ORIGINAL RESEARCH

Observation on the Curative Effect of Different Anti-infective Treatment Regimens for Children with Acute Appendicitis

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ABSTRACT

Objective • To observe the efficacy of different anti-infective treatment regimens on acute appendicitis in children, a retrospective study was conducted by collecting previous cases.

Methods • Ninety children with acute appendicitis who received laparoscopic appendectomy from May 2020 to September 2022 were included in this retrospective study. According to the different anti-infective treatment regimens, they were divided into Piperacillin-Tazobactam group, Piperacillin-Tazobactam+Metronidazole group, and Cefminox+Metronidazole group (n=30). Three groups of children received medication treatment before surgery. The postoperative recovery, treatment effect, bacterial clearance, complication rate, pharmacoeconomic evaluation, and adverse reactions were compared.

Results • The effective rates in the three groups were 83.33%, 90.00%, and 90.00%, respectively ($P > .05$). There were no differences in the bacterial clearance, complication incidence, and incidence of pharmaceutical side effects among the three groups ($P > .05$). The total hospitalization cost, total drug cost, and antimicrobial drug cost in Cefminox + Metronidazole group were lower than those in Piperacillin-Tazobactam group and Piperacillin-Tazobactam + Metronidazole group, respectively ($P < .05$). The intensity of antibacterial drug use in Piperacillin-Tazobactam group was the lowest, followed by Piperacillin-Tazobactam + Metronidazole group and Cefminox + Metronidazole group ($P < .05$).

Conclusion • The three anti-infective regimens have the same therapeutic effect on acute appendicitis in children. However, the regimen of Cefminox + Metronidazole is the most economical option and can be used as the preferred treatment for acute appendicitis in children. As the preferred treatment for acute appendicitis in children. The Piperacillin-Tazobactam group has the lowest intensity of antibiotic use and can reduce bacterial resistance. (*Altern Ther Health Med.* [E-pub ahead of print.])

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INTRODUCTION

Acute appendicitis is a common disease in children. Clinical manifestations are characterized by crying, abdominal pain, fever, nausea and vomiting, abdominal distension, and diarrhea.[1] The clinical presentations are different among children of different ages and are often misdiagnosed and mistreated, which even induces life-threatening.[2] In children, the appendix is thin-walled, and the greater omentum is incompletely developed, which makes it prone to perforation and diffuse peritonitis, and surgical resection is usually the mainstay after diagnosis.[3] The appendix, which is connected to the colon, has a thin lumen containing various microorganisms. These microorganisms can easily multiply in the presence of inflammation.[4] Surgery and antimicrobial therapy are the main treatment choices for acute appendicitis.[5]

According to the Guidelines for the Clinical Use of Antimicrobial Drugs, appendectomy is a Class II or Class III incision, and appendicitis has both infected organisms and a large number of human parasitic flora present in the surgical incision, such as gram-negative bacilli and anaerobic bacteria.[6] The correct application of antimicrobial drugs in the perioperative period is a proven countermeasure to reduce surgical site infections.[7] Specifically, the first-generation cephalosporin (cefazolin) has the strongest bactericidal activity against G^+ Staphylococcus in the head, neck, limbs, and other incisions.[8] The second-generation cephalosporin (cefuroxime) is widely used to prevent infection of thoracic, abdominal, and pelvic surgery sites.[9] For complex major surgeries with a high risk of infection, the third-generation cephalosporin (ceftriaxone) can be used when necessary.[10] When obvious infections occur during gastrointestinal surgery (or trauma), antibiotics should be used to cover common anaerobic bacteria.[11] Due to the complexity of the microbial community, in order to have good antibacterial activity against G - bacteria such as Pseudomonas aeruginosa, G+ bacteria such as Enterococcus, and some anaerobic bacteria, second-generation and third-generation cephalosporins or piperacillin with metronidazole and tazobactam are commonly used.

