the inflammatory process as the etiology of the adhesion formation (Replogle ~~and Johnson~~ *et al*, 1966).

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LITERATURE REVIEW

John Hunter (1828 - 1793), London Surgeon and Anatomist described sticky substance named "Gluten' responsible for the production of Intestinal adhesions. In 1802, Bichat, first published his paper on peritoneal diseases, especially peritonitis and peritoneal adhesions. In 1887, Weigert developed, a specific stain for Hunter's 'Gluten', which he named, thereafter as 'Fibrin'.

Muller (1886) advocated the introduction of large quantity of Normal saline in peritoneal cavity before closure of abdomen. In this way, he believed that injured peritoneal surfaces could be separated and no adhesions would result.

Vogel (1902) attempted to prevent formation of fibrinous adhesions by introducing citrate solution in the peritoneal cavity. He reported good results after using citrate with gum arabica. The development of permanent adhesion was mainly dependent upon the size and depth of peritoneal injury. The possibility of adhesion formation was dependent upon the length of time for which injured peritoneal surfaces faced each other. It was obvious that a permanent adhesion might develop between intact and damaged peritoneal surface.

Pope (1914) investigated that hypertonic glucose and intraperitoneal injection of saline egg albumin alone or with citrate solution was ineffective in prevention of peritoneal adhesions. He did an extensive experimental study

using 2 per cent solution of sodium citrate alongwith 3 per cent solution of sodium chloride for the prevention of peritoneal adhesions and results were satisfactory.

Hertzler (1915) showed that incclean peritoneal wounds exudate is laid down in a few minutes after the peritoneal surfaces are sewn together. In 10 minutes fibrin bundles appear and in a few hours they are fully developed. The fibrin changes into fibrous tissue on the 4th day. This becomes connective tissue by the end of week.

Williamson and Mann (1922) employed a combination of gum acacia with gelatin and found that it was helpful in reducing the peritoneal adhesions.

Payr (1922) advocated the use of pepsin-gel-iodine in the peritoneal cavity in order to prevent adhesions.

Ochsner and Garside (1932) deprecated washing of surgical gloves in antiseptic solution, because it lead to formation of adhesions. They reported good results after use of papain in prevention of (formation and recurrence) adhesions. They also used trypsin, but results were not good. They suggested that mechanical trauma to the peritoneum in the form of rough handling, slipping of the retractors, hooks, gauze packs and blunt trauma to the abdominal wall are the common causes of peritoneal adhesions.

Rea and Weingstein (1933) had done experiments with saline to prevent formation and reformation of peritoneal adhesions without good effect in prevention of adhesions.

Turunun (1933) from his clinical and experimental investigations suggested that mechanical trauma to the peritoneum was the chief cause of post-operative peritoneal adhesions. He thought that bacterial infection seemed to be less important. Adhesion formation is due to high temperature exposure of viscera to air and it is aggrevated by paralytic ileus. He stated that non-peritonised ligatures and sutures act as foreign body and thus cause adhesion formation.

Johnson (1936) postulated that bovine allantoic membrane was least irritating and therefore cause least amount of reaction and fibrosis in human beings. On the basis of his findings he sacrified the bowel wall and peritoneum in animals and found that this helps in prevention of peritoneal adhesions.

Noble (1937) developed a technique to prevent peritoneal adhesions. This technique consists of joining adjacent loops of small gut together in step ladder fashion by suturing the serosa of intestine. No inhibitory effect of papain on the peritoneal adhesions was reported by Donaldson (1938).

Choe et al. (1940) observed that amniotic membrane act as a foreign body for a short time and get absorbed in one month. Adhesion formation did not occur when the amnion was applied but it did occur when the other material used e.g., Fasciolate, fat and plain catgut.

Totten (1940) reported favourable results in rebbits after use of 20 per cent glucose intraperitoneally.

Lehman and Boys (1940) observed that character of the adhesions markedly changed, the bands of adhesions become less dense and easily separable. These workers also noted that heparin checked the recurrence of adhesions after lysis. They also reported non-inhibitory effect of papain on the formation of peritoneal adhesions.

Brimbran (1940) advocated the vitreous humor of calves eye, experimentally in prevention of peritoneal adhesions.

Kredil and Smithy (1941) assessed that use of burning hot laperotomy mops might injure the peritoneum and may lead to adhesion formation.

Boys (1942) studied the mechanism of adhesion formation, he suggested various methods in prevention of peritoneal adhesions and classified them as (i) to prevent peritoneal injury, (ii) peritonealization of raw surfaces, (iii) to prevent coagulation of serous exudate, (iv) to

dissolve the deposited fibrin, and (v) to keep apart the fibrin coated peritoneal surfaces.

Behan (1942) pointed out the significance of depth of injury in adhesion formation and suggested that operative trauma to serosa and collection of blood in the peritoneal cavity from damaged surface provide a favourable condition for adhesion formation. He considered that after operation the continuous pressure exercised by distended intestine on the two peritoneal surfaces in contact with each other, lead to damage of serosa and consequently formation of adhesions. It was generally recognised that physical trauma to the peritoneal surfaces could lead to agglutination of these surfaces even in the absence of infection.

Weed and Grooves (1942) found that contamination of peritoneal cavity by foreign material is greatest during operation. Besides, the use of different suture material for different surgical procedures, glove powder proved to be a common source of contamination.

Crutcher et al. (1943) reported the formation of granuloma and extensive adhesions, after the intraperitoneal use of sulphonamides. They suggested that it should not be used in the prevention of peritoneal adhesions.

German (1943) found that cotton gauze, lint and other thread material leads to formation of granuloma and adhesion in the abdominal cavity.

Bloor et al. (1947) opined that heparin was not effective in prevention of peritoneal adhesion, after intraperitoneal administration.

Krook (1947) stated that recurrence of intestinal obstruction due to adhesion in humen and found that chronic infection played an important part in recurrence of adhesions.

Sexen and Tuovinen (1947) identified Talc powder or [redacted] sulpha powder as source of adhesion formation.

Kubonyi (1947) used fresh amniotic membrane of homologous nature for prevention of adhesions. His findings were, after about 12 weeks of grafting, adhesions has disappeared completely and parent epithelium was restored over the intestines.

Straube (1945) recommended the use of polyvinyl-pyrrolidone (peristone) in prevention of peritoneal adhesions in dogs.

Davidson (1949) found in dogs that heparin given by any route, was effective in decreasing the number and density of adhesions.

Lord et al. (1949) reported that human patients [redacted] died of haemorrhage, after intraperitoneal use of heparin, for the prevention of peritoneal adhesions.

Minge and Dennis (1949) studied the effect of dicumarol after lysis of adhesions in dogs. They reported that adhesions reformed to the same extent or more and 40 per cent animals died of haemorrhage.

Robbins et al. (1949) were able to show that in animals and human beings, both extensive peritoneal injury might heal without adhesion formation. They observed that reperitonealisation of certain areas were not possible, then this factor alone should not be of great concern in possible subsequent development of adhesions.

Stoppelman (1949) believed that adhesions were prevented by the suppression of fibroblastic activity by hyaluronidase.

Ruttenberg et al. (1949) found that emulsified fat and hyaluronidase in peritoneal cavity form adhesions.

White (1949) used dicumarol orally for prevention of peritoneal adhesions after lysis. He found moderate reduction of adhesion formation and adhesions produced were thinner, elastic and more easily separable. Heparin was more effective alone as compared to the combined dicumarol and heparin therapy.

The liquid human fat rendered from lipoma or subcutaneous tissue to prevent adhesions was used by Siemer (1950).

Vandyk (1950) obtained encouraging results after use of heparin in dogs and he concluded that it was not so effective as claimed by other workers.

Thomas et al. (1950) reported that hyaluronidase did not prevent the formation or recurrence of adhesions even with large doses, but they confirmed the observations of Robbins et al. (1949), after their experimental work in rabbits and guinea pigs.

Connolly and Richard (1951) were of opinion that hyaluronidase decrease the number and character of adhesions after surgical division and when used in large doses locally, it completely prevented the adhesion formation. They found experimentally in dogs that talc induced adhesions were fewer in number and filmy in character when hyaluronidase was used intraperitoneally as compared to control animals.

Scheinberg et al. (1951) observed that cortisone and corticotropine (ACTH) were effective in considerably reducing the number of intra-abdominal adhesions in dogs and rats.

Schmoreul(1951) used liquid fat of human origin to prevent adhesions, and found good results.

Lee et al. (1952) found that starch may produce granulomas when improperly used, which are the sites of adhesion formation.

Singleton et al. (1952) found that any form of reperitonealization probably increased the incidence of peritoneal adhesions.

Marshall and Forse (1952) reported a case of paraffinoma on reoperation of a case, after use of paraffin in the prevention of peritoneal adhesions.

Chikelsir and Miretzake (1953) found that Barium sulphate may reach the peritoneal cavity after perforation of gastrointestinal tract during radiological investigation and lead to adhesion formation. They showed that intraperitoneal granuloma forms around the mercury which was thrown into the peritoneal cavity from the ruptured intestinal tubes used for aspiration purposes.

Hubay et al. (1953) evaluated the effect of cortisone in large doses on the formation of adhesions secondary to denuded areas of jejunum in the dog and found it effective in prevention of adhesions.

Wilder (1953) concluded after his experiments that hyaluronidase did not prevent the formation or recurrence of adhesions, even with high doses.

Luttwak et al. (1954) reported that streptokinase-streptodornase diminishes the number of talc induced granulomas and adhesions.

Zecharise (1954) noted that hydrocortisone was less effective on the reformation of adhesion after their lysis. He observed that it was uneble to dissolve or diminish the existing adhesions.

Martin and Magarity (1954) performed plication of intestine in dogs, they found unsatisfactory results on exploration after 2 - 9 months.

