Metronidazole in Acute Non-perforated Appendicitis

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ABSTRACT

Objective — *To compare the infective complication rate after open appendicectomy in patients with non-perforated appendicitis receiving cefazolin with metronizadole and cefazolin alone.*

Study design — *Randomised controlled trial.*

Place & Duration of study — *PAEC General Hospital Islamabad, from March 2015 to June 2016.*

Methodology — *Patients with acute non-perforated appendicitis were divided into two groups. Group A patients received cefazolin with metronizadole and Group B received only cefazolin. A total of three doses were given, one preoperatively and two postoperatively in each group. Patients in both groups were followed up for 30 days postoperatively for any surgical site infections (SSI).*

Results — *A total of* 242 *patients were operated of whom* 11 *were excluded as they did not come for follow-up. There were* 111 *patients in group A and* 120 *in group B. Infection rate in group A patients was 7.21 % and in group B, 8.33%. There was no significant difference of wound infection in both the groups (p=0.427).*

Conclusion — *Addition of metronizadole in patients with non-perforated acute appendicitis did not reduce the rate of surgical site infection.*

Key words — *Acute Appendicitis. Surgical site infections. Cefazolin. Metronizadole. Appendicectomy.*

INTRODUCTION:

Acute appendicitis is one of the commonest surgical emergencies.[1] Diagnosis of acute appendicitis is made on clinical history, physical examination, laboratory and radiological findings.[1,2] *E. coli* and *Bacteroides fragilis* (anaerobe) are the main pathogens involved in pediatric appendicitis-related peritonitis.[3-5] *E. coli* was identified in 81% of peritoneal swab specimens in appendicitis patients followed by anaerobes (54%), *Pseudomonas aeruginosa* (6%) and *Streptococcal* species were identified in 7% specimens.[6]

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The incidence of postoperative surgical site infections after appendicectomy in patients with non-perforated appendicitis has been reported to range from 0% to 11%.[7-12] Disease process at the time of operation and the use of appropriate prophylactic antibiotics significantly affects the risk for postoperative surgical site infections in addition to patient's factors.[8,12] The efficacy of antibiotics in reducing the risk of surgical site infections following appendicectomy has been well established in the literature.[13] In most of the cases of appendicitis, metronizadole is used either intravenously or orally as it is among the most effective drug against anaerobic bacteria.[7-14]

Role of metronidazole in the treatment and prevention of infective complications in cases of acute non-perforated appendicitis following appendicectomy has not been adequately addressed in the literature. The aim of the present study was to compare the infective complication rate after open appendectomy

for non-perforated appendicitis in patients receiving first generation cephalosporin, with and without metronizadole as prophylaxis.

METHODOLOGY:

This was a randomized controlled trial conducted in the Department of Surgery, Pakistan Atomic Energy Commission General Hospital, Islamabad, Pakistan, from March 2015 to June 2016. IRB approval was taken. Informed consent was taken from all the patients.

Patients who were admitted with the clinical diagnosis of acute appendicitis and scheduled for open appendicectomy, were considered eligible for this study. Patients who had received oral or intravenous (I/V) antibiotics within 72 hours of admission, age < 5 or > 60 year, diabetics, pregnant, immunocompromised or had complicated appendicitis (mass, perforation or abscess) or normal appendix on histopathology, were excluded from study. In addition those patients who were lost to follow up were also excluded.

Patients were alternately allocated into group A and B. Group A patients received a preoperative single dose of cefazolin and metronidazole, and two doses postoperatively. Group B patients received single dose of cefazolin preoperatively and two doses postoperatively. Open appendicectomy was performed by the standard operating technique. All the specimens were sent for histopathological examination. Patients of both the groups were discharged when they were fully mobilized, afebrile, could tolerate normal diet, with evidence of normal bowel activity and had adequate pain control on oral analgesics. On discharge, patients were booked for follow-up visit in surgical clinic on the 4^{th}, 7^{th} and 10^{th} postoperative day for wound assessment. Stitches were removed on 10^{th} postoperative day. They were also advised to report immediately to the hospital in case of fever, tenderness or any discharge from the wound site. Last follow-up visit was arranged 20 days after removal of stitches. Surgical site infection was defined as fever above 38^{o} F for at least 24 hours or pus discharge from the wound that necessitated wound opening and drainage. Intra-abdominal collection was defined as the fluid collection inside the peritoneal cavity confirmed by ultrasound or computed tomography that required drainage. All the infected wounds were managed by laying open the wound, wound toilet with normal saline, and loose packing of the wound followed by secondary closure or healing by secondary intention.