Anti infection is an important tool for treating the appendix. There are many anti infection plans for appendicitis in clinical practice, but there is no consensus on the most effective and economical plan. In this study, a retrospective analysis was conducted to compare the therapeutic effects of Piperacillin-Tazobactam, Piperacillin -Tazobactam + Metronidazole, and Cefminor+Metronidazole in the treatment of pediatric appendicitis after laparoscopic appendectomy. In the absence of significant differences in efficacy, the Cefminor + Metronidazole regimen is the most economical and can be used as the preferred option for acute appendicitis in children, reducing treatment and medical costs. The use of antibiotics in the Piperacillin-Tazobactam group is the lowest, which can minimize the production of bacterial resistance. Obtaining the most effective and economical treatment plan can not only improve patient prognosis, reduce the probability of postoperative infections and complications, accelerate patient recovery and discharge, reduce overall treatment costs, but also reduce the degree of pain during the treatment process.

SUBJECTS AND METHODS

General information

This study was approved by the Ethics Committee of the Baoding Childen's Hospital. All patients' guardians gave informed consent before treatment. Ninety children with acute appendicitis who received laparoscopic appendectomy in the Baoding Childen's Hospital from May 2020 to September 2022 were included in this retrospective study. Randomly number the enrolled children, select the corresponding sample size in random numerical order, and assign them to the Piperacillin-Tazobactam group, Piperacillin-Tazobactam+Metronidazole group, and Cefminox + Metronidazole group (n=30)

Inclusion and exclusion criteria

Inclusion criteria: (1) children aged 2 to 18 years; (2) Normal liver and renal function; (3) No use of steroids or immunosuppressive drugs.

Exclusion criteria: (1) Patients with penicillin or cephalosporin allergy; (2) children with persistent respiratory tract infections; (3) children with underlying disease; (4) infections other than the primary cause for change of antimicrobial drugs; (5) Intermediate transfers to the intensive care unit or a different hospital; (6) children with undergoing non-surgical treatment; (7) pathological findings showing non-appendicitis.

Treatment methods

Laparoscopic appendectomy: After general anesthesia, lie on the operating table and first establish a pneumoperitoneum to form a surgical space for the surgery. After determining the specific position of the appendix, peel off the surrounding mucosal tissue layer by layer to fully expose the appendix and its mesentery. Use a separating forceps to make a small hole at the root of the appendix, use a 4-7 mousse thread to ligate the appendix and mesentery. After the ligation is firm, cut off the appendix and mesentery about 10 cm away from the ligation site. At the same time, use an electrocoagulation rod to treat the residual end of the appendix. When it is confirmed that there is no bleeding or oozing at the broken end, rinse the abdominal cavity with physiological saline, place a drainage tube, and suture the incision layer by layer.

Antibacterial drug use

In Piperacillin-Tazobactam group, piperacillin-tazobactam (North China Pharmaceutical Co., Ltd., H20100062) was given 0.5-1 h before surgery. 100 mg/kg was used for those weighing <40 kg, Q8h. For those weighing > 40 kg, 1.25 g/kg was used, Q8h. In Piperacillin-Tazobactam+Metronidazole group, piperacillin-tazobactam + metronidazole was given 0.5-1 h before surgery. The dosage of piperacillin-tazobactam was the same as that in Piperacillin-Tazobactam group. Metronidazole (Hebei Tiancheng Pharmaceutical Co., Ltd., H20033943) was given at 7.5 mg/kg for Q8h. In Cefminox+Metronidazole group, cefminox + metronidazole was given 0.5-1 h before surgery. The dosage of metronidazole was the same as in Piperacillin-Tazobactam+Metronidazole group. Cefminox (Fuan Pharmaceutical Group Qing Yu Tang Pharmaceutical Co., Ltd., H20163075) was sued as 20 mg/kg, Q8h. For those weighing >40 kg, the dose was 1 g/kg, Q8h. All three groups received the same treatment of amino acid supplementation and correction of electrolyte disorders. Blood analysis was reviewed regularly after the operation. If the body temperature and blood examination were normal and positive signs were not obvious, the treatment was promptly switched to oral administration.