Hiroshi Asch (1954) concluded after his experiments that fibrinolysin has no effect in prevention of peritoneal adhesions. He also suggested that gelatin membrane can prevent peritoneal adhesions in rabbits when applied on the denuded surfaces. He thought that it prevented fibrin formation.

Barron and Fallis (1955) reported good results of plication of intestine after lysis of adhesions.

Desanctis et al. (1955) found that, when hydrocortisone acetate applied topically and instilled in peritoneal cavity, it reduces the quantity and alter the quality of peritoneal adhesions in dogs.

Gustavsson et al. (1955) found that streptokinase with plasminogen prevents the intraperitoneal adhesions.

Sherry (1955) was of the opinion that high doses of intravenous streptokinase could modify the development of adhesions.

Hartwell (1955) described that serosal cells present adhesions by combining their fibrinolytic power with their epithelial like function of extending themselves as a solid sheet of cells to cover smoothy raw area. If fibroplasia appears before motion or before serosal cells grow to cover the area then permanent adhesion will be formed.

Fries (1956) used hyaluronidase inhibitor (polyphyloretin) in prevention of adhesions in rabbits. He concluded that it reduces the adhesion formation while hyaluronidase had no effect on the formation of adhesions.

Upplegger (1956) reported the use of peristone (polyvinyl pyrrolidone) in prevention of peritoneal adhesions on the basis of clinical and experimental study in dogs.

Craig and Bianchi (1956) were of the opinion that hyaluronidase in large doses for long time could reduce the density of adhesions and not their number. Injury to the peritoneum results in out pouring of exudate. The fibrinogen in the exudate is activated to fibrin which may cause abdominal viscera to adhere to adjacent structures within as little as three hours time.

Mussgnug (1956) reported good results with peristone-N (Kollidone), a polyvinyl pyrrolidone derivative in prevention of peritoneal adhesions.

Discesaro and Rodolico (1957) noted that hydrocortisone was less effective on the reformation of adhesions after their lysis.

Luttwak et al. (1957) had done comparative study of effects of fibrinolytic agents and corticosteroids on talc induced adhesions in rats. They found that instillation of hydrocortisone, intraperitoneally superior to cortisone and streptokinase-streptodornase in prevention of adhesions and granuloma formation.

Jackson (1958) observed that during the process of exudation, there is collection of fluid in peritoneal cavity, decrease in pulsation of vase-rectae, relative anoxaemia and diminuation of peristalsis. The fibrinous exudate in peritoneal cavity undergo certain changes due to the protec-lytic enzyme secreted by white blood cells. These enzymes affect the organised fibrinous exudate and leads to resorption of fibrin, along with this process, there was recanalisation of capillaries, return of arterial pulsation and resumption of peristalsis. It takes 72 - 96 hours from the onset of trauma to the return of normal bowel function. If, whole of the fibrin is absorbed, no adhesion forms; otherwise fibrin left behind is transformed into collagen by fibroplasia and that in turn forms thick fibrous adhesion. He found that resolution process depends upon the physical condition of

animal. He used heparin and found that it inhibits adhesions only before the stage of fibrinous deposition, while streptokinase activates fibrinolysin to destroy early fibrinous film.

Eisenschmid (1958) found that petrolatum causes adhesion formation. Thomaschek (1959) combined hydrocortisone and oxytetracycline and showed that reduction in formation of adhesions occurred in rats which was not obtained by other means.

Miller (1959) mentioned that reversal of inflammation and edema are produced by anti-inflammatory drugs, probably by competing with the inhibitors of plasmin at the site of inflammation. Plasmin digest the abnormally present proteins at the site.

Connolly and Smith (1960) stated that most of the lubricants recommended for the prevention of peritoneal adhesions act as foreign bodies and cause adhesion formation rather than to prevent them.

Schulze (1960) thought that mechanism of action of polyvinyl pyrrolidone was to form a thin film over the intestinal loops which make them slippery. It also causes peritoneal effusion, which persists for several days. He contreindicated it's use in peritonitis.

Huttle and Somogyi (1960) assessed that polyvinyl pyrrolidone inhibit inflammatory reaction of peritoneum and thus it may have favourable effect on post-operative adhesions.

Laurentaie et al. (1961) evaluated the effect of non-steroid anti-inflammatory agent, Irgapyrin and found effective in preventing adhesions formation.

Brighina and Rizzo (1961) performed experiments in rabbits and proved that oxyphenbutazone (Tendril), an anti-inflammatory drug has a clear prophylactic effect against post-operative peritoneal adhesions.

Huttle et al. (1962) used ACTH in prevention of adhesions but results were very poor. They reported good results after administration of hydrocortisone and peritone-N (Polyvinyl pyrrolidone) but parenterally administration of ACTH, Vitemine E and Peristone-N were ineffective.

Volpe and Santoro (1962) suggested the use of lysozyme solution in prevention of adhesions post-operatively. They reported good results after its local use in guinea pigs.

Knightly et al. (1962) concluded from their experiments that fibrinolysin in single dose was more effective than heparin.

Ellis (1962) opined that the tissue anoxia increases the possibility of adhesion formation. He suggested that

adhesion formation was not initiated by serosal defects unless there was underlying vascular injury. This theory seemed to provide the explanation of the observations concerning the correlation between depth and extent of damage to the peritoneum and development of adhesions. The repair of peritoneal defects cause tissue tension and ischaemia, which lead to adhesion formation. He studied the relation between sutures and abdominal adhesions. He found that sutures as such were not responsible for development of adhesions but tight sutures caused tissue tension and ischaemia leading to formation of adhesions.

Kolliginnins (1962) could prevent talc induced peritoneal adhesions in rats by the administration of polyvinyl pyrrolidone. He suggested mechanism of action of polyvinyl pyrrolidone was dilution of exudate, lubrication, protection, sealing of capillaries, binding of histamine like tissue substances, slow absorption and favourable influence on coagulation of fibrin.

Rijwani et al. (1963) observed that small quantity of talcum powder which may be introduced from the gloves into the peritoneal cavity during operation in rabbits produced adhesions.

Yamakawa (1963) was of the opinion that hydrocortisone diminished adhesions both quantitatively and qualitatively by affecting the fibrinous exudate formation. He found that

the hydrocortisone effect continuous for seven days single local application.

Banks (1963) reported that large pieces of skin and vast quantity of hair, which must have been left in the peritoneal cavity cause adhesions, which will subsequently interfere with the natural function of bowel and other abdominal organs in dogs.

Eskeland (1963a) suggested that exudation with formation of fibrin immediately after trauma played an important part in adhesion formation. He noted that absorption was delayed and exudation was inhibited in rats treated with intraperitoneal administration of prednisolone tertiary butyl acetate. He noted considerable reduction in albumin content and total volume of peritoneal fluid after 24 hours. Further, he concluded that exudation of fibrinogen was probably inhibited to a little or greater degree and consequently fibrin formation was reduced considerably.

Eskeland (1963b) found that prednisolone tertiary butyl acetate was more effective than prednisolone acetate, when administered intraperitoneally in the prevention of peritoneal adhesions in rats.

Takita et al. (1964) observed that dexamethasone application locally prevented intestinal obstruction in rabbits, by affecting the production of glucosamine and

hydroxyproline in traumatised intestinal serosa. They reported that one per cent chondroitin sulphate prevents intra-peritoneal adhesions in rabbits, it greatly inhibited the fibrin formation and thus prevented adhesion formation.

Tsugimura (1964) noted that cortisone and chondroitin sulphate prevented adhesion formation. He suggested the use of chloramphenicol alongwith these agents to check adhesion formation in cases of peritonitis. He found that anti-inflammatory drug (Tendril) prevents formation of peritoneal adhesions when used for three days, before production of experimental adhesions.

Benzer et al. (1964) applied Kabikinase intra-peritoneally to prevent talc induced peritoneal adhesions and reported good results.

Zukerman (1964) found that amnion graft was allied to the peritoneum and could serve as a substitute for the peritoneum.

Coletti et al. (1964) reported that peritoneal adhesions after a successful operation may result in a case of intestinal obstruction in human beings.

Choalte and Justaviera (1964) used dextran intra-peritoneally in the experimental study of intra-peritoneal adhesion formation in rats with good results. They suggested that perhaps a non-polar substance like dextran may mediate

the electrolytical difference between the normal and injured surfaces, thus preventing adhesion formation. They reported that dextran act probably by interfering with the appearance of fibrin, it also reduces the contact time of raw surfaces by its siliconizing properties.

Mazuji et al. (1964) studied the mechanism of action of polyvinyl pyrrolidone, and found that it forms a thin film on the intestinal loops, which makes them slippery. It also causes peritoneal effusion, which persists for several days. They recommended use of a plasdone-C (polyvinyl pyrrolidone) as a 6 per cent sterile solution in the peritoneal cavity, which has preventive action on reformation of abdominal adhesions in rabbits.

Faued et al. (1964) performed the experimental laparotomies on 40 rabbits, to see the effect of different salts of penicillin instilled intra-peritoneally. They concluded that procaine penicilline-G and streptomycin powder, oily solution of procain penicillin resulted in adhesion formation. Crystalline penicilline-G and streptopenicilline in aqueous solution did not give rise to adhesions.

Mion (1965) found that indwelling tubes, when used after operations may cause adhesion formation in human beings.

Negate (1965) noted the influence of chondroitin sulphate on the collagen formation exerted inhibitory effect

on the production of the hyaluronic acid and hydroxyproline, which were produced at the site of injured intestine helping fibrin formation.

Jewet (1965) concluded after his experiments that fibrinolysin has no effect in prevention of peritoneal adhesions. He tried seven different enzymes in three different species of animals (rat, rabbits and dogs) but found that none of the enzyme has any significant action on peritoneal adhesions.

Bates (1965) observed that starch may produce granuloma, when it is improperly used in the peritoneal cavity.

Salzmann Miniates (1965) used Rebacetin powder to prevent the adhesion formation in operated cases of human being and reported good results.

