

Role of Postoperative Antibiotics After Appendectomy in Non-Perforated Appendicitis

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ABSTRACT

Objective: To determine the role of postoperative antibiotics in reducing the surgical site infections (SSIs) after open appendectomy in patients with non-perforated appendicitis (NPA).

Study Design: Randomized controlled trial.

Place and Duration of Study: The Department of Surgery, King Saud Medical City, Riyadh, Kingdom of Saudi Arabia, from January 2010 to July 2011.

Methodology: Three hundred and seventy seven patients, who underwent appendectomy for NPA and fulfilled the selection criteria, were randomized into two groups. The patients in group A received a single dose of pre-operative antibiotics (cefuroxime sodium and metronidazole), while the group B patients received one more dose of the same antibiotics postoperatively. Patients of both the groups were followed-up for 30 days to assess the postoperative infective complications.

Results: Group A had 195, while group B comprised of 182 patients. The groups were comparable in the baseline characteristics. Statistically there was no significant difference in rates of SSIs between both the groups ($p = 0.9182$). Mean hospital stay was 2.29 ± 0.81 and 2.35 ± 0.48 days for group A and B respectively ($p = 0.4403$). None of the patients developed intraabdominal collection.

Conclusion: Single dose of pre-operative antibiotics (cefuroxime and metronidazole) was sufficient in reducing the SSIs after appendectomy for NPA. Postoperative antibiotics did not add an appreciable clinical benefit in these patients.

Key words: *Acute appendicitis. Postoperative antibiotics. Prophylactic. Antibiotics. Appendectomy. Surgical site infection. Non-perforated appendicitis.*

INTRODUCTION

Appendicitis is the most common cause of acute abdominal pain, requiring surgical intervention and appendectomy, is the most frequently performed emergency operation. Upto 20% of the population has a life-time risk of developing acute appendicitis.¹ Cases of non-perforated appendicitis (NPA) and perforated appendicitis (PA) are categorized as clean contaminated and contaminated respectively. Several studies have proved the efficacy of pre-operative prophylactic antibiotics in reducing the postoperative infective complications after appendectomy.¹⁻⁵ Therefore, virtually all the patients undergoing appendectomy in our hospital are given pre-operative prophylactic antibiotics.

Patients with perforated appendicitis after appendectomy are universally treated with a variable course of postoperative therapeutic antibiotics because of heavy

contamination of wound and peritoneal cavity.^{6,7} However, the role of postoperative antibiotics in reducing the infective complications in NPA is still controversial.⁶⁻⁸ The practice of prescribing postoperative antibiotics varies enormously around the globe and no consensus exists on whether postoperative antibiotics are beneficial for preventing infective complications in NPA. Therefore, this trial was conducted to determine the role of postoperative antibiotics in reducing the surgical site infections (SSIs) and intra-abdominal abscess formation after open appendectomy in patients with NPA, and to define the uniform guidelines in the management of these patients in our institution.

METHODOLOGY

Between January 2010 and July 2011, a randomized controlled trial was conducted in the Department of Surgery, King Saud Medical City, Riyadh, Kingdom of Saudi Arabia, after the approval of departmental research and ethical committee. All the patients, who were admitted with the clinical diagnosis of acute appendicitis undergoing emergency open appendectomy, were considered eligible for this study. Patients, who had received antibiotics within 72 hours of admission or who were diabetics, immunocompromised or pregnant, were excluded from the study. In addition,

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those patients who were found to have complicated appendicitis (gangrenous, perforated, appendicular mass or abscess) or normal appendix per-operatively, were excluded as well. After discharge, the patients, who lost to follow-up in the out patient department, were also excluded from the study. Informed consent has been taken from all the patients, enrolled for this study.

