



Original Research Paper

Rational Use of Antibiotics in Patients Undergoing Appendectomy: A Prospective Study

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Abstract

Background & Objectives: Empirical antibiotics are being administered pre and post-operatively in acute appendicitis. The routine, widespread indiscriminate and prolonged antibiotic course has become an ailment in itself, as it gives rise to resistant strains of organisms. The present study was conducted in a tertiary care center, to formulate a plan for the rational use of antibiotics after appendectomy, so effective treatment could be given to those at high risk of developing septic complications.

Methods: This is a prospective study done in General Surgery department at a Tertiary Care Centre from September 2014 to December 2016. 360 cases of appendectomy were studied in this study. Out of which 72 cases belonged to interval appendectomy group, 168 acute appendicitis and 120 cases belonged to the group appendicitis with complications like perforation and gangrene. Patients undergoing interval appendectomy received single dose of antibiotics. Patients having acute appendicitis (uncomplicated) received three doses of antibiotic prophylaxis and patients having complications like perforation and gangrene received antibiotic for 5 days. Post-operative complications like wound infection, wound gaping, etc. were recorded.

Results: The study included 360 patients out of which there were 169 males (65%) and 91 (35%) females with a M: F ratio of 1.86:1. The incidence of wound infection in interval appendectomy, uncomplicated and complicated appendicitis was found to be 6.94%, 8.93% and 13.33% respectively. Incidence of post-operative complications was found to be highest in cases with complicated appendicitis (16.7%) followed by uncomplicated appendicitis (12.50%). Least postoperative complications were seen in patients who had undergone interval appendectomy (6.95%). The difference in white blood cell count, timing of prophylactic antibiotic before surgery, operation time and duration of hospital stay were found to be statistically significantly different in these groups. Statistical analysis was done using SSPE 17.0 software. P value less than 0.05 was taken as statistically significant.

Conclusion: In patients with appendicitis the rational use of antibiotics will reduce the incidence of antibiotic resistance and treatment cost without increasing post-operative complications.

Keywords: Acute appendicitis, appendectomy, perforated appendix, Antibiotics resistance.

Introduction

Appendicitis is the one of the most common cause of acute abdominal pain requiring prompt surgical intervention. The incidence of appendicitis is generally reported to be 10 out of 100,00 inhabitants annually, and the accumulative life risk is reported to be 7%^[1]. Acute appendicitis usually presents with classical symptom of periumbilical pain which later may shift to right iliac fossa. The other symptoms of appendicitis include pain in right iliac fossa, anorexia, nausea and vomiting. In most of the cases the management of appendicitis is surgical^[2,3]. Use of Prophylactic antibiotics is recommended in patients with appendicitis in whom appendectomy is planned^[4,5,6]. Many studies have concluded that postoperative antibiotics may be unnecessary in unruptured appendix but due to fear of development of sepsis and septic shock antibiotics are being routinely administered preoperatively as well as postoperatively even in uncomplicated appendicitis^[7]. This may not only be associated with increased cost of treatment but also may be responsible for emergence of drug resistant bacteria^[8].

It is reported that 3.8% of patients with appendicitis may have associated appendicular abscess or phlegmon. These patients are usually managed conservatively as immediate surgery may be associated with unacceptably high morbidity. The diagnosis of acute appendicitis is usually suspected clinically and confirmed on the basis of ultrasound imaging. However it must be noted that ultrasound is highly operator dependent modality and hence there are chances of false negative results. The common conditions which may mimic appendicitis include pelvic inflammatory disease, biliary colic, renal colic, inflammatory bowel diseases, diverticulitis and ovarian torsion. The use of cross section imaging modalities such as CT and MRI can aid in the diagnosis and also may show presence of free fluid in abdominal cavity. The rational use of imaging including ultrasound and Computed Tomography of abdomen (in cases in whom it is

not contraindicated) has improved the diagnosis of enclosed inflammation and made drainage of intra-abdominal abscesses easier. The risk of recurrence with nonsurgical treatment is found to be approximately 7.4%, and a malignant disease on histopathology is found in 1.2% of patients during follow-up^[9]. With respect to antibiotic therapy, there is variability in the choice, duration of treatment, and route of administration in acute appendicitis. Moreover, there is an increasing problem with antibiotic resistance among bowel pathogens with an increased rate of drug resistant bacteria^[10,11]. Even after antibiotic therapy of relatively short duration, extended spectrum beta-lactamase (ESBL) resistance has been found resulting into increased costs, extended duration of hospitalization and increased morbidity and mortality^[12]. Since improper use of antimicrobial agent is a common risk factor for emergence of antimicrobial resistance, optimum use of antibiotics is essential. In every case of appendicitis treating surgeon must take a rational decision regarding antibiotics use. On one hand inadequate doses of antibiotics in patients may lead to complications such as wound infection, sepsis and pelvic abscess on the other hand irrational and prolonged use of antibiotics may lead to antibiotic resistance. With these facts in mind we conducted this study of 360 patients with appendicitis to formulate a Plan for the rational use of antibiotics after appendectomy, so the effective treatment could be given to those at high risk of developing septic complications.

