

Original Research Article

A comparative study to determine the role of pre and post-operative antibiotic therapy versus only pre-operative antibiotic therapy in patients of non-perforated acute appendicitis

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Received: 11 July 2020

Revised: 02 September 2020

Accepted: 03 September 2020

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ABSTRACT

Background: If properly used in appendicitis, antibiotics can reduce the rate of infection by 50%. The use of post-operative antibiotics for preventing infective complications in non-perforated cases is still controversial.

Methods: A randomised prospective study was conducted in the Department of Surgery, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi with patients who presented acute appendicitis. A minimum number of 30 patients each in group A (pre-operative and post-operative antibiotics) and group B (only pre-operative antibiotics) were evaluated for 18 months, from January 2018 to June 2019.

Results: The mean age of group A is 29.9 ± 15.16 years and in group B is 25.97 ± 9.470 years (p value=0.122, insignificant). There was male preponderance. The seroma formation in both the groups was 10.00% and no patients developed intra-abdominal abscess. The incidence of local site oedema was 10% in both the groups A and B and their p value is insignificant. In both the groups A and B, 10% of the people developed pus discharge from the stitch line and the p value is insignificant. In group A, 6.67% of the patients and in group B 10.00% of the patients developed stitch line inflammatory changes and the p value insignificant. In group A, 13.3% and in group B, 10.00% of the patients developed fever and their p value is 1. The mean length of hospital in case 1.23 ± 0.5 days (group A) and is 1.17 ± 0.45 days (group B) (p value=0.508).

Conclusions: Hence we can conclude that a well-chosen and adequately-timed pre-operative antibiotics are adequate in preventing post-operative complications and post-operative antibiotics do not affect the same.

Keywords: Acute appendicitis, Seroma, Surgical site infections

INTRODUCTION

Appendicitis is the most common cause of acute abdominal pain requiring emergency surgery where luminal obstruction plays a key pathogenic role by increasing mucus production and bacterial overgrowth, increasing the intra-luminal pressure and in turn it decreases blood flow to the appendiceal wall resulting in necrosis and perforation of the appendix.¹⁻³ Patients with an appendicular rupture at the time of surgery have been

shown to have a higher risk of intra-abdominal and pelvic abscesses, surgical site infection (SSI), and postoperative paralytic ileus (39% versus 8%).^{4,5} Before puberty the male to female ratio is equal which increases to 3:2 at the age of 25.⁶ The accumulative life risk is 7%.⁷ The risk of recurrence with nonsurgical treatment is 7.4%, and malignant disease is detected in 1.2% of patients during follow-up.

Post-operative wound complications in the form of post-operative pain, hospital stay, sepsis and patient dissatisfaction can increase morbidity.⁸⁻¹⁰ The chance of wound infection in non-perforated acute appendicitis is less than 10% while perforated appendicitis has an infection rate of 15-20%.⁸ Infection is greatest in diffuse peritonitis (35%).⁸

Appendicectomy in non-perforated acute appendicitis is a clean contaminated surgery.¹¹ Therefore the standard protocol is giving preoperative antibiotics in all the patients undergoing appendicectomy, reducing the rate of infection by half.^{12,13} Patients with perforated appendicitis are put on antibiotics even in the post-operative period. This is necessary to reduce the SSI and pelvic abscess which may be due to contamination of the wound and the peritoneal cavity.¹¹ On the other hand, however, the use of postoperative antibiotics for avoiding infectious complications in non-perforated cases is still needs further probing.^{11,14} The practice of giving post-operative antibiotics in non-perforated acute appendicitis varies and no consensus exist on its use.¹¹ Since antimicrobial use proceeds to the emergence of antimicrobial resistance, optimized use of antibiotics is required. The purpose of this review is to provide an overview of studies on antibiotics for acute appendicitis treated operatively and to see whether evidence-based recommendation can be suggested.

METHODS

This was a randomized prospective study conducted in the Department of Surgery, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi who presented with acute appendicitis. A minimum number of 30 patients in group A receiving pre-operative and post-operative antibiotics and minimum 30 patients in group B receiving only pre-operative antibiotics were evaluated for the study period of 18 months, from January 2018 to June 2019.

Inclusion criteria

All patients presenting to surgical out patients/emergency department with uncomplicated acute appendicitis.

All patient aged more than 12 years.