All the patients received a pre-operative dose of cefuroxime sodium and metronidazole, on call to operation theatre (half an hour before surgery). Open appendectomy was performed by the standard operating technique through right lower quadrant incision. The wound was closed primarily in all the patients after washing with normal saline. After the surgery, patients with intra-operative diagnosis of NPA were randomized by opening the sealed envelopes into two groups. Patients, who were not given any postoperative antibiotics, were included in group A, while the group B comprised of all those patients who received a single dose of cefuroxime sodium and metronidazole, 8 hours postoperatively. All the appendices 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, the patients were booked for follow-up visit in surgical clinic on the 10th postoperative day for removal of stitches and wound assessment. They were also advised to report immediately to the emergency department of the hospital in case of fever, tenderness or pus discharge from the wound. Second follow-up visit was arranged after a month of surgery.

Surgical site infection (SSI) was defined as 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.

The data regarding the demography, duration of symptoms, temperature and white cell count on admission, duration of surgery, operative findings, post-operative antibiotics, hospital stay, and complications were collected on the proforma and tabulated into Microsoft Office Excel 2007 for the calculation of mean values and standard deviation. Student's t-test was used to compare the continuous variables. The rates of SSIs for both the groups were calculated on Microsoft Excel 2007 and categorical variables were compared by chi-square test. The p-value of < 0.05 was considered as statistically significant.

RESULTS

During the study period, 563 patients were admitted with the clinical diagnosis of acute appendicitis for open appendectomy. One hundred and eighty six patients were excluded from the sample because of pre-defined exclusion criteria, shown in Table I. Patients diagnosed to have NPA, intra-operatively were randomized for the study. After randomization, 27 patients failed to report for follow-up, were also excluded from the study. Finally, 377 patients were subjected to statistical analysis.

One hundred and ninety five patients received only a single dose of pre-operative antibiotics (group A); while 182 patients received one dose of postoperative antibiotics in addition to pre-operative antibiotics (group B). Statistically there was no significant difference between mean age, duration of symptoms, admission temperature and WBC count and duration of surgery between the groups (Table II).

Nine patients (4.6%) in group A and 8 patients (4.3%) in group B developed SSIs ($p = 0.9182$). They were managed by the standard protocol. All the wounds healed in 30 days follow-up. None of the patients developed intra-abdominal collection. Mean hospital stay was 2.29 ± 0.81 and 2.35 ± 0.48 days for group A and B respectively ($p = 0.4403$). There was no peri-operative mortality amongst our patients during this study period.

Table I: Excluded patients.

Exclusion criteria	Number of patients	Percentage
Pre-admission antibiotics	18	09.7%
Diabetes mellitus	23	12.4%
Steroid therapy	08	04.3%
Pregnancy	09	04.8%
Alternate diagnosis/normal appendix	39	21.0%
Complicated appendicitis (perforated, gangrenous, mass or abscess)	62	33.3%
Post randomization exclusion	27	14.5%
Total	186	100%

Table II: Comparison between group A and B.

Variables	Group A (No post-operative antibiotics)	Group B (Postoperative antibiotics)	p-value
Number of patients	195	182	
Male to Female ratio (M:F)	1.18:1	1.16:1	
Mean age (years)	32.78 ± 10.62	31.70 ± 9.96	0.3189
Duration of symptoms (days)	1.84 ± 0.72	1.78 ± 0.58	0.3699
Admission temperature (degree Celsius)	37.48 ± 0.34	37.52 ± 0.32	0.2875
Admission white cell count ($10^9/L$)	12.67 ± 1.23	12.76 ± 1.25	0.4577
Duration of surgery (minutes)	52.72 ± 17.30	54.72 ± 16.20	0.2391
Hospital stay (days)	2.29 ± 0.82	2.35 ± 0.48	0.4403
Surgical site infections	9 (4.6%)	8 (4.3%)	0.9182

