The Intraperitoneal Use of Cephazolin: A Novelty in the Prevention of Intra-abdominal Abscess after Laparoscopic Appendectomy in Children

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Background: Laparoscopic appendectomy followed by postoperative intravenous (IV) antibiotics is the standard of care for acute appendicitis and postoperative prevention of intra-abdominal abscesses. The aim of or study was to determine if intraperitoneal irrigation with antibiotics could help prevent intra-abdominal abscess formation after laparoscopic appendectomy for complicated appendicitis in pediatric patients.

Methods: A retrospective study was conducted on consecutive pediatric patients with acute appendicitis who had appendectomy in our Pediatric Surgery Department between August 2020 and February 2022. We compared two groups with similar age and symptoms. The first group (A) was treated with the normal standard of care, i.e., laparoscopic appendectomy and postoperative IV antibiotic therapy. For the second group (B) intraperitoneal cefazoline irrigation was added at the end of the laparoscopic procedure. Postoperative intra-abdominal abscess was diagnosed with ultrasound examination, performed after clinical suspicion/abnormal blood test results.

Results: One hundred sixty patients (males:females 109:51; median age 10.5 years [range 3–17 years]) who had laparosopic appendectomy for complicated appendicitis were included, 82 in group A and 78 in group B. In the first 7 days after surgery, 18 patients in group and 5 in group B developed an intra-abdominal abscess ($p < 0.005$). Drains were positioned in 38 patients in group A vs. 9 in group B. One patient in group A had a different complication which was infection of the surgical incision.

Conclusions: Intraperitoneal cefazoline irrigation at the end of the laparoscopic appendectomy in pediatric patients significantly reduces the formation of intra-abdominal abscesses

Keywords: appendicitis; intra-abdominal abscess; intraperitoneal irrigation; children

Introduction

Appendectomy is the most commonly performed emergency operation in general surgery as well as the most frequent emergency requiring abdominal surgery in children.

Surgical laparoscopic appendectomy followed by postoperative intravenous (IV) antibiotics is the standard of care for acute appendicitis. Although appendectomy is associated with low morbidity and mortality rates, serious postoperative complications such as intra-abdominal abscesses can occur.

Local antibiotic treatment is used for superficial wounds and infections. Intraperitoneal administration of antimicrobial drugs provides high concentrations at the site of infection and therapeutic plasma concentrations [1, 2, 3, 4, 5, 6, 7].

The purpose of this study was to determine if total length of hospital stay and the incidence of post appendectomy peritoneal abscesses in pediatric patients with complicated appendicitis could be reduced by intraoperative intraperitoneal administration of cephazolin followed by an intravenous antibiotic regimen as compared to an intravenous antibiotic regimen alone.

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Materials and Methods

A retrospective study was conducted on consecutive pediatric patients (<18 years of age) with acute appendicitis who underwent appendectomy at our pediatric surgery unit between August 2020 and February 2022. We excluded from the study all the patients who were not treated with laparoscopy (such as traditional open appendectomy or interval appendectomy for peritoneal abscess at onset) as well as those with pathologic or intraoperative findings other than complicated appendicitis. Patients were divided into two groups, patients who did not receive intraoperative intraperitoneal cefazolin (group A) and patients who did (group B). All patients received postoperative IV antibiotic therapy, with ceftazidime (100 mg/kg/day) and metronidazole (24 mg/kg/day). At the end of the surgical procedure, in group B a solution composed of 1 g of cefazoline diluted in 20 mL of 0.9% saline solution was irrigated in the peri-

Table 1. Treatment protocol.

Operative protocol	
Antibiotic prophylaxis	Cefazolin 25 mg/kg one shot
Operative setting	Laparoscopic when possible
Peritoneal irrigation	Mean of 3.5 L of saline solution
Peritoneal antibiotic	2 g cefazolin in 20 mL saline solution: 10 mL in the right flank and 10 mL in the Douglas Pouch
Drains	Avoid if possible
Postoperative protocol	
IV antibiotic regimen	Metronidazole 22.5 mg/kg/day in three doses + Ceftazidime 150 mg/kg/day in three doses
Postoperative blood work	postoperative day 4 → blood count + CRP
Postoperative ultrasound	Only if: - persistent alteration of WBC count or CRP level - fever - abdominal pain
After discharge antibiotic	5 days cefixime (8 mg/kg/day) + 7 days metronidazole (22.5 mg/kg/day in three doses)
Post discharge clinical evaluation	One week after discharge in the clinic

IV, intravenous; CRP, C-reactive protein; WBC, white blood cell.

Table 2. Patient characteristics and perioperative factors.

	Peritoneal lavage only (Group A)	Intraperitoneal Cefazolin (Group B)	*p*
Total number of patients	82	78	
Median age, range (years)	10 (3–17)	11 (4–17)	n.s.
White blood cell count at presentation ($10^3/\mu$L)	13,255	13,462	n.s.
Time interval between onset and operation (minutes)	404 (352–487)	370 (347–452)	n.s.
Intraperitoneal swab positive, n	47	50	
Postoperative intra-abdominal abscess, n	18	5	$p < 0.005$
Length of stay (days) median (range)	7.9 (2–45)	5.6 (1–33)	0.048
Major complications (i.e., adhesive small bowel obstruction), n	1	0	n.s.

n.s., not significable.

toneal cavity (10 mL in the right flank and 10 mL in the Douglas Pouch). In the case of drain positioning, drains were kept closed for the first 6 hours post surgery in order to ensure a local permanence of the antibiotic.