Exclusion criteria

Patients with co-morbid conditions as chronic obstructive pulmonary disease (COPD), benign prostatic hyperplasia (BPH), coagulopathies and diabetes mellitus (DM).

High risk patients like immune-comprised and pregnant females.

Patients with suspected perforated appendix requiring lower midline laparotomy incision.

All matched patients, selected for the study by applying inclusion and exclusion criteria, were grouped into two groups, namely group A and group B by means of closed envelop technique (a method of sealed, numbered envelopes opened in sequence). The envelope was opened once the operating surgeon rules out the last exclusion criteria. Group A patients were subjected to pre-operative and post-operative antibiotic therapy and patients from group B were subjected to only pre-operative antibiotic therapy after appendectomy in patients with non-perforated acute appendicitis. All surgeries were performed under spinal anaesthesia/general anaesthesia (Figure 1). All patients were given antibiotic prophylaxis with a pre-operative dose of injectable ceftriaxone 1g and metronidazole 500 mg and group A patients were given single dose of injectable ceftriaxone 1 g and metronidazole 500 mg. Patients were followed up post operatively on day 1, day 2, day 7, day 14, and day 30 for the following parameters: seroma formation, SSI, intraabdominal abscess (using ultrasound or computed tomography scan) and length of hospital stay.



Figure 1: Appendicectomy procedure.

Sample size was determined based on the ability to determine the role of post-operative antibiotics in reducing SSIs. With 342 patients in each group, there was 80% power at an alpha 0.05 to show that the number of patients with surgical site infections would be 50% lower in the subjects receiving post-operative antibiotics. We chose a 10% baseline ratio of SSIs based on a previous study indicated a similar protocol. The formula for calculated sample size is given below:

$$n = Z_{1-\alpha/2} \times \sqrt{2P(1-P)} + Z_{1-\beta} \times \sqrt{P_1(1-P_1) + P_2(1-P_2)} \div (P_1 - P_2)^2$$

where $Z_{\alpha/2}$ is the critical value of the normal distribution at $\alpha/2$ (e.g. for a confidence level of 95%, α is 0.05 and the critical value is 1.96), Z_{β} is the critical value of the normal distribution at β (e.g. for a power of 80%, β is 0.2) and P_1 and P_2 are the expected sample proportions of the two groups.

Since the study is time bound, all consecutive patients meeting the eligibility criteria during the study period will be enrolled. It is expected from the previous experience that about 30 patients per group will be enrolled.

Statistical testing was conducted with the statistical package for the social science system (SPSS) version 17.0. The comparison of normally distributed continuous variables between the groups was performed using student's t test. Nominal categorical data between the groups was compared using chi-squared test or Fisher's exact test as appropriate. Non-normal distribution continuous variables was compared using Mann Whitney U test. For all statistical tests, a p value less than 0.05 was taken to indicate a significant difference.²¹

RESULTS

This study was conducted in the Department of Surgery, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi. In a group of 30 patients, Group A received pre-and post-operative and Group B received only pre-operative antibiotics and patients were followed upto 30th day, the following observations were made.

Age wise distribution

The mean age in group A is 29.9 with a standard deviation of ±15.16 and the mean age in group B is 25.97 with a standard deviation of ±9.47. The p value of age distribution of patients was found to be 0.122, which is statistically insignificant (Table 1).

Table 1: Mean age of occurrence of non-perforated acute appendicitis with standard deviation and its p value.

Age (years)	Group A	Group B
Sample size	30	30
Mean±standard deviation	29.9±15.16	25.97±9.47
Median	27.5	26
Minimum age - maximum age	12-70	12-45
Interquartile range	19-36	19-30

Gender distribution

The incidence of non-perforated acute appendicitis is 23.33% in females and 76.67% in males, which is same in the both the groups A and B as far as sex distribution is concerned and the p value is 1, which is statistically insignificant. The sex distribution in the study showed male preponderance (Table 2).

Table 2: Sex distribution of patients and their p value in both the groups A and B.

Sex	No. of patients (%)		Total (%)	P value
	Group A	Group B		
Female	7 (23.33)	7 (23.33)	14 (23.33)	1.000
Male	23 (76.67)	23 (76.67)	46 (76.67)	
Total	30 (100.00)	30 (100.00)	60 (100.00)	

Seroma formation

Among the patients in group A 10.00% developed seroma and 10.00% of patients developed seroma in group B and the p value is 1, which is statistically insignificant. It infers that post-operative antibiotic therapy does not reduce seroma formation (Table 3).

