TOPICAL AMPICILLIN FOR PROPHYLAXIS AGAINST WOUND INFECTION IN ACUTE APPENDICITIS

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A total of 249 patients, undergoing appendectomy for acute appendicitis, were prospectively randomized into two groups. Group I, comprising 132 patients, received sterile normal saline irrigation to the surgical wound at closure. Alternatively, Group II included 117 patients, who received intraoperative topical ampicillin irrigation of the wound. Both groups were comparable with regard to age, sex, duration of symptoms, and severity of appendicitis. All patients additionally received preoperative systemic gentamicin and Flagyl. Wound infection occurred in 5.3% of Group I compared to only 0.9% of Group II ($P<0.05$). The reduction in infection rate was significant ($P<0.05$) in histologically proven appendicitis. We conclude that the addition of intraoperative topical ampicillin to systemic gentamicin and Flagyl augments prophylaxis against wound infection in acute appendicitis. *Ann Saudi Med 1994;14(3):233-236.*

A considerable morbidity following appendectomy is caused by wound infection,[1-5] the rate of which ranges from 9% to 30% in early appendicitis and may reach up to 70% in advanced appendicitis.[3-6] Systemic antibiotics were shown to reduce the wound infection rate significantly.[3,4,7] *In vitro* studies demonstrated 100% kill rates with clinically usable concentrations of antimicrobials in irrigating solutions after only 60-second exposure of the organisms.[8,9] Unlike parenterally administered antimicrobials, topical usage was found to attain prolonged effective local concentrations when used in the powder form.[10]

Experimental studies have shown that the combined use of systemic and topical antibiotics is better in advanced appendicitis than systemic antibiotics alone.[11] Similarly, Seco et al.[12] have concluded in a clinical study that prophylaxis with a combination of systemic clindamycin and topical ampicillin solution, when compared with systemic clindamycin alone, was more effective in preventing wound infection after appendectomy, especially in patients with high wound contamination. However, the study of Seco et al. was criticized because the control group wounds were not irrigated with normal saline and clindamycin may not be the systemic antibiotic of choice for many surgeons. This communication aims at investigating the efficacy of the addition of topical ampicillin to systemic antimicrobials in reducing post appendectomy wound infection rate in a properly controlled randomized prospective study.

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Material and Methods

All patients who underwent appendectomy through gridiron incision for clinically suspected acute appendicitis were considered for the study. Exclusion criteria were allergy to ampicillin and other systemic diseases requiring systemic antibiotic administration and therefore three patients who were allergic to ampicillin were excluded from the study, as well as another two patients who had valvular heart disease warranting preoperative prophylactic systemic ampicillin in addition to the systemic gentamicin and Flagyl. A total of 254 patients fulfilled the criteria of the study and were randomized into two groups using sealed envelopes that were opened intraoperatively after the peritoneum was closed. Five patients were withdrawn from the study due to protocol violation. Two patients who were randomized to Group I received their sealed envelopes opened in the beginning of the procedure and were therefore withdrawn because we thought that opening the envelopes before peritoneal closure could be a source of bias. One patient who was randomized to Group II was withdrawn because the appendix was removed through a midline incision. The other two patients were not given topical ampicillin by mistake, despite being randomized to Group II. This left 249 patients who were eligible for the study and further analysis.

Intraoperatively, swabs from the abdominal cavity and from the wound were collected and sent for culture and sensitivity. Both the peritoneal and wound swabs were

inoculated and processed as described by Isenberg et al.[13] Antibiotic susceptibility testing was performed using the Bauer and Kirby procedure.[14]

The wounds of 132 patients of Group I were irrigated with 100 ml of sterile normal saline at closure. Alternatively, in Group II, 117 patients had their wounds irrigated with 1 g ampicillin powder dissolved in 100 ml sterile normal saline. All patients received intravenous metronidazole (500 mg for adults and 15 mg/kg/body weight for children) and gentamicin (75 mg for adults and 1.5 mg/kg/body weight for children) one hour before surgery. If the appendix was found to be gangrenous or perforated, antibiotics were continued for five days postoperatively. Development of wound infection or completion of one month without wound infection were considered end points for the study. Wound infection was defined as the presence of purulent discharge in the wound regardless of the culture results or occurrence of serous discharge with a positive growth on culture.[15] Local erythema and/or pain in the absence of discharge or positive culture were not interpreted as wound infection, since it could be due to local hypersensitivity. Bed stay was estimated in both groups so as to calculate the amount of financial savings made by reducing post appendectomy wound infection.

Chi-square "z" test of proportion and Fisher's exact test were used for comparison and the chosen level of significance was 5%. Comparison of the length of hospital stay of patients with and without wound infection was carried out using the Mann-Whitney U-Wilcoxon Rank Sum W Test.

Results

Groups I and II were comparable for age, sex, severity of appendicitis, and duration of symptoms before surgery (Table I). Of those who were withdrawn from the study, the only patient who developed wound infection was one of the two patients who were, by mistake, not given ampicillin, and pathological examination of his appendix revealed that it was acutely inflamed.

Wound infections occurred in 3.2% of the total patients and were equally distributed among the operating surgeons. There were no wound infections in patients with histologically normal appendices.

The median hospital stay in patients who developed wound infection was 5.5 days (range 3 to 11 days), whereas it was only 3.0 days (range 2 to 11 days) in the remaining patients ($P<0.05$).

Seven patients (5.3%) out of 132 developed wound infection in Group I compared to one patient (0.9%) out of 117 patients in Group II (Table 2). The only patient who developed wound infection in Group II was a five-year-old child with gangrenous appendicitis.

