A Cohort Study of Preoperative Single Dose Versus Four Doses of Antibiotics for Patients With Non-Complicated Acute Appendicitis

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Abstract

Objective: To Test the efficacy of single preoperative dose of Cefotaxime 1gm and Metronidazole 500mg in reducing the surgical site infections (SSIs) after open appendectomy in patients with non-complicated appendicitis (NCA)

Place and Duration of Study: Al Hilla General Teaching Hospital, Babel Governorate-Iraq, from January 2013 to January 2014.

Patients & Methods: 100 patients, who underwent appendectomy for NCA and fulfilled the selection criteria, were randomized into two groups. The patients in group A received a single dose of pre-operative antibiotics (Cefotaxime sodium and metronidazole), while the group B patients received three more dose of the same antibiotics postoperatively. Patients of both groups were followed-up for 30 days to assess the postoperative infective complications.

Results: Group A had 48, while group B comprised of 52 patients. The groups were comparable in the baseline characteristics. Statistically, P value in rates of SSIs between both the groups was 0.9182. None of the patients developed intra-abdominal collection.

Conclusion: Single dose of pre-operative antibiotics (Cefotaxime 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: Preoperative antibiotics, Appendectomy, Surgical site infection, Non-complicated appendicitis

Abbreviations: SSI: Surgical Site Infection, NCA: non-complicated appendicitis CDC Center of Disease Control.
Introduction

Appendicitis is the most common cause of acute abdominal pain, requiring surgical intervention and appendectomy, is the most frequently performed emergency operation. Up to 20% of the population has a life-time risk of developing acute appendicitis. (Liu &McFadden, 1997)

Cases of non-complicated appendicitis (NCA) and perforated appendicitis 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. (Liu &McFadden, 1997; Addiss et al., 1990; Schwartz, 2008; Wilcox &Traverso, 1997; Graffeo & Councilman, 1996) Data regarding risk factors and use of antibiotics in surgical patients is essential for preventing and treating surgical site infections (SSI) which is defined as Infection occurs within 30 days after the operation if no implant is left in place or within one year if implant is in place and the infection appears to be related to the operation and infection involves any part of the anatomy (e.g., organs and spaces) including the incision which was opened or manipulated during an operation and at least one of the following:

1. Purulent drainage from the incision or the drain that is placed through a stab wound into the organ/space.
2. Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space
3. An abscess or other evidence of infection including redness and tenderness or swelling involving the skin/Fascia/Muscles/organ or spaces that is found on direct examination, during reoperation, or by histopathologic or radiologic examination. (Horan et al., 1992).

Appendectomy is one of the most common surgical procedures (Andersen et al., 2005) with SSI complicating 1–5% of appendectomy cases (NNIS, 2004; Hale et al., 1997; Koch et al., 2000). One established risk factor for SSI in appendectomy is the duration of operation (Andersen et al., 2005).

While antibiotic prophylaxis is common in surgical procedures (Dellinger et al., 1994; Gyssens et al., 1996), inappropriate use of antibiotics occurs in 25–50% of general elective surgeries (Gyssens et al., 1996; Silver et al., 1996; Bedouch et al., 2004; Pons-Bousom et al., 2004; Dahms et al., 1998). The efficacy of antibiotic prophylaxis in patients undergoing appendectomy has been examined in several randomized and observational studies (Koch et al., 2000; Lau et al., Liberman et al., 1995; Soderquist-Elinder et al., 1995; Nguyen et al., 1992; Gorecki et al., 1999; Tonz et al., 2000;
Charalambous et al., 2003; Lau et al., 1986; Al-Dhohayan et al., 1993) showing that appropriate use of antibiotics reduces the risk of SSI following appendectomy by 40–60% which was given 30 minutes prior to the incision where the antibiotic reaches its maximum plasma concentration (Lim, 1997).

In Iraq, some hospitals had their own internal antibiotic prophylaxis guidelines. However, standardized national guidelines for antibiotic prophylaxis among appendectomy patients have not yet been established. Simple appendicitis is treated according to surgeons’ discretion, which results in use of many different agents.

According to our online and manual search in several major Iraqi universities, no study has been conducted of the efficacy of single preoperative antibiotic prophylaxis on risk of SSI in patients undergoing appendectomy in Iraq. We aimed to examine the use of single preoperative antibiotic prophylaxis, and the efficacy of antibiotic prophylaxis in reducing SSI among appendectomy patients in Iraq.

**Methods**

This is a randomized controlled trial was conducted in the Department of Surgery, Al Hilla general Teaching Hospital, Al-Hilla, Babel Governorate-Iraq, Between January 2013 and January 2014.

All the patients, who were admitted on our call of duty 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, 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 outpatient 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 IV Cefotaxime 1gm and IV metronidazole 500mg, 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 non-complicated appendix were divided blindly and randomly into two groups by giving the case papers a closed envelope opened at the surgical ward and referred the patient to which group is added. Patients, who were not given any postoperative antibiotics, were included in group A, while the group B comprised of all those patients who received three dose of IV 1gm Cefotaxime and IV Infusion metronidazole 500 mg, 8 hourly 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 3rd for wound assessment and on the 10th postoperative day for removal of stitches.

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.

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, postoperative 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 Excel2007 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, 202 patients were admitted with the clinical diagnosis of acute appendicitis for open appendectomy. 85 patients were excluded from the sample because of pre-defined exclusion criteria, shown in Table I.

