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Evidence-based optimisation of empirical antibiotic regimens in paediatric complicated appendicitis: a retrospective study of 94 patients

Filippo Gerber[a], Jean-Marc Joseph [a], Pierre-Alex Crisinel [b], Véronique Andrey[a]

[a] Unit of Paediatric Surgery, Department Woman-Mother-Child, Lausanne University Hospital (CHUV), Lausanne, Switzerland
[b] Unit of Paediatric and Infectious Diseases and Vaccinology, Department Woman-Mother-Child, Lausanne University Hospital (CHUV), Lausanne, Switzerland

Summary

BACKGROUND: Acute appendicitis is the most frequent surgical emergency in the paediatric population. Complicated appendicitis accounts for 30% of cases and is inextricably linked to postoperative infectious complications. A study at our institution showed that amoxicillin-clavulanate resistant *Escherichia coli* in complicated appendicitis was significantly linked to postoperative infectious complications. These findings led to a change in the empirical antibiotic protocol (amoxicillin-clavulanate changed to ceftriaxone + metronidazole as of 2017), intending to reduce postoperative infectious complications in complicated appendicitis in our institution.

AIM OF THE STUDY: This study aimed to analyse the microbiology and resistance profiles of pathogens of complicated appendicitis at our institution since implementing the new antibiotic protocol and the postoperative infectious complications rate.

METHODS: We designed a retrospective comparative cohort study. During the defined study period (01 January 2017 to 31 July 2020), medical records were analysed for cases of acute appendicitis, complicated appendicitis and postoperative infectious complications, retaining only those who fulfilled inclusion criteria. Postoperative outcomes, microbiology and antibiotic resistance of peritoneal swabs were analysed.

RESULTS: During the study period, 95 patients presented with a complicated appendicitis, and 11 (12%) developed postoperative infectious complications. The most frequent pathogens found in complicated appendicitis were *E. coli* (66%), *Streptococcus anginosus* (45%), and *Bacteroides fragilis* (22%). *Pseudomonas aeruginosa* was present in 17% of complicated appendicitis. Pathogens involved in postoperative infectious complications mirrored the distribution found in complicated appendicitis without postoperative infectious complications. Antibiotic susceptibility analysis showed that 10 (15%) of *E. coli* strains were resistant to amoxicillin-clavulanate but sensitive to ceftriaxone + metronidazole, with only one strain responsible for causing a postoperative infectious complication. Six additional strains of *E. coli* (9%) were resistant to amoxicillin-clavulanate and our empirical antibiotic regimen but were not associated with an increase in postoperative infectious complications. Compared with our previous study, there was a decrease in postoperative infectious complications from 16% to 12%. Postoperative infectious complications caused by amoxicillin-clavulanate-resistant *E. coli* decreased from 28% to 9%.

CONCLUSION: This retrospective study demonstrated a decrease in the rate of postoperative infectious complications due to amoxicillin-clavulanate-resistant *E. coli* in complicated appendicitis. These findings accentuate the need to implement evidence-based treatment protocols based on local microbiology profiles and resistance rates to optimise post-operative antibiotics in complicated appendicitis.

Correspondence:
Véronique Andrey, MD
Lausanne University Hospital (CHUV)
Rue du Bugnon 46
CH-1011 Lausanne
veronique.andrey[at]chuv.ch

Introduction

Acute appendicitis is the most frequent paediatric surgical emergency worldwide [1, 2]. Complicated appendicitis, defined as the presence of perforation, peritonitis, gangrene or an intra-abdominal abscess, accounts for 10–40% of cases [3–5]. Complicated appendicitis is inextricably linked to postoperative infectious complications. Frequent postoperative infectious complications includes intra-abdominal abscesses, occurring in up to 25% of complicated appendicitis and are an important source of morbidity [6–9].

