

Preoperative administration effect of metronidazole, ceftriaxone sodium and their combination on stenotic index of jejunal anastomotic segment of dogs

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Abstract : The jejunum is the longest part of the small intestine and its lumen is mainly involved in the absorption of the nutrients. The present study was conducted to evaluate the effects of metronidazole, ceftriaxone sodium and their combination on the stenotic index of the end to end jejunal anastomotic site. To accomplish this, 20 healthy stray dogs were subjected to end to end jejunal anastomosis. Dogs in Group A (control) underwent jejunal anastomosis with no antibiotic prophylaxis, while those in Group B received surgery and metronidazole alone at 50 mg/kg, those in Group C received ceftriaxone sodium intravenously at 30 mg/kg body weight prior to surgery and dogs in Group D were given metronidazole in combination with ceftriaxone sodium at 50 mg/kg and 30 mg/kg, respectively, 2 h before surgical intervention. No significant difference ($p > 0.05$) in the stenotic index was observed at 14 days after jejunal anastomosis. These findings indicate that prophylactic administration of metronidazole and ceftriaxone sodium alone or in combination had no significant effect on the stenotic index of the jejunum.

Keywords : anastomosis, ceftriaxone sodium, jejunum, metronidazole, stenotic index

Introduction

Intestinal anastomosis is an important surgical procedure that connects two ends of the intestine after diseased portion has been removed. Irresolvable intestinal obstruction or devitalization is benefitted from intestinal resection, which reconnects the intestine end-to-end [5, 26]. Numerous surgical procedures have been described to relieve gastric out flow obstruction [7, 20]. Intestinal resection and anastomosis are most commonly performed in dogs and cats for the reason that of foreign bodies, intussusceptions, neoplasia, abscess, trauma, volvulus or torsion, herniation, neurologic disorders, chronic constipation (e.g. feline idiopathic mega-colon) and ulceration etc. [2, 6, 11, 19, 28]. From 1940 to 1965, the antibiotics were in use after gastrointestinal surgical procedures and the use of antibiotics before surgery was controversial during that period. The advances in the prophylactic use of antibiotics recognized the difference between prophylactic and therapeutic use of antibiotics in surgery [15].

Recently Chemoprophylaxis is mostly done to reduce intra-luminal concentrations of bacteria. Bacterial contamination from the contents of intestinal lumen suggests that col-orectal surgery is connected with a predominantly high risk

of surgical wound infections. If antibiotic prophylaxis is not used, almost 40% of human patients develop wound infections after surgical anastomosis. This numeral can be reduced to about 11% when patients take delivery of some form of antimicrobial prophylaxis [23].

As the prophylactic use of different antibiotics has become the current standard of care for gastrointestinal surgical procedures to minimize the chances of postoperative infection. Previous studies showed that such prophylactic use of antibiotics in surgical interventions of intestine might influence the intestinal stenotic index which is described as, "measurement of narrowing/reduction in luminal diameter of intestine". Keeping in view the described facts, the present study was aimed to evaluate the effect of different antibiotics on the stenotic index of the jejunal lumen of dog's small intestine as it is the largest part of small intestine which is mainly involved in the absorption of nutrients. In this study we employed prophylaxis of metronidazole and ceftriaxone sodium alone and in combination before end to end jejunal anastomosis because according to published literature, metronidazole and parenteral cephalosporins are so broadly used and well thought-out as chemoprophylaxis agents for gastrointestinal anastomosis in comparison to the other choices.

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Material and Methods

Experimental Design

Twenty healthy stray dogs were used in this study and randomly divided into four groups A to D with five animals in each group. The studying animals were comprised of twelve males and eight females weighing between 12 to 18 kg. These experimental dogs were identified by collar tags. The dogs of Group A were kept as control and operated for jejunal anastomosis without administering any prophylactic antibiotic regime. The animals of Group B were only given prophylactic metronidazole at the dose rate of 50 mg/kg body weight intravenously, 2 h before surgery. While the Group C dogs were administered intravenously with ceftriaxone-sodium alone at the dose rate of 30 mg/kg, two hours before surgical intervention. The intravenous administration of metronidazole and ceftriaxone-sodium were given in combination to animals of Group D at the dose rate of 50 mg/kg and 30 mg/kg body weight respectively, 2-h prior to surgery [10, 29].