Data regarding the demography, fever and white cell count at admission, operative findings, postoperative antibiotics, hospital stay, and complications were collected and tabulated into Microsoft Office Excel 2007 for the calculation of mean values and standard deviation. Student t-test was used to compare the continuous variables. The rates of surgical site infections for both the groups were calculated on SPSS 16 and categorical variables were compared by Chi square test. The p-value of < 0.05 was considered as statistically significant.

RESULTS:

A total of 242 patients, who fulfilled the inclusion criteria, were alternately assigned to either of the groups A and B. Ten patients in group A and one in group B were lost to follow, leaving 111 patients in group A and 120 in group B. There was no significant difference between mean age, WBC count and duration of hospital stay between the groups (table I).

One hundred and eleven patients received cefazolin and metronidazole in perioperative period while one hundred and twenty patients received cefazolin only. Eight patients in group A (7.21%) and ten patients in group B (8.33%) developed surgical site infection (p = 0.427). They were managed by the standard protocol. All the infected wounds had healed within 30 days of follow-up. None of the patients developed intra-abdominal collection. Mean hospital stay was

Table I: Comparison between group A and B

Variables	Group A	Group B	p-value
Number of patients	111	120	
Male to Female ratio (M:F)	1.13:1	1.12:1	
Mean age (Year)	24.71 ± 10.54	26.72 ± 8.28	0.111
Admission white cell count (10^9/l)	10118 ± 2855	9997 ± 2652	0.741
Hospital stay (Days)	2.61 ± 0.59	2.52 ± 0.50	0.227
Surgical site infections	8 (7.21%)	10 (8.33%)	0.427

2.61 ± 0.59 for group A and 2.52 ± 0.5 days for group B patients (p = 0.227). There was no mortality amongst patients during the study period.

DISCUSSION:

Appendicectomy for acute appendicitis is a potentially infected surgery with the risk of developing wound infection of up to 11%.[15] Rate of infection greatly depends on the severity of appendicular inflammation or perforation and also on the use of appropriate antibiotics. The role of preoperative antibiotics in surgical prophylaxis is clearly defined. First generation cephalosporin or amoxicillin plus clavulanic acid and metronizadole are traditionally prescribed in cases of acute appendicitis. Role of metronizadole in preventing infective complications in cases of acute non perforated appendicitis is not clear**.** Risk of wound infection by gram positive cocci is the greatest, and the use of metronidazole remained controversial.[16]

al-Dhohayan A et al reported amoxicillin plus clavulanic acid to be as effective and well-tolerated as metronidazole/gentamicin in the prevention of wound infection following appendicectomy. The overall incidence of wound infections in a study in the amoxicillin plus clavulanic acid group was 8% as compared to 14% in the metronidazole/gentamicin group.[16] In our study, we also found no benefit of adding metronizadole in preventing wound infections.

In 1995, Liberman and colleagues reported a high rate of wound infection (11.1%) among the patients who had received only preoperative cefoxitin compared to the patients who were given both pre and postoperative cefoxitin (1.9%). However, they found no infective complication in their third group of patients, who had received a single dose of preoperative cefotetan. Thus, they recommended a single dose of preoperative cefotetan or pre and postoperative Cefoxitin as the optimal prophylaxis for non-perforated appendix[17]. They did not include metronizadole in antibiotic regimen. Therefore, the choice of preoperative antibiotic is an important issue, rather than addition of postoperative antibiotics.

Le and associates retrospectively compared patients of nonperforated appendicitis who received a single dose of preoperative antibiotics with those who were given postoperative antibiotics in addition to preoperative prophylaxis.[18] They observed no significant difference in surgical site infection rate between the groups (10% vs. 9%, p = 0.64). In our study we used single preoperative antibiotic dose and two postoperatively. There was no significant difference of wound infection rate between the two groups.

Metronizadole has different side effects like unpleasant metallic taste or dry mouth, stomach pain, diarrhea, dizziness, loss of balance, vaginal itching or discharge, cough, sneezing, runny or stuffy nose, swollen or sore tongue, but sometimes it can cause fatal side effects like encephalopathy.[19] In our study, we did not compare the side effects of metronizadole in between two groups which might add more value in our study.

CONCLUSIONS:

Prophylactic combination of metronizadole and first generation cephalosporin had no added benefit in preventing post appendicectomy wound infection in non perforated acute appendicitis. Moreover, such cases may be managed by single agent prophylaxis i.e first generation cephalosporin as supported by our study.

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