



Efficacy and Safety of Three Doses of Ceftriaxone and Metronidazole as Prophylactic Uses during Acute Non-Perforated Appendicitis Surgical Operation: A Randomized Control Trial

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Abstract

Background: This study compared the efficacy of prophylactic antibiotics with seven days of conventional antibiotics. **Objective:** This present study was carried out to evaluate the effectiveness of three doses of prophylaxis with ceftriaxone and metronidazole. **Methodology:** This parallel arm, randomized control trial was conducted among fifty patients, consisting of 25 cases and 25 controls, with acute appendicitis admitted at Dhaka Medical College Hospital, Popular Medical College Hospital, Dhaka, and Ad-din Barrister Rafique Ul-Haq Hospital, Dhaka, during the period of November 2021 to April 2022. This study was done to evaluate the efficacy of three doses of combined prophylactic antibiotics, ceftriaxone and metronidazole, in acute non-perforated appendicitis cases. The patients in the control group were treated with seven days of conventional antibiotic therapy to compare the efficacy with three doses of prophylactic antibiotics. **Results:** Among 9 wound infections (15%), 4 patients were in the control group (36.5%), and 5 (40.5%) were in the case group in the study group with combined surgical prophylaxis of ceftriaxone and metronidazole ($P=0.001$). One patient develops both a wound infection and an intra-abdominal abscess. The study also found that amount to patient (3.3%) with intra-abdominal abscess formation 01 (50%) in control group and 01(50.0%) in combined prophylaxis group (ceftriaxone and metronidazole) ($P>0.3$). **Conclusion:** In conclusion no significant difference could be found between the patients who received combined three doses of ceftriaxone and metronidazole and the control groups with regard to age, sex, distribution of symptoms before admission, preoperative temperature, duration of surgery, hospital stay, and concomitant diseases both overall and within each of the three groups of appendiceal examination. [*Bangladesh Journal of Infectious Diseases, June 2023;10(1):11-15*]

Keywords: Prophylaxis; appendicitis; appendectomy

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Introduction

Surgical prophylaxis is used to prevent infection following a surgical procedure¹. Surgical prophylaxis is better and more preferable to long-term conventional therapeutic antibiotic treatment because it is less expensive and because overuse of antibiotics can lead to superinfection by suppressing normal gut flora and the development of antibiotic resistance by plasmid or bacterial genetic mutation². Without antibiotic prophylaxis, the wound infection rate is even higher, increasing to 30.0% when appendices are phlegmonous or gangrenous³⁻⁵.

Two drugs, like ceftriaxone and metronidazole, have been used in this study because bacteriological examination of the inflamed appendix and pus from subsequent wound infections after appendectomy often reveal a mixture of both aerobic and anaerobic organisms like *Escherichia coli* and *Bacteroides fragilis*⁶. Ceftriaxone is active against all the clinically important gram-negative facultative bacteria except pseudomonas and many *Enterobacter* species.

Therefore, the administration of prophylactic combined ceftriaxone and metronidazole covers the possible infective organism and provides suitable prophylaxis against wound infection and intra-abdominal abscess formation following appendectomy. The aim of this study was to evaluate the efficacy and safety of three doses of combined surgical prophylaxis with ceftriaxone (1 gram) and metronidazole (500 mg). Given the circumstances, the first dose was given before the operation, the second dose 12 hours after the appendectomy, and the third dose 24 hours after the operation.

Methodology

Study Settings and Population: This was a single centre, parallel arm, open level randomized control trial. This study was conducted with patients who were clinically diagnosed as having acute appendicitis and admitted to the surgery departments of Dhaka Medical College Hospital, Dhaka, Bangladesh; Popular Medical College Hospital, Dhaka, Bangladesh; and Ad-din Barrister Rafique Ul Huq Hospital, Dhaka, Bangladesh. The study period was from November 2021 to April 2022, a period of six months. The study population was divided into the intervention group and control group. Patients with appendicitis who were admitted to the surgery departments of the Popular Medical College Hospital, Dhaka, Bangladesh and the Ad-Din

Barrister Rafique Ul Huq Hospital, Dhaka, Bangladesh were selected as the study population.