Clinical Examination

Before experimentation, acclimatizing period of fourteen days was provided to all the dogs, so that they get used to the new environment to avoid stress factors. During this acclimatization period, the dogs were subjected to thorough physical and clinical examination for the evaluation of their health status. Hematological parameters including hemoglobin, hematocrit values, total erythrocyte and leukocyte count were determined [12]. Experimental dogs were kept in-door in separate clean stainless steel cages for two weeks pre-operatively to rule out the possibility of any latent or nosocomial infection. Physiological parameters like body temperature, pulse and respiration rates were also recorded daily for one week preoperatively to obtain the baseline data and two weeks following surgical intervention. The experimental dogs were fed on bread and milk. Fresh water was available *ad libitum* except three hours before surgical intervention and six hours post-operatively.

Pre-operative preparations and surgical procedure

Following adequate aseptic preparation of the skin, each dog was positioned as 30° tilted to the horizon in the dorsal recumbency on the Table and whole body was covered with drapes, except the site of surgical intervention. Before the administration of anesthesia, pre-medication of each dog from all four groups was done by administering atropine-sulphate at 0.045 mg/kg body weight through subcutaneous route, half an hour prior to surgical intervention to minimize secretions of the salivary glands and respiratory tract [18]. Thiopentone sodium (Sodium Pentothal; Abbott Laboratories, USA) was used as general anesthesia. It was administered by the slow vein puncture of cephalic vein, at a dose rate of 25 mg/kg body weight.

Firstly, laprotomy procedure was performed described as; umbilicus was considered as surgical landmark. Ventral mid-

line incision of about 12 cm length was made through the skin and subcutaneous tissue with the help of scalpel blade. The dissection was made along the natural lines of cleavage over the lineaalba. Minor bleeding arteries were managed either by surgical gauze and artery forceps. Then peritoneal cavity was opened carefully by a stab incision and the falciform ligament was resected with scissors. This permitted uniform peritoneal contact at the closure, and minimized any risk of wound dehiscence [25]. After exposing the abdominal viscera; a part of the jejunum was selected and packed off for resection. Common jejunal and mesenteric arteries supplying to the selected part were isolated and ligated. The jejunum was transected with a scalpel between the crushing and non-crushing forceps along the edges of the crushing forceps. The resected section of the jejunum, with the two crushing forceps, was removed. The anatomical site of jejunum was then examined critically for the patency and anastomotic leaks. Closure of the abdomen was accomplished by suturing in three layers. Peritoneum and abdominal muscles were sutured together with chromic catgut and by applying simple interrupted sutures. It was followed by a covering continuous subcutaneous sutures applied on the fascia. The skin edges were approximated by the series of horizontal mattress suture with monofilament nylon [6, 28].

Post-operative Observations

Then each animal was then observed for recovery and placed back in the dog ward after recovery. Water was offered *ad libitum* followed by the milk on the postoperative Day 2 and a soft diet on Day 3 postoperatively. Body temperature, pulse and respiration readings were recorded twice a day for the fourteen days after operation. Each animal was given complete antiseptic dressing once daily. After 14 days, dogs were euthanized to find out the effect of treatments on stenotic index.

For determining stenotic index, twelve centimeter long jejunal segments including the anastomotic site were resected and properly washed with saline. A 25% weight by volume solution of barium sulphate saline was made by dissolving it in 100 mL normal saline. Then jejunal segments, sutured on one side by monofilament nylon, were gravity filled with 25% weight by volume solution of barium sulphate. After suturing the other end also, the X-rays of these segments were taken using 60 mm × 50 KVs × 12.5 MAs. The obtained radiographs were used for the assessment of the stenotic index by the following formula [16]. The results for the studied parameter were evaluated after statistical analysis [24].

$$\text{Stenotic index (\%)} = 100 [1 - \{2x / (y + z)\}]$$

Where; x = lumen diameter (cm) at the anastomotic site

y = lumen diameter (cm) 2 cm proximal to the anastomotic site

z = lumen diameter (cm) 2 cm distal to the anastomotic site

Results

For the control group (Group A), average preoperative lumen diameter of jejunum was measured as 1.90 cm. After surgical intervention at Day 14 post-operatively it reduced to 1.12 cm that showed a decrease by 32.75%. The average pre-operative lumen diameter of animals that were treated with metronidazole (Group B) was 1.75 cm, which reduced to 1.26 cm at Day 14 of surgical intervention. The average percentage decrease in lumen diameter of jejunum was 34.61%. The pre-operative average lumen diameter of jejunum for the dogs that were treated with Ceftriaxone sodium (Group C) was 1.81 cm, which on post-operative surgical intervention reduced to 1.30 cm at 14th day. The average percentage reduction in lumen diameter of jejunum in this group was 35.66%. The average lumen diameter of jejunum for the animals that were treated with combination of Ceftriaxone sodium and metronidazole (Group D) was 1.60 cm, which reduced to 1.28 cm at 14th post-operatively. The average percentage reduction in the lumen diameter in this group was 37.83%.

