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Original Article

Single-dose Antibiotic Therapy for Acute Appendicitis

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Abstract

Background: Acute appendicitis is the most common cause of acute abdomen, and appendectomy is the most frequently performed emergency operation. Despite the fact that the mortality rate has been dramatically reduced following appendectomy over the last three decades, septic complications continue to be a significant problem, occurring in a large percentage of patients.

Materials and Methods: This is a multicenter prospective randomized clinical trial conducted on the surgical patients with a diagnosis of acute appendicitis. 150 consenting patients were enrolled in the study. The patients were randomly allocated into three groups. Group "A" received metronidazole, group "B" received cefotaxime, and group "C" received both cefotaxime and metronidazole. The single-dose antibiotic was given to all patients belonging to their respective groups intravenously 1 h before the surgery to all the groups. All operations were performed by resident surgeons under direct attending supervision. To maintain uniformity in the operative procedure, a standard operative protocol was followed. This included a 10 min Lodophor® preparation, use of Steridrape®, right lower quadrant muscle splitting (grind-iron/McBurny's) incision, minimal handling of the appendix, appendiceal stump inversion, glove change before closure, wound closure with absorbable (polyglycolic acid) sutures.

Result: A total of 150 patients were included in this multicener prospective randomized study. In Group "A" 50 patients received only metronidazole, in Group "B" 50 received only cefotaxime and in Group "C" 50 patients received both metronidazole and cefotaxime. In the present series, 91 males (60.7%) were found to be more affected than 59 females (39.3%), the ratio being 3:2.

Conclusion: The extended single drug empirical regime of cefotaxime for 5 days in complicated (perforated/abscessed) appendicitis is effective in reducing the post-operative infection rate. Specific anaerobic coverage of metronidazole is unnecessary and may be contraindicated, since injudicious use of anaerobically oriented antibiotics for prophylaxis may result in untoward side effects and will, undoubtedly, play a role in the development of resistant microbes which will preclude the use of these agents for later specific therapy.

Keywords: Anti-bacterial agents, Antibiotic prophylaxis, Postoperative complicatons, Risk factors, Surgical wound infection

INTRODUCTION

References about antibiotic therapy for acute appendicitis can be found in ancient time's literatures. However, significant development in the prophylactic management of post-operative complications is seen within the last century.[1-6] Many studies have been done on the prophylactic antibiotic therapy for acute appendicitis. Few of them which have been done on single-dose are as follows:

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MATERIALS AND METHODS

The samples collected were processed as follows:

a. Direct microscopic examination of gram stained smear.
b. Inoculation of the samples onto different culture media for aerobic and anaerobic organisms.
c. Preliminary identification.
d. Biochemical tests.
e. Antibiotic sensitivity.

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a. Direct microscopy
   Using the 1st swab, a smear was made on a clean glass slide and stained by Gram-staining. The smear was screened for pus cells, the gram reaction, morphology, arrangement, and number of types of organisms was noted.
b. Culture for aerobic organisms
   The 2nd swab was inoculated onto plates of MacConkey agar and 5% sheep blood agar by rolling the swab over the agar and streaking from the primary inoculums, using a sterile bacteriological loop. These plates were incubated at 37°C for 24-48 h. The primary plates were observed for any visible growth after 24 h and if there was no growth within 24 h, subcultures were made from nutrient broth onto the same solid media. All types of colonies on the primary plates were examined macroscopically using a magnifying lens, and the colony characteristics recorded. Smear was made from isolated colonies, stained by Gram-staining and were observed under oil immersion objective for the size, shape, gram reaction, arrangement, presence or absence of specific structures like granules which would help in preliminary identification.

MacConkey Agar

After 24-48 h of incubation, the colony characteristics were noted along with color to detect lactose utilizing properties of the organism. Lactose fermenting bacteria produced colonies that were in varying shades of red, often mucoid and non-lactose fermenting bacteria appeared colorless or transparent. On Gram-staining, often Gram-negative bacilli and sometimes pleomorphic and coccobacillary forms were seen.

