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Comparison of Mono Therapy with Tazobactam Versus Multi Drug Therapy for Treatment of Perforated Appendix in Children

Nadir Aman[1], Asad Munir[1], Kashif Bashir[1], Mariam Rafique[1], Mahwish Noor ul Haq[1], Zuha Zafer[1]

[1]Department of Pediatric Surgery, King Edward Medical University, Mayo Hospital, Lahore, Punjab, Pakistan.

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Corresponding Author: Nadir Aman, Department of Pediatric Surgery, King Edward Medical University, Mayo Hospital, Lahore, Punjab, Pakistan.
Email: nadiraman93@gmail.com

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ABSTRACT

Introduction: Appendicitis stands as the predominant surgical emergency among pediatric patients. Despite its high occurrence rate, there remains a lack of agreement concerning the diagnostic and treatment approaches for this condition. This study aims to assess and compare the surgical results of open appendectomy in children with perforated appendicitis, utilizing either a perioperative multiple antibiotic regimens or a single antibiotic regimen. **Patients and Methods:** The investigation was carried out on pediatric patients who underwent open appendectomy due to perforated appendicitis at the Pediatrics Surgery Department in Mayo Hospital between December 2023 and June 2024. A total of 74 children were enrolled in the research. One group, Group A, received monotherapy with piperacillin/tazobactam, while another group, Group B, received multiple drug therapy with Metronidazole and Meropenem. **Results:** The mean age of patients in group A was 9.76±2.488 years and in group B was 9.86±2.406 years. In group-A (Tazobactam monotherapy), intra-abdominal collection was noted in 4(10.8%) patients and 3(8.1%) patients in group-B (Multi-drug therapy) with a p-value of 0.691. The mean hospital stay in Tazobactam monotherapy group was 7.92±0.829 days and in Multi-drug therapy group as 7.16±0.727 days ($p<0.05$). **Conclusion:** In the current study population, the use of monotherapy antibiotic treatment for perforated appendix in children demonstrated comparable effectiveness to triple antibiotic therapy in mitigating infectious morbidities, suggesting that the choice between these two approaches may not significantly impact the clinical outcomes of patients in this particular cohort.

INTRODUCTION

Appendicitis, which refers to the inflammation of the appendix, stands out as the leading reason necessitating abdominal surgical interventions among children, with statistics indicating a higher prevalence compared to other abdominal conditions that may require surgical management, highlighting the significance of this condition in pediatric surgery.[1] Clinical manifestations commonly observed in patients with acute appendicitis encompass lower right abdominal pain, tenderness, rebound tenderness, reduced appetite, feelings of nausea, episodes of vomiting, and elevated body temperature, with surgical intervention widely accepted as the mainstay therapeutic approach.[2]

Studies have indicated that postoperative infectious complications following appendectomy for acute appendicitis have been documented to have a frequency ranging from 8% to 25%, underscoring the importance of vigilant monitoring and preventive measures in the management of this condition. It is imperative for healthcare providers to remain vigilant for signs of infectious complications post-surgery to promptly address

and mitigate potential adverse outcomes in patients with acute appendicitis.[3-5]

It is noted in scientific literature that an increased level of resistance to antibiotics correlates with a higher probability of being the root cause of the issue at hand, suggesting a direct relationship between resistance and causation.[6-7] The incidence of perforation in pediatric appendicitis varies widely, ranging from 23% to 73%, and in cases where perforation does happen, individuals frequently require extended hospital stays as a result of complications like surgical site infections, intra-abdominal abscesses, and post-operative intestinal obstructions, which significantly impact their recovery and overall health outcomes.[8]

In the historical context, it was common practice to employ three distinct modalities of treatment following surgical intervention for perforated appendicitis in pediatric patients. These included the repetitive delivery of antibiotic agents such as ampicillin in combination with gentamicin, alongside the conventional approach of utilizing clindamycin or metronidazole as part of the standard therapeutic regimen. The rationale behind this multifaceted treatment strategy was grounded in the aim of mitigating the risk of postoperative complications and ensuring optimal recovery outcomes for young individuals undergoing appendectomy.[9-10]

Recent reports indicate that the efficacy of a single administration of broad-spectrum antibiotics is comparable to that of multiple therapy involving two or more antibiotics, suggesting that there may be potential for simplifying treatment regimens in certain cases, which could have significant implications for clinical practice and patient outcomes.[11] In this study, an examination was conducted on the duration of hospitalization and clinical outcomes of pediatric patients receiving treatment with tazobactam as a single therapy in comparison to a combination therapy involving Meronem and metronidazole for the management of perforated appendicitis.