Patients diagnosed to have non-complicated Appendicitis, intra-operatively were randomized for the study. After randomization, 17 patients failed to report for follow-up, were also excluded from the study. Finally, 100 patients were subjected to statistical analysis. 48 patients received only a single dose of pre-operative antibiotics (group A); while 52 patients received three doses 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). 4(8.3%) in group A and 5 (9.6%) patients 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 34± 4.81 and 35 ± 5.48 hours for group A and B respectively (p = 0.4403). There was no perioperative mortality amongst our patients during this study period.
### Table I: Excluded patients

<table>
<thead>
<tr>
<th>Exclusion criteria</th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-admission antibiotics</td>
<td>8</td>
<td>3.9</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>23</td>
<td>11.3</td>
</tr>
<tr>
<td>Steroid therapy</td>
<td>1</td>
<td>0.49</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>4</td>
<td>1.9</td>
</tr>
<tr>
<td>Alternate diagnosis/normal appendix</td>
<td>7</td>
<td>3.4</td>
</tr>
<tr>
<td>Complicated appendicitis (perforated, gangrenous, mass or abscess)</td>
<td>44</td>
<td>21.7</td>
</tr>
<tr>
<td>Post randomization exclusion</td>
<td>17</td>
<td>8.4</td>
</tr>
<tr>
<td>Total</td>
<td>102</td>
<td>50.4</td>
</tr>
</tbody>
</table>

### Table II: Comparison between group A and B

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group A</th>
<th>Group B</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>48</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>Male to Female ratio</td>
<td>1.8:1</td>
<td>1.5:1</td>
<td></td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>32.78 ± 10.62</td>
<td>31.70 ± 9.96</td>
<td>0.3189</td>
</tr>
<tr>
<td>Mean Duration of symptoms (Days)</td>
<td>1.84 ± 0.72</td>
<td>1.78 ± 0.58</td>
<td>0.3699</td>
</tr>
<tr>
<td>Mean Admission temperature (degree Celsius)</td>
<td>37.48 ± 0.34</td>
<td>37.52 ± 0.32</td>
<td>0.2875</td>
</tr>
<tr>
<td>Mean Admission white cell count x 10^3</td>
<td>9.0 ± 3.23</td>
<td>10 ± 1.25</td>
<td>0.4577</td>
</tr>
<tr>
<td>Mean Duration of surgery (minutes)</td>
<td>32.72 ± 7.30</td>
<td>34.72 ± 6.20</td>
<td>0.2391</td>
</tr>
<tr>
<td>Mean Hospital stay (hours)</td>
<td>34 ± 4.81</td>
<td>35 ± 5.48</td>
<td>0.4403</td>
</tr>
<tr>
<td>Mean Surgical site infections</td>
<td>4 (8.3%)</td>
<td>5 (9.6%)</td>
<td>0.9182</td>
</tr>
</tbody>
</table>
Discussion

The incidence of postoperative Surgical Site Infections (SSIs) after appendectomy in patients with non-complicated Appendicitis (NCA) has been reported to range from 0% to 11%. (Mui et al., 2005; Le et al., 2009; Ravari et al., 2011; Liberman et al., 1995; Coakley et al., 2011) 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. (Mui et al., 2005; Liberman et al., 1995).

The efficacy of pre-operative antibiotics in reducing the risk of SSIs following appendectomy has been well established in the literature. (Gorecki et al., 1999; Tonz et al., 2000; Charalambous et al., 2003; Lau et al., 1986; Al-Dhohayan et al., 1993) However, the role of postoperative antibiotics in these patients has not been clearly defined (Al-Dhohayan et al., 1993). Only few studies have evaluated specifically the clinical benefits and the disadvantages of administering postoperative antibiotics in addition to adequate pre-operative antibiotics prophylaxis (Mui et al., 2005; Le et al., 2009; Ravari et al., 2011; Liberman et al., 1995; Coakley et al., 2011; Al-Meferji, 2006).

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%). (Liberman et al., 1995). 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. (Al-Dhohayan et al., 1993). 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. (Al-Dhohayan et al., 1993). 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. (Mui et al., 2005).

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 Cefotaxime 1gm and metronidazole 500mg, for a broader coverage. Moreover, high risk patients (diabetics, immunocompromised, pregnant) were excluded from our 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. (Coakley et al., 2011) 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. (Coakley et al., 2011)

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 postoperative 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. (Al-Dhohayan et al., 1993; Lim, 1997; Mui et al., 2005; Le et al., 2009; Ravari et al., 2011; Liberman et al., 1995; Coakley et al., 2011; Al-Meferji, 2006)

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. while it was consistent with others’ reports.(Ravari et al., 2011; Liberman et al., 1995; Coakley et al., 2011).

Intra-abdominal abscess formation has rarely been reported after appendectomy in non-complicated Acute Appendicitis, but it accounts for 2 – 3% of patients in complicated appendicitis.(Ibar et al., 2012). This complication was not seen in these patients. In the surgical practice, the supplementary postoperative antibiotics have been used increasingly, because of the fear of developing postoperative SSIs. Postoperative antibiotics cannot be the substitute of good surgical and aseptic techniques. The overuse of antibiotics is associated with the increase risk of antibiotic related complications, bacterial antibiotic resistance and cost of care.(Gorecki et al., 1999; Al-Dhohayan et al., 1993; Lim, 1997; Mui et al., 2005; Le et al., 2009; Ravari et al., 2011; Liberman et al., 1995; Coakley et al., 2011; Al-Meferji, 2006). 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 postoperative infectious complications.Van et al., 2010; Ibar et al., 2012; Henry et al., 2007).

**Conclusion**

Single dose of pre-operative antibiotics (cefuroxime and metronidazole) was sufficient in controlling the SSIs after appendectomy for non-complicated Acute Appendicitis. 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


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