The microbiology of acute appendicitis is well documented, implicating aerobic and anaerobic bacteria [2, 10–12]. Microorganisms resistant to or not covered by current empirical antibiotic regimens, such as *Pseudomonas aeruginosa* , present in 10–30% of cases of complicated appendicitis, are increasingly cited [11, 13–15]. Isolation of amoxicillin-clavulanate-resistant *Escherichia coli* in peritoneal fluid samples has also been associated with postoperative infectious complications in complicated appendicitis [15, 16].

Intravenous postoperative antibiotics are considered the gold standard of postoperative care in complicated appendicitis; however, treatment protocols vary globally, with little or no official consensus between institutions [17–19]. The optimal selection of an empirical postoperative intravenous antibiotic regimen (EAR) remains contested. Most single antibiotic agents are ineffective alone owing to the polymicrobial nature of complicated appendicitis and postoperative infectious complications [7].

For decades, triple antibiotic administration of ampicillin, gentamicin, and metronidazole/clindamycin was considered the optimal treatment. Several recent publications challenge this combination. A plethora of retrospective studies comparing the efficacy and cost-effectiveness of dual versus triple antibiotic therapy in complicated appendicitis demonstrated no significant difference in the rate of postoperative infectious complications [14, 20, 21]. Some institutions suggest using single broad-spectrum antibiotics in complicated appendicitis [22–24]. Generalised EAR also include the risk of new antimicrobial resistances [25–28].

Until 2013 at our institution, a triple EAR was prescribed (amoxicillin-clavulanate + aminoglycoside + metronidazole). Internal reviews (2012–13) of the bacteriology and local resistances demonstrated low rates of amoxicillin-clavulanate-resistant *E. coli* (less than 15%). Following SIS-IDSA guidelines, a downgrade from a triple EAR to a monotherapy empirical regimen of amoxicillin-clavulanate was made [28].

Since these changes, we have closely monitored the bacteriology of complicated appendicitis via peritoneal sampling and the rate of postoperative infectious complications. We published a retrospective cohort study of patients treated for complicated appendicitis, which showed an increase in the rate of amoxicillin-clavulanate resistant *E. coli* and a significant association between these isolates and postoperative infectious complications [16]. Additional findings included an alarming rate of infection with *P. aeruginosa*. Modification of our EAR from amoxicillin-clavulanate to a bitherapy of ceftriaxone and metronidazole was made as supported by existing literature [20, 21, 28]. There was insufficient evidence from either our study or the literature to introduce a broad spectrum antipseudomonal antibiotic.

This study's primary objective was to describe and analyse microorganisms' microbiology and antibiotic susceptibility in complicated appendicitis since 2017. Secondary objectives included evaluating the change of EAR on the rate of postoperative infectious complications in complicated appendicitis and identifying possible determinants of postoperative infectious complications in our population.

Methods

Study design

This retrospective, comparative, single-centre cohort study was carried out in a tertiary care hospital (Lausanne University Hospital, Lausanne, Switzerland) in the department of child and adolescent surgery. Inpatient and outpatient medical records for all children and adolescents under the age of 18 who underwent an appendectomy between 01 January 2017 and 31 July 2020 were retrospectively reviewed. Eligibility criteria included the intraoperative diagnosis of complicated appendicitis by the surgeon and peritoneal sampling. Patients not meeting these two criteria were excluded. Standard postoperative follow up occurred, with the only relevant data being hospital readmission. The study was written in accordance with the STROBE (Strengthening The Report of Observational Studies in Epidemiology) guidelines.

Data collection

Patient electronic records were accessed via the electronic health record system (Soarian – Cerner, North Kansas City, MI, USA) under our hospital's data protection and data mining protocols. The following patient data and variables were extracted manually by retrospective review: demographic information (e.g., gender and age), clinical characteristics (e.g., duration of symptoms), microbiological information (e.g., bacteria isolated, antibacterial resistance), management (e.g., surgical procedure, antibiotic treatment) and complications (infectious versus non-infectious). No data were missing for the variables included in this study.