Benek (1966) studied the mode of action of Tendril in reducing the formation of peritoneal adhesions, was by inhibiting the local inflammatory process.

Glucksman et al. (1966) confirmed the observations of Robbins et al. (1949). They found that extensive peritoneal injury might heal without adhesion formation.

Vorster (1966) showed that Trasylol (Kallikren inhibitor) had proved its value in prevention of peritoneal adhesions in experimental animals. The mechanism and diminution of the fibrin formation.

Glucksmann and Warren (1966) corticosteroids did not show any reduction in number or extent of adhesions either after trauma or lysis in dogs.

Gross et al. (1966) used dextran and gelatin, Ringer's lactate and normal saline and hydroxyethyl starch, and found that they decreased adhesion formation.

Replogle et al. (1966) observed that by the local use of dexamethasone and phenargan, the inflammatory exudate that followed trauma was minimised and organisation of inflammatory exudate into fibrinous adhesions could be delayed. This delay allowed the serosal cells to proliferate and cover the denuded bowel which otherwise led to adehsions. They considered inflammatory reaction as etiology of adehsion formation. Due to inflammation, macroproteins such as fibrin, form in the tissue spaces. These complex proteins are hydrophilic. As they swell, pressure is exerted on the surrounding capillaries and clots forms inside these blood channels. Impairment of delivery of oxygen, humoral antibodies and administered antibacterial drugs to the disease follows. Carbondioxide and other products of metabolism are not removed from the site.

Lenggerhagger (1966) found that resolution process depends upon the presence of leucocytes in exudate. He suggested that fibrinous exudate was dissolved by proteolytic enzymes elaborated by leucocytes.

Swolin (1966) has reported good results with use oflubricants in the prevention of peritoneal adhesions. He found that hydrocortisone diminished adhesions both quantitatively and qualitatively. After use of 2 per cent liquid emulsion with 2.5 per cent prednisolone in 88 per cent of animals. The instillation of either lipid or prednisolone was ineffective.

Belzer (1967) mentioned that venous obstruction increases the possibility of adhesion formation; it was more important than the obstruction to the arterial blood flow.

Goldman et al. (1967) tried the 5-flurouracil, which is the inhibitor of the normal wound healing process, considering the peritoneal adhesion formation equal to that for the wound healing. They found that formation of adhesion was prevented by using 5-flurouracil, subcutaneously in rats.

Polishuk and Aboulfia (1967) observed that 40 to 60 per cent dextran solution remain in the peritoneal cavity for 10 - 11 days and it was completely absorbed in 21 days. These workers postulated that mechanical factors separating the serosal surfaces play a role in the prevention of adhesions but anti-thrombogenic and siliconising effect of dextran may also be an additional factor.

Dieulfae and Dieulfae (1967) reported after their experimental and clinical test, that alpha chymotrypsin was effective in preventing adhesions. They suggested its use clinically in human beings.

Tocco et al. (1967) were of the opinion that a new anti-inflammatory agent, Benzydamine, was effective in prevention of peritoneal adhesions, they suggested its use clinically.

Sakakihara (1967) suggested that low molecular dextran was more effective than the high molecular dextran in the prevention of peritoneal adhesions.

Aboulfia and Polishuk (1967) used dimethylpolysiloxane intraperitoneally in rabbits for the prevention of peritoneal adhesions and found excellent results with dimethylpoly-siloxane in dogs.

Tsugu (1967) observed that fibrinolysin and chondroitin sulphate reduced the edema and inflammation of sub-serosal and muscular tissue and so helped in preventing adhesions.

Broody and Frey (1968) were of the opinion that dimethylopolysiloxane did not prevent adhesion formation in rats. The adhesions in silicone treated animals were thicker and more vascular as compared with control animals. The thickness of adhesion was more on account of granulomas

in adhesions. They suggested that silicone liquid should not be used intraperitoneally in human beings.

Schede et al. (1968) did the ultrastructural study of adhesion formation in rats. They have produced adhesions by silica injections and observed that in one minute silica particles were absorbed by surface mesothelial cells of villi. Silica was seen in cytoplasm of the cells at 5 minutes. By the end of 4 hours microvilli greatly decreased in number and mesothelial cells were beginning to separate from each other and the underlying basement membrane. At the 7th hour most of mesothelial cells had desquamated and the exposed basement membrane is covered with fibrin. They noted that fibrinous adhesions were widespread by 12 hours, fibroblasts and new collagen were evident by the 6th day. They concluded that desquamation of epithelial cells preceeds adhesion formation. The fibrin deposit on the exposed surfaces (basement membrane) lead to fibrous adhesions, which becomes collagenous by 10th day.

Kapoor et al. (1968) used low molecular dextran, and reported significant results in the prevention of peritoneal lesions, at the time of production or lysis of adhesions.

Stevens (1968) reported no inhibitory effect of papain in the formation of peritoneal adhesions.

Kho et al. (1969) used promethazine, dexamethazone combined for the prevention of peritoneal adhesions in the dogs and found this combination effective. Kapoor et al. (1969) used an anti-inflammetory agent, Tandril (Oxyphen-butazone) for prevention of peritoneal adhesions. They found excellent results. They suggested that factor of lubrication of low molecular dextran helps in prevention of peritoneal adhesions.

Gulati et al. (1972) reported the inhibitory action of the oral administration of pepase in the formation of intraperitoneal adhesions before and after lysis in monkeys and rabbits. They reported the efficacy of oxyphenbutazone in reducing or preventing the formation of adhesions. They found that intraperitoneal instillation of low molecular dextran helped in reducing the formation of adhesions.

Shun-Kwun et al. (1973) suggested that methyl prednisolone prevents reformation of peritoneal adhesions after adhesiolysis of mature 3 months old adhesions in Macca monkeys.

Gazzaniga et al. (1975) were of the opinion that human fibrinolysin Thrombolysin when used in combination of methyl prednisolone and promethazine intra-peritoneally which virtually eliminated adhesion formation in rats. They found that methyl prednisolone and dexamethasone,

depending on the route of administration, modified the total number of adhesions but did not modify their severity, when compared to control animals (rats). They found that promethazine by itself modified peritoneal adhesions in rats. When methylprednisolone and promethazine modifies adhesions but not substantially better than the combination of dexamethasone and promethazine.

Kapoor et al. (1976) demonstrated that intra-peritoneal instillation of periston did not produce any marked change in performation of the adhesions as compared to peristone-N, which significantly reduces the adhesions after lysis.

Shetty et al. (1981) found that intra-peritoneal instillation of chloramphenicol probably may be the cause of post-operative adhesions which may lead to post-operative intestinal obstruction.

Young et al. (1981) found that intravenous aprotenin (Trasylol) was effective in the prevention of peritoneal adhesions in rats.

Gulati et al. (1981) suggested that Betamethasone was effective in reducing peritoneal adhesions significantly in albino rats. They found that xanthinol nicotinate and Indomethacin when given combined were effective in reducing the adhesions significantly in rats but there was no appreciable decrease in peritoneal adhesions with Indomethacin therapy.

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MATERIALS & METHODS

Forty apparently healthy mongrel dogs were taken for the study. These animals were divided randomly in four groups having ten dogs in each group. First group was kept as control, second group was administered Phenylbutazone and Amidopyrine*, third group was administered Betamethasone** and frouth group was administered Indomethacin***.

Instruments:

Following instruments were incorporated in the surgical pack used for creating trauma on the serosa of the stomach, small intestine and large intestine.

1.	Bard-Parker handle No. 4	One
2.	Allis tissue forceps	Two
3.	Backhaus towel clamp	Four
4.	Thumb forceps	Two
5.	Mayohager's Needle holder	One
6.	Mayo Scissors	Two
7.	Suturing Needles, half curved -	
	Traumatic	One
	Atraumatic	One
8.	Mosquito artery forceps	Two
9.	Pean's artery forceps	Two
10.	Kocher's artery forceps	Two
11.	Nylon Surgeon's scrubbing brush	One
12.	Suture material	Silk

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* Esgipyrin, Suhrid Geigy Limited, Baroda

** Betnesol, Glaxo Laboratories, Bombay.

*** Idicin, Indian Drugs and Pharmaceuticals Limited, Hyderabad.

The rubbing of the surface was continued with scrubbing brush till the petechial haemorrhagic spots were seen on the injured area. The organs were replaced in the abdominal cavity. The peritoneum and linea alba were closed in layers with continuous sutures of silk thread. The skin incision was closed by interrupted silk sutures. No antibiotic was given post-operatively.

Drug Schedule:

All the dogs were allowed for post-anaesthetic recovery on the operation day. Supplementation of drugs was started on the same day. Dogs were fed on the standard maintenance ration of wheat porridge.

Drugs Administered:

Name of the drug	Dose	Mode of administration	Frequency
Group A (Control)	No drug was administered		
Group B Phenylbutazone and Amidopyrine*	10 mg/kg Body wt.	I/M	Regularly for 7 post-operative days
Group C 16-Beta-Methyl-9-Alpha fluroprednisolone (Betamethasone)**	0.6 mg/kg Body wt.	I/M	Regularly for 7 post-operative days.
Group D 1-p-Chlorobenzyl-5-methoxy-2-methylindole-3-acetic acid (Indomethacine)***	1.5 mg/kg Body wt.	Orally	Regularly for 7 post-operative days

* Esgipyrin, Suhrid Geigy Limited, Baroda.

** Betnesol, Glaxo Laboratories, Bombay.

*** Idicin, Indian Drugs and Pharmaceuticals Limited, Hyderabad.

The surgical pack was autocleved at 240 degree Fahrenhite at 15 pounds per square inch pressure for 15 to 20 minutes.

The animals were kept off feed for twelve hours prior to surgery. Thiopentone sodium* was used as a general anaesthetic 60 milligrams of thiopentone sodium was dissolved in one millilitre of distilled water. The anaesthetic solution was injected at the rate of 60 milligrams per two kilogram of body weight.