Other postoperative complications were infrequent. One patient in each group had some redness in the wound accompanied by pain that subsided spontaneously and was ascribed to the local effect of the adhesive plaster used for dressing. None of the patients developed intra-abdominal or pelvic abscesses. Two patients in Group I and one patient in Group II developed postoperative ileus that resolved on conservative treatment. Three patients in Group II and two patients in Group I developed immediate postoperative fever that was attributed to atelectasis and resolved with chest physiotherapy and early ambulation.

Positive cultures from both the intraoperative abdominal and wound swabs were frequent with advanced appendicitis; less common with acute appendicitis ($P<0.05$) (Table 3). *E. coli* was the most frequent aerobic organism isolated, followed by klebsiella, streptococci, staphylococci, enterococci and pseudomonas species. Almost all streptococci and enterococci were sensitive to ampicillin besides 30% of the *E. coli* isolates.

Wound infection occurred more frequently when the intraoperative cultures were positive. The incidence of wound infection was only 0% to 2% when the intraoperative cultures were negative. With positive intraoperative wound cultures, a significant reduction in

TABLE 1. *Characteristics of the groups.*

	Group I	Group II
Age mean (range)	21 (5-80)	24 (4-66)
Sex (male/female)	90/42	77/40
Normal appendix (total)	27	26
Acute appendicitis (total)	102	88
Advanced appendicitis* (total)	3	3
Duration of symptoms in days		
Mean (range)	1(0.5-4) days	1(0.5-3)
Total	132	117

*=histologically proven gangrenous or perforated appendix.

TABLE 2. *Wound infection rate.*

	Group I	Group II	
Normal appendix	0/27	0/26	ns
Acute appendicitis	6/102 (5.9%)	0/88	$p<0.05$
Advanced appendicitis	1/3 (33.3%)	1/3 (33.3%)	ns
Total	7/132 (5.3%)	1/117 (0.9%)	ns

ns=not significant.

TABLE 3. *Positive intraoperative culture results according to the type of appendicitis.*

Histology	Positive abdominal culture		Positive wound culture	
Normal	7/53	(13%)	4/49	(8%)
Acute appendicitis	42/1	(23%)	34/177	(19%)
Advanced appendicitis	5/6	(83%)	4/6	(67%)
Total	54/242	(22%)	42/232	(18%)

TABLE 4. *Correlation of postoperative wound infection with intraoperative culture results.*

Intraoperative cultures	Group I			Group II			Z	P
	Total	Infected	%	Total	Infected	%		
Abdominal								
+ve	30	5	17	24	1	4	1.452	ns
-ve	99	2	2	89	0	0	1.348	ns
Wound								
+ve	19	5	26	23	0	0	2.621	sig.
-ve	106	2	2	86	1	1	0.402	ns

Sig=significant; ns=not significant.

wound infection occurred in Group II ($P<0.05$) (Table 4). Postoperative cultures from the infected wounds showed *E. coli* in five patients, *Pseudomonas aeruginosa* in addition to *E. coli* in one patient, staphylococcus in one and no growth was found in one patient.

Discussion

Wound infection is still the most common complication following appendectomy and is an important cause of morbidity.[1] The significantly longer hospital stay in our study of the infected group is in agreement with previous studies.[4-7]

Prophylactic use of systemic antibiotics, many of which have been used either alone or in combination, has resulted in a significant reduction in wound infection rate.[2-4] Gentamicin is effective against *E. coli,* which was the most common aerobic organism cultured from the wound and abdomen in our study and this is in agreement with previous studies.[16,17] Unfortunately, culture for anaerobes was not carried out in our study in view of lack of facilities in the emergency setting of our hospital. However, since *Bacteroides fragilis* has been reported to be the most common anaerobic organism in acute appendicitis,[16,17] we believe that systemic Flagyl, which was given routinely in all patients, is an adequate prophylaxis against bacteroides.

A total of 21% (53 patients) of the appendices removed in this study turned out to be normal. This is within the range reported in other places[18] and reflects our attitude of early surgical intervention and is the reason that only six patients with advanced appendicitis were encountered in this study.

Topical antibiotics were found to reduce wound infection following appendectomy.[5-7,11,12,16] Specifically, topical ampicillin was shown to reduce wound infection after colonic,[19] biliary and gastrointestinal surgery[20] and after appendectomy.[21,22] Ampicillin effectiveness is based on its activity against streptococci, enterococci and 30% of the *E. coli* isolates in our study. Its effectiveness against some aerobic and anaerobic bacteria has been also shown by others.[23] Addition of topical antibiotics to systemic antibiotics was found beneficial in advanced appendicitis.[24,25] Bergamini et al.[11] demonstrated in an experimental study that when wound contamination is great, a combination of topical and systemic antibiotics becomes more effective. In this study, we demonstrated that the addition of topical ampicillin to systemic gentamicin and Flagyl also significantly reduces post appendectomy wound infection in early acute appendicitis, which could only be ascribed to the ampicillin effect and not to the mechanical effect of saline irrigation, since a similar benefit was not seen in the control group.

In conclusion, we have demonstrated that the addition of topical ampicillin to systemic gentamicin and Flagyl significantly reduces post appendectomy wound infection rate. This efficacy was well seen in patients with acute appendicitis. In advanced appendicitis, conclusions cannot be drawn due to the small sample size. In our hospital, each bed stay costs approximately SR 1000/day, which is quite remarkable considering the large number of patients undergoing appendectomy. Indeed, hospital bed stay was reduced by 2.5 days/patient by avoidance of wound infection. Our study therefore suggests that the hospital bill can be reduced by routine topical ampicillin application with appendectomy.

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