Surgical intervention(s)

A paediatric surgeon established the indication for surgery based on their clinical diagnosis of appendicitis or with the help of a radiological examination (i.e., echography, followed by a computed tomography scan in the absence of direct or indirect signs of acute appendicitis). The surgical intervention consisted of a laparoscopic appendectomy or open (McBurney) approach. The surgeon then confirmed the diagnosis of complicated appendicitis based on the presence of perforation, peritonitis, gangrene and/or an intra-abdominal abscess. Visualisation of peritoneal liquid or pus prompted surgeons to take samples for aerobic and anaerobic culture. Intraoperative and postoperative antibiotics were administered following the antibiotic protocol highlighted below. Postoperative infectious complications were defined as new intra-abdominal abscesses (confirmed radiographically) or surgical site infections, with their management being decided individually for each patient by the paediatric surgeon on call. When possible, conservative treatment was preferred. If unsuccessful, percutaneous drainage by the interventional radiologist was favoured, and if not technically possible, a second surgery was performed.

Empirical intravenous antibiotic regimen

The new EAR was implemented throughout this study but exclusively only from 2018. The anaesthetist gave the first dose of antibiotics at induction or, in cases when surgery was delayed, at diagnosis (NB: administration of this first dose was in all cases within 24 hours before surgery). Antibiotics consisted of a dual intravenous therapy of ceftriaxone (50–75 mg/kg) and metronidazole (15 mg/kg). In the case of acute appendicitis, no further doses were necessary. In complicated appendicitis, the duration of antibiotic therapy depended on the clinical evolution. Modification of the EAR occurred upon receiving the preliminary bacteriological results (within 48 hours after surgery) and again upon publication of the final results. When possible, antibiotics with the narrowest spectrum were chosen. In the event of worsening clinical symptoms in the first 48 hours (e.g., fever, lower right quadrant pain, nausea, and vomiting), piperacillin-tazobactam 100 mg/kg/dose) was administered.

Statistical analysis

Demographic information, clinical characteristics, microbiological information, and management were compared between groups using either the Student's t-test or the Kruskal–Wallis test for continuous variables, and the chi-square test or Fisher's exact test for categorical variables. All tests were two-tailed, and a resulting p-value <0.05 was statistically significant. Variables with a p-value <0.05 were included in a multivariable logistic regression model for which adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. Statistical analyses were computed using STATA software (Stata/SE 16.1 for Mac StataCorp, Lakeway, TX).

Ethical considerations

Owing to its retrospective and anonymous design, informed consent was not requested with no anticipated harm to the patients. The study was approved by the Human Research Ethics Committee of the Canton of Vaud, Switzerland, and conducted per the principles of the World Medical Association's Declaration of Helsinki, as well as the standards of Good Clinical Practice and in line with Swiss regulatory requirements.

Results

Patient inclusion criteria and demographics

During the study period, 553 patients under the age of 18 underwent an appendectomy. Of these, 458 (83%) presented with acute appendicitis and 94 (17%) met the required inclusion criteria for complicated appendicitis. There was a male predominance with 56 (60%) and a male to female ratio of 1.4:1. The median age was 9years (Interquartile range [IQR] 5–13). The median duration of symptoms before hospital presentation was 2 days (IQR 1–3), with patients staying hospitalised for a median of 6 days (IQR 4–7). The majority of patients with complicated appendicitis (n = 79, 84%) presented with localised perforated appendicitis, with the rest having a collected abscess (n = 8, 9%) or diffuse appendicular peritonitis (n = 7, 8%). Laparoscopy was performed in 88 (94%) patients, with three cases (3%) converted to an open appendectomy. The remaining 3% (n = 3) of patients underwent primary exploratory laparotomies owing to clinical severity or surgeon's preference. A summary of patient characteristics and potential risk factors for postoperative infectious complications is shown in table 1.