Technique :

The operative area on the midline of abdomen was selected. The site was prepared thoroughly for aseptic surgery by clipping, sheving and scrubbing with savlon solution. The operative area was painted with tincture cetavlon. Animal was secured in the dorsal recumbancy on the operation table. The abdomen was opened by a 4 - 5 cm long midline incision. Exploration of the peritoneal cavity was done to confirm that there was no intraperitoneal adhesion. The stomach and intestines were exteriorised and serosa of the stomach, small intestine and large intestine were denuded of the peritoneal covering with the help of the sterilized scrubbing brush at 20 places (four on anterior surface of stomach, eight on the anti-mesenteric border of the small intestine and eight on the anti-mesenteric border of the large intestine). Each area was five centimeter in length.

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* Intreval sodium, May and Baker, Bombay.

Sutures were removed on 10th post-operative day.

Re-explorations:

The animals were euthanised after a period of two weeks. The abdomen was opened through the same incision. Exploration of the peritoneal cavity was done to look for the adhesions. Discovered adhesions were labelled according to grade. The grading was done as follows :

Grade 0	:	No adhesions seen.
Grade I (+)	:	A single band of adhesion between viscera or viscera and abdominal wall.
Grade II (++)	:	Two bands of adhesions between viscera or viscera and abdominal wall.
Grade III(+++)	:	More than two bands of adhesions or whole of the intestine in a mass.

The grading of adhesions were done, because it was difficult to measure the adherent area. The number of adhesions were counted in all the experimental animals and samples of adhesions were collected for histopathological studies.

Histopathological Study :

Of adhesions samples were taken and preserved in 10 per cent formaline. The paraffin blocks were prepared

and sections were cut with the help of microtome at 5 micron and stained with Haemotoxylin and Eosin. The slides were examined to note inflammatory or foreign body reactions.

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RESULTS & DISCUSSION

In the present study traumatisation of the visceral peritoneum has been used for the production of adhesions, because the viscera is prone to injury.

The use of talc in production of experimental peritoneal adhesions is an unsatisfactory method because under normal operative conditions talc is never placed in the peritoneal cavity.

It is, further corroborated by this experimental work that the mechanical trauma, is the etiological factor in the production of adhesions (Table I) since the control group (A) has developed 100 per cent of the adhesions.

The formation of peritoneal adhesions is a dynamic, non-specific, indiscriminate response of the peritoneum to any type of the trauma regardless of the nature and site of the traumatising agent (Oschner and Garside, 1932; Turunun, 1933; Ruttenberg et al., 1949 and Miller, 1959).

Majno and Palade (1961) postulated that trauma to the peritoneum initiates an inflammatory response. It is well known fact that trauma to the peritoneum causes an increase in vascular permeability resulting in exudation of a protein rich material. This is followed by coagulation of the exudate and production of microscopic fibrin net work. Body defence mechanism resolve most of the fibrinous strands by phagocytosis and enzymatic digestion.

Fig. 1 : Showing a loop of normal small intestine with it's mesentery, revealing '0' grade adhesion.

If the trauma involves a considerably large area or there is low concentration of enzymes and leucocytes, it leads to collagen deposition and further strengthening of the fibrinous adhesions (Connolly and Smith, 1960).

The difficulties in assessing value of prophylactic measures in peritoneal adhesions has been emphasized by many workers (Boys, 1942). The assessment of prevention of peritoneal adhesions and comparison of effects of various drugs in the prevention of peritoneal adhesions was done by counting number of adhesions, extent of adhesions and site of adhesions based upon the numeric score system. A statistical analysis of scores thus obtained were made and effect of different drugs in the prevention of peritoneal adhesions was evaluated.

TABLE I : SHOWING PERCENTAGE OF ADHESIONS FORMED DURING THIS EXPERIMENTAL STUDY.

Group	No. of animals	No. of animals with adhesions	Per cent with adhesions	No. of animals without adhesions	Per cent without adhesions
A (Control)	10	10	100	0	0
B (Zsgipyrin)	10	9	90	1	10
C (Betnesol)	10	6	60	4	40
D (Idicin)	10	7	70	3	30

Fig. 2 : Showing small intestine with artificially created trauma on the serose revealing an area (A - A') of petechial haemorrhage at the antimesenteric border.


A
A'

In the present study, a comparative study of the anti-inflammatory drugs (Baygipyrin, Betnesol and Idicin) has been conducted for the prevention of experimental peritoneal adhesions in dogs. These drugs were choosen because of their marked anti-inflammatory action with a relatively low degree of toxicity.

Boys (1942) and Replogle et al. (1966) suggested a few factors for the prevention of peritoneal adhesions. The approaches suggested by them may act singly or in a combined form. Their suggestions are -

(1) To reduce the amount of exudate,

(2) To prevent coagulation of exudate,

(3) To reduce contact between traumatized surfaces,

(4) To remove fibrin after it's appearance.

(5) To stop proliferation of fibroblasts.

In the present work anti-inflammatory drugs have been used for the prevention of peritoneal adhesions. Anti-inflammatory drugs competes with the plasmin inhibitors to bring about mentioned changes. Plasmin inhibitors do not allow the plasmin to digest the abnormally present proteins at the site of inflammation (Miller, 1960). Four out of the five factors suggested by Boys (1942) and Replogle et al. (1966) work together when anti-inflammatory drugs are used for the prevention of peritoneal adhesions. These are suggestion No. 1, 2, 4 and 5 of the above mentioned five factors.

Fig. 3 : Showing I (+) grade of adhesion,
a single band of adhesion (A) between
small intestine and mesentery.

In the past anti-inflammatory drugs have been tried in almost every sort of inflammatory condition, but very little work has been done about the use of this property for the prevention of peritoneal adhesions.

On exploration, after two weeks of the initial trauma, it was found that all of the dogs of group A (Control) developed adhesions. These findings of study was consistent with the observations of several workers, who have experimentally produced adhesions in different animals (Aboulafia and Polishuk, 1967; Knightly et al. 1962; Kapoor et al., 1967 and Kapoor et al., 1969).

The group B (Esgipyrin group) developed maximum adhesions in 90 per cent of the animals as compared to 60 per cent adhesions of the group C (Betnesol group) and 70 per cent adhesions of group D (Idicin group).

The number of adhesions was highest in the control group (Group A) and minimum in Betnesol group (Group C).

TABLE II : SHOWING GRADE OF ADHESIONS IN EACH GROUP.

Group	No. of animals	No. of animals with grade of adhesions				
		0	I(+)	II(++)	III(+++)	Total
A (Control)	10	0	0	3	7	10
B (Esgipyrin)	10	1	3	4	2	10
C (Betnesol)	10	4	5	1	0	10
D (Idicin)	10	3	2	3	2	10
Total	40	8	10	11	11	40

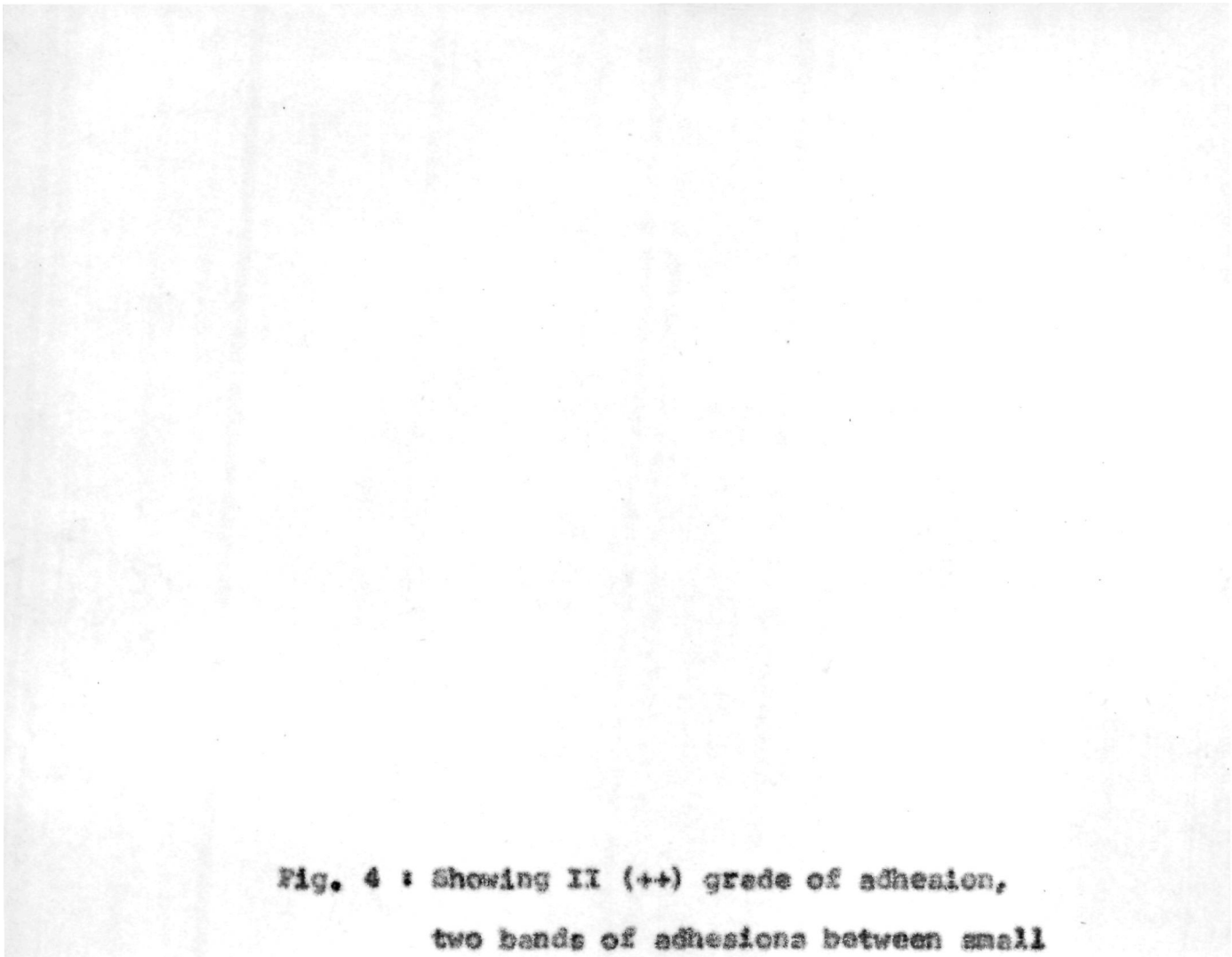


Fig. 4 : Showing II (++) grade of adhesion, two bands of adhesions between small intestine and mesentery (A & B).

