



*Research Article*

# **Comparative Prophylactic Administration Effect of Metronidazole, Ceftriaxone Sodium and their Combination on the Tensile Strength of End-to-End Jejunal Anastomotic Site in Dogs**

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## **Abstract**

Intestinal resections are most commonly performed in dogs and currently it is involved with extensive use of different antibiotics before surgical intervention. Metronidazole and cephalosporins are considered as best choice for prophylactic use in gastrointestinal operations. Therefore, the study is established to reveal the comparative effect of metronidazole, ceftriaxone sodium and their combination on the tensile strength of jejunal anastomotic site. A total of twenty healthy stray dogs were included in this study. These dogs were randomly divided into four groups, which underwent end to end jejunal anastomosis. The dogs in Group I (control) were operated for jejunal anastomosis without any antibiotic prophylaxis. The metronidazole alone was administered intravenously to dogs in Group II at the dose rate of 50mg/kg while the dogs in Group III were administered with intravenous ceftriaxone sodium at the dose rate of 30mg/Kg body weight two hours prior to surgery. The dogs in Group IV were given metronidazole in combination with ceftriaxone sodium by intravenous route at the dose rate of 50mg/Kg and 30mg/kg respectively two hours before surgical intervention. A significant difference was noted in the tensile strength between the four studied groups ( $P < 0.05$ ). The study concluded that the combination of ceftriaxone sodium with metronidazole was found to enhance the gain in tensile strength significantly i.e. 47.50 %.

**Keywords:** Jejunum, End- to- end anastomosis, Metronidazole, Ceftriaxone sodium, Tensile strength.

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## Introduction

Surgical anastomosis of various parts of intestine is most commonly performed in animals especially in dogs and cats to relieve out the irresolvable intestinal obstruction or de-vitalization (Tobias and Ayres, 2006; Gregory, 2003; Rasmussen, 2002). Jejunum is the longest part of small intestine that increases its possible chance to the surgical intervention at some specific location (Dilawar *et al.*, 2011).

Surgical wound infections are frequent complications following gastrointestinal tract surgery. Infections related to surgical wound consequence in the administration of additional antimicrobial agents. It is extensively approved that appropriate antimicrobial prophylaxis is favorable in gastrointestinal surgery that has high risk to intestinal flora (Dellinger *et al.*, 1994).

Prior 1970, the intestinal anastomotic resections were fraught with post-operative infectious complications which occurred in more than 30-50% of all the surgical approaches to the intestine. Due to recognition of the importance of appropriate prophylactic antimicrobial therapy directed at both aerobic and anaerobic species of bacteria, surgeons have been able to perform single-stage intestinal resections with primary anastomosis routinely. The current century brought the revolution in gastrointestinal surgery, resulting in significant decrease in infectious complications, in animals including dogs with the reduced postoperative complications due to the antibiotic prophylaxis, improved surgical techniques, new anesthesia drugs and protocols as well as both pre & post-surgical management (Nichols *et al.*, 2005). The prophylactic use of antimicrobial agents is the current standard of care prior to gastrointestinal surgery (Basany *et al.*, 2005).

Recently, pre-operative prophylactic antibiotics became a foundation of therapy, the accurate and judicious administration of antibiotics have become performance measures for the excellence perfection and safe surgical procedures worldwide. As it is

obvious from the published literature, to minimize the chances of postoperative infections for the gastrointestinal surgical procedures, the prophylactic use of different antibiotics has become the current standard of care. Metronidazole and ceftriaxone sodium are most commonly administered prophylactic agents for gastrointestinal anastomosis and considered as best choice as compared to other options. Keeping in view the highlighted facts, the purpose of present study was to evaluate the comparative effect of most commonly used prophylactic metronidazole and ceftriaxone sodium on the tensile strength of the jejunal anastomotic segment of dogs.

## Material and Methods

The study comprised of twenty healthy stray dogs that were randomly divided into four groups, with five animals in each group. The studying animals included twelve males and eight females weighing between 14 to 18 kilograms. Each studied group included three male and two female stray dogs. These experimental dogs were identified by collar tags. The dogs of Group-I were kept as control and operated for jejunal anastomosis without administering any prophylactic antibiotic regime. The animals of Group-II were only given prophylactic metronidazole at the dose rate of 50 mg/Kg body weight intravenously, two hours before surgery. While the Group-III 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-IV at the dose rate of 50 mg/Kg and 30 mg/Kg body weight respectively, two hours prior to surgery (Hinchey *et al.*, 1983; Woodfield *et al.*, 2003).

## 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 minimize 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 by following the methods as described by Jain (1986). 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.