Microbiology and antibiotic susceptibility

The full classified list of microorganisms identified in peritoneal swab cultures can be seen in table 2. Single isolates were identified in 23 (24%) patients and multiple isolates in 66 (70%) patients. Cultures remained sterile in 11% of cases (n = 10). The most common isolated pathogen was *E. coli* (n = 65, 68%, fig. 1), followed by *Streptococcus anginosus* in 47 (48%) of isolates. *Bacteroides fragilis* was present in 22% (n = 22) of cultures. *P. aeruginosa* was isolated in 20% (n = 19) of cultures. Multiple isolates demonstrated intermediate or full resistance to one or more antibiotics. Ten of the *E. coli* isolates (15%) were resistant to amoxicillin-clavulanate, all of which were susceptible to our EAR and did not prove to be significantly associated with postoperative infectious complications (p = 0.859). Six strains of *E. coli* isolates (9%) demonstrated resistance to cephalosporins and thus to the EAR due to broad-spectrum beta-lactamase (ESBL) production. ESBL-producing strains did not prove to be significantly associated with postoperative infectious complications (p = 0.357). No meropenem or metronidazole resistance existed.

Antibiotic treatment and coverage

A summary of the antibiotics administered at all phases of this study can be found in table 3. Upon induction, the most frequently administered antibiotic was ceftriaxone/metronidazole (n = 65, 68%). Concerning the EAR, ceftriaxone/

Table 1:
Patient characteristics and potential determinants for post-operative infectious complications.

		Entire population (n = 94)	No postoperative infectious complications (n = 83)	Postoperative infectious complication (n = 11, intra-abdominal abscess formation)	p-value*
Gender, n male (%)		56 (60)	49 (59)	7 (64)	0.770
Age, median years (IQR)		9 (5–13)	9 (4–12)	13 (8–14)	0.045
Symptom duration, median days (IQR)		2 (1–3)	2 (1–3)	3 (1–7)	0.285
Abscess at presentation, n (%)		8 (9)	6 (7)	2 (18)	0.448
Laparoscopy, n (%)		88 (94)	78 (94)	10 (91)	0.622
P. aeruginosa positive, n (%)		19 (20)	17 (20)	2 (18)	0.858
Co-amoxicillin-resistant E. coli, n/total (%)		10 (11)	9 (11)	1 (9)	0.859
ESBL, n (%)		6 (6)	6 (7)	–	0. 357
Empirical antibiotherapy chosen	Co-amoxicillin, n (%)	6 (7)	6 (7)	–	
	Piperacillin-tazobactam, n (%)	31 (33)	25 (30)	6 (55)	
	Ceftriaxone-metronidazole, n (%)	54 (57)	49 (59)	5 (45)	
	Other **	3 (3)	3 (3)	-	

ESBL: broad-spectrum beta-lactamase; IQR: interquartile range.

*Univariable analysis comparing patients with and without postoperative infectious complications: Student's t-Test or the Kruskal-Wallis test for continuous variables and chi-squared or Fischer's exact test for categorical variables.

** Due to known allergy an alternative regimen was administered.

metronidazole was predominant (n = 54, 57%), followed by the broad-spectrum antibiotic piperacillin-tazobactam (n = 31, 33%). Based on these figures, the adherence rate to the new EAR for all years combined was 57%. The adherence rate per year was at a low of 21% in 2017, rising to 59%, 79% and 88% for the following years. The median duration of antibiotic treatment in all patients was 10 days (IQR 10–14) and 15 days (IQR 12–22) for the subgroup with postoperative infectious complications (p = 0.0034). EAR lasted for a median duration of 5 days (IQR 4–7), and antibiotics upon discharge lasted for 7 days (IQR 4–10) for all patients. Most patients (n = 83, 87%) were discharged with oral antibiotics, primarily amoxicillin-clavulanate (n = 35, 37%), followed by a dual therapy comprised of a quinolone (most frequently ciprofloxacin) and metronidazole (n = 24, 25%). The EAR correctly covered 74% (n = 69) of cases and their respective pathogens; it was inappropriate for the remaining 26% (n = 25), and therefore a change in antibiotic was necessary, often upgrading to a broad-spectrum antibiotic such as piperacillin-tazobactam. Of the patients with *P. aeruginosa*, only three (16%) did not need upgrading to a broad spectrum antibiotic due to an unremarkable clinical course. The remaining 84% (n = 16) required an upgrade from ceftriaxone/metronidazole to piperacillin-tazobactam, with the change taking place on postoperative day two.

