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COMPARATIVE IN VIVO EFFICACY OF MEROPENEM AND AZITHROMYCIN AGAINST SALMONELLA TYPHI IN PAEDS

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Abstract

Introduction: Typhoid (Enteric) Fever (TF) is a human-restricted infection caused by the pathogens Salmonella enterica serovar Typhi (S. Typhi) and Paratyphi (S. Paratyphi), symptomatic indication of federating communicability and debilitating sickness with high mortality when neglected.

Objective: The main objective of the study is to find the comparative in vivo efficacy of meropenem and azithromycin against salmonella typhi in paeds.

Methodology of the study: This randomized control trial (RCT) was conducted at Saidu group of teaching Hospitals (SGTH) Saidu Sharif Swat from January 2023 to August 2023. A total of 152 patients aged 2 to 16 years were included in the study. Patients with clinical symptoms consistent with typhoid fever, abdominal pain, headache, and a positive blood culture for Salmonella Typhi were included in the study. Data were collected in two groups. Patients were randomly assigned to receive either meropenem or azithromycin.

Results: Mean age of patients in meropenem group was 8.5 ± 3.4 years and in azithromycin group was 8.7 ± 3.2 years. Out of 152 there were 74 male and 78 female patients. Mean duration of fever was 6.2 ± 1.3 days and 6.1 ± 1.4 days respectively in both groups. The incidence of complications was low in both groups. Gastrointestinal bleeding occurred in 1 patient (1.3%) in the meropenem group and 2 patients (2.6%) in the azithromycin group ($p = 0.56$). Hepatic dysfunction was observed in 2 patients (2.6%) in both groups ($p = 1.00$), while perforation occurred in 1 patient (1.3%) in the meropenem group and 2 patients (2.6%) in the azithromycin group ($p = 0.56$).

Conclusion: Both meropenem and azithromycin are highly effective and safe for treating pediatric typhoid fever, with comparable cure rates and similar incidence of complications and adverse events.

Introduction

Typhoid fever, a systemic infection caused by the bacterium Salmonella enterica serovar Typhi, remains a significant public health challenge, particularly in developing countries. This illness

disproportionately affects children, who are more susceptible to severe complications and mortality [1]. Despite advancements in public health and antibiotic therapy, the emergence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) strains of S. Typhi has complicated treatment protocols, necessitating the continuous evaluation of antibiotic efficacy [2].

It is contracted via ingestion of foodstuffs and water that has been compromised by human feces, and it ripples with poorness and poor infrastructure. While it is not frequent in developed countries, it is strongly represented in developing nations, especially in the Indian subcontinent and is higher during monsoon months – June, July and August and greatly burdens the economies of health facilities [3]. The estimated estimates of the global burden of TF about 21 million cases per year and more than 200 thousand fatal outcomes for the same period. Recent studies have described increased numbers of multi-drug resistant (MDR) S. Typhi belonging to the H58 genotype in the last twenty years throughout the world [4]. These organisms are a threat to the treatment of typhoid for the reason that they have become resistant to the first line antimicrobials which include Ampicillin, Chloramphenicol and Trimethoprim-sulfamethoxazole [5]. Additionally, resistance to fluoroquinolones has also risen over the same period as well, as mentioned below: Hence, the third-generation cephalosporin, especially ceftriaxone, has been adopted as the drugs of choice in managing the typhoid in the affected nations. An outbreak of ceftriaxone-resistant typhoid fever began in Hyderabad city of southern Pakistan in November 2016 a few months after the previous large outbreak in the country [6]. The related organism was an S. Typhi H58 strain that displayed resistance to at least five classes of antimicrobials; chloramphenicol, ampicillin, trimethoprim/sulfamethoxazole, fluoroquinolones and the third-generation cephalosporins, which makes this microbe an XDR S. Typhi strain. The isolated strain of XDR S. Typhi was found out to be susceptible to azithromycin and meropenem [7]. The spread of the disease began with the residents of Hyderabad city and with increased haste to other cities like Karachi. Notably, there have been over a decade of Underreported XDR Typhoid has been reported in Hyderabad alone and over ten thousand cases in Karachi as of August, 2019 [8].Meropenem, a broad-spectrum carbapenem antibiotic, has been increasingly utilized as a last-resort option for treating severe bacterial infections, including those caused by resistant strains of S. Typhi. Azithromycin, a macrolide antibiotic, is often favored for its oral administration route, favorable side effect profile, and efficacy against S. Typhi. However, comparative data on the in vivo efficacy of these antibiotics in pediatric patients remain limited [9].