In the group A (Control group), 70 per cent animals has developed III (+++) grade of adhesions, II (++) grade adehsions developed in 30 per cent of animals. There was no animal, without adhesions in the control group. In addition, to the absence of '0' grade adhesions, I (+) grade adhesion was also absent.

In the group B (Asgipyrin group) III (+++) grade of adhesions developed in only 20 per cent animals, while II(++) grade adhesions were present in 40 per cent of animals. I (+) grade of adhesions developed in 30 per cent of cases but adhesions were absent in 10 per cent of animals.

In the group C (Betnesol group), III (+++) grade adhesions were completely absent, while 10 per cent of the animals developed II (++) grade of adhesions. I (+) grade of adhesions were present in maximum 50 per cent animals. Adhesions were absent in 40 per cent animals.

Group D (Idicin group) developed adhesions in 70 per cent of animals. III (+++) grade adhesions were present in 20 per cent animals. II (++) grade adhesions developed in 30 per cent of animals. Twenty per cent animals in this group developed I (+) grade adhesions. It was found that 30 per cent of animals, developed '0' grade adhesions.

The III (+++) grade adhesions, were maximum in group A, while minimum in group C, and Group B and group D have developed same percentage (20%) of III (+++) adhesions.

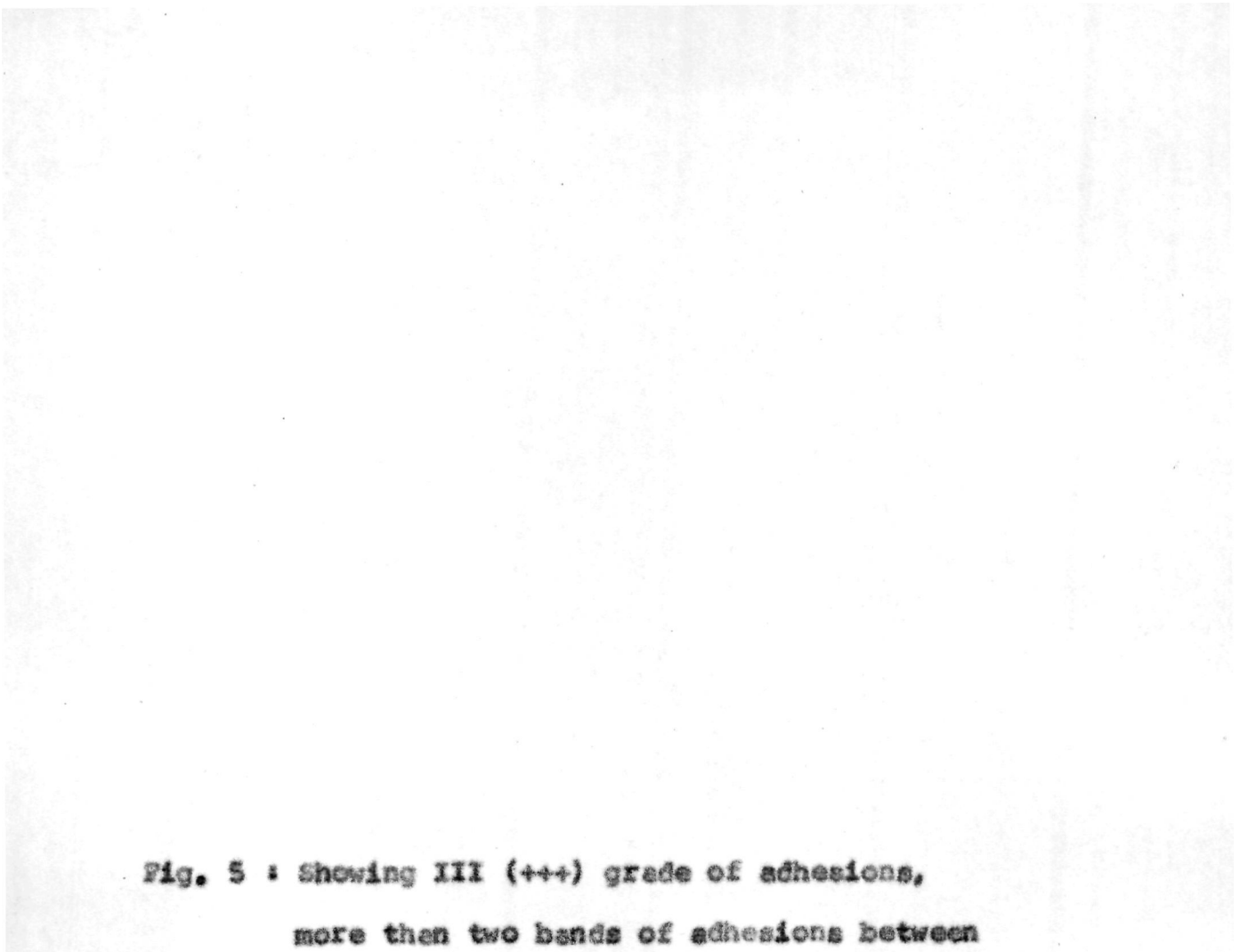


Fig. 5 : Showing III (+++) grade of adhesions, more then two bands of adhesions between loops of small intestine (A, B and C).

II (++) grade adhesions were maximum in the group B, while minimum in the group C, group A and group D developed same percentage of II (++) adhesions, i.e. 30 per cent.

The I (+) grade adhesions were maximum in group C and minimum in group A. Thirty per cent animals developed I (+) grade of adhesions in group B and 50 per cent of I (+) grade adhesions were present in group C.

Maximum number of animals without adhesions were in group C (40%) and group D (30%). In group B 10 per cent of animals were without adhesions (Fig. 7).

TABLE III : SHOWING COMPARISON OF RESULTS AND EXTENT OF ADHESIONS (Grade '0' and I(+) were considered mild, Grade II(++) as moderete and Grade III(+++) as severe extent of adhesions).

Group	Number of animals with adhesions					
	Mild		Moderate		Severe	
	No.	%	No.	%	No.	%
A (Control)	0	0	30	30	7	70
B (Esgipyrin)	4	40	4	40	2	20
C (Betnesol)	9	90	1	10	0	0
D (Idicin)	5	50	3	30	2	20

By comparison of the extent of adhesions, it was found that in group A (Control group) mild adhesions were absent. The moderate adhesions were present in 30 per cent

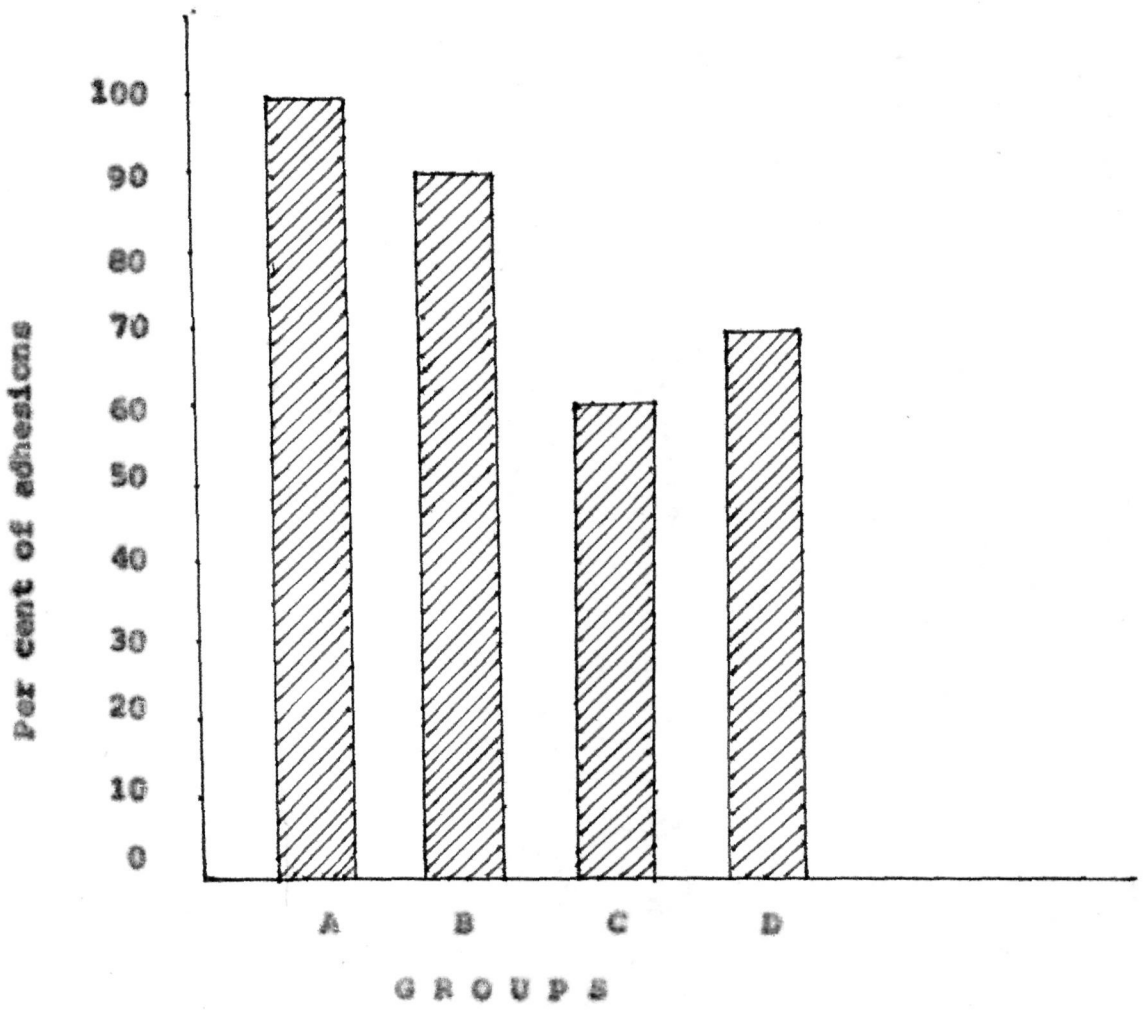


Fig. 6 : Showing the percentage of adhesions.

