Antibiotics and postoperative abscesses in complicated appendicitis: is there any association?

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ABSTRACT

Introduction: Complicated appendicitis has significant infective postoperative morbidity. There is no universally-accepted antibiotic regime, although traditionally, triple antibiotics are recommended. Our complicated appendicitis clinical pathway recommends ceftriaxone and metronidazole. The study aimed to determine if choice of antibiotics influenced the risk of infective complications.

Methods: We reviewed all paediatric appendicectomy patients between January 1, 2005 and December 31, 2005. All patients with intraoperative diagnosis of perforated appendicitis were recruited, excluding infants, immunocompromised patients, and patients allergic to the guideline antibiotics. All operations were performed by registrar/consultant surgeons and were laparoscopic, unless technically not feasible.

Results: There were 82 patients with perforated appendicitis. 62 patients (76 percent) followed pathway antibiotics, and 20 patients (24 percent) deviated from the pathway by receiving additional empiric gentamycin. We compared the pathway compliant and deviation groups, and found no significant differences in patient characteristics, clinical presentation, operation, length of stay and infective complications. Overall there was one wound infection and five (six percent) postoperative abscesses. Initial peritoneal cultures and subsequent drainage cultures of patients who developed abscesses were sensitive to treatment antibiotics.

Conclusion: In complicated appendicitis, empirical perioperative addition of gentamycin to ceftriaxone and metronidazole did not reduce the risk of developing intra-abdominal abscess, compared to changing antibiotics on clinical grounds. Patients developed postoperative abscesses despite initial peritoneal cultures growing organisms sensitive to treatment antibiotics.

Key words: appendicitis, complicated appendicitis, perforated appendicitis, postoperative abscess, postoperative infection

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INTRODUCTION

Appendicitis is one of the most common childhood illnesses, and complicated appendicitis, in particular, has a greater risk of postoperative infective morbidity.[1] Traditionally, broad-spectrum antibiotic coverage with multiple drugs has been advocated,[1-3] although there is no universally accepted regime. There has been a recent trend towards single or dual drug regimes,[4,5] in order to reduce cost and simplify dosing schedules. Likewise, our department started a clinical pathway in 2003 for complicated appendicitis using intravenous ceftriaxone and metronidazole. However, there remained significant clinician concern that this was inadequate[6] to cover *Pseudomonas* and *Bacteroides*, whose prevalence in appendix specimens is reported to be as high as 40% and 73%, respectively.[7] This study was carried out to determine if the choice of antibiotics in complicated appendicitis influenced the risk of infective complications. Our secondary hypothesis was that postoperative abscesses occurred in patients with organisms resistant to the treatment antibiotics.

METHODS

Approval was granted for this study by the hospital ethics and research committee. Retrospective chart review was carried out on all patients between the ages of one and 16 years and who underwent appendicectomy between January 1, 2005 and December 31, 2005. All patients with an intraoperative diagnosis of perforated appendicitis were recruited. We excluded infants under one year of age, immunocompromised patients and patients who were allergic to the guideline antibiotics. Registrar or consultant grade paediatric surgeons performed all operations. Since 2004, our department did laparoscopy routinely for complicated appendicitis. Registrars (advanced trainees) were allowed to perform laparoscopic appendicectomies independently only after fulfilling standard training numbers. The decision to convert was at the surgeon's discretion.

A standard three-port technique was used with absorbable suture with pre-tied knot (Vicryl endoloop, Ethicon Inc, Somerville, NJ, USA) for the appendix base. Visible peritoneal pus was routinely aspirated into a specimen trap for culture, and saline lavage carried out for peritoneal contamination. Placement of drains was

Table I. Patient characteristics and operations.

Followed pathway	Pathway compliant (n = 62)	Pathway deviator (n = 20)	Total (n = 82)	p-value
Age (years)	10.0 ± 3.2	9.5 ± 3.4	9.8 ± 3.2	0.55
Gender				
Male: female (% male)	40:22 (65)	13:7 (65)	53:29 (65)	1.00
Duration of symptoms preoperatively (days)	2.8 ± 1.6	2.5 ± 1.0	2.7 ± 1.5	0.43
Temperature (°C)	38.2 ± 0.7	38.1 ± 0.7	38.1 ± 0.7	0.58
Total white blood cell count (× 10^9/L)	18.2 ± 5.2	18.3 ± 3.7	18.2 ± 4.8	0.94
No. laparoscopic (%)	51 (82)	17 (85)	68 (83)	1.00
No. drains (%)	45 (73)	17 (85)	62 (76)	0.37

Table II. Postoperative outcomes.