DISCUSSION

The incidence of postoperative SSIs after appendectomy in patients with NPA has been reported to range from 0% to 11%.⁶⁻¹¹ The stage of the disease process at the time of operation and the use of appropriate prophylactic antibiotics significantly affects the risk for postoperative SSIs in addition to patient's factors.^{7,10} The efficacy of pre-operative antibiotics in reducing the risk of SSI following appendectomy has been well established in the literature.¹⁻⁵ However, the role of postoperative antibiotics in these patients has not been clearly defined.⁶ Only few studies have evaluated specifically the clinical benefits and the disadvantages of administering postoperative antibiotics in addition to adequate pre-operative antibiotics prophylaxis.⁶⁻¹¹

In 1995, Liberman and colleagues reported a high rate of wound infection (11.1%) among the patients who had received only pre-operative cefoxitin compared to the patients who were given both pre- and postoperative cefoxitin (1.9%).⁹ However, they found no infective complication in their third group of patients, who had received a single dose of pre-operative cefotetan. Thus, they recommended a single dose of pre-operative cefotetan as the optimal prophylaxis for NPA. Therefore, the choice of pre-operative antibiotic is an important issue, rather than addition of postoperative antibiotics.

Mui and coworkers conducted a randomized trial on 269 patients to define the optimum duration of prophylactic antibiotics in NPA.⁶ They found no significant difference in the wound infection rate between three study groups, who received varied period of prophylactic antibiotics. They concluded that single dose of pre-operative antibiotic could adequately prevent the postoperative infective complications.⁶

Le and associates retrospectively compared patients of NPA, who received a single dose of pre-operative antibiotics with those who were given postoperative antibiotics in addition to pre-operative prophylaxis.⁷ They observed no significant difference in SSIs rate between the groups (10% vs. 9%, $p = 0.64$). Their wound infection rate was higher than the present study. This difference might be due to type of antibiotics used. Instead of cefoxitin, we used a combination of cefuroxime sodium and metronidazole, for a broader coverage. Moreover, high risk patients (diabetics, immunocompromised, pregnant) were excluded from this study.

Recently, Coakley and colleagues compared the outcomes of large number of patients (728) treated with antibiotics before and after appendectomy with those, who received only pre-operative antibiotics.¹⁰ They concluded that the addition of postoperative antibiotics did not reduce the infectious complications, rather significantly increased the morbidity in the terms of higher rates of antibiotic-associated diarrhea and *Clostridium difficile* infection. In addition, postoperative

antibiotics had significantly prolonged the hospital stay and increased the treatment cost without affording any appreciable clinical benefit.¹⁰

In the present study, there was no significant difference between the rates of SSIs among the patients with NPA, who did (group B) and who did not receive postoperative antibiotics (group A). Therefore, the addition of post-operative antibiotics with single dose of pre-operative antibiotic did not reduce the rate of SSIs further in patients with NPA. These findings are in accordance with other studies.⁶⁻¹¹ Both groups were comparable in terms of patients demographics. The high risk patients, (diabetic, immunocompromised, pregnant) were excluded from the study to eliminate the patient factors of developing SSIs and to define precisely, the real advantages of postoperative antibiotics.

There was no antibiotic related complication in both the groups, because of short course of antibiotics. There was no significant difference in the hospital stay of our patients in both the groups. However, it was shorter than that of Mui *et al.*⁶ while it was consistent with others' reports.^{8,10} Intra-abdominal abscess formation has rarely been reported after appendectomy in NPA, but it accounts for 2 – 3% of patients in complicated appendicitis.¹² This complication was not seen in these patients.