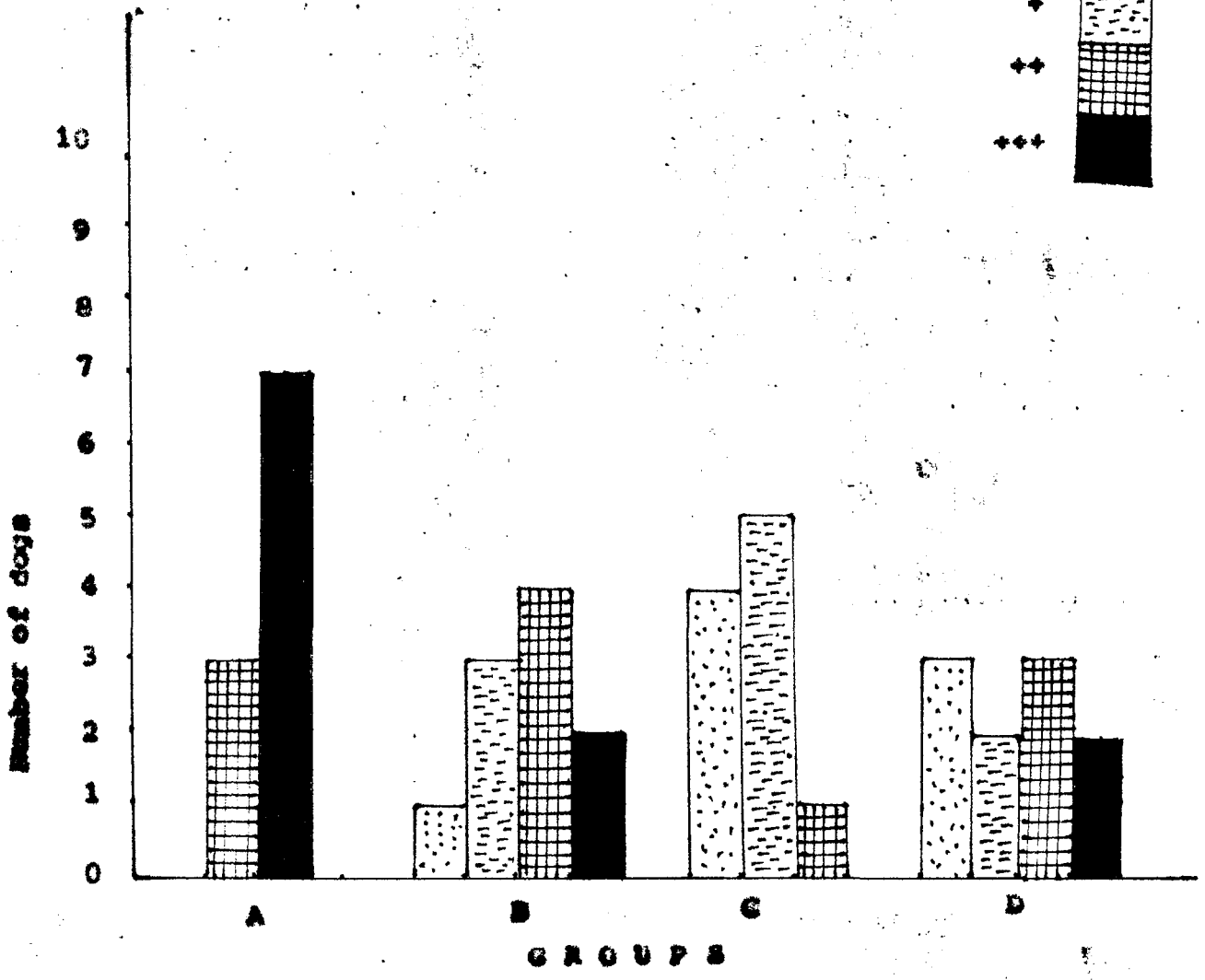


Fig. 7 : Showing grade of adhesions.

of animals, while severe adhesions were found in 70 per cent of animals.

In the group B (Esgipyrin group) mild adhesions were present in 20 per cent of animals. In 40 per cent of animals, moderate adhesions were present, 20,per cent animals of this group were found with severe adhesions. So the administration of Esgipyrin was definitely responsible for the decreased severity of adhesions, when compared with those of group A.

In the group C (Betnesol group) mild adhesions were present in 90 per cent of the animals, while moderate adhesions were present in 10 per cent animals. Absence of severe adhesions in the Betnesol group is indicative of decrease in the extent of adhesions.

In the group D (Idicin group), it was found that 50 per cent of the animals were having mild adhecions, while 30 per cent animals were with moderate adhesions. Severe adhesions were present in 20 per cent animals. These findings confirms the marked anti-inflammatory property of Indomethacin and its help in prevention of peritoneal adhesions.

Mild adhesions were maximum in the group C (Betnesol group). Moderate adhesions were maximum in the group B (Esgipyrin group), and severe adhesions were maximum in group A (Control group), while mild adhesions were minimum (Absent) in

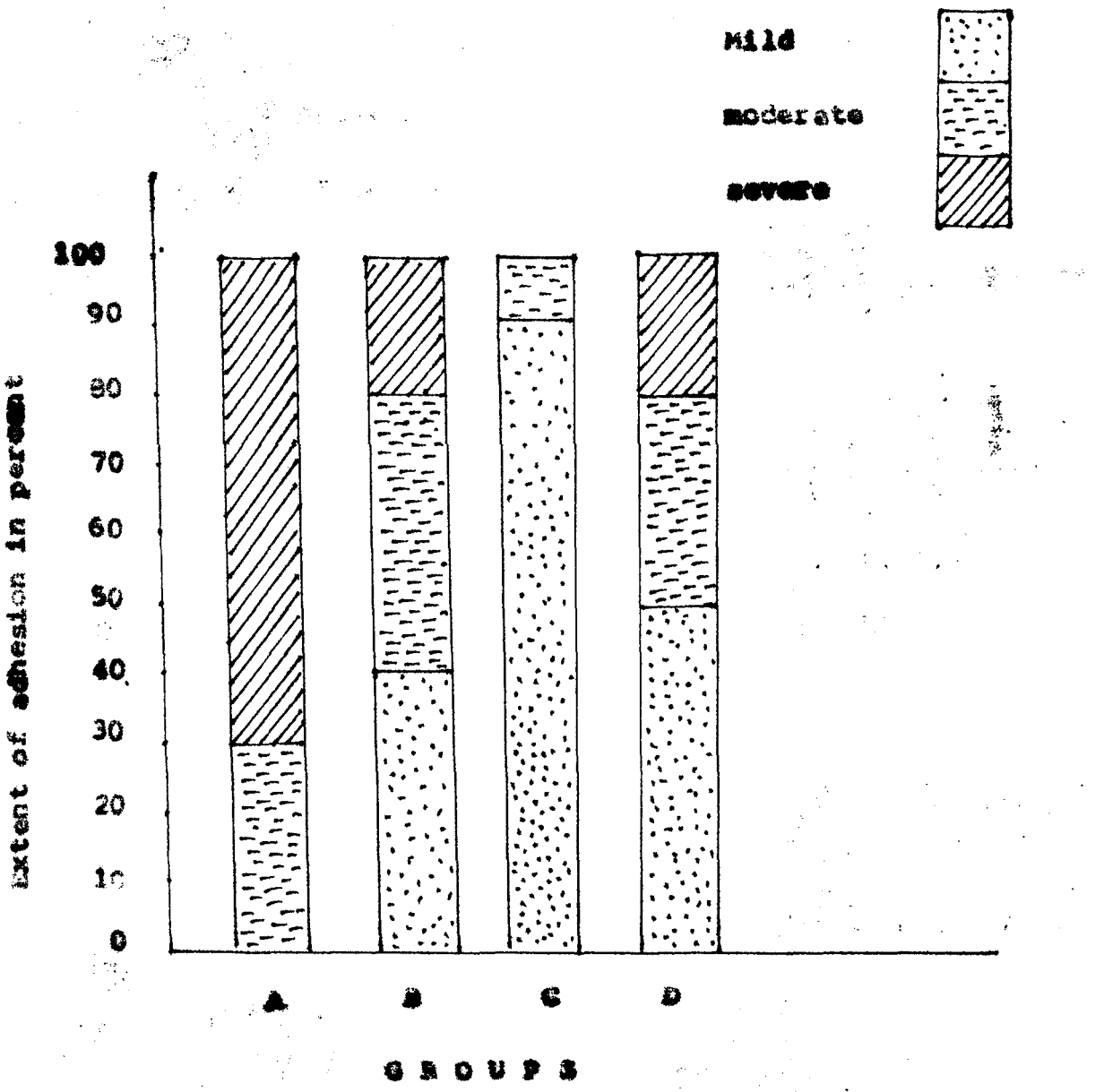


Fig. 8 : Showing the extent of adhesions.

group A (control group), as compared to group B (Esgipyrin group). Moderate adhesions were minimum in group C (Betnesol group), and maximum in group B (Esgipyrin group). Severe adhesions were minimum in group C (Betnesol group) and maximum in group A (Control group) (Fig. 8).