Observation indicators

(1) Baseline information, including age, gender, body weight, surgery time, and intraoperative bleeding. (2) Post-operative recovery: time to first bed activity, time to anal discharge, leukocyte count at 5 days postoperatively ($\times 10^9$/L), C-reactive protein at 5 days postoperatively (mg/L), length of stay in hospital (day) were collected. (2) Effect of treatment: Clinical efficacy is divided into three grades: significant, effective, and ineffective. Significant effect: No fever, no suppuration of the wound; Effective: Mild fever, redness and swelling of the wound, and signs of suppuration; Ineffective: Continuous fever and pus production from the wound. Total

Table 1. Baseline information of children in the three groups

Groups	Age (years)	Gender (cases)		Body weight (kg)	Surgery time (min)	Intraoperative bleeding (ml)
		Males	Females			
Piperacillin-Tazobactam group	7.37±0.97	15 (50%)	15 (50%)	40.94±8.02	34.83±8.22	10.03±0.93
Piperacillin-Tazobactam + Metronidazole group	7.51±0.97	16 (53.33%)	14 (46.67%)	39.40±10.79	34.33±6.40	10.17±0.94
Cefminox + Metronidazole group	7.41±1.10	18 (60.00%)	12 (40.00%)	39.93±11.21	37.31±5.84	10.18±1.05
F/χ^2	0.151	0.627		0.180	1.607	0.222
P value	.860	.731		.836	.206	.801

Table 2. The postoperative recovery of the three groups of children

Groups	Time to first bed activity (h)	Time to anal discharge (h)	Time to recovery of gastrointestinal function (h)	Leukocyte count at 5d postoperatively (×10⁹/L)	C-reactive protein at 5d postoperatively (mg/L)	Length of stay in hospital (d)
Piperacillin-Tazobactam group	18.09±3.24	27.54±5.19	14.03±2.56	11.07±2.01	33.16±6.64	5.00±0.26
Piperacillin-Tazobactam + Metronidazole group	19.00±2.96	29.25±4.48	14.87±2.29	11.92±1.66	34.36±4.94	5.19±0.59
Cefminox + Metronidazole group	18.96±2.79	27.16±4.63	15.42±2.31	11.78±2.00	33.29±6.14	5.15±0.43
F	0.880	1.630	2.574	1.732	0.368	1.503
P value	.418	.202	.082	.183	.694	.228

effective rate = significant effective rate + effective rate. (3) Bacterial clearance: subcutaneous needle puncture at the right lower abdominal appendix point to make microscopic bacterial smear of the puncture fluid (4) Incidence of postoperative complications: The postoperative complications in each patient were recorded, including wound infection, pneumonia, precision dehiscence, intestinal obstruction, abscess, and readmission within 30d. (5) Pharmacoeconomic evaluation: The treatment expenses were sorted out, including the total cost of hospitalization, including total hospitalization costs, types of antibiotics, and total cost of antibiotics. (6) Incidence of adverse drug reactions: Inform the patient's adverse reactions through daily inspections and inquiries. (7) Antimicrobial drug indicators, including intensity and rate of use.

Effectiveness evaluation

Clinical symptoms and signs disappeared, no right lower abdominal pain on physical examination, no fever, white blood cells normalized or tended to be normalized in routine blood examination, no residual abscess in color ultrasound abdominopelvic cavity shown under ultrasound (cure); clinical symptoms and signs decreased, slight right lower abdominal pain on physical examination, no fever, white blood cells normalized or tended to be normalized in routine blood examination, no residual abscess in color ultrasound abdominopelvic cavity shown under ultrasound (effective); clinical No change or worsening of clinical symptoms and signs, with right lower abdominal tenderness on examination, fever, higher than normal white blood cells in routine blood tests, and residual abscesses in the abdominopelvic cavity on ultrasound (invalid).

Statistical analysis

Data were analyzed using SPSS 26.0 software. The measurement data were described as mean ± standard deviation (SD. The count data were described as n(%), with χ^2 test at $\alpha = 0.05$. *t* test was used to compare the differences between the two groups. One-way ANOVA was used to compare the differences among the three groups. $P < .05$ was considered significantly different.