METHODOLOGY

The research was carried out at the Department of Pediatrics Surgery, Mayo Hospital, Lahore, spanning from December 25, 2023, to June 24, 2024. A total of 74 patients from the age groups of 4-13 years, with a diagnosis of perforated appendix and deemed suitable for antibiotic treatment, were included in this study, with 37 patients in each group. Patients with an acutely inflamed appendix, children who underwent open appendectomy, those who were prescribed a different antibiotic regimen, and those who did not provide informed consent were not considered for inclusion in this study.

Sample size of 74 cases was calculated by using 95% confidence level, 80% power of test and the mean hospital stay as 7±1.5 in multiple drug therapy and 8.5±2 in monotherapy goup.[12] Written informed consent was obtained and patient demographic information (name, age, gender) was recorded. Patients were randomly divided in two equal groups by computer generated method, thirty-seven each were placed in group-A (tazobactam) and in group-B (meronem and metronidazole).

All patients were administered a single dose of pre-operative Amoxicillin Clavulanate within 30 minutes prior to surgery. A standard surgical procedure was carried out, incision given on right side of iliac fossa skin and subcutaneous tissue cut with mono polar cautery incise externa oblique muscle, retraction of internal oblique and transversus abdominus muscle. open peritoneum, identify appendix, ligate mesoappendix, appendectomy done.

The prescribed dosage of Piperacillin/tazobactam was 100 mg/kg every 8 hours (up to a maximum of 4 grams per dose), , Meronem 20mg/kg every 8hourl and Metronidazole was given at a dosage of 10 mg/kg (up to a maximum of 500 mg per dose). Following discharge, patients were scheduled for a review at the outpatient clinic one week later.

Residual intra-abdominal collection was defined as any post-operative intra-abdominal collection after surgery diagnosed by ultrasound associated with fever and aspirated fluid was positive for the culture. Surgical site infection was defined as any discharge from any of the wounds within one month of surgery associated with redness, tenderness and/or fever. Hospital stay was noted in days. All the data was collected through a pre-designed proforma (attached).

Data was inputted and analyzed using the statistical software SPSS v25.0. Categorical

variables such as gender and outcomes (SSI, intra-abdominal collection) were subjected to frequency and percentage analysis. Quantitative measurements like age and outcome (hospital stay) were analyzed for mean and standard deviation. Chi-square test was utilized to compare SSI and intra-abdominal collection across different groups, whereas an independent sample t-test was conducted to compare hospital stay between groups. A p-value of ≤0.05 was deemed as statistically significant.

RESULTS

Total 74 children diagnosed with perforated appendix were enrolled in this study. Patients were divided in two treatment groups i.e. Group-A (Tazobactam monotherapy) and Group-B (Multi-drug therapy). In group-A, there were 21(56.8%) were males and 16(43.2%) were females, while in group-B, 20(54.1%) were males and 17(45.9%) were females.

The mean age of patients in group A was 9.76±2.488 years and in group B was 9.86±2.406 years. In group-A, there were 11(29.4%) patients in 4-8 years age group and 26(70.3%) in 9-13 years age group, while in group-B, 10(27.0%) patients in 4-8 years age group and 27(73.0%) in 9-13 years age group.

In group-A (Tazobactam monotherapy), intra-abdominal collection was noted in 4(10.8%) patients and 3(8.1%) patients in group-B (Multi-drug therapy) with a p-value of 0.691. In group-A (Tazobactam monotherapy), SSI was noted in 5(13.5%) patients and 4(10.8%) patients in group-B (Multi-drug therapy) with a p-value of 0.722. The mean hospital stay in Tazobactam monotherapy group was 7.92±0.829 days and in Multi-drug therapy group as 7.16±0.727 days (p<0.05).

