

Brief communication (Original)

Optimum duration of perioperative antibiotic therapy in patients with acute non-perforated appendicitis: a prospective randomized trial

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Background: Inappropriate use of antibiotics for perioperative antimicrobial therapy can cause considerable complications including emergence of antibiotic resistance, risk of drug reactions and economic implications.

Objective: We assessed the use of antibiotics in patients with acute non-perforated appendicitis.

Methods: The study was performed on 317 patients aged 15 to 70 years with non-perforated appendicitis who were undergoing open appendectomy. All patients received intravenous ceftriaxone (1 g) and metronidazole (500 mg) immediately after appendectomy. Patients were randomized into one of the following three treatment protocols; A: no further antibiotics, B: three more doses of antibiotics for 1 day (ceftriaxone 1 g every 12 hours and metronidazole 500 mg every 8 hours), or C: a 3-day course of antibiotics (ceftriaxone 1 g every 12 hours and metronidazole 500 mg every 8 hours) as the postoperative antibiotic regimen. Postoperative infective complication was the primary endpoint within the 10-day postoperative follow-up period.

Results: A total of 291 patients (female 37.5%), were subjected to final analysis. This included 97 patients in each group. Twenty-six patients failed to return for wound assessment. The groups were comparable in baseline characteristics including age and gender. The Overall frequency of surgical site infection was 6.25%, with 8.2% in group A, 6.25% in group B and 5.2% in group C. The rate of postoperative surgical infection was not significantly different among all groups. There were no perioperative mortalities. No untreated control group could be included for ethical reasons.

Conclusion: A combined preoperative single dose of metronidazole and ceftriaxone appears to be sufficient for the prevention of surgical site infections in patients with uncomplicated appendicitis.

Keywords: Acute appendicitis, ceftriaxone, metronidazole, prophylactic antibiotic therapy

Acute appendicitis is a common cause of acute abdominal pain that requires surgical intervention [1]. Appendectomy is one of the most common surgical procedures [2], which may result in surgical site infection could complicate 1 to 5% of appendectomy cases [3-5]. Duration of operation is one of the risk factors for surgical site infection in appendectomy [1].

Although antibiotic prophylaxis is common in surgery, inappropriate use of antibiotics occurs in 25

to 50% of general elective surgical procedures [6-10]. The efficacy of antibiotic prophylaxis in acute appendicitis has been examined in several studies [5, 11-15]. Several trials have shown that prophylactic antibiotic therapy can significantly reduce the risk of surgical site infection in non-perforated appendicitis compared with placebo [16-19]. However, few studies have addressed the optimum duration of prophylactic antibiotic administration for non-perforated appendicitis. Therefore, the present study sought to investigate this issue in a prospective randomized trial in Iranian patients with non-perforated appendicitis.

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Methods

This prospective randomized study was conducted from May 2006 to May 2007 at the Ghaem Hospital (Mashhad, Iran). Patients aged 15 to 70 years who were admitted with the clinical diagnosis of acute appendicitis, and were undergoing open appendectomy through a right lower quadrant incision were considered to be eligible for this study.

The project was approved by the Ethics Committee of the Mashhad University of Medical Sciences. Informed consent for the study was obtained from patients. Excluded were patients with diabetes mellitus, history of preadmission antibiotics and/or steroid and/or immunosuppressive therapy, allergy to any of the medications, ruptured appendicitis and appendiceal mass or abscess formation. Pregnant women and patients who refused to consent to the study were also excluded.

Intravenous ceftriaxone (1 g) and metronidazole (500 mg) were given at the time of induction of general anesthesia. Immediately after appendectomy, patients who were diagnosed with non-perforated appendicitis were randomized into one of the following 3 treatment protocols; A: no further antibiotics, B: three more doses of i.v. antibiotics for 1 day (ceftriaxone (1 g) every 12 hours and metronidazole (500 mg) every 8 hours), or C: a 3-day course of antibiotics (ceftriaxone (1 g) every 12 hours and metronidazole (500) mg every 8 hours) as the postoperative antibiotic regimen. Open appendectomy was performed through right lower quadrant incision by muscle-splitting approach and appendices were removed in the standard fashion.

Operating time was recorded from the time of first incision to closing skin, ranging between 32 to 46 minutes. All removed appendices were examined histologically. The wound was inspected daily for signs of infection, defined as discharge of pus that required

surgical drainage before discharge. After discharge, all patients were followed for wound infection for 10 days.

Statistical analyses were performed using SPSS software (version 11). Group comparisons were made using one-way analysis of variance (ANOVA) for numerical variables, and chi-square (χ^2) test for categorical variables. A *p*-value of <0.05 was considered to be statistically significant.