Materials and Methods

A total of 360 cases of appendectomy were included in this study on the basis of a predefined inclusion and exclusion criteria. The patients were divided into 3 groups.

In preoperative phase, patients were examined thoroughly and clinical diagnosis was established. In females, gynecological conditions mimicking appendicitis were ruled out. After admission, thorough evaluation of the patients was done. Patients were subjected to routine investigations

viz., CBC, kidney function tests, serum electrolytes and plain x-ray abdomen, USG abdomen & pelvis. History and demographic

details were noted in detail. Antibiotics were given as per table 1.

Table 1: Groups of the patients on the basis of type of appendicitis and treatment given

Group	Type of Appendicitis	IV Antibiotics
Group A -	Interval appendectomy (72 cases)	IV Cefotaxime 1 gm 30 min before incision
Group B	Uncomplicated appendicitis (168 cases).	IV Cefotaxime 1gm + IV Metronidazole 500mg three doses given First dose administered on admission. Second dose was given intra-operatively and Third dose was given post operatively six hours after surgery.
Group C	Complicated appendicitis (120 cases) which included gangrenous and perforated appendicitis.	IV Cefotaxime 1gm 8hrly + IV Gentamicin 80mg 12hrly + IV Metronidazole 500mg 8 hourly for 5 days.

Operative Procedure

Patients were explored by McBurney's grid iron incision for interval and emergency appendectomy, while lower midline incision was taken for suspected appendicular perforation. On exploration, the gross features of the appendix were noted and appendectomy was done. Peritoneal lavage with normal saline was given only for localized serous collection and normal saline with Metronidazole for purulent collection. Insertion of peritoneal drain in perforated appendix was left to the choice of the surgeon. Wound was irrigated with normal saline and povidone iodine to skin closure. Post operatively patients were monitored with respect to pulse, blood pressure, temperature and condition of the wound. Appropriate IV fluid and antibiotics (depending upon the group of patient) was given.

Post-operative care

Wounds were inspected routinely after 72 hours and then on 7th post-operative day, when stitches were removed. If the patient had fever and tachycardia in the immediate post-operative period, then dressing was opened after 48 hours. If the wound was found to be healthy and patient stable then no further antibiotics were given. If the wound was unhealthy swab was taken from the wound for culture and sensitivity. Wound infection was defined according to SSI grading. Post-operative antibiotics were given according to the protocol above. Additional post-operative antibiotic therapy (IV Piperacillin-Tazobactam)

was given if the patient had signs of wound infection, fever, tachycardia or wound discharge etc.

The patients in Group A and B were discharged after 24 hours whereas patients in group C were discharged depending upon clinical condition. All patients were asked to come for stitches removal.

Inclusion Criteria

1. Patients of appendicitis.
2. Age more than 18 years
3. Those who have informed consent.

Exclusion Criteria

1. Those who refused consent.
2. Patients with appendicular abscess or lump however they were followed up and later on included in interval appendectomy group.
3. Patients with medical illnesses such as severe anemia, diabetes mellitus, tuberculosis and ischemic heart disease were also excluded from this study

The statistical analysis was done using SSPE 17.0 software. P value less than 0.05 was taken as significant for statistical purposes. Microsoft office was used for preparing charts and graphs.

Results

The study included 360 patients out of which there were 169 males (65%) and 91 (35%) females with a M: F ratio of 1.86:1.

