ORIGINAL ARTICLE

Prophylactic antibiotics in patients undergoing appendicectomy: one versus three doses of antibiotics

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Abstract:

Objective: To compare the rate of surgical site infection using single dose versus three doses of prophylactic antibiotics in patients undergoing emergency appendicectomy.

Study Design: Randomized controlled trial.

Setting and Duration: Surgical "A" ward, Khyber Teaching Hospital Peshawar from September 2009 to August 2010.

Methodology: In this study 292 patients were randomly allocated to two groups, A and B (146 patients in each group). Group A received single prophylactic dose of intravenous cefuroxime and metronidazole at induction of anaesthesia and Group B received three doses of cefuroxime and metronidazole i-e at induction of anaesthesia, 8 and 16 hours post-operatively. All the patients were followed up for 10days post operatively. Patient's demographics including age, gender and outcome in terms of surgical site infection (SSI) were recorded on a standardized proforma. Statistical analysis was performed using SPSS version 11 with proportions and mean ± SD calculated for categorical and continuous variables, respectively. Probability ≤ 0.05 was taken as significant.

Results: Two hundred and ninety two patients were analyzed (146 in Group A and 146 in Group B). The two groups were comparable in terms of demographic variables like age and gender. There was no significant difference between the two groups regarding overall SSI rate (P = 0.304).

Conclusion: A single-dose systemic regimen of cefuroxime with metronidazole given during the immediate preoperative period is safe and reduces the chances of surgical site infection.

Keywords: Appendicectomy, Surgical Site Infection (SSI), Antibiotic Prophylaxis.

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Introduction:

Appendicitis is one of the commonest emergencies faced by a General Surgeon. There is 5-10% lifetime risk, higher in males with a peak age between 15-25years but affect all age groups. Appendicitis is sufficiently common that appendicectomy is the most frequently (16% of the population) performed urgent abdominal operation and is often the first major procedure performed by a Surgeon in training[1].

Surgical Site infection (SSI) is the most common post-operative complication occurring in 5-10% of all patients1. The organisms responsible are usually a mixture of Gram-negative bacilli and anaerobic bacteria, predominantly bacteroids species and anaerobic streptococci[2].

Surgical Site Infection (SSI) result in increased post-operative morbidity and financial cost[3,4]. The benefit of prophylactic antibiotics to reduce complications following open appendicectomy has been demonstrated5. Single dose prophylactic antibiotic (2gm intravenous cefuroxime + 500mg of metronidzole) at the time of induction of anaesthesia decreases the SSI to 6.5%[6]. Whereas multiple doses of the same antibiotics given at different intervals reduces the SSI to 0.32%[5]. The optimum time and schedule of antibiotics is unknown and thus there is the potential

for either under treatment with increased risk of post-operative infections or over treatment with the risk of developing microbial resistance[5].

In our setup, as evident from the previous records, appendicectomy is performed frequently (upto 15 cases per week). The injudicious prescription of antibiotics in the peri-operative period is a common practice and this amounts to a higher cost on behalf of patient and the hospital. In this study we aimed to compare the effectiveness of single dose prophylactic antibiotics to three doses for the same reasons, and thus develop a protocol for administration of prophylactic antibiotics in patients undergoing appendicectomy.

Materials and methods:

This study was conducted at Surgical 'A' Unit, Department of Surgery, Khyber Teaching Hospital, Peshawar, Pakistan, from September 2009 to August 2010, as part of a single center, prospective, single blind, randomized clinical trial. The objective of the study was to compare the rate of surgical site infection using single dose versus three doses of prophylactic antibiotics in patients undergoing emergency appendicectomy. Based on current literature findings, we hypothesized that there is no difference between single dose and three doses of prophylactic antibiotics in preventing surgical site infection in patients undergoing appendicectomy. Approval for the study was obtained from the Ethics Committee of the hospital.

In this study, a total of 292 consecutive patients presenting through outpatient department (OPD) or emergency with signs and symptoms suggestive of acute appendicitis, age between 11 to 50 years, of both gender and American Society of Anesthesiologists class I were registered for the study. Any patient with perforated or gangrenous appendix, pus in the peritoneal cavity, or who were diabetic, immunocompromised, allergic to Cefuroxime and failing to abide by the follow up protocol, were excluded from the study.