Blood Agar

After 24-48 h of incubation, the colony characteristics were noted and the plates were examined to detect hemolytic reactions on the agar. Convex, 2-3 mm creamy yellowish to white colonies with entire edges, often beta-hemolytic were seen. On Gram-staining, Gram-positive cocci arranged in clusters were seen. All in embers of the Enterobacteriaceae produced relatively large, dull, gray, dry or mucoid colonies on blood agar. Based on the above observations, the organisms were grouped mainly into Gram-negative bacilli and cocci, Gram-positive cocci and bacilli.

Gram-negative Bacilli

The isolates were confirmed by the following tests:

Catalase test

About 1 ml of 3% hydrogen peroxide was taken in a sterile test tube. A small amount of the culture was picked from a colony on MacConkey agar with a thin glass rod. The glass rod was inserted into the Hydrogen peroxide solution. The production of effervescence immediately from the surface of the solid culture material indicated a positive test.

Oxidase test (dry filter paper method)

A speck of culture was rubbed onto moistened filter paper disks, impregnated with freshly prepared 1% tetramethyl-p-phenylene-diamine dihydrochloride. An intense deep purple hue, appearing within 5-10 s indicated a positive reaction.

Motility

Motility was tested by hanging drop preparation from a 2 to 4 h growth in peptone water medium.

Biochemical tests

i. Nitrate reduction test
   The test organism was inoculated in nitrate broth containing 0.02% concentration of potassium nitrate and incubated for 96 h. Equal volumes of nitrate test reagents, A and B were mixed before use and 0.1 ml added to test culture. A red color developing within a few minutes indicated presence of nitrites and hence the ability of the organism to reduce nitrate.
ii. IMVIC tests
   a. Indole test
      About 2-3 ml of peptone water was inoculated with the test organisms and incubated for 48 h at 37°C. 0.5 ml of Kovac's reagent was added. The test was interpreted as positive if there was a change in color to red in the alcohol layer or negative if no change in color.
   b. Methyl red test
      A pure culture of the test organism was inoculated into 5 ml of glucose phosphate peptone water medium. After incubation for 48-72 h, 5 drops of methyl red reagent was added directly to the broth. The development of bright red color indicated a positive test and negative was yellow.
   c. Voges–proskauer test
      The test organism was inoculated into glucose phosphate peptone water and incubated at 37°C for 48 h only. Acetoin formation can be detected in the test mediuln by observing the development of an eosin pink color in 2-5 min, after adding 1 ml of 40% potassium hydroxide and 3 ml of a 5% solution of alpha-naphthol in absolute ethanol.
   d. Citrate utilization test
      A well isolated colony was picked up from the MacConkey plate and inoculated on the slant surface of the Simmon's citrate agar tube and incubated for 96 hrs at 37°C. The production

of a blue color in the test medium indicated the presence of alkaline products and a positive citrate utilization test.

iii. Urease production
The surface of a Christensen's urea agar slant was inoculated heavily and incubated at 37°C. After 4 h or overnight incubation, a red color in the slant or throughout the medium indicated a positive test for urea hydrolysis.

iv. Fermentation tests
   a. Sugar fermentation tests
   A speck of solid culture or a drop of liquid culture was inoculated into 5 ml of peptone water containing 0.5% test sugar compound, 1% Andrade's indicator and Durham's tube. After incubation for 24-48 h, the media was examined for the presence of a color change indicating acid production and for gas formation in the Durham's tube.
   b. TSI
   Using a straight wire the colony was first stabbed deep into the butt of the TSI agar, streaked over the surface of slant and incubated aerobically at 37°C for 24 h. The phenol red indicator shows different colors at different pH. Yellow coloration was seen when the medium is acidic due to sugar fermentation and pink color was seen due to the alkaline nature of the medium, when oxidative decarboxylation of the proteins take place. Hydrogen sulfide produced was visualized as a black precipitate.

v. Phenylalanine deaminase test
   The test organism was inoculated heavily onto a phenylalanine test medium and incubated overnight at 37°C. 4-5 drops of ferric chloride solution were added; the test was interpreted as positive if a green color developed.

Blood Agar

After 24 h of incubation, the colony characteristics such as size, form, elevation, margins, color, surface, density, and consistency are observed. The plates were examined to detect hemolytic reactions in the agar.