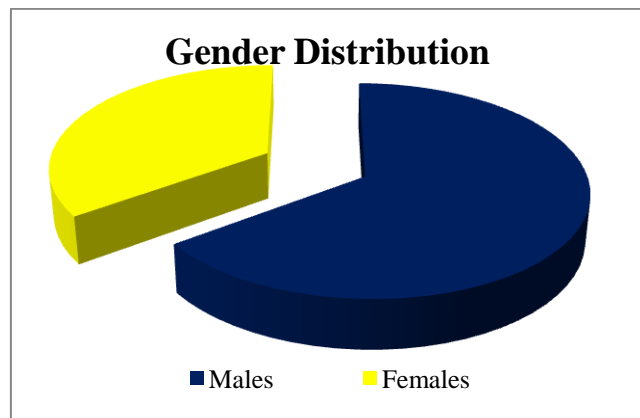


Figure 1: Gender Distribution of the studied cases

The analysis of age groups of the patients showed that the mean age of Group A patients was 26 ± 6.24 years. The mean age of the patients in group B and Group C was found to be 24.06 ± 6.12 and 24.02 ± 5.67 years respectively. The difference in age groups of the studied cases was found to be statistically significant ($P = < 0.05$).

Table 2: Mean age of the studied cases

	Mean Age +/- Std Deviation	Test Of Significance
Group A	26 ± 6.24	P= < 0.05 Significant
Group B	24.06 ± 6.12	
Group C	24.02 ± 5.67	

The analysis of total white blood cells count showed that the highest mean WBC count was highest in group C (12150.48 ± 2022.90) followed by Group B (11285.63 ± 1890.35) and Group A (6706.57 ± 1484.99). The difference in WBC count of the studied cases was found to be statistically significant ($P = < 0.05$).

Table 3: Mean White blood cell count of the studied cases

	White blood cell (WBC) count (cells per cubic mm)	Test Of Significance
Group A	6706.57 ± 1484.99	P= < 0.05 Significant
Group B	11285.63 ± 1890.35	
Group C	12150.48 ± 2022.90	

The analysis of timing of prophylactic antibiotics showed that prophylactic antibiotics were given 30 minutes before in Group A. While in Group B and Group C prophylactic antibiotic were given 31.09 ± 3.21 and 31.47 ± 3.70 minutes before surgery. The difference was found to be statistically significant ($P = < 0.05$).

Table 4: Timing of prophylactic antibiotic before surgery (in minutes)

	Timing of prophylactic antibiotic before surgery (in minutes)	Test Of Significance
Group A	30.00 ± 0.0	P= < 0.05 Significant
Group B	31.09 ± 3.21	
Group C	31.47 ± 3.70	

Duration of operation time was longest in Group C (38.97 ± 6.37 minutes) followed by Group B (25.79 ± 5.29 minutes) and Group A (23.64 ± 3.44 minutes). The difference in duration of operation time was found to be statistically significant ($P = < 0.05$).

Table 5: Duration of operating time (in minutes)

	Duration of operating time (in minutes)	Test Of Significance
Group A	23.64 ± 3.44	P= < 0.05 Significant
Group B	25.79 ± 5.29	
Group C	38.97 ± 6.37	

The incidence of wound infection was: group A (6.94%); group B (8.93%) and in group C (13.33%). It was the lowest in interval appendectomy group and highest in patients who underwent emergency appendectomy for perforated and gangrenous appendicitis (13.33%). The incidence of post-operative complications was high in group C (16.7%) followed by in group B (12.50%) and Group A (6.95%). Post operatively fever and tachycardia was most commonly encountered, next common was post-operative wound discharge; wound gape was least common. Additional antibiotics (IV piperacillin-tazobactam) were needed in 8.33% patients in group C (that is in addition to the doses given in protocol). On histopathology acute-on-chronic appendicitis was found in 41.52% cases, acute appendicitis in 40.98% and acute suppurative with peri-appendicitis was a feature in 17.5% cases.

Table 6 : Surgical Site infections in the studied groups

Characteristic	Group A (n=72)	Group B (n=168)	Group C (n=120)	p value
Surgical Site Infection	5(6.94)	15(8.93)	16(13.33)	0.295 Not Significant
Superficial Surgical Site Infection	5(6.94)	12(7.14)	6(5.00)	0.747 Not Significant
Deep Surgical Site Infection	0(0)	0(0)	10(8.33)	-
Organ Surgical Site Infection	0	0	0	-

When there were no complications, the mean hospital stay was 2 days in group A and group B, and 5.6 days in group C. It was slightly higher when there were complications i.e. 4.3, 6.60 and

7.2 in group A, B & C respectively. The difference was found to be statistically significant (P<0.05).