However, all these results concluded that the differences in the post-operative narrowing of jejunum (bowel stenosis) among the animals of all the studied four groups were statistically non-significant.

However, all these results as shown in Table. 1 and Fig. 1 concluded that the differences in the post-operative narrowing of jejunum (bowel stenosis) among the animals of all the studied four groups were statistically non-significant.

Table 1. Statistical analysis for stenotic index

Experimental groups	Mean stenotic index (%)
Control	32.8 ± 4.40
Metronidazole	34.6 ± 5.68
Ceftriaxone sodium	35.7 ± 4.37
Ceftriaxone sodium + Metronidazole	37.9 ± 5.87

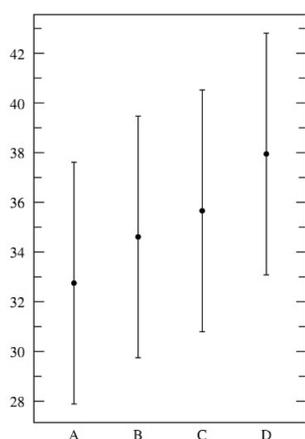


Fig. 1. Graphical representation of stenotic index for studied groups. (A) Control group. (B) Metronidazole administered group. (C) Ceftriaxone sodium administered group. (D) Ceftriaxone sodium + Metronidazole administered group.

Discussion

In recent times, Intestinal surgery has undergone a lot of trials and tribulations. Intestinal anastomosis, that reconnects the intestine end-to-end, has a key concern in resolving the intestinal obstruction and segmental dysfunction/devitalization. The principles for the resection and anastomosis are similar throughout the gastrointestinal tract. In end-to-end intestinal anastomosis/resections, subsequent peritonitis, anastomotic dehiscence and leakage at anastomotic site have been found to be more common in the lower gastrointestinal tract [8, 26]. Post-operative surgical wound infections are a frequent complication of intestinal anastomosis and usually, it is associated with a high incidence rate of post-operative infectious complications and major cause of morbidity and mortality that range from 30–51%, when antimicrobial prophylaxis is not used. While less than 10% of post-operative infectious complications have been reported, in the patients receiving suitable antimicrobial prophylactic agents that has coverage against both aerobic and anaerobic pathogenic micro-organisms [9, 14, 17, 22].

Recently, third generation cephalosporin (Cefotaxime, Ceftriaxone sodium etc.) antibiotics have been extensively administered to attain the effective prophylaxis against the pathogens that cause post-operative surgical complications. Single pre-operative intravenous dose of Ceftriaxone sodium, a third generation cephalosporin antibiotic in combination with metronidazole found to be most effective in dealing with post-operative infections as compared to other first generation and second generation cephalosporin [14, 21, 29]. The combination of ceftriaxone sodium with metronidazole provides wide coverage against both aerobic and anaerobic pathogens [3, 4, 21, 27]. As the lumen of intestine is mainly involved in the absorption and narrowing of intestinal lumen in any case affects the natural absorption rate, it indicates the significance of stenotic index. Keeping in view the above mentioned scenario this study was designed to evaluate the effect of extensively used antimicrobial agents in gastrointestinal interventions.

The barium contrast radiographs study for anastomotic site of jejunum revealed significant decrease in the diameter at anastomotic site of all groups at Day 14 postsurgical intervention. However, differences in the mean stenotic indexes of the dogs of four groups were statistically non-significant. However according to the results, obtained from this study, lowest reduction in the lumen diameter of anastomotic site for jejunum was recorded in Group A (Control) *i.e.* 32.80 ± 4.40%, followed by 34.60 ± 5.68% in Group B (metronidazole) and 35.70 ± 4.37% in Group C. The highest decrease in the luminal diameter of anastomotic site for jejunum 37.90 ± 5.87% was observed in Group D (ceftriaxone sodium + metronidazole). These findings were incongruent with those reported by the Khan *et al.* [13] and Athar *et al.* [1].

These findings could be due to uniformity of the operating procedure and suturing technique adopted. Because through-

out the study same surgical procedure and simple interrupted suturing technique was used for end- to-end jejunal anastomosis [1], as it is the simplest, fastest, safest and biologically sound technique. The simple interrupted suturing pattern results is the lesser adhesions, minimal lumen compromise and a rapid gain in tensile strength, this might be taken as a logical cause for these results [25].

The prophylactic efficacy of these antimicrobials was evaluated in terms of their effect on stenotic index. Among all the four studied groups, no significant difference ($p > 0.05$) was found in terms of stenotic index as significant decrease in the luminal diameter of jejunum was observed in all the dogs of four different groups. The study suggests that the metronidazole and ceftriaxone sodium alone or in combination have no significant effect on the stenotic index of jejunum in the dogs.

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