Gram-positive Cocci

Catalase and oxidase tests were done by picking up culture material from center of isolated colonies from blood agar plate.

Slide Coagulase Test (Willams and Harper, 1946)

A colony suspected of being a staphylococcal species was emulsified in a drop of sterile saline on a clean glass slide with a minimum of spreading. A drop of citrated Human plasma was stirred into the staphylococcal suspension on the slide. Similar suspensions were made with known positive and negative Staphylococcal strains to confirm the proper reactivity of plasma. Coarse clumping of the cocci when visible to the naked eye within 10 s, indicated the organism was slide coagulase positive. The test was confirmed with a tube coagulase test.

Tube Coagulase Test

About 1 ml volumes of I in 6 dilution of plasma (0.85% NaCl) were taken in small test tubes. A colony of the staphylococcus under test was mixed in a tube of diluted plasma. Positive and negative controls and a tube of unseeded diluted plasma were set-up, tubes were incubated at 37°C for 4 h. They were examined at 1, 2 and 4 h for clot formation and any degree was read as positive. The plasma was converted into a stiff gel that remained in place when the tube was tilted. If no clot was observed, the tube was re-incubated at room temperature and read again after 18 h. Clot formation confirmed the slide test and the organism was identified as *Staphylococcus aureus*.

Bacitracin Sensitivity

Three to four isolated colonies of the beta-hemolytic streptococci were picked using a cotton swab and streaked on a blood agar plate. A 0.04 unit bacitracin disk was placed on the inoculum and incubated at 37°C. Any zone around the disk was considered as sensitive, which differentiates Group A streptococci from other beta-hemolytic streptococci which are resistant and grow right up to the disk.

CAMP Test

Beta-hemolytic Staphylococci were streaked down the center of a blood agar plate. An inoculum of the beta-hemolytic streptococcus to be identified was streaked perpendicular to the Staphylococcal streak, without intersecting. Known A and B streptococcal strains are similarly inoculated on the same plate as negative and positive controls, respectively. The plate was incubated at 37°C for 18-24 h. Group B streptococci were identified with the appearance of an arrow head shaped area of increased hemolysis, near the area where the two streaks were closest.

Antibiotic Sensitivity

Antibiotic sensitivity of isolates was tested using the modified Kirby-Bauer method (NCCLS). Two or three identical colonies were taken from the primary culture plates with sterile loop and suspended in sterile saline in a test tube. The turbidity was compared and adjusted to 0.5 MacFarland tube turbidity standard. A sterile swab was dipped into the inoculum. Excess Inoculum was removed by pressing and rotating the swab firmly against the side of the tube, above the level of the liquid. The swab was streaked all over the surface of a Mueller-Hinton agar

plate three times, rotating the plate through an angle of 60° after each application. Finally, the swab was passed round the edge of the agar surface.

Culture for Anaerobic Organisms

The aspirate in the syringe or the 3rd swab was inoculated into a plate of freshly poured 5% blood agar, a plate of blood agar with hemin 5 μg/ml and menadione 10 μg/ml and a blood agar plate with gentamicin 10 μg/ml. The plates were placed in the anaerobic jar of Dynamicro GR anaerobic system. Silicon grease was applied on the rim of the jar and lid generously. The contents of the dyanox anaerobic charge (P2) were placed at the bottom of the jar. 40 ml of 1:4 sulfuric acid was poured on the charge quickly; the plates were placed the lid closed and clamped tightly. The external cup was filled with saturated sodium carbonate solution a vigorous bubbling was seen immediately. A plate of blood agar streaked with a known pseudomonas strain was kept inside the jar as a biological indicator. The anaerobic plates are incubated at 370C for 48-72 hrs. Subcultures were done similarly from the RCMB after 4 days when there was no growth on the primary plates. Colony morphology was recorded in detail; this included colony size, shape, color, internal appearance profile, opacity, general appearance (e.g., mucoid, glistening, breadcrumb like, dull), and other distinctive characteristics. Transmitted light was used to look for beta hemolysis, a double zone of beta-hemolysis and greening of the agar which usually is more apparent after exposure to air.