Table 3: Seroma formation and their p value.

Seroma formation	No. of patients (%)		Total (%)	P value
	Group A	Group B		
No	27 (90.00)	27 (90.00)	54 (90.00)	1.000
Yes	3 (10.00)	3 (10.00)	6 (10.00)	
Total	30 (100.00)	30 (100.00)	60 (100.00)	

Intra-abdominal abscess formation

No patients in group A or group B developed intra-abdominal abscess.

Local site edema

Among the patients in group A 10.00% developed local site oedema and 10.00% of patients developed local site oedema in group B and their p value is 1, which is statistically insignificant. It infers that postoperative antibiotic therapy does not reduce local site oedema (Table 4).

Table 4: Local site edema development and their p value.

Local site oedema	No. of patients (%)		Total (%)	P value
	Group A	Group B		
No	27 (90.00)	27 (90.00)	54 (90.00)	1.000
Yes	3 (10.00)	3 (10.00)	6 (10.00)	
Total	30 (100.00)	30 (100.00)	60 (100.00)	

Pus discharge from the stitch line

In both the groups 10% of the people developed pus discharge from the stitch line and the p value is 1. It infers that that there is no significant difference in the two groups (Table 5).

Stitch line inflammatory changes

In group A, 6.67% of the patients and in group B, 10.00% of the patients developed stitch line inflammatory changes and the p value is 1. It infers that postoperative antibiotic therapy does not reduce the stitch line inflammatory changes (Table 6).

Table 5: Pus discharge from the stitch line and their p value.

Pus discharge	No. of patients (%)		Total (%)	P value
	Group A	Group B		
No	27 (90.00)	27 (90.00)	54 (90.00)	1.000
Yes	3 (10.00)	3 (10.00)	6 (10.00)	
Total	30 (100.00)	30 (100.00)	60 (100.00)	

Table 6: Stitch line inflammatory changes.

Stitch line inflammation	No. of patients (%)		Total (%)	P value
	Group A	Group B		
No	28 (93.33)	27 (90.00)	55 (91.67)	1.000
Yes	2 (6.67)	3 (10.00)	5 (8.33)	
Total	30 (100.00)	30 (100.00)	60 (100.00)	

Fever

In group A 13.3% and in group B 10.00% of the patients developed fever and their p value is 1. It infers that post-operative antibiotic therapy does not decrease fever development (Table 7).

Table 7: Fever in the both groups A and B.

Fever	No. of patients (%)		Total (%)	P value
	Group A	Group B		
No	28 (86.67)	27 (90.00)	55 (88.33)	1.000
Yes	4 (13.33)	3 (10.00)	7 (11.67)	
Total	30 (100.00)	30 (100.00)	60 (100.00)	

Table 8: Length of hospital stay mean values and p value.

Length of hospital stay	Group A	Group B	P value
Sample size	30	30	0.508
Mean±standard deviation	1.23±0.5	1.17±0.46	
Median	1	1	
Min-max	1-3	1-3	
Inter quartile range	1-1	1-1	

Length of hospital stay

The mean length of hospital in case group A is 1.23 with a standard deviation of ±0.5 and the mean length of hospital stay in group B is 1.17 with a standard deviation of ±0.45. The p value of length of hospital stay of patients was found to be 0.508, which is statistically insignificant (Table 8).

DISCUSSION

SSI in appendectomies is alarming for the patients and the operating surgeons. The factors involved include duration of pre-operative symptoms (hours), stage of the disease, choice and pre-operative use of antibiotics, management practices of the hospital and the factors relating to the individual patient. Antibiotics heavily influence the rate of SSIs in non-perforated appendectomy cases.^{16,17} In fact, there are studies that indicate their use in the post-operative period is without benefit and even controversial for non-perforated appendectomy cases. In our present study, there was no significant difference between the rates of SSIs among the patients with non-perforated acute appendicitis between two groups. Therefore, the addition of post-operative antibiotics with single dose of pre-operative antibiotic did not reduce the rate of SSIs in patients with non-perforated acute appendicitis. The incidence of post-operative SSIs after appendectomy in patients with non-perforated acute appendicitis has been reported to range from 0% to 11%.¹⁵⁻²⁰

