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Bacteriologic epidemiology and empirical treatment of pediatric complicated appendicitis

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Abstract

Preoperative samples in the context of complicated appendicitis (CA) are rarely collected, and there is no consensus regarding the optimal antibiotic therapy in children. To help optimize empirical preoperative treatment, we studied clinical and bacteriologic data from a prospective cohort of 93 children with CA in a French hospital. All the bacteria isolated from peritoneal fluids were identified, using phenotypic and/or molecular techniques. The most commonly recovered species were *Escherichia coli* (71%), *Streptococcus* group *milleri* (34%), anaerobes (20%), and *Pseudomonas aeruginosa* (19%). The association piperacillin–tazobactam is an accurate choice of empirical therapy as it is active against 97% of bacteria. A third-generation cephalosporin with metronidazole in association with an aminoglycoside is a good alternative. Although antibiotic use may be considered as an adjunct to surgical intervention of CA, the appropriate use of preoperative antibiotics is essential and must be constantly reevaluated according to the bacterial epidemiology.

Keywords: Appendicitis; Children; Bacteria; Epidemiology; Peritoneal fluid

1. Introduction

Acute appendicitis is the most common visceral emergency in children. The positive effect of prophylactic antibiotic therapy on reducing postoperative complications in patients with acute nonperforated appendicitis is well established (Bauer et al., 1989; Gutierrez et al., 1987). However, there is no consensus regarding the optimal antibiotic therapy after appendectomy for children with perforated appendicitis, the most common cause of peritonitis in children. According to Nadler et al., after an appendectomy, these children should be treated in the same way as adults, until there is no further clinical evidence of infection. It appears that no single antibiotic regimen outperforms any other, as long as adequate Gram-negative and anaerobic coverage is provided. Monotherapy with broad-spectrum agents is as effective as but more cost-effective than multidrug therapy and should be considered for first-line therapy (Nadler & Gaines, 2008). The French recommendations for community-acquired peritonitis in the adult population suggest the use of any of a large choice of antibiotics (Montravers, 2001). Recently, Solomkin et al. (2010) published new Infectious Diseases Society of America (IDSA) guidelines for management of intra-abdominal infection, including recommendations for post-surgical treatment in children. These authors also proposed a large choice of antibiotics, either administered alone (ertapenem, meropenem, imipenem, ticarcillin–clavulanate, and piperacillin–tazobactam) or in combination (third-generation cephalosporin associated with metronidazole, aminoglycoside associated with metronidazole or clindamycin, with or without ampicillin).

In the department of pediatric surgery of our hospital, we currently use 2 different empirical antibiotic regimens for complicated appendicitis (CA) according to surgeon

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preference. If the preoperative evaluation suggests a perforation, antibiotic therapy is started before surgery with either amoxicillin–clavulanate (amoxi/clav) + gentamycin or, alternatively, cefotaxime/ceftriaxone + gentamycin + metronidazole. In cases of confirmed CA, an aminoglycoside is given for 2 days and other antibiotics are administered for 5–7 days unless continued sepsis warrants further treatment. To develop a local consensus concerning empirical preoperative antibiotherapy, we investigated whether the antibiotics currently used are adapted to the sensitivity of bacteria most commonly found in the peritoneal fluid of children. We also wanted to gain an understanding of the current bacterial epidemiology of appendicitis in France through studying a large cohort of children undergoing surgery for acute appendicitis.

2. Patients and methods

2.1. Study population

Between March 1, 2006, and May 31, 2008, we collected clinical and bacteriologic data for all cases of CA among the 322 emergency appendectomies for acute appendicitis performed in the pediatric surgery department of the Necker-Enfants Malades hospital. We considered that the appendicitis was complicated if at least 1 of the 4 following features was present: perforated appendicitis, purulent liquid, presence of abscess, or fibrinous membranes. Delayed appendectomies for acute appendicitis primarily treated by antibiotics were excluded.