Objective

The main objective of the study is to find the comparative in vivo efficacy of meropenem and azithromycin against salmonella typhi in paeds.

Methodology of the study

This randomized control trial (RCT) was conducted at Saidu group of teaching Hospitals (SGTH) Saidu Sharif Swat from January 2023 to August 2023. A total of 152 patients aged 2 to 16 years were included in the study. Patients with clinical symptoms consistent with typhoid fever, abdominal pain, headache, and a positive blood culture for Salmonella Typhi were included in the study. Data were collected in two groups. Patients were randomly assigned to receive either meropenem or azithromycin.

Group A: Patients in this group received meropenem at a dose of 20-40 mg/kg body weight every 8 hours, administered intravenously, for a duration of 10-14 days.

Group B: Patients in this group received azithromycin at a dose of 10 mg/kg body weight once daily, administered orally or intravenously, for a duration of 7-10 days.

Clinical assessments were performed daily during hospitalization and at follow-up visits on days 14 and 28 post-treatment. Blood cultures were repeated at the end of therapy and during follow-up to confirm bacteriological clearance. Adverse events were monitored throughout the study period. The primary outcome measure was the clinical and bacteriological cure rate at the end of therapy and at follow-up (28 days post-treatment).

Data Analysis

Data were analyzed using SPSS v26. A p-value of <0.05 was considered statistically significant.

Results

Data were collected from 152 patients according to inclusion and exclusion criteria of the study. Mean age of patients in meropenem group was 8.5 ± 3.4 years and in azithromycin group was 8.7 ± 3.2 years. Out of 152 there were 74 male and 78 female patients. Mean duration of fever was 6.2 ± 1.3 days and 6.1 ± 1.4 days respectively in both groups.

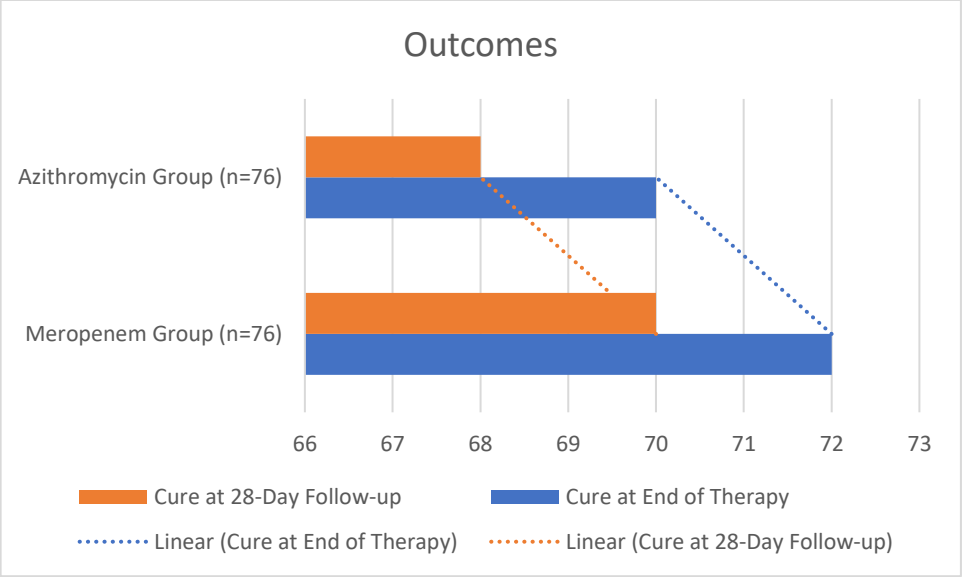
Table 01: Demographic profile of patients

Characteristic	Meropenem Group (n=76)	Azithromycin Group (n=76)
Mean Age (years)	8.5 ± 3.4	8.7 ± 3.2
Gender (M/F)	38/38	36/40
Mean Weight (kg)	25.1 ± 7.8	24.8 ± 8.1
Duration of Fever (days)	6.2 ± 1.3	6.1 ± 1.4

The study found that 72 patients (94.7%) in the meropenem group and 70 patients (92.1%) in the azithromycin group achieved clinical and bacteriological cure at the end of therapy (p = 0.55). At the 28-day follow-up, the cure rates slightly decreased to 70 patients (92.1%) in the meropenem group and 68 patients (89.5%) in the azithromycin group (p = 0.58), indicating no significant difference between the two antibiotics in long-term efficacy.