Randomization and Allocation: The intervention group received three doses of combined surgical antibiotic prophylaxis with ceftriaxone and metronidazole. The alternative patients, who were admitted to the same hospital with acute appendicitis during the same period but were given a conventional 7-day antibiotic regimen, were taken as the control group by way of a semi-structured questionnaire. An observational checklist was used for the collection of socio-demographic information and the collection of information by taking history. clinical examination of the patients with acute appendicitis and the findings of their relevant laboratory investigations like TC, DC, USG of the abdomen, X-ray KUB. Information was also collected regarding postoperative complications like wound infections and intra-abdominal abscess formation.

Surgical Intervention: Before operation, patients were excluded who had a known allergy to ceftriaxone, were moribund comatose with renal function or in shock, or had taken antibiotics within 3 days before surgery, were lactating or pregnant, were children under the age of 12 years, or had a ruptured or burst appendix. Appendectomies were performed according to routine procedures normally performed by younger doctors. Only absorbable suture materials were used, except for skin, where non-absorbable material was used.

Follow-Up and Outcome Measures: The patients were observed for signs and symptoms of wound infection and intra-abdominal abscess. At least two of the following characteristics were present like continuous pyrexia, a palpable mass in the right iliac fossa or discharge from the rectum like post-operative diarrhea. Peak temperature was recorded daily throughout the hospitalization. At discharge from the hospital, the wound was inspected, and a digital perineal examination was done. Ages, sex, duration of symptoms and signs before admission, concomitant diseases, and operation time were recorded.

Statistical Analysis: After the collection of all response data, it was processed accordingly, and the results were analyzed with SPSS and presented in tables. Different associations were assessed with the help of relevant statistical tools and techniques. Pearson's chi-square test was used in order to make certain that there was no significant difference between the two treatment groups.

Ethical Clearance: All procedures of the present study were carried out in accordance with the principles for human investigations (i.e., the Helsinki Declaration) and also with the ethical guidelines of the Institutional Research Ethics. Formal ethics approval was granted by the local ethics review committee. Participants in the study were informed about the procedure and purpose of the study and the confidentiality of the information provided. All participants consented willingly to be a part of the study during the data collection periods. All data were collected anonymously and analyzed using the coding system.

Results

Among 50 patients with clinically diagnosed as acute appendicitis, 20(41.6%) patients of them were male and 30(54.4%) patients were female. Females were significantly affected, and the female-to-male ratio was 1.4:1. The mean age of patients was 23.5 yeSD (\pm SD 5.38) with a range from 12 years to 46 years and maximum age group were 12 to 17 years like 8(32%) cases followed by 18 to 22 years 6(24%) cases (Table 1).

Table 1: Age Distribution of the Patients (n=50)

Age Group	Intervention Group	Control Group
12 to 17 Years	8(32.0%)	8(32.0%)
18 to 22 Years	6(24.0%)	6(24.0%)
23 to 28 Years	5(20.0%)	5(20.0%)
29 to 34 Years	3(12.0%)	3(12.0%)

Age Group	Intervention Group	Control Group
35 to 40 Years	2(8.0%)	2(8.0%)
41 to 46 Years	1(4.0%)	1(4.0%)
Total	25(100.0%)	25(100.0%)

In this study, patients were divided into 3 groups: normal, acutely inflamed appendix, and gangrenous (Table 2).

Table 2: Distribution of the Patients with State of Appendix

State of Appendix	Intervention Group	Control Group
Normal	24	21
Acute	16	14
Gangrenous	4	6

The study findings revealed that no significant difference could be found between the patients who received combined 3 doses of ceftriaxone and metronidazole (the prophylaxis group) and the control groups with regards to age, sex distribution, duration of symptoms before admission, duration of surgery, and concomitant diseases (Table 3).

The study finding showed that among 9 wound infections (15%), 4 patients were in the control group (36.5%), and 5 (40.5%) were in the case group in the study group with combined surgical prophylaxis of ceftriaxone and metronidazole ($P = 0.001$). One patient develops both a wound infection and an intra-abdominal abscess (Table 4).