### **Surgical Procedure**

Before the administration of thiopentone sodium (general anesthetic agent), each dog from all four groups was pre-medicated by administering atropine-sulphate @ 0.045 mg/ Kg body weight through subcutaneous (S/C) route, half an hour prior to surgical intervention to minimize secretions of the salivary glands and respiratory tract (Plumb, 2008). Thiopentone sodium was administered by the slow vein puncture of cephalic vein, at a dose rate of 25 mg/ Kg body weight. Then laprotomy procedure was performed by following adequate pre-operative measures. Each dog was positioned as 30° tilted to the horizon in the dorsal recumbency and umbilicus was considered as surgical landmark. Ventral midline incision of about 12 cm length was made through the skin and subcutaneous tissue with the help of scalpel blade. 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 (Tavakoli *et al.*, 2007). 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 anastomotic site of jejunum was then examined critically for the patency and anastomotic leaks. Suturing in three layers was accomplished for the closure of the abdomen (Weisman *et al.*, 1999; Fossum, 2007).

After the surgical intervention each dog 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, all the dogs were euthanized to find out the effect of treatments on the tensile strength.

### **Tensile Strength Measurement**

The tensile strength (TS) of the anastomotic site was recorded at day 14<sup>th</sup> post-operatively with a device Schopper's tensile strength tester No. 114-SC type (Yasuda Seiki Seisakusho, Japan). The instrument is specially designed for measuring the tensile strength of vinyl, rubber, leather, copper-wire, fabric and cord etc. This tester is designed and manufactured in accordance with Schopper's mechanism on the basis of principle of balance for measuring tensile strength. For this purpose, the 6 cm intestinal segments containing jejunal anastomotic site were cut 14 days after the operation by euthanizing the all dogs. Following washing of the specimen with normal saline, three 1 x 2 cm strips containing the anastomotic site in the center and three same sized strips from the un-operated part of the jejunum (as control) were cut. Each piece was clumped in the upper and lower chucks of the Schopper's Tensile Strength Tester leaving 1 cm<sup>2</sup> area on the either side of the healing line and subjected to the instrument for the

measurements. Tensile strength was noted as the force units (grams) indicated by the pointer on the holding scale of the tensile tester when the rupture occurred. Similar strips from the healthy (control strips) intestinal segment of all dogs were also evaluated for their tensile strength. The percent gain in the tensile strength (using means of 3) was calculated by the formula (Booth, 1968).

Gain in the tensile strength =  $\frac{\text{Mean TS of strips with anastomotic site}}{\text{Mean TS of control strips}} \times 100$

Mean TS of control strips

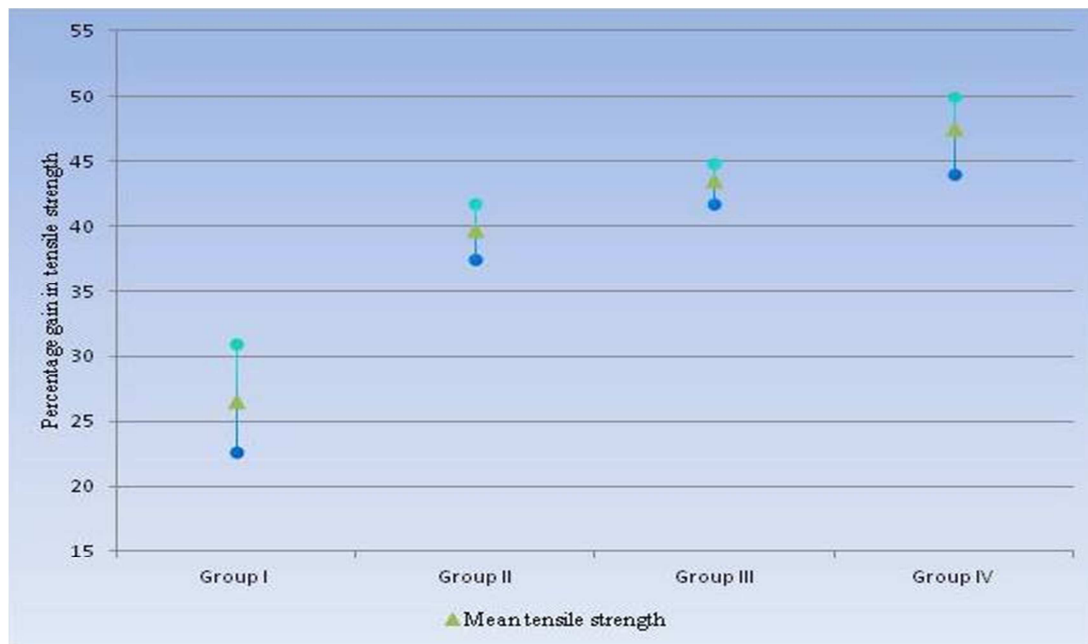
### Results

The average gain in the tensile strength of the Group I animals was 26.50 percent. For this group, the results for gain in tensile strength were ranging between 22-31 percent. The lowest gain in tensile strength, in this group, was 22.73 percent. While the highest gain in tensile strength 30.95 percent was recorded in this group. The dogs that were prophylactically administered with metronidazole (Group II) revealed 39.70 percent average gain in the tensile strength. The percentage gain in tensile strength of this group was found to