Table 3. The treatment effects of the three groups of children

Groups	Significant effect	Effective	Ineffective	Total effective rate
Piperacillin-Tazobactam group	10 (33.33)	15 (50.00)	5 (16.67)	25 (83.33)
Piperacillin-Tazobactam + Metronidazole group	12 (40.00)	15 (50.00)	3 (10.00)	27 (90.00)
Cefminox+Metronidazole group	11 (36.67)	16 (53.33)	3 (10.00)	27 (90.00)
χ^2				0.829
P value				.661

RESULTS

Baseline information

The average age in Piperacillin-Tazobactam group, Piperacillin-Tazobactam + Metronidazole group, and Cefminox+Metronidazole group was 7.37±0.97, 7.51±0.97, and 7.41±1.10. There were 15 males and 15 females in Piperacillin-Tazobactam group. There were 16 males and 14 females in Piperacillin-Tazobactam+Metronidazole group. There were 18 males and 12 females in Cefminox + Metronidazole group. According to the Table1, the *P* values for body weight, surgical time, and intraoperative bleeding in the three groups were 0.180, 1.607, and 0.222, respectively, with no significant differences ($P > .05$).

Post-operative recovery

According to Table 2, the *P* values of the three groups in terms of first post-operative bed movement, anal discharge, recovery of gastrointestinal function, post-operative 5-d white blood cell count, C-reactive protein, and length of hospital stay were .418, .202, .082, .183, .694, and .228, respectively, and there were no differences ($P > .05$).

Effect of treatment

According to Table 3, the effective rates were 83.33%, 90.00%, and 90.00% in Piperacillin-Tazobactam group, Piperacillin-Tazobactam + Metronidazole group and Cefminox + Metronidazole group,with a *P* value of .661, respectively, with no statistical difference in comparison ($P > .05$).

Bacterial clearance

As shown in Table 4, compared with the preoperative period, the bacterial positivity rate of children in the three groups decreased 7 d after surgery ($P < .05$). Still, there was a distinction between the groups ($P > .05$).

Table 4. Bacterial clearance of children in the three groups

Groups	Preoperative		7d post-op	
	Positive	Negative	Positive	Negative
Piperacillin-Tazobactam group	29 (96.67)	1 (3.33)	2 (6.67)[a]	28 (93.33)
Piperacillin-Tazobactam + Metronidazole group	30 (100.00)	0 (0.00)	1 (3.33)[a]	29 (96.67)
Cefminox+Metronidazole group	29 (96.67)	1 (3.33)	1 (3.33)[a]	29 (96.67)
χ^2	1.023		0.523	
P value	.600		.770	

[a]Compared to the same group preoperatively, $P < .05$

Table 5. Incidence of postoperative complications in the three groups

Groups	Wound infection	Pneumonia	Incision dehiscence	Intestinal obstruction	Abscess	Readmission within 30 d
Piperacillin-Tazobactam group	2 (6.67%)	2 (6.67%)	0 (0.00%)	3 (10.00%)	1 (3.33%)	1 (3.33%)
Piperacillin-Tazobactam + Metronidazole group	0 (0.00%)	0 (0.00%)	1 (3.33%)	1 (3.33%)	0 (0.00%)	0 (0.00%)
Cefminox + Metronidazole group	1 (3.33%)	0 (0.00%)	0 (0.00%)	2 (6.67%)	0 (0.00%)	0 (0.00%)
χ^2	2.069	4.091	2.023	1.071	2.023	2.023
P value	.355	.129	.364	.585	.364	.364

Table 6. Comparison of pharmacoeconomic indicators among children in the three groups

Groups	Total cost of hospitalization (Yuan)	Total drug costs (Yuan)	Cost of antibacterial drugs (Yuan)
Piperacillin-Tazobactam group	10651.69±518.58	2207.64±316.19	1079.18±153.57
Piperacillin-Tazobactam + Metronidazole group	10898.03.±556.87	2194.84±321.75	1109.62±172.30
Cefminox+Metronidazole group	9915.55±533.01[a,b]	2004.74±392.62[a,b]	698.74±71.92[a,b]
F	27.247	3.249	80.715
P value	<.001	.044	<.001