TABLE IV : SHOWING SITE OF ADHESIONS FORMATION.

Group	No. of animals	Peritoneal adhesions				
		Suture line	Small intes-tine	Large intes-tine	Stomach	Other Viscera
A (Control)	10	17	28	3	1	0
B (Esgipyrin)	10	10	9	2	0	0
C (Betnesol)	10	6	1	0	0	0
D (Idicin)	10	7	8	1	0	0

While considering the site of adhesion formation, it was concluded that the common sites for the adhesions formation were suture line, small intestine and large intestine. Maximum number of adhesions were present on the small intestine and suture line, stomach developed rare adhesions, as other viscera.

It was found that a maximum number of adhesions occurred in the group A (control group) which reveals the total number of adhesions to be 49, while it was minimum in the group C (Betnesol group). The total number of adhesions in group C was 7. In group B, total number of adhesions was 21 as compared to group D which revealed total number of adhesions to be 16 only(Table V).

TABLE V : SHOWING THE NUMBER OF PERITONEAL ADHESIONS.

Group	Dog No.	Peritoneal adhesions			Remarks	
		Suture line	Other than suture line	Total		
A	1	1	3	4		
	2	1	6	7		
	3	2	2	4		
	4	1	3	4		
	5	3	2	5	Total No. of adhesions	49
	6	2	3	5		
	7	1	4	5	Average	4.9
	8	3	2	5		
	9	2	3	5		
	10	1	4	5		
B	1	1	1	2		
	2	1	0	1		
	3	0	0	0	Total No.of adhesions	21
	4	2	4	6		
	5	1	1	2	Average	2.1
	6	1	3	4		
	7	1	1	2		
	8	1	0	1		
	9	1	1	2		
	10	1	0	1		
C	1	1	0	1		
	2	0	0	0		
	3	1	0	1		
	4	1	0	1	Total No.of adhesions	7
	5	1	0	1		
	6	0	0	0	Average	0.7
	7	1	0	1		
	8	1	1	2		
	9	0	0	0		
	10	0	0	0		
D	1	0	0	0		
	2	1	1	2		
	3	1	2	3		
	4	0	0	0	Total No.of Adhesions	16
	5	1	1	2		
	6	1	2	3	Average	1.6
	7	0	0	0		
	8	1	3	4		
	9	1	0	1		
	10	1	0	1		

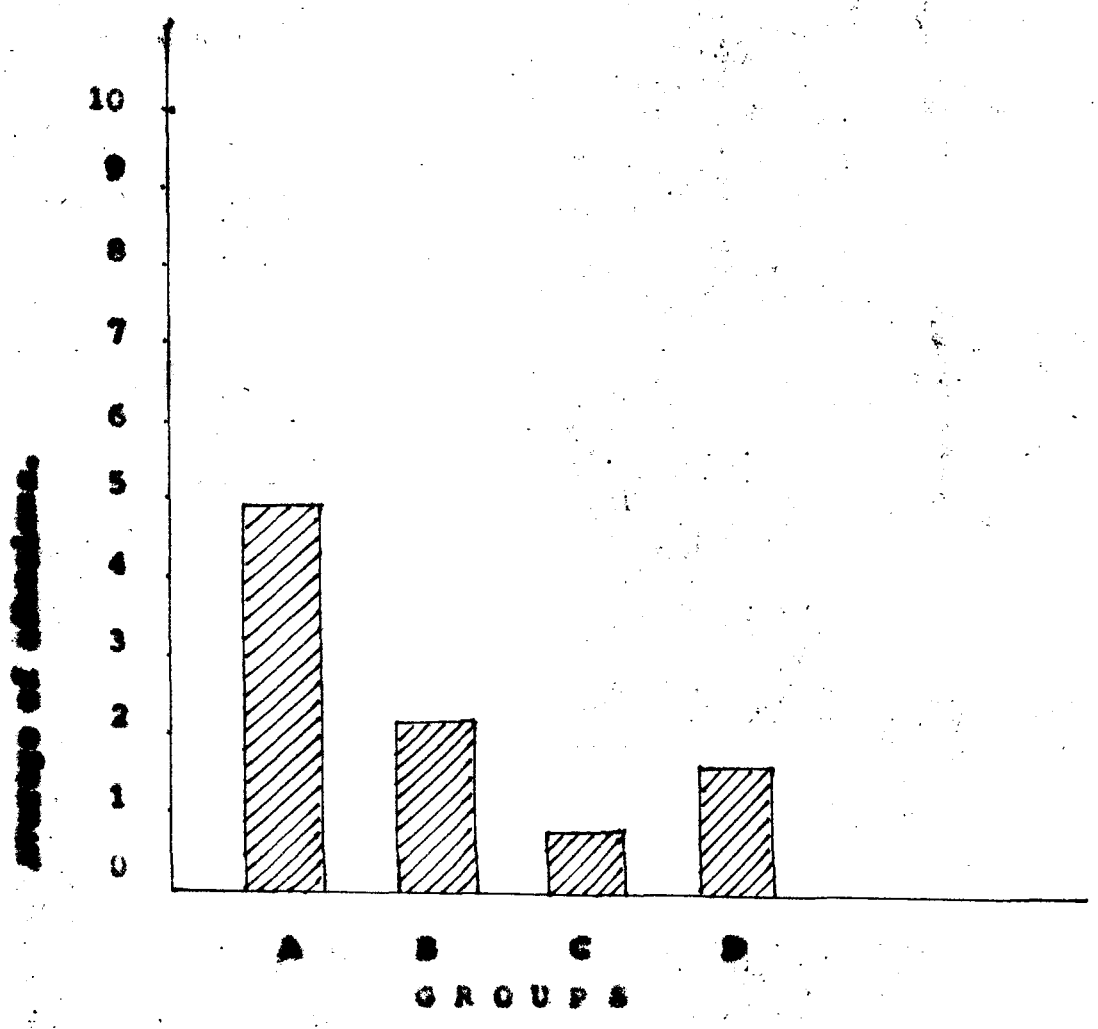
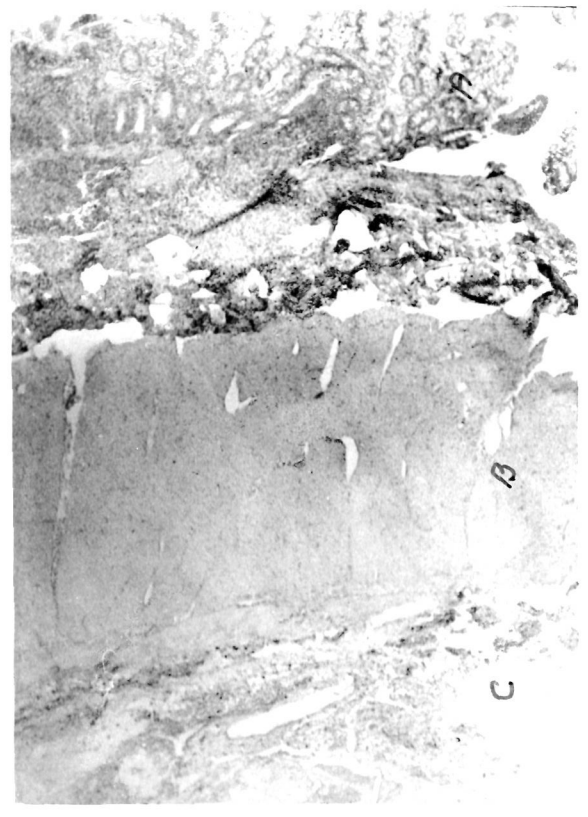


Fig. 9 : Showing number of adhesions.

Fig. 10 : Photomicrograph showing normal mucosa (A), Submucosa (B) and Muscular layer (C), of small intestine revealing '0' grade adhesion (H & E, 35X).


B
C

It is concluded by comparing the mean of the adhesions, Betnesol has got its clear cut effect on prevention of peritoneal adhesions. The Idicin being superior to that of Esgipyrin, because of the mean difference of 0.3.

The average of adhesions was minimum, 0.7 in the group C (Betnesol group) and maximum 4.9 in the group A (Control group). The group B (Esgipyrin group) has got average of adhesions to be 2.1 and group D (Idicin group) to be 1.6(Table V).

Histopathological study:

The histological study of adhesions showed intestinal mucosa, submucosa and muscular layer to be normal (Fig. 10). Marked inflammatory reaction was revealed in mucosa and submucosa. These two layers showed acute inflammatory cellular infiltration mostly neutrophils and exudate formation with occasional mononuclear cells. The actual band of adhesion was markedly congested and showed area of haemorrhage (Fig. 11). There were areas having macrophages and mononuclear cells in the adhesions with little vascularisation and exudate formation (Fig. 12). There was marked proliferation of fibroblasts and mononuclear cells (Lymphocytes and monocytes) with occasional polymorphs in exudate (Fig. 13).

Fig. 11 : Photomicrograph of I (+) grade of adhesion showing marked congestion and area of haemorrhage in mucosa, with acute inflammatory cellular infiltration mostly neutrophils and exudate formation with occasional mononuclear cells (H & E, 100X).

Fig. 12 : Photomicrograph of II (++) grade of adhesion, showing macrophages and mononuclear cells in the adhesion with little vascularisation and exudate formation (H & E, 450X).