Followed pathway	Pathway compliant (n = 62)	Pathway deviator (n = 20)	Total (n = 82)	p-value
Days till afebrile (excluding abscess cases)	2.3 ± 1.1	2.7 ±1.0	2.5 ± 1.1	0.28
No. wound infection (%)	0	1 (5%)	1 (1%)	0.24
No. postoperative abscess (%)	4 (6%)	1 (5%)	5 (6%)	1.00
Length of stay (days)	6.4 ± 3.4*	6.3 ± 2.4**	6.4 ± 3.1	0.90
Length of stay (days) excluding outliers	5.7 ± 2.1	5.7 ± 1.0	5.6 ± 1.4	1.00

*includes four postoperative abscess cases with prolonged length of stay and one outlier with adhesive obstruction length of stay of 16 days
**includes one postoperative abscess case and one open operation wound infection

surgeon-dependent. Intravenous ceftriaxone (50 mg/kg daily) and metronidazole (7.5 mg/kg q8H) was started at induction of anaesthesia or prior to that in the ward if time was required for preoperative resuscitation. Postoperative antibiotics were continued intravenously until the patient had been afebrile for at least 24 hours and converted on hospital discharge, to oral antibiotics for 5–7 days. During the study period, the clinical pathway guidelines for simple appendicitis recommended gentamycin and metronidazole for 24 hours. Hence, if a preoperative diagnosis of simple appendicitis were changed intraoperatively to complicated appendicitis with perforation, the postoperative antibiotics would be altered to ceftriaxone and metronidazole accordingly.

Patients clinically suspected of a postoperative abscess underwent computed tomography of the abdomen. Upon confirmation, drainage of the abscess was undertaken, where feasible, by interventional radiology or operative methods. Cultures were taken if the abscess was drained and antibiotics were changed following clinical criteria. All continuous data in the tables are reported as mean and standard deviation. Statistical analysis was calculated using the Fisher's exact test for categorical variables and Student's *t*-test for continuous variables. Statistical significance was accepted when $p < 0.05$.

RESULTS

There were 219 appendicectomies performed in the year 2005. The intraoperative diagnosis was perforated appendicitis in 84 patients (38%). Two of the 84 patients with complicated appendicitis were allergic to cephalosporins, leaving 82 cases for analysis. Regarding antibiotic usage, 62 patients (76%) followed pathway guideline antibiotics and 20 patients (24%) deviated from the pathway because they received additional empiric gentamycin from operation day. Of the pathway compliant group, 53 (85%) received ceftriaxone and metronidazole only, while nine (15%) had a change in their antibiotic regime after three or more days for clinical reasons (eight for persistent fever, and one following culture sensitivity). We compared the pathway compliant and pathway deviation groups. There were no differences in patient characteristics of age, gender and clinical presentation (Table I). The outcomes of both groups were similar in terms of length of stay and infective complications (Table II).

Overall infective complications among the 82 patients included one wound infection that occurred in an open case and five cases (6%) of postoperative intra-abdominal abscess formation. In three cases, intraoperative peritoneal cultures grew multiple organisms and all were sensitive to the treatment antibiotics. In the other two cases, the culture showed mixed bacterial growth (Table III). Repeat cultures taken at drainage of abscess showed either sensitive organisms similar to initial peritoneal cultures or no bacterial growth. Peritoneal cultures showing specific organisms were obtained in only 34 out of 82 patients (41%), of which 11 had a single organism identified, 21 had two organisms and two had three organisms. The rest showed a mixed bacterial growth pattern in 26 cases (32%), no bacterial growth in 16 (20%), and cultures could not be taken or retrieved in six cases (7%).

Table III. Details of postoperative intra-abdominal abscess cases.

Case	Initial peritoneal culture	Postoperative abscess drainage culture	Compliance to pathway	Initial operation	Drainage operation
1	*Klebsiella* spp. and *E. coli*	No bacterial growth	No (Empirical gentamicin added from operation day)	Open (conversion)	LA
2	*S. milleri* and *E. coli*	*E. Coli* and *Prevotella loescheii* (anaerobe)	Yes (Antibiotics changed 10 POD)	LA	Open
3	*S. milleri* and *E. coli*	*S. milleri* and *E. coli*	Yes (Antibiotics changed 8 POD)	Open (conversion)	LA
4	Mixed bacterial growth	Not drained	Yes (Antibiotics restarted and changed 14 POD)	LA	Treated antibiotics
5	Mixed bacterial growth	Mixed bacterial growth	Yes (Antibiotics changed 3 POD)	Open (conversion)	Percutaneous CT-guided

LA: laparoscopic; POD: postoperative day; CT: computed tomography; *E.: Escherichia; S. : Steptococcus*
All specific cultures grew organisms that were sensitive to pathway antibiotics

Among the 34 patients who had specific cultures, 25 (74%) had organisms that were sensitive to the guideline antibiotics. Among the nine (26%) patients with resistant organisms, five did not have antibiotic change because of good clinical response and no complication occurred. *Pseudomonas* was found as one of multiple organisms in five cases (15%). Of these five patients, one received only guideline antibiotics, two received gentamycin empirically in addition to the guideline antibiotics, while the final two patients received gentamicin several days later when the antibiotic regime was changed (one based on culture results and one because of persistent fever). None developed wound infection or abscess.