[a]Compared with Piperacillin-Tazobactam group, $P < .05$
[b]Compared with Piperacillin-Tazobactam+Metronidazole group, $P < .05$

Table 7. Comparison of adverse drug reactions among the three groups of children[n/(%)]

Groups	Nausea and vomiting	Itchy skin	Dizziness
Piperacillin-Tazobactam group	3 (10.00)	2 (6.67)	2 (6.67)
Piperacillin-Tazobactam + Metronidazole group	5 (16.67)	4 (13.33)	3 (10.00)
Cefminox+Metronidazole group	7 (23.33)	3 (10.00)	3 (10.00)
χ^2	1.920	0.741	0.274
P value	.383	.690	.872

Table 8. Antimicrobial drug index situation in three groups

Groups	Utilization rate (%)	Intensity of use
Piperacillin-Tazobactam group	100.00	20.70±2.34
Piperacillin-Tazobactam+Metronidazole group	100.00	82.89±18.64[a]
Cefminox+Metronidazole group	100.00	181.27±25.64[a,b]
χ^2/F	—	583.900
P value	1.000	<.001

[a]Compared with Piperacillin-Tazobactam group, $P < .05$
[b]compared with Piperacillin-Tazobactam+Metronidazole group, $P < .05$

Incidence of postoperative complications

According to Table 5, the postoperative complications mainly included wound infection, pneumonia, incision dehiscence, intestinal obstruction, abscess, and readmission within 30 d, with *P* values of .355, .129, .364, .585, .364, and 0.364, respectively, there was no significant differences in the incidences of complications among the three groups after surgery ($P > .05$).

Pharmacoeconomic evaluation

According to Table 6, the total cost of hospitalization, total drugs, and the antimicrobial drugs were collected in the three groups. The total cost of hospitalization was the least in Cefminox + Metronidazole group, followed by Piperacillin-Tazobactam+Metronidazole group and Piperacillin-Tazobactam group. Similarly, the cost of total antimicrobial drugs were the least in Cefminox + Metronidazole group, followed by Piperacillin-Tazobactam + Metronidazole group and Piperacillin-Tazobactam group ($P < .05$).

Incidence of adverse drug reactions

According to Table 7, there were three main adverse drug reactions among the three groups, including nausea and vomiting, itchy skin, and dizziness, with *P* values of .383, .690, .872, there was no notable difference in adverse drug reactions among the three groups ($P > .05$).

Antimicrobial drug indicators

As shown in Table 8, there was no statistical difference in the comparison of the utilization of antibacterial drug rate use among the three groups (100% vs. 100% vs. 100%, $P > .05$). However, the intensity of antibacterial drug use in Piperacillin-Tazobactam group was the least, followed by Piperacillin-Tazobactam + Metronidazole group and Cefminox + Metronidazole group ($P < .05$). Therefore, in order to reduce bacterial resistance during treatment, the Piperacillin-Tazobactam group is more likely to be considered.

According to a retrospective study, there was no significant statistical difference in postoperative recovery, treatment efficacy, bacterial clearance rate, incidence of postoperative complications, and incidence of adverse drug reactions among the three treatment regimens($P > .05$). However, in pharmacoeconomic evaluation, Cefminox + Metronidazole group had the lowest total cost, followed by the Piperacillin -Tazobactam+Metronidazole group and Piperacillin-Tazobactam group. In terms of antimicrobial indicators, there was no statistical difference ($P > .05$) in utilization rate, but the Piperacillin-Tazobactam group had the lowest intensity of antimicrobial use, followed by Piperacillin-Tazobactam + Metronidazole group and Cefminox + Metronidazole group.