In our study among the patients in group A 10.00% developed seroma and 10.00% of patients developed seroma in group B and the p value is 1 (>0.05) which is statistically insignificant. It infers that post-operative antibiotic therapy does not reduce seroma formation and it is comparable with the study by Le et al, 2006, in which they reviewed retrospectively 763 patients who underwent appendectomy for non-perforated appendicitis. Comparing patients who did and did not receive post-operative antibiotics no significant differences in the rates of all SSIs (10% versus 9%, p=0.64), superficial SSIs (9.3% versus 5.4%, p=0.13), deep SSIs (0.3% versus 0.5%, p=1.0), organ space SSIs (2.8% versus 2.7%, p=0.87), urinary tract infections (0.6% versus 0.5%, p=1.0), and diarrhoea (2.5% versus 1.1%, p=0.34) were found between groups.

In our study analysis among the patients in group A 10.00% developed local site oedema and 10.00% of patients developed local site oedema in group B and their p value is 1 (>0.05) which is statistically insignificant. It infers that post-operative antibiotic therapy does not reduce local site oedema formation and this is consistent and comparable with the study by Sadraei-Moosavi, 2017. During the study period, 152 patients were admitted with acute appendicitis for open appendectomy. Seventy-six patients received only a single dose of pre-operative antibiotics (group A); while 76 patients received post-operative antibiotics up to 24 hours after surgery plus pre-operative antibiotics (group B). One patient in group A and one, patient in group B developed SSIs two groups. There was no statically significant difference in the rate of SSIs in two groups in this study.

In the subgroup analysis in both the groups A and B, 10% of the people developed pus discharge from the stitch line and the p value is 1 (>0.05) which is statistically insignificant. It infers that that there is no significant

difference in the two groups. This is consistent with the study by Coakley et al.¹⁷ In total, 728 cases contained sufficient follow-up data for analysis; 334 of these patients received postoperative antibiotics and 394 did not. There were no significant differences in patient demographics and medical comorbidities.

In our study analysis, in group A 6.67% of the patients and in group B 10.00% of the patients developed stitch line inflammatory changes and the p value is 1. It infers that post-operative antibiotic therapy does not reduce the stitch line inflammatory changes. Coakley et al have compared the outcomes of large number of patients (728 subjects) treated with antibiotics before and after appendectomy with those who have received only pre-operative antibiotics. They concluded that the addition of post-operative antibiotics did not reduce infectious complication.¹⁵

In our study, in group A 13.3% and in group B 10.00% of the patients developed fever and their p value is 1. It infers that post-operative antibiotic therapy does not decrease fever development. This observation is consistent with the three studies Mui et al, Coakley et al and Rafiq which included 400 patients in 2015.²¹

In the subgroup analysis, the mean value of group A is 1.23 and mean value of group B is 1.¹⁷ and the p value is 0.508, which is statistically insignificant. It infers that post-operative antibiotic therapy does not decrease the length of hospital stay and this is consistent with the study by Mui et al conducted a randomized trial on 269 patients to define the optimum duration of prophylactic antibiotics in non-perforated appendicitis.¹⁷ They found no significant difference in the wound infection rate between three study groups. rather, they showed that in non-perforated appendectomy cases, the addition of post-operative antibiotics not only failed to add any benefit, but also worsened post-operative morbidity with prolonged hospital stay and increase in antibiotic-associated diarrhea and treatment cost.¹⁵

In our study analysis no patients in both the groups developed intra-abdominal abscess. This is consistent with the study by Rafiq which included 400 patients in 2015. The intra-abdominal abscess formation has rarely been reported after appendectomy in non-perforated acute appendicitis.²¹

CONCLUSION

Hence we can conclude from our study that a well-chosen and adequately timed pre-operative antibiotics are adequate in preventing seroma formation, SSIs, local site oedema, pus discharge from the stitch line, intra-abdominal abscess formation, local site oedema and length of hospital stay in cases of non-perforated appendicitis. Post-operative antibiotics do not affect the rate of occurrence of the above mentioned parameters.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Chowdegowda GK, Arya SV, Sharma AK, Kalwaniya DS, Bajwa JS. A comparative study to determine the role of pre and post-operative antibiotic therapy versus only pre-operative antibiotic therapy in patients of non-perforated acute appendicitis. *Int Surg J* 2020;7:3305-10.