Postoperative complications and hospital readmissions

A total of 11 patients (12%) developed postoperative infectious complications. Over the study period, the majority (n = 5, 45%) of cases of postoperative infectious complications occurred in 2017. Patients who developed postoperative infectious complications were significantly older (p = 0.045), with a median age of 13 (IQR 9–14). These patients were also more likely to have an increased length of

Table 2:
Microorganisms identified in peritoneal swab cultures sent for aerobic and anaerobic analysis.

Microorganisms		n (%)
Gram negative	*Escherichia coli*	65 (68)
	Pseudomonas aeruginosa	19 (20)
	Bacteroides fragilis	22 (23)
	Comamonas kerstersii	3 (3)
	Citrobacter koseri	1 (1)
	Proteus gr. *Vulgaris*	1 (1)
	Klebsiella gr. *Oxytoca*	1 (1)
	Haemophilus parainfluenzae	1 (1)
	Haemophilus influenzae	1 (1)
	Eikenella corrodens	1 (1)
	Citrobacter freundii	1(1)
Gram positive	*Streptococcus anginosus*	44 (46)
	Streptococcus pneumoniae serotype 11	1 (1)
	Streptococcus mitis	3 (3)
	Enterococcus avium	3 (3)

Figure 1: Microorganisms identified in cases of complicated appendicitis (displayed as a percentage per year). This bar chart shows that the most common microorganism found was *Escherichia coli* peaking at 86% in 2018.

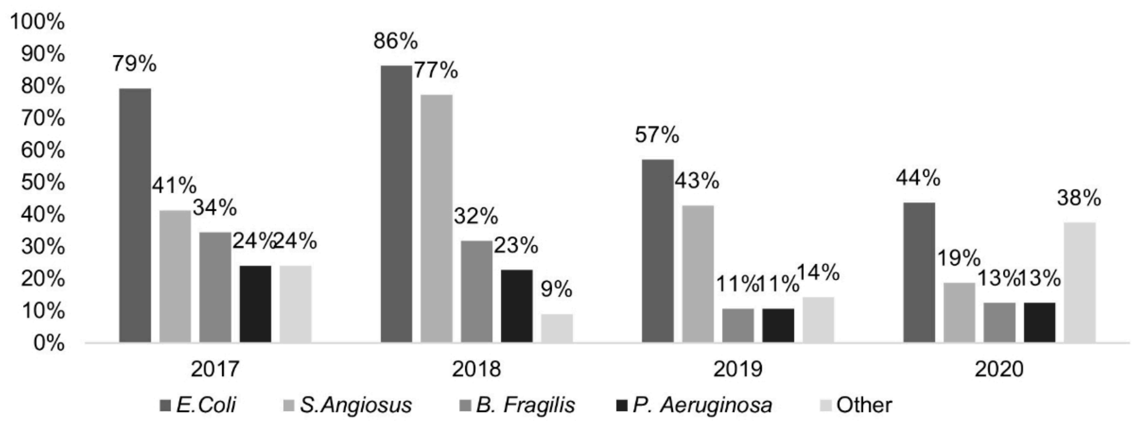

Table 3:
Summary of antibiotics administered throughout this study at all possible stages (induction, postoperatively, discharge) for all years combined (2017–2020, n = 94).