DISCUSSION

The choice of antibiotics for complicated appendicitis varies widely among institutions.[4] A commonly-followed guideline[2] recommends triple antibiotics, and similarly, we used to prescribe the combination of ampicillin, gentamicin and metronidazole. In a bid to improve efficiency, our institution preferred a cheaper combination with a simpler dosing schedule. As generic ceftriaxone became easily available and limited the ototoxicity and nephotoxicity risks without the need for checking drug levels, it was chosen for our complicated appendicitis clinical pathway guidelines after consultation with the hospital microbiologist, the infectious disease physician and pharmacists. In our study, we found no difference in infective complications and length of stay in the pathway compliant group (which received ceftriaxone and metronidazole only) compared to the pathway deviator group (which received additional empiric gentamicin). As to the reason why some surgeons deviated from the pathway guidelines, we speculated that either the pathway deviator cases appeared more severe, or that some risk-adverse surgeons were uncomfortable with the guideline antibiotics. As the cases were similar in both groups in terms of patient characteristics and clinical presentation, we suspect it is the latter reason.

A particular concern among some surgeons was that the guideline antibiotics do not cover *Pseudomonas*.[6] Our study found that none of the patients with *Pseudomonas* in their initial cultures developed complications despite 60% receiving no or late gentamycin. Although inconclusive because of the small numbers, like other series,[8,9] it seems to suggest that *Pseudomonas* obtained as one of multiple colonic flora in complicated appendicitis is different from single agent *Pseudomonas* infection and does not require the usual dual drug regime for *Pseudomonas*. Contrary to our expectations, we found that postoperative abscesses occurred in patients who had organisms on culture that were sensitive to the treatment antibiotics. It could be argued that standard hospital laboratory cultures do not isolate the most pathogenic organisms as some paediatric series have shown that taking intraoperative peritoneal cultures does not change management.[8,10] Unlike Kokoska et al,[8] we found that drainage culture of the postoperative abscess did correlate with initial peritoneal culture, although this did not alter management. In fact, two cases with specific organisms in their repeat drainage cultures had organisms that were still sensitive to the treatment antibiotics despite therapy for more than a week. On the other hand, cases with resistant organisms on culture but which did not change antibiotics also did not develop complications. This suggests that host factors play a greater role in infectious complications. Alternatively, it could be that the postoperative abscess cases had a higher pathogen load at the end of surgery.

Notably, three postoperative abscess cases occurred in the conversion/open group (21%), compared to two in the laparoscopic group (3%).

Laparoscopy has the advantage of providing a good view to irrigate the entire peritoneal cavity.[11] Hence, it is possible that cases that could be completed laparoscopically had a reduced pathogen load at the end of operation because of better irrigation. Another possible mechanism is that in open cases, increased intestinal handling predisposes to early postoperative adhesions that wall off pathogens from the reach of antibiotics. Our series' open cases comprised 12 that were converted to avoid intestinal injury (eight because of poor visualisation of the appendix base, three for dense adhesions, one to repair caecal perforation) and two that were done primarily open for septicaemic shock. The postoperative abscess cases had been converted for better appendix visualisation (two cases) and adhesions (one case). Routine peritoneal cultures in complicated appendicitis were taken during the study period based on previous departmental data (unpublished) that suggested it was useful in detecting resistant organisms. Likewise, up to 67% of paediatric surgeons still take peritoneal cultures in certain circumstances.[3] Our department has stopped this practice after the results of this study.

The main criticism of our study will be that it is underpowered to detect a difference in the two groups receiving different antibiotic regimes. As *a priori* power calculations show that the sample size to detect a halving of postoperative abscess formation rate from 10% to 5% is 950, we felt that we would not be able to achieve enough numbers in our standard practice to prove statistical significance in this study. In our review of the literature, we were unable to find adequately-powered paediatric trials,[5,9,12,13] while the randomised trials in adults fail to show any difference in antibiotic regimes.[14] Our overall intra-abdominal abscess rate of 6% is comparable to 3.3%–8.8% in recent paediatric open series[2,5,8,15] and non-operative management,[16] while our wound infection rate of 1% is on the lower end of quoted rates of 1%–18%.[2,8,10] As previously reported,[11,17] our department is comfortable with laparoscopy for complicated appendicitis and find that the rate of intra-abdominal abscess formation should be no different or even less than open surgery.

Postoperative abscess formation is likely multifactorial, encompassing host and operative factors, in addition to antibiotics. The search for the best antibiotic regime for appendicectomy persists.[4,5,18,19] Our study findings suggest that our current guideline antibiotics are adequate to treat most cases of perforated appendicitis, and changing antibiotics on clinical grounds does not result in an increased infectious complication rate or length of stay. A multicentre prospective randomised trial will be required to achieve adequate numbers to show significant improvement in the low complication rates of most modern paediatric centres.

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