Catalase Test

About 1 ml of 15% hydrogen peroxide was taken in a test tube; the suspected colonies were harvested on a glass rod and dipped into the hydrogen peroxide solution. The evolution of bubbles denoted a positive test.

Spot Indole Test

The growth from the blood agar plate was rubbed into filter paper saturated with para-dimethylaminocinnamaldehyde reagent. A blue color denotes a positive test.

Aerotolerance Test

Each colony type on the anaerobic blood agar plates was subcultured onto two plates of blood agar and one was incubated aerobically and the other anaerobically. If there was growth on the aerobic plate, the organisms were considered aerobes and correlated with the aerobic culture; if there was no growth in the aerobic plate and growth was seen only in the anaerobic plate, the organisms were considered anaerobes.

Special Potency Antibiotic Disc Susceptibility

Colistin 10 μg, vancomycin 5 μg and Kanamycin 1 mg disks were placed on the first quadrant of a well streaked blood agar plate. A zone size of 10 mm or less was considered resistant. These disks were used as an aid in determining grams reaction, and in separating the bacteroides and Fusobacterium species Gram-positive organisms are resistant to Colistin and sensitive to Vancomycin, whereas Gram-negative organisms are resistant to Vancomycin. Fusobacterium are susceptible to both Kanamycin and Coiistin and Bacteroides are generally resistant to Kanamycin but variable in susceptibility to Colistin. All the results were recorded. The standard reference strains of *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27852 ("Boston" strain), and *S. aureus* ATCC 25923 were used as internal controls with the facultative organisms. Two control strains of *Bacteriodes fragilis* (UCLA #55973 and #55711) were tested simultaneously with all anaerobic isolates. Antimicrobial susceptibility testing of facultative organisms was performed by the ICS-WHO agar dilution method[2]. The following ranges of drug concentrations were tested: Cefotaxime: 30 μg/ml and metronidazole: 0.25-16 μg/ml. An inoculum of approximately 10^4 organisms diluted from broth cultures in the logarithmic phase of growth was used. Anaerobic bacteria were tested by the agar dilution method, using Wilkins-Chalgren medium (pH = 7.2).[3] The following ranges of drug concentrations were tested: Cefotaxime: 30 μg/ml; metronidazole: 0.25-16 μg/ml. An inoculum of 10^5 organisms was used after 72 h incubation on blood agar and an18-24 h incubation in Schaedler broth at 37°C. The plates were read after incubation at 37°C in a GasPak® jar for 48 h.

RESULTS

A total of 150 patients were included in this prospective randomized study. In Group "A" 50 patients received only metronidazole, in Group "B" 50 received only cefotaxime, and in Group "C" 50 patients received both metronidazole and cefotaxime. In the present series, 91 males (60.7%) were found to be more affected than 59 females (39.3%), the ratio being 3:2 (Table 1).

The most common age in this study was between 15 and 25 years which constituted 67 cases (44.6%), the next common being 26-35 years 42 cases (28%) followed by the age group 4-14 years 27 cases (18%). Acute appendicitis was uncommon before the age of 4 years and less common between 36 and 45 years was seen in only 8 cases which constituted (5.3%). The incidence of appendicitis between the age group 46 and 55 years constituted only 2 cases (1%) and in age group 56-65 only 3 cases (2%). The youngest case recorded of 4 years of age and the oldest 70 years (Table 2).

The most common presenting symptom was pain in the abdomen which was present in all the 150 cases (100%). The next common symptom was vomiting which was present in 120 (80%) of cases followed by constipation

Table 1: Distribution of sex

Sex	Group A number patients % age	Group B number patients % age	Group C number patients % age	Total number patients % age	Kini's series 1950
Male	32 (64)	28 (56)	31 (62)	91 (60.7)	81.7
Female	18 (36)	22 (44)	19 (38)	59 (39.3)	17.7
Total	50 (100)	50 (100)	50 (100)	150 (100)	

