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Comparison of Monotherapy with Piperacillin/Tazobactam Versus Multidrug Therapy for Treatment of Perforated Appendix in Children

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Disclaimers

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ABSTRACT

Background: Appendicitis is the most common surgical emergency in pediatric patients, with perforated appendicitis posing significant risks due to postoperative complications. The optimal antibiotic regimen to manage these risks remains debated.

Objective: To compare the efficacy of piperacillin/tazobactam monotherapy versus ceftriaxone and metronidazole multi-drug therapy in children undergoing open appendectomy for perforated appendicitis.

Methods: This randomized study included 74 pediatric patients (aged 4-13 years) diagnosed with perforated appendicitis at the Pediatric Surgery Department, Mayo Hospital, between December 2023 and June 2024. Patients were randomized into two groups: Group A received piperacillin/tazobactam monotherapy, and Group B received ceftriaxone and metronidazole. The primary outcomes were surgical site infections (SSI), intra-abdominal collections, and hospital stay. Data were analyzed using SPSS version 25, with significance set at $p \leq 0.05$.

Results: Intra-abdominal collection occurred in 2 patients (5.4%) in Group A and 3 patients (8.1%) in Group B ($p=0.643$). SSI rates were 13.5% in Group A and 10.8% in Group B ($p=0.722$). The mean hospital stay was significantly shorter in Group B (7.16±0.727 days) compared to Group A (7.92±0.829 days, $p<0.05$).

Conclusion: Monotherapy with piperacillin/tazobactam demonstrated comparable effectiveness to multi-drug therapy, but multi-drug therapy resulted in a shorter hospital stay.

INTRODUCTION

Appendicitis is the most common cause of acute abdominal emergencies requiring surgery in children, making it a critical area of focus in pediatric surgical care. Among pediatric patients, perforated appendicitis is a significant concern due to its higher risk of complications and prolonged recovery periods, especially when compared to non-perforated cases. The management of perforated appendicitis has long been debated, particularly concerning the use of antibiotic regimens to minimize postoperative infections and other complications. Surgical intervention remains the primary treatment modality, and it is typically followed by antibiotic therapy to prevent the development of infectious morbidities such as surgical site infections (SSI) and intra-abdominal abscesses (1).

Historically, the management of perforated appendicitis involved the use of multi-drug therapy, often comprising combinations of antibiotics such as ampicillin, gentamicin, and metronidazole. This approach was believed to provide broad-spectrum coverage and reduce the risk of postoperative infections (2). However, recent studies have questioned the necessity of multi-drug regimens, suggesting that single-drug therapies, such as piperacillin/tazobactam, may offer similar outcomes in terms of efficacy while simplifying treatment protocols (3). The potential for monotherapy to reduce the complexity of treatment regimens without compromising clinical outcomes is of particular interest, given the increasing concerns over antibiotic resistance and the need for judicious use of antibiotics in clinical practice (4). Perforated appendicitis in children is associated with a higher risk of postoperative complications, including prolonged hospital stays and the development of intra-abdominal abscesses. These complications contribute to increased healthcare costs and patient morbidity, underscoring the importance of optimizing antibiotic regimens to minimize adverse outcomes while also addressing concerns related to antibiotic overuse (5).

In this context, it is crucial to evaluate whether monotherapy with piperacillin/tazobactam can provide comparable clinical outcomes to the traditional multi-drug regimens, such as those involving ceftriaxone and metronidazole. The aim of this study is to compare the efficacy of monotherapy with piperacillin/tazobactam against multi-drug therapy in pediatric patients undergoing open appendectomy for perforated appendicitis. By examining the incidence of postoperative complications, including surgical site infections, intra-abdominal collections, and length of hospital stay, this study seeks to provide evidence on

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whether monotherapy can be a viable alternative to multi-drug therapy in this patient population. The findings from this research could have significant implications for clinical practice, particularly in terms of reducing the burden of antibiotic administration and minimizing the potential for antibiotic resistance, while still ensuring optimal patient outcomes (6).

MATERIAL AND METHODS

The study was conducted in the Department of Pediatric Surgery, Mayo Hospital, Lahore, from December 2023 to June 2024. A total of 74 pediatric patients, aged between 4 and 13 years, who were diagnosed with perforated appendicitis and met the inclusion criteria, were enrolled in the study. Sample size calculation was based on a 95% confidence level, 80% power of the test, and the mean hospital stay of 7±1.5 days in the multi-drug therapy group and 8.5±2 days in the monotherapy group (12). Patients were randomly assigned to two groups: Group A received monotherapy with piperacillin/tazobactam, while Group B received a combination of ceftriaxone and metronidazole. The randomization process was performed using a computer-generated sequence, with 37 patients assigned to each group.