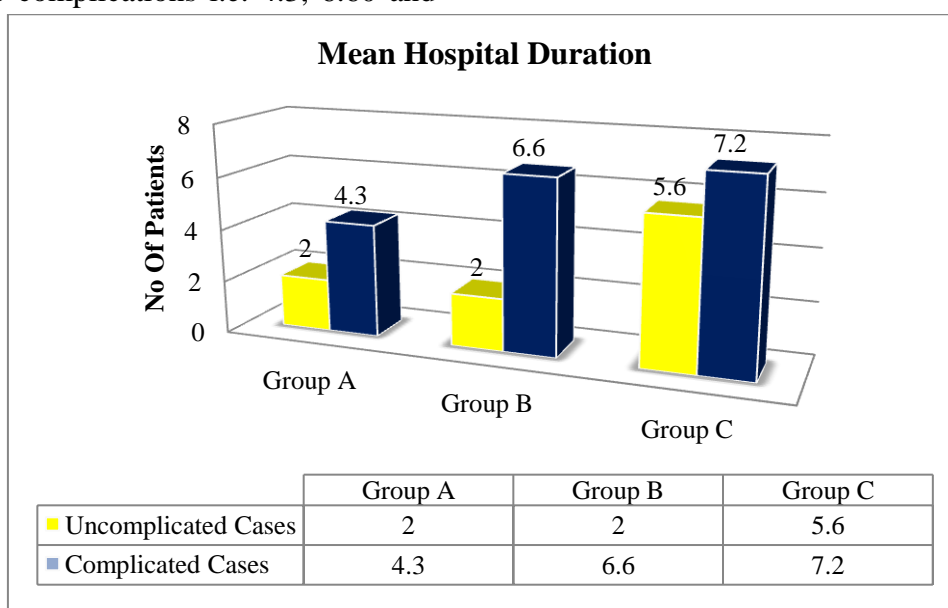


Figure 2: Mean Duration of Hospital Stay in the studied cases

Discussion

Many studies have reported that nonsurgical management of uncomplicated appendicitis by conservative measures such as antibiotics is associated with considerably low rates of complications their efficacy is found to be low as compared to surgical treatment. Uses of parenteral broad spectrum antibiotics have found to be effective in unruptured appendicitis by many studies^[13]. Even if surgical interventions are planned intravenous antibiotics are indicated to reduce the complications in these patients such as infection and sepsis. Various meta-analyses found that the complication rates in patients undergoing appendectomy were considerably less in patients who received parenteral antibiotics during and after surgical procedure^[14].

In our study majority of the patients were found to be in between the age group of 20-30 years. The mean age of patients in group A, group B and group C was found to be 26, 24.06 and 24.02 years. The overall mean age of the studied cases was found to be 24.69 years. The appendicitis is reported to be usually affecting the patients in the young age group. In a study of 321 cases Oguntola AS^[15] et al found the mean age of the patients to be 25.79 years. In another large study of patients with acute appendicitis Mohammed Al-Omran et al^[16] found the mean age of the affected patients to be 26 years. In this regard our study was found to be comparable to the studies conducted by Oguntola AS et al and Mohammed Al-Omran et al^[15,16].

The analysis of total leucocyte count of the studied cases showed that the highest rise in total leukocyte count was seen in patients in Group C (complicated appendicitis) followed by the patients in group B (uncomplicated appendicitis). Leukocytosis was not a feature of patients who had undergone interval appendectomy. In a study of 456 patients Al-Gaithy Z K et al found that mean WBC count in patients with complicated appendicitis was 14340 /mm³ whereas in uncomplicated appendicitis this was found to be 14340/mm³. The findings of our study were found to be comparable to the findings of the study conducted by Al-Gaithy Z K et al^[17].

From this prospective study we could conclude that in cases with interval appendectomy, single dose antibiotic for the purpose of prophylaxis is sufficient. Proper sterilization techniques and normal immune system are sufficient to prevent wound infection in these patients. As far as uncomplicated acute appendicitis (group B) is concerned only 3 doses of peri-operative antibiotics (cefotaxime and metrogyl) were found to be enough to prevent infection. Since in patients undergoing appendicitis the source of infection ie inflamed appendix is removed there are less chances of infections. However it is important that in case of symptomatic patients (fever, malaise or chills) broad spectrum antibiotics coverage is essential. Finally in cases of complicated appendicitis (Group C) administration of parenteral antibiotics is essential for prevention of complications such as wound infection, sepsis and septic shock. In a study of 263 patients DJ pinto et al^[18] concluded that antibiotics are not likely to reduce incidence of wound infection in patients with normal or even inflamed appendices. Similar conclusions were drawn by the authors such as David IB et al and Xu S et al^[19,20].