All the patients were selected through non-probability consecutive technique. Patients were included in the study after taking informed and written consent. Complete history was taken and thorough examination was done. When the diagnosis of appendicitis was established and antibiotic sensitivity checked, patients were allocated to either group A or B using sequential method. Bias and confounders in the study were controlled by strictly following the exclusion criteria. Group "A" received single prophylactic dose of intravenous 1.5gm Cefuroxime + 500mg Metronidazole at induction of anaesthesia and Group "B" received three doses of prophylactic antibiotics intravenously i-e 1.5gm Cefuroxime + 500mg Metronidazole at induction and then 750mg Cefuroxime + 500mg Metronidazole at 8 and 16 hours post-operatively.

The patients in both groups were operated by consultant surgeon, under general anesthesia. Skin was prepared with aqueous povidine iodine solution. The patients in group "A" were given a single prophylactic parenteral dose of Cefuroxime (1.5gm) and Metronidazole (500mg) at induction as part of the protocol, and patients in group "B" were given two more doses of Cefuroxime (750mg) and Metronidazole (500mg) antibiotic postoperatively at 8 and 16 hours respectively. Open appendectomy was performed through Grid iron incision. After the incision, the external oblique was incised and the internal oblique and transversusabdominus muscle were splitted, the peritoneum was accessed. Appendix was identified and the mesoappendix was ligated with vicryl 1 after creation of a window in its base. The base of the appendix was crushed and ligated using Vicryl 1 and removed. The wound was closed in layers. The skin incision closed with subcuticular skin stitches using polypropylene 2/0 and aseptic dressing was done. Postoperatively, the patients were kept nill by mouth until they were fully recovered from anesthesia and had their bowel sounds returned when clear fluids were started. Soft diet followed by regular diet was introduced when the patients tolerated the liquid diet and had passed flatus. Patients were discharged once they were, able to take regular diet, afebrile, ambulatory, and had good pain control. Before discharging the

patient from the hospital, the dressing was removed to examine the surgical site.The patients were asked for follow up visit with in ten days. Complete examination especially of the wound was done at follow up visit. A standardized questionnaire was used to record the data like age, gender and SSI for the two groups.

Surgical site infection was defined, using center for disease control and prevention (CDC) classification, incisional and deep SSI. Incisional SSI was further divided into superficial and deep with involvement of superficial subcutaneous tissue and deep subcutaneous tissue and muscles, respectively. The findings/features of purulent or seropurulent discharge, redness or pain, at the incision site within 10 days postoperatively were used to identify SSI. A febrile patient with fever, elevated white cell count (WBC > 10,000g/dl), paralytic ileus and imaging detected fluid collection with characteristics of an abscess were labeled as having intra-abdominal abscess.

Statistical analysis:

The data was analyzed with the help of computer software SPSS® for windows version 11.0. Age was presented as mean and standard deviation. Gender distribution was described in percentages. Proportions of patients with surgical site infection in Group A and B was recorded in tabular form and both the groups were compared using chi-square test. P value of ≤ 0.05 was considered significant.

Table 1: *Age distribution of patients*

Age Range (years)	Group A N (%)	Group B N (%)	Total N (%)
11-20	20 (13.7)	34 (23.3)	54(18.5)
21-30	83 (56.9)	80 (54.8)	63(55.8)
31-40	32 (21.9)	27 (18.5)	59(20.2)
41-50	11 (7.5)	5 (3.4)	16(5.5)
Total	146 (100)	146 (100)	292(100)

Table 2: *Gender Distribution*

	Group A N (%)	Group B N (%)	Total N (%)	P value
Male	80 (54.8)	82 (56.2)	162 (55.5)	0.814
Female	66 (45.2)	64 (43.8)	130 (44.5)	
Total	146 (100)	146 (100)	292 (100)	

Table 3: *Surgical site infection*

	Group A N (%)	Group B N (%)	Total N (%)	P value
Yes	10 (6.9)	6 (4.1)	16 (5.5)	0.304
No	136 (93.1)	140 (95.9)	276 (94.5)	
Total	146 (100)	146 (100)	292 (100)	

Results:

In this study 292 patients were included, 146 patients in group A, who received single prophylactic dose of intravenouss 1.5gm of cefuroxime + 500mg of metronidazole at induction of anaesthesia and 146 patients in group B who received three doses of prophylactic antibiotics intravenously i-e 1.5gm of cefuroxime + 500mg of metronidazole at induction of anaesthesia and 750mg of cefuroxime + 500mg of metronidazole at 8 and 16 hours post-operatively.