Antibiotic of choice	Induction	Post-op	Discharge
Amoxicillin-clavulanate, n (%)	20 (21)	6 (6)	35 (37)
Ceftriaxone and metronidazole, n (%)	64 (68)	54 (56)	–
Piperacillin/tazobactam, n (%)	5 (5)	31 (33)	2 (2)
Other, n (%)	5 (5)	3 (3)	57 (60)

stay (p = 0.0001), with a median of 10 days (IQR 8–16). Age upon multivariate analysis adjusting for infection with amoxicillin-clavulanate resistant *E. coli* was on the limit of statistical significance (p = 0.05, table 4). The three most frequently found microorganisms in patients who developed postoperative infectious complications were *E. coli* (n = 7, 64%), *S. anginosus* (n = 7, 64%), and *B. fragilis* (n = 7, 64%). Other bacteria isolated in lower numbers included *P. aeruginosa* (8%), *Citrobacter freundi* (9%) and *Citrobacter koseri* (9%). Two pathogens presented resistance to amoxicillin-clavulanate, an *E. coli* isolate and a *C. freundi* isolate. In both cases, isolates were susceptible to our EAR. Both instances of postoperative infectious complications caused by *P. aeruginosa* received broad spectrum antibiotics without a postoperative delay.

The majority (n = 7, 64%) of patients in the postoperative infectious complications subpopulation demonstrated unfavourable clinical evolution during their initial hospitalisation and received treatment immediately. In our study, a total of eight patients (9%) were readmitted, four for non-infectious reasons (postoperative haematomas or ileus;[n = 4/83, 5%) and the remaining four with postoperative infectious complications, leading to a readmission rate of 36% for the subpopulation presenting with postoperative infectious complications (p = 0.006). A total of 5 (45%) were treated conservatively with antibiotics, four (36%) via surgical intervention (exploratory laparotomy), one patient (9%) via interventional radiology, and one patient (9%) underwent an initial surgical intervention later followed by CT-guided drainage.

Discussion

Postoperative infectious complications such as intra-abdominal abscesses in complicated appendicitis remain a significant source of morbidity in the paediatric population [22, 29]. It follows that the optimisation and streamlining of its treatment and clinical care pathways should be a priority for all paediatric surgical departments. The choice of EAR has been intensely debated in the literature, and despite existing evidence, wide variability remains between surgeons and institutions [24]. Nevertheless, two common trends are becoming apparent. Firstly, antibiotics should address local patterns of microorganisms, choosing to cover the most frequently found pathogens while remaining vigilant to antimicrobial resistance and the increasing risk it poses to global health [15, 26]. Secondly, intravenous antibiotic choice should be simplified from triple to dual therapy or even single broad-spectrum therapy and continuously reviewed, and updated by institutions [30]. Our institution is adamant about following these two trends. Internal reviews and a published study [16] demonstrated that our EAR (amoxicillin-clavulanate) was no longer adequate owing to the significant role that amoxicillin-clavulanate-resistant *E. coli* played in causing postoperative infectious complications, thus prompting a change to a dual therapy with ceftriaxone/metronidazole. This analysis and conclusion led to the present study.

We retrospectively reviewed cases of complicated appendicitis after introduction of our new EAR. Complicated appendicitis was present in 17% of patients with a postoperative infectious complication rate of 12%, a decrease of 3% and 4%, respectively, versus the previous cohort. These rates are on the lower limit of those published, ranging from 15–40% for complicated appendicitis and 4-20% for postoperative infectious complications [14, 20, 23, 31, 32]. These favourable rates could be due to our definition of complicated appendicitis, which may differ from other institutions. The initial presentation of complicated appendicitis (e.g., abscess, perforation, appendicular peritonitis), the surgical technique used and gender all had no significant impact on the rate of postoperative infectious complications. In line with the current surgical trends in surgery, there was a 38% increase in the rate of laparoscopy as the primary approach, which occurred in 94% of cases in our current study.