DISCUSSION

Acute appendicitis in children accounts for approximately 20%-30% of acute abdominal pain in pediatric surgery. It is often thought to be caused by obstruction of the appendiceal cavity by fecal debris or lymphoid tissue growth, resulting in high pressure in the cavity and compromising the integrity of the mucosa, leading to infection and eventual morbidity.[7,12] Some patients with acute appendicitis were found to be better treated with conservative antibiotics than with surgical resection,[13] and recent studies have shown that anti-infective therapy is usually safe and effective in simple appendicitis.[14]

If left untreated, acute appendicitis can be followed by perforation, leading to the entry of large numbers of pathogenic bacteria into the peritoneal cavity, increasing the likelihood of intra-abdominal infection and incisional contamination following surgical treatment.[15,16] Antibacterial drugs are commonly used in surgery, but due to the development of bacterial resistance, the minimum inhibitory concentrations of some bacteria in the blood are increasing, leading to a higher rate of bacterial resistance and the rapid development of the disease in children, which makes it more difficult to treat these diseases clinically.[17]

Escherichia coli is the most common causative agent of acute appendicitis. WSES guidelines state that postoperative antimicrobial therapy is unnecessary in patients with simple abdominal infections in the acute appendicitis category.[18] Piperacillin tazobactam is a semi-synthetic acyl urea-based broad-spectrum penicillin,[19] whereas piperacillin is a broad-spectrum semi-synthetic penicillin, and tazobactam is a potent inhibitor of a variety of β-lactamases. The combination of the two effectively extends the antimicrobial spectrum of the former, with high antibacterial activity against most plasmid-mediated Klebsiella pneumonia, Aspergillus, Escherichia coli, and Salmonella. This drug is, therefore, used more frequently in abdominal infections.[20] Metronidazole is a broad-spectrum, highly effective anti-anaerobic drug that acts directly on bacterial DNA, inhibiting DNA synthesis and promoting DNA breakdown, causing bacterial death and inhibiting bacterial multiplication, which is important for suppressing local infections caused by anaerobic bacteria and reducing the inflammatory response.[21] Cefminox belongs to the β-lactam class of antibacterial drugs, which mainly inhibits the synthesis of bacterial cell walls to exert antibacterial effects. It has obvious antibacterial effects on Gram-positive, Gram-negative, and anaerobic bacteria, especially Escherichia coli and Klebsiella pneumonia. It is usually used to treat infectious diseases in clinical practice.[22]

In clinical practice, the widespread use of antibiotics leads to bacterial resistance, while the emergence of multidrug-resistant bacteria reduces the lifespan of antibiotics, posing risks and difficulties in the treatment of future bacterial infections. How to properly collocate and use antibiotics is a key issue in controlling bacterial resistance.

In this study, three different anti-infective regimens of piperacillin-tazobactam, piperacillin-tazobactam + metronidazole, and cefminox + metronidazole were administered to patients with acute appendicitis 0.5-1 h before laparoscopy. There were no distinctions in the rates of bacterial clearance, complications, and adverse drug reactions among the three groups, indicating that the three anti infection regimens have achieved significant results in children, providing a clearer treatment plan for acute appendicitis in children, improving their postoperative recovery process, and enhancing their quality of life. In terms of pharmacoeconomics, the total cost of hospitalization, drugs, and antibacterial drugs was lower in Cefminox + Metronidazole group than in Piperacillin-Tazobactam group and Piperacillin-Tazobactam + Metronidazole group, indicating that the anti-infective regimen of Cefminox + Metronidazole was less costly and more economically feasible, given comparable treatment outcomes. This not only reduces the economic pressure on patient families, but also maximizes allocation when hospital resources are limited.

The reason is that piperacillin-tazobactam is suitable for appendicitis and peritonitis caused by piperacillin-resistant, β-lactamase-producing Escherichia coli and Mycobacterium avium, and piperacillin/tazobactam is also effective against some anaerobic bacteria, so the combination with metronidazole is not necessary. Cefminox has good antibacterial activity against most Gram-positive, Gram-negative, and anaerobic bacteria and can be used alone to achieve better therapeutic effects, while metronidazole is easier and cheaper to use as it does not need to be supported by anaerobic culture results in clinical use.