Table 3: Patients Population According to Gender, Duration of Symptoms Before Admission, Concomitant Diseases and Duration of Surgery

Variables	Normal		Acute Appendicitis		Normal	
	Intervention Group	Control	Intervention	Control	Intervention	Control
Male/Female (20/30)	1/2	1/2	14/17	4/3	2/4	3/6
Duration of Symptoms Before Admission (Hours)	36.2	36.3	24.1	24.8	27.6	38.2
Concomitant Diseases	1	1	2	3	6	5
Surgery Duration(Minutes)	44.2	44.6	41.6	40.5	40.3	41.0

Table 4: Wound Infection after Appendectomy (n=25)

State of Appendix	Intervention	Control	P value
Normal	1(3.3%)	1(3.3%)	<0.001
Acute	1(3.3%)	2(6.6%)	<0.0001
Gangrenous	3(10%)	1(3.3%)	<0.0001
Total	5(16.6%)	4(15%)	<0.0001

The study also found that amount to patient (3.3%) with intra-abdominal abscess formation 01 (50%) in control group and 01(50%) in combined prophylaxis group (ceftriaxone and metronidazole) ($P>0.3$) (Table 5).

Table 5: Intra-abdominal Abscess Formation after Appendectomy

State of Appendix	Intervention	Control
Normal	0/25 (0%)	0/25 (0%)
Acute	0/25 (0%)	0/25 (0%)
Gangrenous	1/25 (3.3%)	1/25 (3.3%)
Total	1/25 (3.3%)	1/25 (3.3%)

Intervention group=Ceftriaxone + Metronidazole Prophylaxis;

Discussion

This study showed that the overall wound infection rate after appendectomy in non-perforated cases of appendicitis can be reduced with combined three doses of prophylactic ceftriaxone and metronidazole. However, regarding intra-abdominal abscess formation, no significant difference was found between the two groups. Factors responsible for the incidence of wound infection are abdominal drains; patients with perforated or ruptured appendicitis were excluded from this study. The study findings demonstrated that almost half of the wound infections (5 patients) were detected after discharge from the hospital and also strongly indicate the need for follow-up with the patients.

The patients were observed for signs and symptoms of wound infection and intra-abdominal abscess. A wound infection was defined as the discharge of pus from the wound, and an intra-abdominal abscess was diagnosed either by rectal examination, by using ultrasonography, or when at least two of the following three characteristics were present like continuous pyrexia with any other focus after operation, a palpable mass in the abdomen or a discharge of pus from the rectum, i.e., postoperative diarrhoea. Peak temperature was recorded daily throughout the hospitalization.

By using the combined prophylactic antibiotics ceftriaxone and metronidazole, the incidence of wound infection in this study was definitely lowered ($p=0.001$) than that found in other studies using ceftriaxone, ticarcillin, and metronidazole alone.

The mean hospital stays of wound infection patients that occurred with combined three doses of antibiotic prophylaxis and the control group in this study were almost similar. However, routine three-dose combined antibiotic prophylaxis with ceftriaxone and metronidazole can be recommended for appendectomies in patients with acute appendicitis, i.e., the first dose before starting the operation, the second dose 12 hours after the appendectomies, and the third dose 24 hours after the operation.

Conclusion

This study established the value of three- dose combined prophylactic antibiotics of ceftriaxone and metronidazole against both anaerobic and aerobic organisms in reducing the incidence of wound infection to a minimum after appendectomy in non-perforated cases. So, routine three-dose combined antibiotic prophylaxis with ceftriaxone and metronidazole can be recommended for appendectomy patients with acute appendicitis. As the sample size of this study was small, further study with a larger sample size could be recommended.

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None

Conflict of Interest

We declare that we have no conflict of interest.

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Contribution to authors:

Quddus MA, Jahan N, Yusuf MA: Conception and design, or design of the research; or the acquisition, analysis, or interpretation of data; conceptualized and designed the overall study. Quddus MA: involved in data collection; Drafting the manuscript or revising it critically for important intellectual content. Quddus MA, Jahan N: involved in data input and data cleaning. Meherun Nesa, Una Jessica sarker: conducted data analysis. Syeed-UI-Alam SM, Talukder AR: drafted the manuscript. All authors reviewed and approved the final manuscript.

Data Availability

Any questions regarding the availability of the study's supporting data should be addressed to the corresponding author, who can provide it upon justifiable request.

Ethics Approval and Consent to Participate

The Institutional Review Board granted the study ethical approval. Since this was a retrospective study, not every study participant provided formal informed consent. Each method followed the appropriate rules and regulations.

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