The mean age of patients in group A and group B were 26.5 ± 7.1 years and 25.2 ± 6.5 years respectively and it was statistically not significant (p = 0.101). Most of the patients were present in age range of 21-30years, 83 (56.9%) patients in Group A and 80 (54.8%) patients in Group B as shown in Table 1.There were 80 (54.8%) males and 66 (45.2%) females in Group A with male to female ratio 1.21 : 1 compared to 82 (56.2%) males and 64 (43.8%) females in Group B with a male and female ration1.28 : 1 (Table 2).

Surgical site infection was observed in 10 patients in Group A and in 6 patients in Group B which was statistically not significant (p = 0.304) as shown in Table 3.

Discussion:

Surgical site infections are a major source of postoperative illness, accounting for approximately a quarter of all nosocomial infections. They are, along with urinary tract infections, pnuemonina and blood borne infections, ranked as the second or third most common type of hospital acquired infections[7]. National studies have defined the patients at highest risk for infection in general and in many specific operative procedures[8]. The use of antibiotic prophylaxis before surgery has evolved greatly in the last 20 years. Improve-

ments in the timing of initial administration, the appropriate choice of antibiotic agents, and shorter durations of administration have defined more clearly the value of this technique in reducing postoperative wound infections.[9]

Acute appendicitis can occur at any age and no age is exempted however maximum number of patients are seen in 2nd and 3rd decade of life. In our study it was 56.9% and 21.9% in Group A and 54.8% and 18.5% in group B in 2nd and 3rd decade of life. Male to female ratio in our study was 1.2 : 1 in Group A and 1.28 : 1 in Group B. The incidence is marginally higher in males as shown in a study conducted byOguntola ASet al.[10]

In this study, 146 patients in Group A received single dose of prophylactic antibiotic at the induction of anaesthesia and 146 patients in Group B received three doses of prophylactic antibiotics intravenously at the induction of anaesthesia and at 8 and 16 hours post-operatively. The antibiotics in Group B were given for longer duration with the assumption that the longer course would be beneficial in reducing the risk of infective complications. The findings of the current study showed that 10/146 (6.9%) patients in Group A and 6/146 (4.1%) patients in Group B developed SSI (overall), the difference was, however, statistically insignificant. Prescribing antibiotics for longer duration does not seem to give additional protection, which was corroborated by other studies[11,12].

Antibiotics are recommended for reducing the incidence of wound infections post-operatively[13]. The optimum duration of antibiotic prescription is currently a topic under review. The Cochrane review of antibiotic prescription in appendicectomy has suggested that single doses may be as effective in reduction of post-operative complications as multiple doses[14]. A randomised controlled trial by Muiet al.[15] looked at the impact of the duration of antibiotics on the incidence of complications in patients undergoing open appendicectomy for non-perforated appendicitis. They failed to demonstrate any significant difference between a single dose, 3-doses and a 5-day course of antibiotics. Interestingly, they noted a higher antibiotic-related complication rate in the group who had the 5-day course of antibiotics.

The choice of parenteral prophylactic antibiotic agents and the timing and route of administration have become standardized on the basis of well-planned prospective clinical studies[16]. It is generally recommended in clean-contaminated procedures that a single dose of cephalosporin, be administered intravenously by anesthesia personnel in the operative suite just before incision. Additional doses are generally recommended only when the operation lasts longer than 2 to 3 hours. The American Society of Health System Pharmacists (ASHP)[17] recommends prophylaxis with cephalosporins for uncomplicated appendicitis, with metronidazole and gentamicin only considered an alternative in cases of penicillin allergy.[17,18]

The improper use of antibiotic agents and inappropriately prolonged duration of antibiotic prophylaxis are likely to cause antimicrobial resistance[19,20]. Surgeons and surgical departments need to update their practices of antibiotic prophylaxis to comply with standard guidelines[15,16] and updated evidencebase.[5]

Conclusion:

There was no significant difference between single dose of cefuroxime with metronidazole given at induction of anaesthesia to three doses of cefuroxime with metronidazole given at induction of anaesthesia, 8 and 16 hours postoperatively in terms of surgical site infection in patients undergoing appendicectomy with the conclusion that increasing the doses of antibiotics does not confer any effect on preventing surgical site infection.

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