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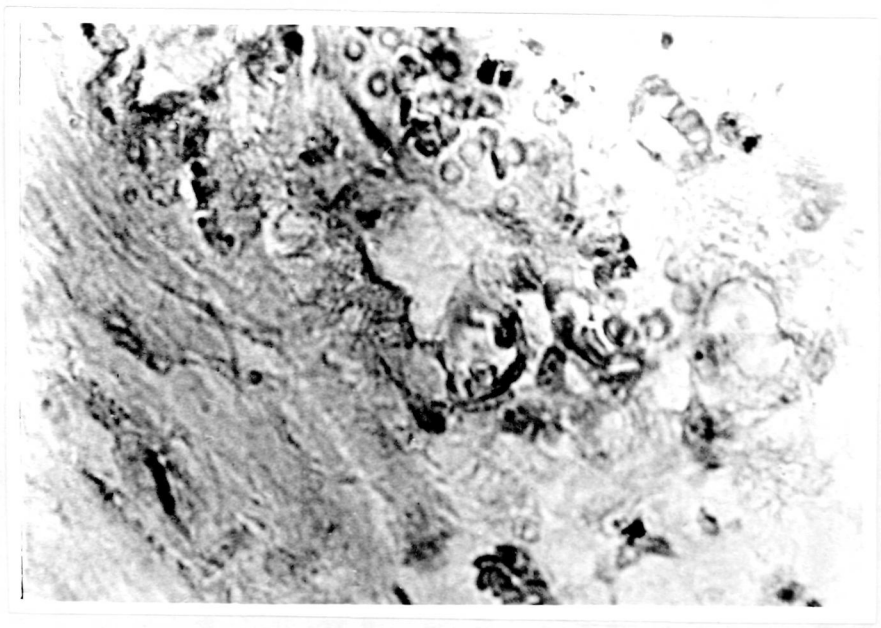

Fig. 13 : Photomicrograph of III (+++) grade of adhesion, showing proliferation of fibroblasts with a few mononuclear cell infiltration and a moderate degree of vesculerization, in the right side a portion of blood vessel (A) (H & E, 450X).

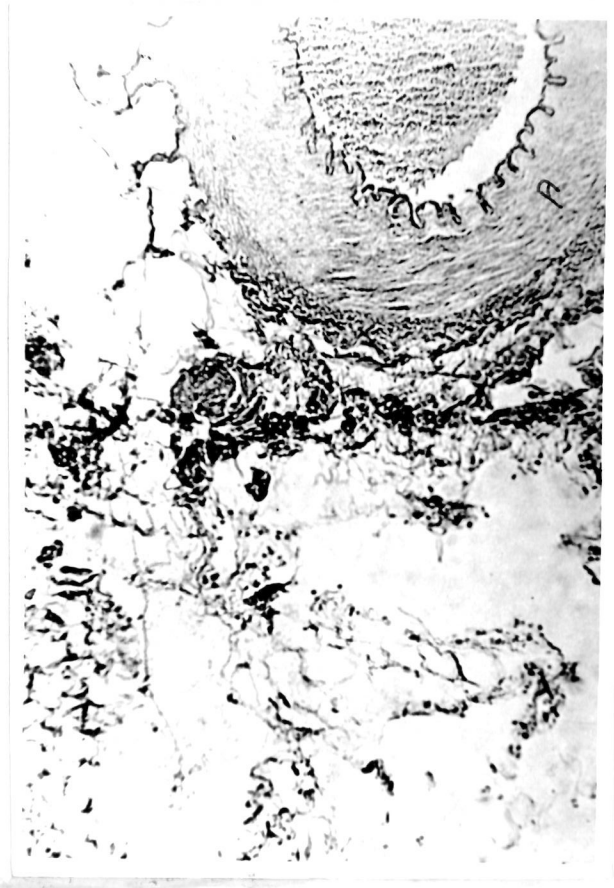

TABLE VI : SHOWING STATISTICAL ANALYSIS.

Group	No. of No.	Difference of Mean±S.E.	'P' value from Statistical test
A. Control B. Esgipyrin	10 10	1.3 ± 3.276	0.397
A. Control C. Betnesol	10 10	2.3 ± 3.269	0.703
A. Control D. Idicin	10 10	1.6 ± 3.283	0.487
B. Esgipyrin C. Betnesol	10 10	1.0 ± 0.366	2.732**
B. Esgipyrin D. Idicin	10 10	0.3 ± 0.475	0.631
C. Betnesol D. Idicin	10 10	0.7 ± 0.427	1.643

Scoring was done by giving numbers

1 to 0 Grade

2 to I (+) Grade

3 to II(++) Grade

4 to III(+++)Grade

It is evident by the comparison of the number of adhesions, extent of adhesion and site of adhesions. The Betnesol group, has got the significant effect on the prevention of adhesions while Idicin has got marked preventing effect against peritoneal adhesions, which is not significant. The difference of mean of Esgipyrin and Idicin groups reveals that basically the Idicin has got better effects than that of Esgipyrin but difference is not significant.

Though, Esgipyrin has got preventing action on adhesions which is evident by difference of mean, between control and Esgipyrin groups, but effect is not significant. It has reduced the density and grade of adhesion formation, as compared to the control group. This reduction of density of adhesions can be explained to be due to anti-inflammatory property of Esgipyrin (Laurentei et al., 1961).

On the other hand, Betnesol in group C, resulted in marked reduction of peritoneal adhesions. The cortico-steroids have been found effective in reducing the peritoneal adhesions by other workers (Gazzaniga et al., 1975; Replogle et al., 1966, Kho et al., 1969 and Gulati et al., 1981).

Beneficial effects of corticosteroids have been attributed to the reduction of exudate caused by inflammatory stimulus and limitation of secondary damage due to inflammation probably by protecting the lysozyme system and stabilizing the

cellular membrane in the presence of permeability factors (Replogle et al., 1966).

Inhibition of fibroblastic proliferation by administration of corticosteroids has been noted to be yet another mode of their action in preventing the peritoneal adhesions (Hubay et al., 1954).

Though, Idicin group has not got significant difference but, basically it has got better effects in reducing the number of peritoneal adhesions and extent of peritoneal adhesions, as compared to the Aspipyrin group. It is because of the fact that Idicin has got very potent anti-inflammatory action (Winter et al., 1963 and Dominjon, 1965) which reduce the chances of development of peritoneal adhesions. Even the adhesions developed in this group of animals were of mild to moderate degree as compared to the group B (Aspipyrin group). Anti-inflammatory property of Idicin has been investigated by various assay methods. Granuloma inhibition test has proved that Idicin has a much higher anti-inflammatory activity (Winter et al., 1963).

Experiments employing corragreen induced edema in the rat paw showed that Indomethacin in a dose of 1 mg/kg body weight and more, was about twice as effective as hydrocortisone and twenty times as effective as phenyl butazone. Morsdorf (1965) found Indomethacine to be active in inhibiting proteolytic activity. Anti-inflammatory action of the Idicin

is exerted without pituitary or edrenal involvement, since it has been proven that it is also manifested in the edrenalectomised animals. Gulati et al. (1981) observed that Indomethacine did not decrease the extent of peritoneal adhesions significantly. On the other hand it is mentioned that anti-inflammatory potency of Indomethacine is 85 times that of phenyl butazone and 4 times that of hydrocortisone (Winter et al., 1963). So the decrease in the quality and quantity of adhesions by the Indomethacine is mainly due to its anti-inflammatory property.

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SUMMARY

The formation of peritoneal adhesion is a dynamic, non-specific and indiscriminate response of peritoneum to any type of the trauma, regardless of the nature and the site of the traumatizing agent.

The present experimental study was undertaken to assess the comparative effects of various drugs in the prevention of peritoneal adhesions in dogs. This study was conducted in the forty apparently healthy dogs. The peritoneal adhesions were produced by traumatisation of the visceral peritoneum with the help of Surgeon's scrubbing brush, made up of Nylon. A constant trauma was created in all the animals, until petechial haemorrhages were seen, at twenty different places (4 at anterior surface of stomach, 8 at antimesenteric border of small intestine and 8 at antimesenteric border of large intestine).

All the animals were divided in four groups, consisting of 10 animals in each group. First group was kept as control, second group was administered Phenyl butazone, third group was administered Betamethasone and fourth group was administered Indomethacine.

All the animals were re-explored after a period of two weeks and adhesions were graded as follows:

Grade 'O' : No adhesions seen.

Grade I (+) : A single band of adhesion between viscera or a viscera and abdominal wall.

Grade II (++) : Two bands of adhesions between viscera or a viscera and abdominal wall.

Grade III (+++) : More than two bands of adhesions between viscera or whole of the intestine in a mass.

The extent of adhesions was considered as 'O' to I(+) grade mild, II (++) as moderate and III (+++) as severe types.

The assessment of prevention of peritoneal adhesions and comparison of effects of various drugs in the prevention of peritoneal adhesions was done by counting number of adhesions, extent of adhesions and site of adhesions based on numeric score system. A statistical analysis thus obtained was made out. The present study has shown that trauma is the important factor in production of adhesion rather than any other substance used to produce adhesions.

The observations have revealed that these substances, have got their important role in the prevention of peritoneal adhesions which is attributed to their anti-inflammatory action.

On exploration of the abdominal cavity after two weeks period, it was found that 16-Beta-Methyl-9-alpha-fluro prednisolone (Betamethasone) intramuscular was most effective in preventing the peritoneal adhesions, when used at the rate of 0.6 mg/kg body weight. It has got significant reduction of peritoneal adhesions, as compared to the phenylbutazone and Indomethacine.

The Indomethacine, when used orally at the dose rate of 1.5 mg/kg body weight had no harmful effect on the animal and it resulted in reduction of quantity and quality of the adhesions as compared to the phenyl butazone, used at the dose rate of 10 mg/kg body weight, intramuscularly.

It was, therefore, concluded that Bethamethasone has got significant effect in prevention of peritoneal adhesions. Indomethacine has got better effects on the prevention of peritoneal adhesions, as compared to Phenyl butazone.

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