However, this study has some limitations. Firstly, the sample size of this study is relatively small. Secondly, as our study is a retrospective analysis, we are unable to determine other variables during the treatment process. It is necessary to design a larger sample size prospective multicenter clinical study to validate the results of this study. In the process of designing a prospective study, more consideration should be given to the patient's condition type, detailed inquiry and statistics should be conducted on postoperative complications, and more standardized applications of antibiotics should be explored.

In the clinical research of using antibiotics for acute appendicitis, reducing bacterial resistance is also something we need to focus on, so we need to pay attention to the long-term outcomes of these three treatment options.

CONCLUSION

In summary, the three anti infective regimens of piperacillin tazobactam, piperacillin-tazobactam + metronidazole, and cefminor + metronidazole have the same therapeutic effect on acute appendicitis in children. However, cefminox + metronidazole is more economical. The selection of anti infection plans for acute appendicitis in children during the treatment process has greater clinical significance. It can choose more suitable and economical plans based on the patient's condition and family economic situation, reduce the treatment burden, and is of great significance in poverty-stricken areas. It can use the smallest resources to achieve the maximum effect. In the study, it was found that the combination of Piperacillin-Tazobactam can reduce antibiotic overuse, reduce antibiotic abuse, and delay the worsening of bacterial resistance. Searching for better antibiotic use plans not only reduces the cost of antibiotic use, but also extends the lifespan of antibiotics. I urge everyone not to overuse antibiotics and to consider the efficacy and cost of antibiotic regimens more when using them.

CONFLICTS OF INTEREST

No conflicts of interest.

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DATA AVAILABILITY

The data used for this study can be obtained from the corresponding author.

REFERENCES

1. Sherratt FC, Allin BSR, Kirkham JJ, et al; Appendicitis Core Outcome Set Study Group. Core outcome set for uncomplicated acute appendicitis in children and young people. *Br J Surg.* 2020;107(8):1013-1022. doi:10.1002/bjs.11508