be significantly higher than Group I. The gain in tensile strength of metronidazole treated group was ranging between 37-42 percent. The highest recorded gain in tensile strength was 41.67 percent, while 37.50 percent was the lowest recorded gain in tensile strength. The group of dogs that were prophylactically administered with only ceftriaxone sodium (Group III), the highest average gain in tensile strength 44.83 percent was recorded. The average gain in tensile strength of this group 43.6 percent was significantly higher from Group I and Group II. The gain in tensile strength of this group was ranging between 41-45 percent, with highest gain in tensile strength recorded as 44.83 percent. While 41.67 was the lowest gain in tensile strength of this group. The average gain in tensile strength recorded, for the animals that were prophylactically administered with combination of ceftriaxone sodium and metronidazole (Group IV), was 47.50 percent which is significantly higher than the dogs of Group I, Group II and Group III. The gain in tensile strength of this group was ranging between 44-50 percent with the highest value of gain in tensile strength recorded as 50.0 percent. However, the lowest gain in tensile strength of this group was 44.0 percent.

**Table I: Pre-Operative Prophylactic Effect of Treatment Groups on Tensile Strength of Anastomotic Portion of Jejunum**

Experimental Groups	Mean Tensile Strength (%)
Control	26.5 ± 3.44
Metronidazole	39.7 ± 1.50
Ceftriaxone Sodium	43.6 ± 1.29
Ceftriaxone Sodium+ Metronidazole	47.5 ± 2.27



**Figure 1: Graphical Representation for the Gain in Tensile Strength of Studied Groups**

### Statistical Analysis

The analysis of variance (ANOVA) statistical test was applied to the data obtained from the findings of mean tensile strength of each group and results expressed that among all the four studied groups, a highly significant difference was observed as probability is less than 0.01 ( $P < 0.01$ ). The highest percentage gain in tensile strength of jejunum  $47.5 \pm 2.27$  percent was observed in animals that were treated with combination of Ceftriaxone Sodium and Metronidazole (Group IV). While the lowest percentage gain in tensile strength  $26.5 \pm 3.44$  was recorded in animals of control group (Group I).

### Discussion

Restoration of normal tissue strength is among the most accepted and reliable indices of wound healing (Van Winkle, 1969; Athar *et al.*, 1996). In case of intestinal anastomosis, tensile strength is not a function of the length of the incision or of the thickness of the tissue rather, it is determined in term of load applied per unit

of cross section area. In the present study, increase in the tensile strength of the anastomosed jejunal segment was measured on day 14 postsurgical intervention following the techniques of Athar *et al.*, (1996). Jejunal anastomotic segments of the dogs that were administered prophylactically with single dose of intravenous ceftriaxone sodium alone (Group III) and in combination with metronidazole (Group IV) had statistically highly significant increments in tensile strength (Table I) as compared to the remaining two regimens i.e. prophylactically single dose intravenous administration of metronidazole alone (Group II) and control group that was not given any prophylactic antibiotic (Group I). Moreover, the jejunal anastomotic segments of the dogs that were administered pre-operatively with single intravenous dose of metronidazole (Group II) also had statistically significant increase in tensile strength (Table I) as compared to control group (Group I). The least gain in tensile strength was observed in control group and it might be related to the

presence of infective organisms at the anastomotic site.

In all three treatment groups (Group II, Group III and Group IV), the gain in the tensile strength seems to be due to reduction in the colonization of normal and pathogenic micro-organisms, which on getting chance might contaminate the anastomotic wound and ultimately causing post-operative infections. These results concur with those reported by Athar *et al.*, (1996), Hayashi and Wilson (2009), Wang *et al.*, (2003), and Woodfield *et al.*, (2003). Statistically lesser gain in tensile strength recorded in the control animals. It was observed that during study, the animals of this group had suffered from fever for three to four days that's why the gain in the tensile strength was lower than the groups having single dose of intravenous antibiotic prophylaxis. These findings are also inline with those of Athar *et al.*, Cai (1992), Leaper (1994), Lindhagen *et al.*, (1981), Mittermayer *et al.*, (1984) Ono *et al.*, (1990) Parker *et al.*, (1985) Playforth *et al.*, (1988) and Takesue *et al.*, (2000). As for the choice of antimicrobial agents, it is general consensus worldwide that administration of prophylactic antibiotics should be intravenous as single dose preferably 1 hour to 30 minutes before surgery. In our study it is thus not surprising that ceftriaxone sodium in combination with metronidazole has more prophylactic efficacy. This high prophylactic efficacy might be due to specific pharmacokinetic profile of these antimicrobials which ensures the bactericidal actions against aerobic and anaerobic pathogenic organisms. Similar results for prophylactic efficacy of ceftriaxone sodium in combination with metronidazole also discussed by Athar *et al.*, (1996), Gravante and Caruso (2009), Lalla (2009), Rau *et al.*, (2000) and Ross *et al.*, (2009).

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