In the surgical practice, the supplementary post-operative antibiotics have been used increasingly, because of the fear of developing postoperative SSIs. Postoperative antibiotics can not be the substitute of good surgical and aseptic techniques. The over use of antibiotics is associated with the increase risk of antibiotic related complications, bacterial antibiotic resistance and cost of care.^{2,6-11} For these reasons, the benefits and side effects of antibiotics therapy have to be evaluated carefully. Moreover, our results are further strengthened by the recent studies showing that the prolong use of antibiotics even in patients with complicated appendicitis does not reduce the post-operative infectious complications.^{13,14}

CONCLUSION

Single dose of pre-operative antibiotics (cefuroxime and metronidazole) was sufficient in controlling the SSIs after appendectomy for NPA. Postoperative antibiotics did not add an appreciable clinical benefit in these patients. Therefore, surgeons need to update their practice of antibiotic prophylaxis according to the standard guidelines and evidence based medicine.

REFERENCES

1. Andersen BR, Kallehave FL, Andersen HK. Antibiotics versus placebo for prevention of postoperative infection after appendectomy. *Cochrane Database Syst Rev* 2005; 3:CD001439.

2. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guidelines for prevention of surgical site infection. *Infect Control Hosp Epidemiol*; 1999 **20**:247-78.
3. Bauer T, Vennits BO, Holm B, Pedersen J, Lysen D, Galatius H, *et al*. Danish multicenter study group III. Antibiotics prophylaxis in acute non-perforated appendicitis. *Ann Surg* 1989; **209**: 307-11.
4. Fraser JD, Aguayo P, Leys CM, Keckler SJ, Newland JG, Sharp SW, *et al*. A complete course of intravenous antibiotics vs. a combination of intravenous and oral antibiotics for perforated appendicitis in children: a prospective, randomized trial. *Pediatr Surg* 2010 **45**:1198-202.
5. St Peter SD, Tsao K, Spilde TL, Holcomb GW 3rd, Sharp SW, Murphy JP, *et al*. Single daily dosing ceftriaxone and metronidazole vs. standard triple antibiotic regimen for perforated appendicitis in children: a prospective randomized trial. *J Pediatr Surg* 2008; **43**:981-5.
6. Mui LM, Ng CS, Wong SK, Lam YH, Fung TM, Fok KL, *et al*. Optimum duration of prophylactic antibiotics in acute non-perforated appendicitis. *ANZ J Surg* 2005; **75**:425-8.
7. Le D, Rusin W, Hill B, Langell J. Postoperative antibiotics use in non perforated appendicitis. *Am J Surg* 2009; **198**:748-52.
8. Ravari H, Jangjoo A, Motamedifar J, Moazzami K. Oral metronidazole as antibiotic prophylaxis for patients with non-perforated appendicitis. *Clin Experiment Gastroenterol* 2011; **4**:273-6.
9. Liberman MA, Greason KL, Frame S, Ragland JJ. Single dose cefotetan or cefoxitin versus multiple dose cefoxitin as prophylaxis in patients undergoing appendectomy for acute non-perforated appendicitis. *J Am Coll Surg* 1995; **180**:77-80.
10. Coakley BA, Sussman ES, Wolfson TS, Bhagavath AS, Choi JJ, Ranasinghe NE, *et al*. Postoperative antibiotics correlate with worse outcomes after appendectomy for nonperforated appendicitis. *J Am Coll Surg* 2011; **213**:778-83.
11. Al-Mefreji KA. Antibiotics prophylaxis in non-perforated appendicitis: a prospective study. *Al-Kindy Col Med J* 2006; **3**: 49-51.
12. Tang E, Ortega AE, Anthonie GJ, Beart RW Jr. Intra-abdominal abscesses following laparoscopic and open appendectomies. *Surg Endosc* 1996; **10**:327-8.
13. Van Wijck K, De Jong JR, Van Heurn LW, Van der Zee DC. Prolonged antibiotic treatment does not prevent intra-abdominal abscesses in perforated appendicitis. *World J Surg* 2010; **34**: 3049-53.
14. Henry MC, Walker A, Silverman BL, Gollin G, Islam S, Sylvester K, *et al*. Risk factors for the development of abdominal abscess following operation for perforated appendicitis in children: a multicenter case-control study. *Arch Surg* 2007; **142**:236-41.