Table 2: Distribution of age

Age in years	Number patients (%)			
	Group A	Group B	Group C	Total
4-14	8 (16)	9 (18)	10 (20)	27 (18)
15-25	24 (48)	24 (48)	19 (38)	67 (44.6)
26-35	16 (32)	13 (26)	13 (26)	42 (28)
36-45	2 (4)	3 (6)	3 (6)	8 (5.3)
46-55	0 (0)	0 (0)	2 (4)	2 (1)
56-65	0 (0)	1 (2)	2 (4)	3 (2)
>65	0 (0)	0 (0)	1 (2)	1 (0.6)
Total	50 (100)	50 (100)	50 (100)	150

Table 3: Clinical features

Clinical features	Present series	Campbell McPhail
	Cases (%)	
Abdominal pain	150 (100)	99
Vomiting	120 (80)	74
Constipation	72 (48)	54
Pyrexia	48 (32)	26
Diarrhea	15 (10)	10
Signs		
Mcburney's tendency	147 (98)	100
Rovsing's	81 (54)	61
Muscle guarding	84 (56)	72

Table 4: Duration of surgery

	Duration in minutes		
	Group A	Group B	Group C
Range	25-100	35-100	25-120
Mean	56±17	61±20	60±23

in 72 (49%) and diarrhea in 15 (9%). Fever was present in 48 (33%) of cases which were never more than 100°F. On examination tenderness at Mcburney's point was seen in 147 (98%) of cases, muscle guarding in 84 (56%) of cases, Rovsing's sign in 81 (54%) of cases (Table 3).

The duration of surgery in minutes in all the groups was similar, Group A (25-100), Group B (35-100), and Group C (25-120) (Table 4).

Sixteen patients in metronidazole group developed wound sepsis compared with five in cefotaxime group and five in the metronidazole and cefotaxime group. The uncomplicated cases which got infected were in Group A (9 cases out of 41 cases), in Group B (2 out of 40 cases) and in Group C (2 out of 38 cases) whereas in complicated cases in Group A (7 out of 9 cases), in Group B (2 out of 10 cases) and in Group C (3 out of 12 cases). The infection rate in uncomplicated was 13 out of 119 cases (11%), in complicated cases 12 out of 31 cases (38.7%), in Group-A 16 out of 50 cases (32%), in Group-B 4 out of 50 cases (8%), and in Group-C 5 out of 50 cases (10%) (Table 5). For statistical analysis, we used the χ^2 test with yates correction. The reduction in the wound sepsis by the use of cefotaxime or the combination of metronidazole and cefotaxime is statistically significant when compared with metronidazole alone. If the appendicitis is subdivided into uncomplicated cases (normal, acutely inflamed or gangrenous) in which a single- dose of antibiotic was used, and the complicated cases (perforated or abscessed) in which a 5-days course of antibiotics was used this difference in the wound sepsis in each of the two subgroups is also statistically significant. There is no statistical difference in wound sepsis between the patients who received cefotaxime alone and those who received a combination of metronidazole and cefotaxime. There was no residual intraperitoneal abscess in this study.

There is increased percentage of positive peritoneal culture in correlation with increased degree of appendiceal inflammation in all groups (Table 6).

No statistical difference between positive aerobic and anaerobic cultures among groups ($P > 0.05$) (Table 7).

Delayed wound sepsis (>7 days) occurred in 17 out of 25 patients (68%), it was common in patients who received any of the antibiotic regimes in the study. Thus, the majority of wound infection was detected after the patients were discharged home. For early wound sepsis (<7days) 8 patients (32%), all wound infections were deep 6 in Group A, 1 each in Groups B and C. There is not much difference in the incidence of superficial infection in all the three groups of patients of early wound sepsis, but there was increased incidence of superficial infection in Group A 6 patients when compared to 1 in each Groups B and C (Table 8).

The average post-operative hospital stay per patient was significantly reduced in Group B to 3.72 days when compared to Groups A and C it was 4.42 days and 4.16 days, respectively. Most of the patients were discharged on the fourth day in all the groups (Table 9).

