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Short Communication

Perforated appendicitis in children: antimicrobial susceptibility and antimicrobial stewardship

Ozden Turel[a,*], Semih L. Mirapoglu[b], Mine Yuksel[a], Aysenur Ceylan[c], Bilge Sumbul Gultepe[c]

[a] Department of Pediatrics, Bezmialem Vakif University Medical Faculty, Istanbul, Turkey
[b] Department of Pediatric Surgery, Bezmialem Vakif University Medical Faculty, Istanbul, Turkey
[c] Department of Microbiology, Bezmialem Vakif University Medical Faculty, Istanbul, Turkey

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ABSTRACT

Objectives: For perforated appendicitis in children, microbiological cultures should always be sought if an adequate sample is available. Knowledge of local epidemiology is important for optimal selection of antimicrobial therapy. The aim of this study was to evaluate the aetiology and susceptibility of pathogens in paediatric patients with perforated appendicitis.

Methods: Microbiological results of tissue samples obtained at surgery from children with acute appendicitis over 24 months were evaluated retrospectively.

Results: Among 209 children operated for acute appendicitis, 62 (29.7%) were perforated appendicitis. Intraperitoneal culture results were available for 42 patients, of which 41 (97.6%) had positive microbiological growth (57 pathogens). The male:female ratio was 1.8 and the mean age at presentation was 11 years (range 4–18 years). The most common pathogen was *Escherichia coli* (66.7%), among which 57.9% produced an extended-spectrum β-lactamase (ESBL). All patients received initial treatment with intravenous antibiotics (ampicillin, gentamicin and metronidazole). The antibiotic regimen was modified in 22 patients (52.4%). Seven patients (16.7%) developed a post-operative complication. No significant difference was observed for development of complications between patients with ESBL-positive and -negative *E. coli* growth ($P = 0.698$).

Conclusion: The high rate of ESBL-positive *E. coli* may indicate bowel colonisation with resistant bacteria even in the community setting. Prospective studies will show whether treatment options should be directed according to identified pathogens.

1. Introduction

Acute appendicitis is one of the most common surgical emergencies. Approximately 300 000 patients are treated for appendicitis annually, utilising 11 million hospital-days [1]. Many surgeons do not take routine cultures for appendicitis. However, identification of pathogens and susceptibility data may facilitate recognition of local changes in resistance that might affect optimal selection of antimicrobial agents for therapy. The aim of this study was to evaluate the aetiology and susceptibility of pathogens in paediatric patients with perforated appendicitis.

2. Methods

Clinical and microbiological data of paediatric cases with perforated appendicitis admitted to Bezmialem Vakif University (Istanbul, Turkey) were collected retrospectively. In all cases, purulent fluid was observed during surgery and perforated appendicitis was identified by histological examination. Peritoneal fluid or appendicular tissue taken intraoperatively was cultured on blood agar and eosin methylene blue agar plates. The antimicrobial susceptibility of isolated bacteria was investigated by the disk diffusion method according to Clinical and Laboratory Standards Institute (CLSI) guidelines [2].

Data were expressed as the mean ± standard deviation. Statistical analysis was performed using IBM SPSS Statistics v.19.0 (IBM Corp., Armonk, NY). Mann–Whitney *U*-test was used to compare length of hospital stay and cost of hospitalisation between patients who did and did not require treatment alteration.

* Corresponding author at: Pediatric Infectious Diseases, Department of Pediatrics, Bezmialem Vakif University Medical Faculty, Adnan Menderes Bulvarı (Vatan caddesi), Fatih, Istanbul 34093, Turkey.
E-mail address: barisbulent98@yahoo.com (O. Turel).

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Table 1
Resistance patterns of Gram-negative bacteria isolated from patients with perforated appendicitis.

Species	No. of isolates[a]	Antimicrobial resistance (%)							
		AMK	AMP	SAM	CAZ	ETP	IPM	TZP	GEN
Escherichia coli, ESBL-negative	16	0	21.4	21.4	0	0	0	20.0	6.3
E. coli, ESBL-positive	22	4.5	81.8	81.8	100	0	4.5	47.6	13.6
Pseudomonas aeruginosa	12	0	100	100	8.3	N/A	16.7	16.7	0
Enterobacter cloacae	1	0	100	100	0	0	0	0	0
Klebsiella pneumoniae	1	0	100	0	0	N/A	0	0	0

AMK, amikacin; AMP, ampicillin; SAM, ampicillin/sulbactam; CAZ, ceftazidime; ETP, ertapenem; IPM, imipenem; TZP, piperacillin/tazobactam; GEN, gentamicin; ESBL, extended-spectrum β-lactamase; N/A, not available.
[a] Not all isolates were tested for susceptibility to all antimicrobial agents.

The χ^2 test and Fisher's exact test were used to evaluate categorical variables. A *P*-value of 0.05 was considered statistically significant.