Table 1

Frequency distribution of gender between groups

Gender	Groups		Total
	Tazobactam monotherapy	Multidrug therapy	
Male	21 56.8%	20 54.1%	41 55.4%
Female	16 43.2%	17 45.9%	33 44.6%
Total	37 100.0%	37 100.0%	74 100.0%

Table 2

Frequency distribution of age groups between groups

Age groups	Groups		Total
	Tazobactam monotherapy	Multidrug therapy	
4-8 years	11 29.7%	10 27.0%	21 28.4%
9-13 years	26 70.3%	27 73.0%	53 71.6%
Total	37 100.0%	37 100.0%	74 100.0%

Table 3

Comparison of intra-abdominal collection between groups

Intra-abdominal collection	Groups		Total	p-value
	Tazobactam monotherapy	Multidrug therapy		
Yes	4 10.8%	3 8.1%	7 9.5%	0.691
No	33 89.2%	34 91.9%	67 90.5%	
Total	37 100.0%	37 100.0%	74 100.0%	

Table 4

Comparison of surgical site infection between groups

SSI	Groups		Total	p-value
	Tazobactam monotherapy	Multidrug therapy		
Yes	5 13.5%	4 10.8%	9 12.2%	0.722
No	32 86.5%	33 89.2%	65 87.8%	
Total	37 100.0%	37 100.0%	74 100.0%	

Table 5

Comparison of hospital stay between groups

	Groups	N	Mean	Std. Deviation	p-value
Hospital stay (days)	Tazobactam monotherapy	37	7.92	0.829	<0.05
	Multidrug therapy	37	7.16	0.727	

DISCUSSION

Appendicitis is considered the most prevalent reason necessitating prompt abdominal surgery among children, with a significant number of pediatric patients being impacted by perforated appendicitis, which further underscores the urgency and importance of timely medical intervention in such cases.[13]

Minimizing morbidity, cost, hospital length of stay, and readmissions continues to be the key

focus of surgical interventions. One of the significant factors impacting these measurable outcomes is post-appendectomy infection, which has a direct correlation with all of these aforementioned parameters. The selection of antibiotic regimens plays a crucial role in influencing each of these aspects, underscoring the importance of judicious antibiotic management in surgical settings.[13]

Approximately 60% of surgeons rely on their personal preferences when it comes to making decisions in the clinical setting for the treatment of patients with perforated appendicitis. This suggests that a substantial portion of healthcare providers may tailor their approach based on subjective factors rather than following standardized protocols or guidelines.[14]

In accordance with the findings of the present research, Adam and colleagues demonstrated that the duration of hospitalization was notably extended in the cohort receiving monotherapy as opposed to those treated with a combination of multiple antibiotics. This observation highlights the potential impact of antibiotic selection on patient outcomes and underscores the importance of considering the efficacy and appropriateness of treatment regimens in clinical practice.[13]

Nadler and colleagues failed to demonstrate any notable variances between the study cohorts in terms of the duration of hospitalization, suggesting that there were no statistically significant distinctions in the lengths of stay among the groups under investigation.[15]

In the current study, there were no statistically significant variances observed in the occurrence of SSI and postoperative residual intraperitoneal collection between the two groups under investigation. However, previous research conducted by Nadler et al exhibited a noteworthy disparity, indicating a notably elevated rate of postoperative infectious complications among participants treated with multi-agent antibiotics compared to those receiving Piperacillin/tazobactam.

The findings from the current study did not reveal any significant disparities in the incidence of SSI and postoperative residual intraperitoneal collection between the groups under examination. Conversely, the research conducted by Nadler and colleagues demonstrated a marked contrast, with a substantially higher prevalence of postoperative infectious complications observed in the multi-agent antibiotics group compared to the Piperacillin/tazobactam group.

The results obtained from the current investigation did not demonstrate any statistically significant distinctions in the rates of SSI and postoperative residual intraperitoneal collection between the two groups analyzed. In contrast, prior studies by Nadler et al reported a significant increase in postoperative infectious complications among participants treated with multi-agent antibiotics when compared to those who received Piperacillin/tazobactam.[15]

In a research conducted by Chun and colleagues, it was observed that there was no significant variance in the occurrence of abscess formation rate, wound infections, and duration of hospital stay when comparing two distinct groups. Consequently, the researchers reached the conclusion that the administration of daily doses with mono-therapy exhibited comparable effectiveness to that of multi-drug therapy. This finding underscores the potential of adopting a simplified treatment regimen without compromising the clinical outcomes for patients undergoing therapy for the conditions studied.[12]

CONCLUSION

The efficacy of a single drug, tazobactam, has been demonstrated to be comparable to that of multi-drug therapy when it comes to the reduction of post-operative complications, leading to a notable decrease in the utilization of hospital resources for patient care.

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