E. coli and *S. anginosus* were the most commonly cultured microorganisms in complicated appendicitis, mirroring our previous study and in line with other published studies [12, 14, 30, 33, 34]. Rate of infection with amoxicillin-clavulanate-resistant *E. coli* remained similar to the last cohort (15% vs 14%). There was a drop from 28% to 9% in postoperative infectious complications due to amoxicillin-clavulanate-resistant *E. coli*. These results confirm that the strategic modification of our EAR now provides better coverage of local resistances, demonstrating the importance of making changes at an institutional level based on local resistance patterns. ESBL-producing *E. coli* increased from 3% in the previous cohort to 9%, with no significant impact on postoperative infectious complications. A study reporting a 57% infection rate of ESBL-producing *E. coli* failed to demonstrate a statistically significant effect on the rate of postoperative infectious complications [32]. With a small sample size, it is difficult to conclude the role of ESBL-producing *E. coli* on postoperative infectious complications. Further investigation is warranted as resistant microorganisms are becoming more common in paediatric patients, and their impact must be elucidated [35].

Age was positively correlated with developing postoperative infectious complications (p = 0.045) and concordant with similar studies [36]. Age was on the limit of statistical significance after multivariate analysis adjusting for the presence of amoxicillin-clavulanate-resistant *E. coli*. Other predictive variables for postoperative infectious complications in complicated appendicitis are described in the literature, such as: C-reactive protein levels at admission superior to 100 mg/dl, higher white blood cell count, and bowel obstruction at presentation [36–38]. These variables were not considered in the present study as they fell beyond the scope of the objectives but prove pertinent for consideration in future prospective studies.

Table 4:
Multivariable analysis.

Predictor	Contrast	Odds ratio (95% confidence interval) for postoperative infectious complications	p-value
Amoxicillin-clavulanate-resistant *E. Coli*	Yes vs no	0.61 (0.07–5.38)	0.654
Age	One year increase	1.18 (0.99–1.39)	0.053
Intercept	–	0.03 (0.003–0.19)	<0.001

Due to the prolongation and the complexity of treatment, patients with postoperative infectious complications had a significantly longer length of stay and total duration of antibiotic therapy, and a tendency to be readmitted. These factors have an essential role in increasing morbidity. Our patients received intravenous antibiotics for a median of 5 days. The optimal length of EAR in complicated appendicitis remains undecided. Recent studies suggest that 2 days of intravenous antibiotics is not associated with a higher risk of postoperative infectious complications, and in parallel, longer duration of antibiotics do not prevent postoperative infectious complications from occurring [5, 17, 37, 39]. Indeed, the World Society of Emergency Surgery (WSES), in their most recent publication on the diagnosis and treatment of acute appendicitis, recommend an early switch (after 48 hours) to oral antibiotics in children with complicated appendicitis [40]. Moreover, an early transition could decrease the overall morbidity by decreasing patient burden, use of hospital resources and length of stay. Further prospective studies are needed.

Due to a transition period between 2017–2018, after the new EAR was established and introduced, a certain number of patients initially received antibiotics with enhanced anti-pseudomonas activity such as piperacillin-tazobactam. We attribute this heterogeneity to the implementation of and potential initial hesitation with the new EAR. Some surgeons most likely opted for a broader spectrum antibiotic when faced with a severe clinical presentation. We have not excluded these patients. It is noteworthy that the most significant number of postoperative infectious complications was during this transition period. We observed a decrease in postoperative infectious complications when adherence rose. Studies have shown that streamlining clinical care pathways can significantly decrease the rate of postoperative infectious complications and length of stay [41].