2. Téoule P, Laffolie J, Rolle U, Reissfelder C. Acute Appendicitis in Childhood and Adulthood. *Dtsch Arztebl Int*. 2020;117(45):764-774.
3. Zavras N, Vaou N, Zouganeli S, Kasti A, Dimitrios P, Vaos G. The Impact of Obesity on Perioperative Outcomes for Children Undergoing Appendectomy for Acute Appendicitis: A Systematic Review. *J Clin Med*. 2023;12(14):4811. doi:10.3390/jcm12144811
4. Steiner Z, Gilad Y, Gutermacher M, Stackievicz R, Bauer-Rusek S, Arnon S. Acute appendicitis in children: reexamining indications for conservative treatment - A large prospective analysis. *J Pediatr Surg*. 2022;57(10):373-379. doi:10.1016/j.jpedsurg.2021.12.012
5. Lee J, Garvey EM, Bundrant N, et al. IMPPACT (Intravenous Monotherapy for Postoperative Perforated Appendicitis in Children Trial): Randomized Clinical Trial of Monotherapy Versus Multi-drug Antibiotic Therapy. *Ann Surg*. 2021;274(3):406-410. doi:10.1097/SLA.0000000000005006
6. Ikegami M, Miyano G, Nojiri S, et al. Indications for Nonoperative Management of Uncomplicated Appendicitis in Children: A Prospective Analysis at a Single Institution. *J Laparoendosc Adv Surg Tech A*. 2020;30(1):70-75. doi:10.1089/lap.2019.0186
7. Walter K. Acute Appendicitis. *JAMA*. 2021;326(22):2339. doi:10.1001/jama.2021.20410
8. Díaz-Brochero C, Valderrama-Rios MC, Nocua-Báez LC, Cortés JA. First-generation cephalosporins for the treatment of complicated upper urinary tract infection in adults: A systematic literature review. *Int J Infect Dis*. 2022;116:403-410. doi:10.1016/j.ijid.2021.12.363
9. van Duin D, Bonomo RA. Ceftazidime/Avibactam and Ceftolozane/Tazobactam: second-generation β-Lactam/β-Lactamase Inhibitor Combinations. *Clin Infect Dis*. 2016;63(2):234-241. doi:10.1093/cid/ciw243
10. Ishikawa K, Matsuo T, Suzuki T, Kawai F, Uehara Y, Mori N. Penicillin- and third-generation cephalosporin-resistant strains of Streptococcus pneumoniae meningitis: case report and literature review. *J Infect Chemother*. 2022;28(5):663-668. doi:10.1016/j.jiac.2022.01.021
11. Könönen E, Gursoy UK. Oral *Prevotella* Species and Their Connection to Events of Clinical Relevance in Gastrointestinal and Respiratory Tracts. *Front Microbiol*. 2022;12:798763. doi:10.3389/fmicb.2021.798763
12. Plataras C, Tsangouri S, Bourikas D, Christianakis E. Acute appendicitis in a child with swine influenza (H1N1). *BMJ Case Rep*. 2015;2015(mar26 1):bcr2014208219. doi:10.1136/bcr-2014-208219
13. Salminen P, Paajanen H, Rautio T, et al. Antibiotic Therapy vs Appendectomy for Treatment of Uncomplicated Acute Appendicitis: The APPAC Randomized Clinical Trial. *JAMA*. 2015;313(23):2340-2348. doi:10.1001/jama.2015.6154
14. Sallinen V, Akl EA, You JJ, et al. Meta-analysis of antibiotics versus appendicectomy for non-perforated acute appendicitis. *Br J Surg*. 2016;103(6):656-667. doi:10.1002/bjs.10147
15. Stokes SC, Theodorou CM, Brown EG. Additional prophylactic antibiotics do not decrease surgical site infection rates in pediatric patients with appendicitis and cholecystitis. *J Pediatr Surg*. 2021;56(10):1718-1722. doi:10.1016/j.jpedsurg.2020.11.014
16. Thapa B, Sutanto E, Bhandari R. Thickness of subcutaneous fat is a risk factor for incisional surgical site infection in acute appendicitis surgery: a prospective study. *BMC Surg*. 2021;21(1):6. doi:10.1186/s12893-020-01029-7
17. Roberts JK, Stockmann C, Constance JE, et al. Pharmacokinetics and pharmacodynamics of antibacterials, antifungals, and antivirals used most frequently in neonates and infants. *Clin Pharmacokinet*. 2014;53(7):581-610. doi:10.1007/s40262-014-0147-0
18. Sartelli M, Chichom-Mefire A, Labricciosa FM, et al. The management of intra-abdominal infections from a global perspective: 2017 WSES guidelines for management of intra-abdominal infections. *World J Emerg Surg*. 2017;12(1):29. doi:10.1186/s13017-017-0141-6
19. Cojutti PG, Morandin E, Baraldo M, Pea F. Population pharmacokinetics of continuous infusion of piperacillin/tazobactam in very elderly hospitalized patients and considerations for target attainment against Enterobacterales and Pseudomonas aeruginosa. *Int J Antimicrob Agents*. 2021;58(4):106408. doi:10.1016/j.ijantimicag.2021.106408
20. Hertz FB, Andreasen MR, Almind SR, et al. Efficacy of piperacillin-tazobactam and cefotaxime against Escherichia coli hyperproducing TEM-1 in a mouse peritonitis infection model. *Int J Antimicrob Agents*. 2022;59(4):106543. doi:10.1016/j.ijantimicag.2022.106543
21. Kashtan MA, Graham DA, Melvin P, et al. Ceftriaxone with metronidazole versus piperacillin/tazobactam in the management of complicated appendicitis in children: Results from a multicenter pediatric NSQIP analysis. *J Pediatr Surg*. 2021; S0022-3468(21)00784-3.
22. Wu S, Bi X, Lin Y, Yang L, Li M, Xie Y. Severe coagulopathy caused by cefminox sodium in a liver cirrhosis patient: a case report. *Infect Agent Cancer*. 2022;17(1):30. doi:10.1186/s13027-022-00446-y