Table 5: Wound infection in relation to degree of appendicitis

Pathological classification	Group "A" metronidazole		Group "B" cefotaxime		Group "C" metronidazole+cefotaxime		Statistical significance
	Number	Infected	Number	Infected	Number	Infected	
Uncomplicated cases	41	9	40	2	38	2	A:B - χ^2=3.81 (P<0.05)
Normal	4	0	4	0	5	0	A:C - χ^2=3.79 (P<0.05)
Acutely inflamed	29	6	28	1	25	1	B:C - not significant
Gangrenous	8	3	8	1	8	1	
Complicated	9	7	10	2	12	3	A:B - χ^2=4.23 (P<0.05)
Perforated	6	5	8	1	10	2	A:C - χ^2=3.82 (P<0.05)
Abscessed	3	2	2	1	2	1	B:C - not significant
Total	50	16 (32)	50	04 (8)	50	05 (10)	A:B - χ^2=7.56 (P<0.05) A:C - χ^2=6.03 (P<0.05) B:C - not significant

Table 6: Positive peritoneal culture in relation to degree of appendicitis

Appendix pathology	Number patients (%)	
	Aerobic	Anaerobic
Normal	1/9 (11.1)	3/9 (33.4)
Acutely inflamed	8/82 (9.85)	8/82 (9.8)
Gangrenous	5/24 (20.8)	7/24 (29.2)
Perforated	12/24 (50)	20/24 (83.3)
Abscessed	4/7 (57.4)	6/7 (85.7)
Total	30/74	44/74

Table 7: Positive peritoneal cultures in relation to groups

Organisms	Number patients (%)		
	Group "A"	Group "B"	Group "C"
Aerobic	11/50 (22)	9/50 (18)	10/50 (20)
Anaerobic	13/50 (26)	15/50 (30)	16/50 (32)
Total	24/50	24/50	26/50

Routinely, aerobic and anaerobic culture swabs were taken from the appendicecal fossa during operation. Positive culture was obtained in 74 swabs (49.7%) and pure growth of bacteria in 40 swabs (26.6%). The most common organisms dated were *E. coli* (30%) and *B. fragilis* (28%) in either pure or mixed growth (Table 10).

DISCUSSION

Our multicenter prospective randomized trail conducted on 150 patients, there was no significant difference in the distribution of cases by age and sex among the three groups. Number of males was 60.75% and female were 39.3% when compared to Kini's series it was 81.7% males and 17.75% females. In our study, Rovising's sign was positive in 54% of cases which is comparable to 61% of positivity in a study conducted by Campbell McPhail *et al*. The duration of the operation in minutes and the pathologic classification of appendix, two factors which would influence the eventual development of post-operative infection, were assessed.[7-10] There was no significant difference in the duration among the three groups. Similarly, classification of the appendix according to gross and microscopic appearance into the categories: Normal, acutely inflamed, gangrenous (uncomplicated) and perforated, abscessed (complicated) related no significant difference among the three groups. Aerobic and anaerobic cultures of appendiceal fossa were obtained in all patients. This demonstrated an increase in positive cultures as the appendicitis progressed from normal, through acutely inflamed, gangrenous, abscessed to perforated appendicitis. There were equal numbers of positive aerobic and anaerobic cultures in the acutely inflamed. In this study, the prophylactic administration of cefotaxime or cefotaxime plus metronidazole was equally effective in significantly reducing the rate of wound infections following appendectomy for both uncomplicated and complicated appendicitis when compared with the administration of metronidazole alone.[11-15]

The use of prophylactic antibiotics in nonperforated (uncomplicated) appendicitis has been questioned by some authors because of relatively minor degree of bacterial inoculation in these patients and the relatively low incidence of infection. However, a large number of reports indicate that despite a positive peritoneal culture in <20% of these patients, the infection rate is significant and ranges from 10% to 20%. Based on the guidelines which have been proposed for appropriate preventive antibiotic usage an incidence of wound infection of approximately 11% in uncomplicated (nonperforated) appendicitis is of sufficient magnitude to justify prophylactic antimicrobial administration. A positive peritoneal culture of 74 swabs in my study yielded *E. coli* in 30% of patients and *B. fragilis* in 28%. In addition, there was a direct correlation with the degree of appendiceal inflammation and the percentage of positive peritoneal and subcutaneous tissue cultures. Post appendectomy infections are in the majority of patients caused by a polymicrobial flora consisting of facultative aerobes and obligate anaerobes.