P. aeruginosa plays a significant role in postoperative infectious complications [15]. Our previous study demonstrated infection rates between 44% and 9%, depending on the year in question. The presence alone of this microorganism was not correlated with postoperative infectious complications and we, therefore, chose not to introduce an antipseudomonal antibiotic into our EAR [16]. Our current study demonstrated a mean overall infection rate of 20% (3% decrease) with no significant contribution to the rate of postoperative infectious complications. *P. aeruginosa* may be one of multiple pathogens found in colonic flora of paediatric patients and differs from single *P. aeruginosa* infections, thus questioning whether its antibiotic coverage is warranted [14].

Multiple retrospective studies have been conducted in children with complicated appendicitis comparing dual EAR versus broader antipseudomonal antibiotics such as piperacillin-tazobactam. The results are often conflicting. Some authors report positive outcomes such as a decrease in the percentage of postoperative infectious complications rates in those receiving broader antipseudomonal antibiotics [42], whereas others report no added advantage [19, 31, 43]. These studies have many drawbacks, notably not detailing the local microbiology and thus the infection rate of *P. aeruginosa*. Guillet-Caruba et al. [44] proposed providing supplemental pseudomonal coverage with an aminoglycoside for a period of 2 days until microbiological results become available. Institutions would then down-grade or maintain their therapy. Reverting to a triple EAR could increase morbidity, which in our view is not recommended. The risk of multidrug resistance and supplemental side effects such as infection with *Clostridium difficile* are important to consider when deciding to implement piperacillin-tazobactam as a first-line regimen [13, 25, 31].

Given the shortfall of evidence in the literature proving a clear added benefit of administering antipseudomonal antibiotics in cases of complicated appendicitis, and with our rate of infection of *P. aeruginosa* stagnating at 20%, we chose not to modify our empirical antibiotic regimen further. Institutions should continue to track and analyse their rates of *P. aeruginosa* infection and other potentially resistant microorganisms and their influence on postoperative infectious complications. Randomised prospective studies are needed to determine whether *P. aeruginosa* coverage is warranted.

The role of peritoneal sampling and cultures has been widely disputed, particularly in acute appendicitis. Indeed, certain authors concluded that it is fruitless as they do not impact clinical outcomes [34]. In complicated appendicitis, the role of peritoneal sampling is equally disputed. Since 2000, many authors have promoted systematic sampling due to its integral part in studying local flora and streamlining clinical pathways [12, 13, 32, 37, 44]. The Study for Monitoring Antimicrobial Resistance Trends (SMART) conducted a surveillance study of the epidemiology and antimicrobial susceptibility of pathogens causing intra-abdominal infections in paediatric patients, concluding that EAR should reflect regional and local resistance patterns, as there can be a large variability between institutions [45], thus confirming the importance of peritoneal sampling. We stand by these guidelines and will continue this practice, which permitted us to modify our EAR and better target resistant microorganisms in our local population.

This study has some limitations. Firstly, its retrospective design and small sample size may rationalise the limited statistically significant data and restrict the validity of our research. In our defense, multiple homogeneous factors are present. Our patients were all treated in the same institution, by the same pool of on-call surgeons, and followed the same EAR. We recognise the inherent possibility of potential biases. Secondly, due to its single-centre design, the results may not be generalisable, as inter-institutional pathogen distribution and local resistance rates can vary. We hope that our study can guide others in their future study designs and, eventually, their choice of EAR in the treatment of complicated appendicitis.

Conclusion

The findings of this study emphasis the need to implement evidence-based treatment protocols based on local microbiology profiles and current resistance rates to optimise postoperative EAR in complicated appendicitis. The change in our EAR permitted us to successfully cover resistant isolates that have been problematic in the past. We do not retain an indication to introduce antipseudomonal coverage. Our study adds to the vast body of literature evaluating management strategies for patients with complicated appendicitis who develop postoperative infectious complications. Postoperative infectious complications are likely multifactorial, and numerous prospective studies are needed to understand better their aetiology and the role of EAR in decreasing their existence. Antimicrobial resistance is on the rise, and institutions should play their role in tackling this global phenomenon.

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