3. Results

From 1 January 2013 to 31 December 2014, 209 patients received a diagnosis of acute appendicitis, among which 62 (29.7%) were perforated appendicitis. Intraperitoneal culture results were available for 42 patients, of which 41 patients (97.6%) had positive microbiological growth (57 pathogens). The mean age at presentation was 11 years (range 4–18 years). The male:female ratio was 1.8. Gram-negative *Escherichia coli* was the most common pathogen (38/57; 66.7%). Other Gram-negative bacteria were *Pseudomonas aeruginosa* (12/57; 21.1%), *Klebsiella pneumoniae* (1/57; 1.8%) and *Enterobacter cloacae* (1/57; 1.8%). Gram-positive bacteria included *Enterococcus avium* (3/57; 5.3%) and *Streptococcus constellatus* (1/57; 1.8%). *Pediococcus pentosaceus* was the sole anaerobic pathogen (1/57; 1.8%). Eight patients (19.0%) had more than one pathogen isolated (four with *P. aeruginosa* + *E. coli*, three with *E. coli* + *Enterococcus* spp. and one with *E. coli* + *P. aeruginosa* + *S. constellatus*). Among the *E. coli* isolates, 57.9% (22/38) produced an extended-spectrum β-lactamase (ESBL). Ampicillin/sulbactam failed to inhibit ≥63% of any species. Imipenem inhibited 97.3% of *E. coli* and 83.3% of *P. aeruginosa* isolates. Amikacin showed activity against all species except for one ESBL-positive *E. coli* isolate. Resistance rates for the different antibiotics are summarised in Table 1.

All patients received initial treatment with intravenous antibiotics (ampicillin, gentamicin and metronidazole). The antibiotic regimen was modified in 22 patients (52.4%) due to ongoing complaints. Moreover, 63.6% of patients with ESBL-producing bacteria required modification of initial therapy, whilst treatment was changed in 42.9% of patients with ESBL-negative isolates ($P = 0.172$). Imipenem/cilastatin was the most commonly used secondary antibiotic therapy (18 patients). Ceftriaxone plus metronidazole (two patients) and either piperacillin/tazobactam (TZP), cefepime or ceftriaxone (each one patient) were other antibiotics used. Seven patients (16.7%) developed a post-operative complication (wound infection, abscess, fluid collection or pleural effusion). No significant difference was observed in the development of complications between patients with ESBL-positive and -negative bacterial growth ($P = 0.698$). Patients were treated for a median of 8.4 days (range 3–20 days). The median cost of hospital stay was 371 US$/case. Length of hospitalisation was longer in patients who received antibiotic modification compared with those who did not ($P = 0.06$). Length of hospital stay and cost of hospitalisation were not significantly different between patients with ESBL-positive and -negative isolates ($P = 0.903$ and $P = 0.808$).

4. Discussion

The rate of perforated appendicitis is reported as 37% among children treated for appendicitis in teaching hospitals [3]. In the current study of children with appendicitis, 29.7% of cases were perforated appendicitis. The mean age was 11 years and 64.4% of patients were male. Perforation is most common in children aged <6 years since the classic pattern of clinical findings is less common or may not occur at all [4]. Karakuş et al. reported that among 314 patients with complicated appendicitis, the mean age of boys and girls was 11.2 ± 5.4 years and 10.4 ± 6.4 years, respectively [5].

The Infectious Diseases Society of America (IDSA) guidelines advise that if there is significant resistance (i.e. 10–20% of isolates) of a common community isolate (e.g. *E. coli*) to an antimicrobial regimen in widespread local use, routine culture and susceptibility results should be obtained for perforated appendicitis and other community-acquired intra-abdominal infections [6]. In the current study, 58.3% of *E. coli* isolates were resistant to ampicillin and 57.9% were ESBL-positive. There is no clear consensus whether culture and susceptibility results have an impact on therapy for lower-severity patients with community-acquired infections. Pathogen-directed therapy is recommended if resistant bacteria are identified and there are persistent signs of infection. The American Pediatric Surgical Association guidelines advise treatment with TZP for perforated appendicitis [7]. In the current study, all patients received triple-antibiotic therapy initially but more than one-half of patients required modification of treatment. In a large review of a database for 32 children's hospitals in the USA, there was significant improvement in terms of length of stay, pharmacy charges and hospital charges, with no increase in hospital re-admissions, among children receiving monotherapy compared with those receiving traditional triple-antibiotic therapy [8]. Nevertheless, the benefit of extended-spectrum antibiotics are not clear. Among 7000 children with complicated appendicitis, treatment failure occurred in ca. 6% of all patients with complicated appendicitis and was increased in patients who received extended-spectrum antibiotics [9]. In the current cohort, the length of hospital stay was longer in patients who required antibiotic modification than in those who received traditional triple-antibiotic therapy.

In conclusion, the high rate of ESBL-positive *E. coli* may indicate bowel colonisation with resistant bacteria even in the community setting. Routine cultures should be taken from patients with perforated appendicitis to recognise local changes in resistance and for optimal selection of antimicrobial therapy. Prospective studies will show whether treatment options should be directed according to identified pathogens.

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Competing interests

None declared.

Ethical approval

Not required.

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