Clinical data collected included age at surgery, sex, preoperative duration of symptoms, antibiotic administration before diagnosis, surgical technique (laparotomy or laparoscopy), macroscopic findings at surgery, type and duration of postoperative antibiotherapy, postoperative infectious complications, and total duration of hospital stay. Infectious complications were defined as those occurring within 30 days of surgery, and included intra-abdominal abscess and/or wound infection.

In addition, we studied clinical and bacteriologic data from cases of uncomplicated appendicitis (UA) in which peritoneal fluid was present and was cultured.

2.2. Specimen culture

Peritoneal fluid or pus specimens were collected from the peritoneal cavity at surgery. The liquid was aspirated into a syringe immediately after opening the abdominal cavity. Fluid specimen was injected into an anaerobic transport vial (Portagerm, bioMérieux, Marcy l'Etoile, France) then, in the microbiological laboratory, used to inoculate 5% horse blood agar, chocolate agar (bioMérieux), and URI4 agar (bioMérieux) and incubated under aerobic and anaerobic atmospheres for up to 48 h. Samples were also cultured on Sabouraud agar (bioMérieux) under an aerobic atmosphere for 5 days. Fifty microliters of liquid was added on each medium. The counting of bacteria in unity forming colonies (UFC) was semiquantitative: $<10^2$ UFC/mL, between 10^2 and 10^3 UFC/mL, and $\geq 10^3$ UFC/mL.

All organisms were identified using conventional methods. The Gram-negative bacilli and anaerobic bacteria were identified by biochemical galleries (API 20E, API 20 NE, Rapid ID 32 A, bioMérieux). In addition, identification disks for anaerobic Gram-negative bacilli were used (colimycin 10 μg, vancomycin 5 μg, kanamycin 1000 μg, bioMérieux). The phenotypic identifications of *Streptococcus* spp. and *Enterococcus* spp. (ID 32 Strep, API 20 Strep, bioMérieux) were confirmed by sequencing the sodA and rpoB genes (Drancourt et al., 2004; Poyart et al., 1998).

Susceptibility to commonly used antibiotics was tested by an agar disc diffusion method. As ticarcillin–clavulanate (ticar/clav) and piperacillin–tazobactam (pip/taz) were not tested in standard diffusion against *Streptococcus* and *Enterococcus*, the minimal inhibitory concentration (MIC) of these antibiotics was tested by the E test method (AB Biodisk, Sweden), in comparison with MIC of amoxi/clav and cefotaxime. Susceptibility to anaerobic bacteria was performed on monomicrobial cultures.

2.3. Statistics

R (language and environment for Statistical Computing, R Foundation for Statistical Computing, Vienna, Austria) was used for statistical analysis.

χ^2 or Fisher exact test was used for analysis of qualitative data, and Student t test was used for numerical data. A P value less than 0.05 was defined as statistically significant.

3. Results

During the study period, we included 93 CA patients. Intraoperative peritoneal specimens for culture were available from 91% of these patients. During the same period, we studied 58 cases of UA for which peritoneal fluid sample volume was sufficient to allow culture. There were no deaths. The demographic and clinical characteristics are summarized in Table 1.

The duration of symptoms before hospital presentation was significantly longer in CA than in UA (Table 1). The majority of CA children did not receive either antibiotics (84%) or nonsteroid anti-inflammatory medication (94%) before diagnosis. On physical examination, temperature and C-reactive protein concentration values were significantly more elevated in CA than in UA (Table 1).

Standard abdominal X-ray, abdominal ultrasonography, and CT scan were performed in 43%, 92%, and 15% of CA and contributed to the diagnosis in 60%, 88%, and 93% of cases investigated, respectively. Overall, the 3 imaging techniques contributed to the diagnosis of CA in 89 cases (96%). The peritoneal fluid of CA was serous in 2%, cloudy in 5%, and purulent in 76% of cases; 29% of patients had