Medical records were retrospectively examined based on the following criteria: white blood cell count, neutrophil percentage and the C-reactive protein (CRP) level on admission, as well as the presence of fever before surgery. Other parameters that were evaluated were preoperative ultrasound findings and the time intercurred between the beginning of the symptoms and surgery. Surgical parameters that we considered were the eventual necessity of conversion from laparoscopic to open traditional incision and the positioning of peritoneal drains at the end of the surgical procedure. Postoperative parameters were the length of hospital stay and the presence of any complications, such as peritoneal abscesses. During every surgery peritoneal liquid samples were sent for microbiological cultures and the results were also evaluated (eventual growth of bacteria, presence of multidrug resistant bacteria).

Blood tests were performed on postoperative day 4 and then every 48 hours until CRP levels were inferior to 1 mg/dL. Our treatment protocol is provided in Table 1.

Statistical Analysis

Dichotomous variables were analyzed using Fisher's exact test, assessing statistical significance at $p < 0.05$ (2-tailed). Data were also correlated by Pearson's coefficient, and 95% confidence intervals were calculated. Statistical tests were performed using GraphPad Prism for Windows (Version 8.0, GraphPad Software Inc., San Diego, CA, USA; http://www.graphpad.com).

Results

There were160 patients (male:female 109:51; median age 10.5 years [range 3–17 years]), 82 in group A and 78 in group B. Background characteristics and perioperative factors of the groups with and without intraperitoneal use of cephazolin are summarized in Table 2. All 160 patients had minimally invasive treatment with a 3-port standard laparoscopic appendectomy. There were no conversions to open. There were no adverse events related to the intraoperative intraperitoneal administration of cephazolin. All patients received the full postoperative course of IV antibiotics according to the same protocol. All patients received a minimum of 2000 mL washout, with a mean of 3500 mL. Eighteen patients in group A vs. 5 patients in group B de-

Table 3. Bacterial growth was detected in the cultures of the peritoneal liquid.

	Peritoneal lavage only (Group A)	Intraperitoneal Cefazolin (Group B)
Total swab positive	47	50
Escherichia Coli	41%	39%
Bacteroides spp.	17%	18%
Enterococcus spp.	10%	12%
Pseudomonas Aeruginosa	9%	8%
S. Anginosus spp.	12%	14%

veloped a postoperative intra-abdominal abscess in the first 30 postoperative days ($p < 0.005$). In all cases surgery was not needed and all patients underwent IV antibiotic treatment. There were no significant differences between the two groups in terms of time to full diet, mobilization or pain resolution. In 47 cases in group A vs. 50 cases in group B bacterial growth was detected in the cultures of the peritoneal liquid (Table 3). Drains were positioned in 38 patients in group A vs. 9 in group B. One patient in group A had a different complication which was the infection of the surgical incision. He was treated with medications in the clinic. All patients attended their outpatient appointments for review. There were no readmissions to our institution for any patient included in this retrospective study.

Discussion

In our series, children having laparoscopic appendectomy were less likely to develop postoperative abscess if they received intraoperative intraperitoneal cefazolin. There were no adverse events related to the intraoperative intraperitoneal irrigation. In group B, the postoperative intraabdominal abscess rate was only 6.4% vs. 21.9% in group B. The incidence of intra-abdominal abscess after appendectomy for complicated appendicitis ranges from 3 to 45%, according to a survey of several datasets in the literature [8, 9, 10, 11]. Therefore, it appears that our strategy does indeed lower the incidence of these abscesses. Although anaerobes, which are known to be the primary cause of these abscesses, are unaffected by cefazolin, a first-generation cephalosporin, the concentration of cephalosporin injected into the peritoneum, which was thousands of times larger than the concentration used for bacterial susceptibility testing, was likely the cause of this decrease in abscess formation. Our choice of cefazolin as an antibiotic to be used intraperitoneally reflects the result of the antibiograms of 100 appendicitis/peritonitis patients who had surgery at our hospital, so as to adapt the local therapy to the population of bacteria most represented in our region. The use of intraperitoneal lavage without antibiotics is also much debated in the international literature, in 1952, Thorek [12] already highlighted how this alone reduced the percentage of mortality from peritonitis from 100% to 33%. Since then, several studies have proven the usefulness of washing alone [13, 14, 15, 16, 17]. In patients who underwent surgery for appendicitis or peritonitis, many writers tested the effects of intraperitoneal antibiotics [1, 2, 3, 4, 5, 6, 7, 8]. It is well known that several antibiotics, including cephalosporins, can be administered intraperitoneally to attain effective blood levels [18]. There are various experimental demonstrations that show the intraperitoneal route to be superior to the systemic route for reducing peritonitis-related mortality and morbidity [19] even if, this treatment modality is not widely used.

The present study has limitations, it is not randomized, and multicenter controlled studies would be needed to assess whether the intraperitoneal use of cephazolin for complicated appendicitis can prevent intra-abdominal abscess.

Conclusions

This study shows that adding intraperitoneal cefazoline irrigation at the end of laparoscopic appendectomy in pediatric patients significantly reduces the formation of intra-abdominal abscesses.

Availability of Data and Materials

The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

SF, IPA, AK designed the research study. TDA, AB, SM performed the research. AA, VP, AI analyzed the data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Bambino Gesù Children's Hospital waived ethical approval for the study as it was a retrospective study. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The patients involved in this series were appropriately consented for this publication using the institution's policy for media consent.

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Conflict of Interest

The authors declare no conflict of interest.

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