Table 8: Early and delayed wound sepsis

Classification of wound	Metronidazole Group A	Cefotaxime Group B	Metronidazole+cefotaxime Group C	Total
Deep	6	1	1	8 (32)
Early (<7 days)	6	1	1	
Superficial	0	0	0	
Deep	6	2	3	17 (68)
Delayed (>7 days)	10	3	4	
Superficial	4	1	1	

Table 9: Post-operative stay

Number of days	Number patients (%)		
	Group A	Group B	Group C
2 days	4 (8)	6 (12)	4 (8)
3 days	20 (40)	28 (56)	23 (46)
4 days	5 (10)	4 (8)	5 (10)
5 days	5 (10)	6 (12)	6 (12)
6 days	10 (20)	2 (4)	8 (16)
7 days	2 (4)	2 (4)	2 (4)
>7 days	4 (8)	2 (4)	2 (4)
Total post-operative days	221	186	208
Average post-operative days/patient	4.42	3.72	4.16

Table 10: Bacteria isolated from appendicular fossa swab culture

Organisms isolated	Metronidazole Group A, (n=26)		Cefotaxime Group B, (n=24)		Metro+cefotaxime Group C, (n=24)		Total
	Pure growth	Mixed growth	Pure growth	Mixed growth	Pure growth	Mixed growth	
Aerobes							
E. coli	6	3	4	3	3	3	22
Klebsiella	1	1	1	1	2	1	7
P. aeruginosa	2	1	1	1	1	1	7
Proteus	1	-	-	-	-	1	2
S. aureus	-	-	-	1	1	-	2
Enterobacter	1	1	1	-	1	-	4
S. faecalis	-	2	-	-	-	-	2
Strep species	-	1	1	-	-	-	2
Alcaligens species	-	-	-	-	-	1	1
Anaerobes							
B. fragilis	4	2	5	3	3	4	21
A. streptococcus	-	1	-	1	1	1	4

E. coli: Escherichia coli, B. fragilis: Bacteriodes fragilis, S. faecalis: Streptococcus faecalis, S. aureus: Staphylococcus aureus, P. aeruginosa: Pseudomonas aeruginosa, A. streptococcus: Anaerobic streptococcus

E. coli is the most frequently cultured aerobic from both contaminated peritoneal fluid and from infected wounds. Of the anaerobes *B. fragilis* the most common pathogen, and in Leigh *et al*. was cultured from the appendiceal fossa in 37% of the patients undergoing appendectomy and 78% of the patients where bacteria were isolated from this sight. Our study supports this finding of the prevalence of *B. fragilis* by 28% from appendiceal fossa contamination in acute appendicitis. Although a wide variety of antimicrobial agents, both singly and combination have been used for and antimicrobial prophylaxis in acute appendicitis, a cephalosporin alone appears to be best suited for this role. The reasons for this include the low incidence of toxicity favorable pharmacokinetic properties which allow rapid equilibration between blood, interstitial fluid, and tissue that result in bactericidal levels when the drugs are administered 30-60 min before surgery and excellent spectrum for facultative pathogens.[15-20]

Similarly, in a study by Busuttil *et al*.,[21] the Administration of cefamandole has reduced the post-operative hospital stay per patient to 2.9 when compared to placebo it was 3.8 and in combination with carbenicillin it was 3.2 days per patient. By the reduction of post-operative days, the cost of hospitalization will be significantly reduced.

CONCLUSION

Based on the results of this study, we recommend that:

1. Pre-operative prophylaxis of single-dose of cefotaxime is efficient for patients who undergo appendectomies for uncomplicated (nonperforated) appendicitis;
2. The drug should be administered 30-60 min before making surgical incision and;
3. The extended single drug empirical regime of cefotaxime for 5 days in complicated (perforated/abscessed) appendicitis is effective in reducing the postoperative infection rate;
4. Specific anaerobic coverage of metronidazole is unnecessary and may be contraindicated, since injudicious use of anaerobically oriented antibiotics for prophylaxis may result in untoward side effects and will, undoubtedly, play a role in the development of resistant microbes which will preclude the use of these agents for later specific therapy.

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