Inclusion criteria for this study involved pediatric patients who had undergone open appendectomy for perforated appendicitis. Exclusion criteria included patients with acute non-perforated appendicitis, those undergoing laparoscopic procedures, patients treated with antibiotic regimens other than the study protocols, and those who did not provide informed consent. Written informed consent was obtained from the guardians of all participants. The study followed the ethical principles outlined in the Declaration of Helsinki, and ethical approval was obtained from the Mayo Hospital ethical review board before the commencement of the research.

Surgical management involved a standard open appendectomy. All patients received a single dose of preoperative amoxicillin-clavulanate within 30 minutes of surgery. A standard surgical technique was applied, with a right iliac fossa incision followed by identification and removal of the appendix. Piperacillin/tazobactam was administered to patients in Group A at a dose of 100 mg/kg every 8 hours (up to a maximum of 4 grams per dose). Group B patients received ceftriaxone at 50 mg/kg/day, administered every 12 hours, and metronidazole at 7.5 mg/kg (up to 500 mg per dose). Postoperative care was standardized across both groups, and all patients were monitored for clinical outcomes.

Data collection was performed using a structured proforma, which recorded demographic details, clinical findings, and outcomes. The primary outcomes measured were the incidence of surgical site infection (SSI), intra-abdominal collection, and length of hospital stay. SSI was defined as any wound discharge occurring within one month of surgery, associated with redness, tenderness, or fever. Intra-abdominal collection was confirmed via ultrasound and characterized by positive culture results from aspirated fluid. Hospital stay was measured in days, from the day of surgery until discharge.

Data were analyzed using SPSS version 25. Descriptive statistics were employed to summarize categorical variables such as gender, SSI, and intra-abdominal collection, which were presented as frequencies and percentages. Quantitative variables, including age and length of hospital stay, were presented as means and standard deviations. A chi-square test was used to compare the frequency of SSI and intra-abdominal collections between the two groups, while an independent sample t-test was conducted to compare the mean hospital stay. A p-value of ≤0.05 was considered statistically significant for all analyses.

RESULTS

A total of 74 children diagnosed with perforated appendicitis were included in this study. They were divided into two equal groups: Group A (piperacillin/tazobactam monotherapy) and Group B (ceftriaxone + metronidazole multi-drug therapy), with 37 patients in each group.

The demographic characteristics of the study population are presented in Table 1. The mean age of patients in Group A was 9.76±2.488 years, and in Group B, it was 9.86±2.406 years. There were 21 males (56.8%) and 16 females (43.2%) in Group A, while Group B had 20 males (54.1%) and 17 females (45.9%).

Table 1: Demographic characteristics of the study population

Group	Mean Age (years) ± SD	Males (%)	Females (%)	Total (%)
Group A (Monotherapy)	9.76 ± 2.488	21 (56.8%)	16 (43.2%)	37 (100%)
Group B (Multi-drug Therapy)	9.86 ± 2.406	20 (54.1%)	17 (45.9%)	37 (100%)

There was no statistically significant difference in the occurrence of intra-abdominal collection between the two groups (p=0.643). Group A had 2 patients (5.4%) with intra-abdominal collection, while Group B had 3 patients (8.1%).

Table 2: Comparison of intra-abdominal collections between groups

Group	Intra-Abdominal Collection	No Intra-Abdominal Collection	Total (%)	p-value
Group A (Monotherapy)	2 (5.4%)	35 (94.6%)	37 (100%)	0.643
Group B (Multi-drug Therapy)	3 (8.1%)	34 (91.9%)	37 (100%)	

The frequency distribution of intra-abdominal collections between groups is shown in Table 2. The rate of surgical site infection (SSI) was similar between the two groups, with Group A reporting 5 cases (13.5%) and Group B reporting 4 cases (10.8%). The p-value for this comparison was 0.722, indicating no significant difference. Table 3 provides a detailed comparison of SSI rates.