Conclusion

Though in complicated appendicitis, antibiotics are needed for a relatively longer time, in cases of uncomplicated appendicitis only 3 doses of peri-

operative antibiotics were found to be sufficient. Rational use of antibiotics in these patients will reduce incidence of antibiotic resistance without compromising the post-operative clinical course of the patients.

Funding: No funding sources

Conflict of interest: None to declare

Ethical approval: The study was approved by the institutional ethics committee

References

1. Andersson RE: Appendicitis: Epidemiology and diagnosis. Doctoral Thesis, Linköpings universitet, Sweden, 1998.
2. O'Connell PR. The vermiform appendix In: Williams NS, Bulstrode CJK, O'Connell PR, eds. Bailey and Love's Short Practice of Surgery. 26th ed. Boca Raton, FL: CRC Press; 2013:1199-1209.
3. Richmond B. The Appendix. In: Townsend CM, Beauchamp RD, Evers BM, Mattox KL, eds. Sabiston Textbook of Surgery. 20th ed. Philadelphia: Elsevier; 2017:1296-1303.
4. Lamont P. Surgical Infection. In: Williams NS, Bulstrode CJK, O'Connell PR, eds. Bailey and Love's Short Practice of Surgery. 26th ed. Boca Raton, FL: CRC Press; 2013:59-62.
5. Barie PS. Surgical Infections and Antibiotic Use. In: Townsend CM, Beauchamp RD, Evers BM, Mattox KL. Sabiston Textbook of Surgery. 20th ed. Philadelphia: Elsevier; 2017:245-7.
6. ASHP Therapeutic Guidelines on Antimicrobial Prophylaxis in Surgery. American Society of Health-System Pharmacists. Am J Health Syst Pharm. 1999;56(18):1839-88.
7. Daskalakis K, Juhlin C, Pahlman L. The use of pre-or postoperative antibiotics in surgery for appendicitis: a systematic review. Scandinavian Journal Surg. 2013;103(1):14-20.

8. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999. Hospital infection control practices advisory committee. *Infect Control Hosp Epidemiol.*1999;20(4):250-78.
9. Andersson RE, Petzold MG: Nonsurgical treatment of appendiceal abscess or phlegmon: A systematic review and meta-analysis. *Ann Surg* 2007;246(5):741–748.
10. Ventola CL. The Antibiotic Resistance Crisis: Part 1: Causes and Threats. *Pharmacy and Therapeutics.* 2015;40(4):277-283.
11. Chabok A, Tarnberg M, Smedh K et al: Prevalence of fecal carriage of antibiotic resistant bacteria in patients with acute surgical abdominal infections. *Scand J Gastroenterology* 2010;45(10):1203–1210.
12. Shaikh S, Fatima J, Shakil S, Rizvi SMD, Kamal MA. Antibiotic resistance and extended spectrum beta-lactamases: Types, epidemiology and treatment. *Saudi Journal of Biological Sciences.* 2015;22(1):90-101.
13. Busuttill RW, Davidson RK, Fine M, Tompkins RK. Effect of prophylactic antibiotics in acute nonperforated appendicitis: a prospective, randomized, double-blind clinical study. *Annals of Surgery.* 1981;194(4):502-509.
14. Fine M, Busuttill RW. Acute appendicitis: efficacy of prophylactic preoperative antibiotics in the reduction of septic morbidity. *Am J Surg.* 1978 Feb;135(2): 210–212.
15. Oguntola AS, Adeoti ML, Oyemolade TA. Appendicitis: Trends in incidence, age, sex, and seasonal variations in South-Western Nigeria. *Ann Afr Med.* 2010 Oct-Dec;9(4):213-7.
16. Al-Omran M, Mamdani MM, McLeod R. Epidemiologic features of acute appendicitis in Ontario, Canada. *Canadian Journal of Surgery.* 2003;46(4):263-268.
17. Al-gaithy Zuhoor K. Clinical value of total white blood cells and neutrophil counts in patients with suspected appendicitis: retrospective study. *World Journal of Emergency Surgery : WJES.* 2012;7:32.
18. Pinto DJ, Sanderson PJ. Rational use of antibiotic therapy after appendectomy. *British Medical Journal.* 1980;280(6210): 275-277.
19. David IB, Buck JR, Filler RM. Rational use of antibiotics for perforated appendicitis in childhood. *J Pediatr Surg.* 1982 Oct;17(5):494-500.
20. Xu S, Yu X, Li Y, et al. Analysis of antibiotics selection in patients undergoing appendectomy in a Chinese tertiary care hospital. *SpringerPlus.* 2016;5(1):1839.