Results

During the study period, 317 patients were diagnosed intraoperatively to have non-perforated appendicitis and underwent open appendectomy. Among them, 26 patients failed to return for wound assessment. Finally, 291 patients (mean age: 26.20 ± 10.28 ; females: 37.5%), were subjected to final analysis. Of these, 97 patients were in group A), 97 patients received 1-day (group B) and 97 patients received 3-day postoperative antibiotic regimen as described above. The groups were comparable in baseline characteristics including age and gender as shown in **Table 1**. Duration of hospitalization was not statistically different between groups B and C ($p > 0.05$). However, both B and C group had significantly higher length of hospitalization compared to group A ($p < 0.001$).

Nineteen surgical site infections were identified in 291 subjects, yielding an overall wound infection rate of 6.52%. Eight patients in group A (8.2%), 6 patients in group B (6.25%), and 5 patients in group C (5.2%) had wound infections (**Figure 1**). These frequencies of postoperative surgical infection were not significantly different among the groups. During the study period, none of the patients developed intra-abdominal collections or abscess nor other antibiotic related complications. There was also no perioperative mortality.

Table 1. Characteristics of study groups

Parameter	Total	Group A	Group B	Group C
Number	291	97	97	97
Mean age (years)	26.20 ± 10.28	24.77 ± 8.79	26.82 ± 11.51	26.93 ± 10.33
Male:Female	182:109	63:34	56:41	63:34
Duration of hospitalization (days)	2.80 ± 0.52	2.24 ± 0.43	$3.02 \pm 0.28^*$	$3.11 \pm 0.31^*$

*Significant difference compared to group A

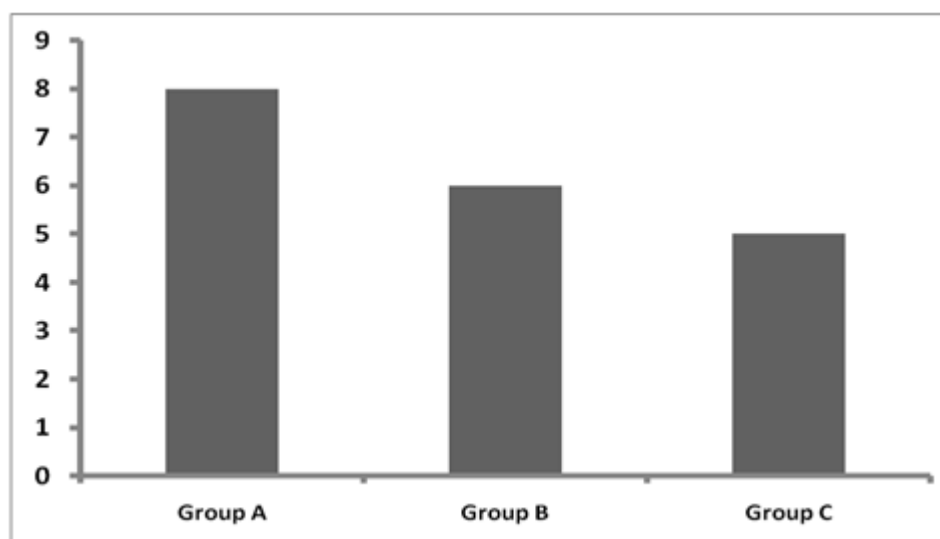


Figure 1. Frequency of infection rate in 3 different treatments

Discussion

Despite improved surgical techniques, postoperative complications including wound infection and intra-abdominal abscess still account for a significant rate of morbidity. It has been shown that antibiotic prophylaxis is effective in prevention of postoperative complications in appendectomised patients, whether the administration is given pre-, peri- or post-operatively [2].

There is variation in the incidence of postoperative infection for non-perforated appendicitis, ranging from 0 to 11.7% [17-21]. These discrepancies could be attributed to differences in the number of patients, type of antibiotics used, follow-up duration and definition of wound infection. In our study, wound infection rate was between 5.2 to 8.2% which is consistent with previous studies [22].

In the present trial, there was no intra-abdominal abscess or collection. In consistence with a previous study [20], our findings showed that a single dose of prophylactic antibiotic is enough to prevent infective complications following open appendectomy for non-perforated appendicitis. Furthermore, our results are supported by recent randomized controlled trials [23, 24], showing that even in complicated appendicitis, prolonged use of antibiotics did not decrease the rate of postoperative infective complications.

The relatively few number of included subjects was a limitation of the present study. Therefore, conducting larger trials may be required to detect

significant differences among treatment arms, if any. Taken together, a combined single dose of metronidazole and ceftriaxone preoperatively appears to be sufficient to prevent surgical site infections in patients with uncomplicated appendicitis. We recommend that preoperative antibiotic prophylaxis be administered to all patients undergoing appendectomy.

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