Table 3: Comparison of surgical site infections (SSI) between groups

Group	SSI	No SSI	Total (%)	p-value
Group A (Monotherapy)	5 (13.5%)	32 (86.5%)	37 (100%)	0.722
Group B (Multi-drug Therapy)	4 (10.8%)	33 (89.2%)	37 (100%)	

The mean hospital stay was shorter in Group B (7.16±0.727 days) compared to Group A (7.92±0.829 days), and this difference was statistically significant ($p<0.05$). Table 4 summarizes the comparison of hospital stay between the two groups. In conclusion, while there were no significant differences in intra-abdominal collections or SSIs between the two groups, the multi-drug therapy group had a significantly shorter hospital stay compared to the monotherapy group. These findings suggest that although both treatment regimens are effective in managing postoperative complications, the multi-drug therapy may contribute to faster patient recovery.

Table 4: Comparison of hospital stay (days) between groups

Group	Mean Hospital Stay (days) ± SD	p-value
Group A (Monotherapy)	7.92 ± 0.829	<0.05
Group B (Multi-drug Therapy)	7.16 ± 0.727	

DISCUSSION

This study compared the efficacy of piperacillin/tazobactam monotherapy with ceftriaxone and metronidazole multi-drug therapy in the management of pediatric patients undergoing open appendectomy for perforated appendicitis. The results showed no statistically significant differences in the rates of intra-abdominal collections or surgical site infections (SSI) between the two groups, although the hospital stay was significantly shorter for the multi-drug therapy group. These findings align with previous research that has demonstrated comparable outcomes between single and multi-drug antibiotic regimens in the treatment of perforated appendicitis (12, 13).

Previous studies have shown a wide range of postoperative infectious complications, particularly following appendectomy for perforated appendicitis, with rates of intra-abdominal collections and SSIs varying significantly. Studies by Nadler et al. and Chun et al. reported similar findings, showing no significant difference in infection rates between monotherapy and multi-drug therapy groups (15). However, some research has suggested that multi-drug regimens may be more effective in reducing postoperative complications in specific clinical scenarios, such as severe perforations or in patients with high risk of abscess formation (14). The current study adds to this body of literature by suggesting that, for the general pediatric population with perforated appendicitis, a single broad-spectrum antibiotic like piperacillin/tazobactam can be just as effective as combination therapy in preventing infectious complications (15).

The observed shorter hospital stay in the multi-drug therapy group may reflect the broader spectrum of activity provided by combining ceftriaxone and metronidazole, which could have facilitated quicker resolution of infection. Although this finding was statistically significant, it is important to consider that the absolute difference in hospital stay was relatively small (less than a day), which may limit its clinical significance. These findings are consistent with other studies that have suggested that multi-drug therapy can reduce hospital stay, particularly in complex or high-risk cases (12).

A notable strength of this study is its randomized design, which helps reduce selection bias and ensures balanced distribution of patients across the two treatment arms. The standardized surgical procedure and postoperative care further enhance the internal validity of the study. However, the study also had several limitations. The sample size, although sufficient for detecting differences in primary outcomes, was relatively small, which may have limited the power to detect smaller differences in secondary outcomes, such as SSIs. Additionally, the study was conducted at a single center, which may limit the generalizability of the findings to other settings or populations with different characteristics.

The reliance on ultrasound to detect intra-abdominal collections is another potential limitation, as it is an operator-dependent modality, and its sensitivity may vary. Future studies could benefit from incorporating other imaging techniques, such as CT scans, to provide a more accurate assessment of postoperative collections. Moreover, the study did not assess long-term outcomes, such as recurrence of infections or long-term complications, which could be valuable in determining the overall efficacy of the antibiotic regimens.

In light of these findings, it may be reasonable to consider the use of monotherapy with piperacillin/tazobactam as an effective and potentially less burdensome alternative to multi-drug therapy in pediatric patients with perforated appendicitis. However, further research is needed to confirm these findings in larger, multi-center studies and to evaluate the cost-effectiveness of monotherapy versus combination therapy. Additionally, investigations into the impact of antibiotic stewardship programs on clinical

outcomes in pediatric surgery may help refine treatment protocols and reduce the development of antibiotic resistance (6).

CONCLUSION

In conclusion, this study demonstrated that piperacillin/tazobactam monotherapy was as effective as ceftriaxone and metronidazole multi-drug therapy in preventing infectious complications following appendectomy for perforated appendicitis in children, with the exception of a slightly shorter hospital stay in the multi-drug therapy group. These results suggest that the choice between these two antibiotic regimens may not significantly impact clinical outcomes, providing flexibility for clinicians in managing pediatric appendicitis while considering factors such as antibiotic stewardship and hospital resource utilization.

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