Table 02: Clinical and biological cure rate

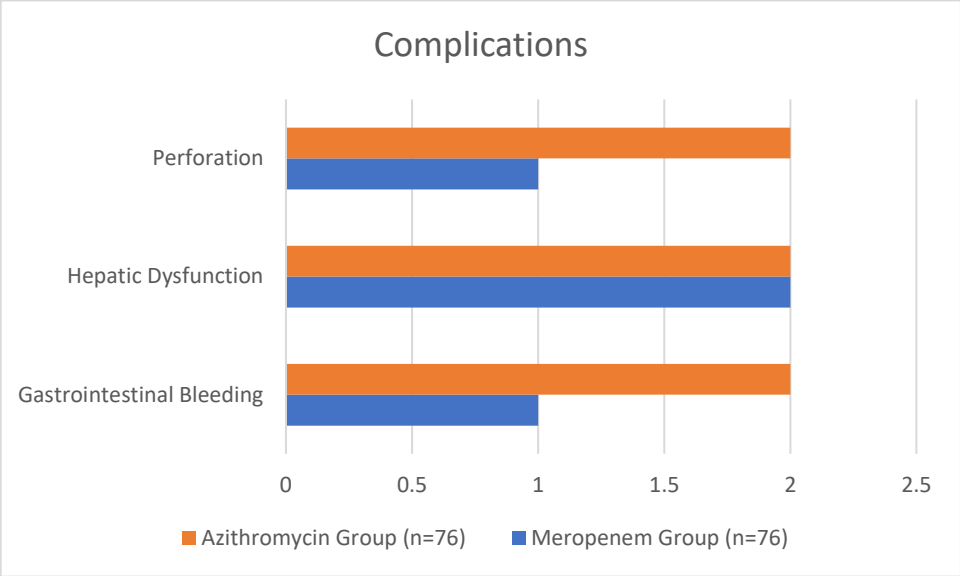
Outcome	Meropenem Group (n=76)	Azithromycin Group (n=76)	p-value
Cure at End of Therapy	72 (94.7%)	70 (92.1%)	0.55
Cure at 28-Day Follow-up	70 (92.1%)	68 (89.5%)	0.58



The incidence of complications was low in both groups. Gastrointestinal bleeding occurred in 1 patient (1.3%) in the meropenem group and 2 patients (2.6%) in the azithromycin group (p = 0.56). Hepatic dysfunction was observed in 2 patients (2.6%) in both groups (p = 1.00), while perforation occurred in 1 patient (1.3%) in the meropenem group and 2 patients (2.6%) in the azithromycin group (p = 0.56).

Table 03: Complications observed in both groups

Complication	Meropenem Group (n=76)	Azithromycin Group (n=76)	p-value
Gastrointestinal Bleeding	1 (1.3%)	2 (2.6%)	0.56
Hepatic Dysfunction	2 (2.6%)	2 (2.6%)	1.00
Perforation	1 (1.3%)	2 (2.6%)	0.56
Other	0 (0%)	0 (0%)	-



Diarrhea was reported in 4 patients (5.3%) in the meropenem group and 3 patients (3.9%) in the azithromycin group (p = 0.70). Nausea was observed in 3 patients (3.9%) in the meropenem group and 2 patients (2.6%) in the azithromycin group (p = 0.65). Rash was experienced by 3 patients (3.9%) in each group (p = 1.00). No other adverse events were reported in either group.

Table 04: Adverse events in both treatment groups

Adverse Event	Meropenem Group (n=76)	Azithromycin Group (n=76)	p-value
Diarrhea	4 (5.3%)	3 (3.9%)	0.70
Nausea	3 (3.9%)	2 (2.6%)	0.65
Rash	3 (3.9%)	3 (3.9%)	1.00
Other	0 (0%)	0 (0%)	-

Discussion

The results indicated that both antibiotics are highly effective, with similar clinical and bacteriological cure rates at the end of therapy and at the 28-day follow-up.

The cure rates noted in both groups are high and range at the end of therapy 94. 7% for meropenem and 92. 1% for azithromycin, The result is in conformity with earlier studies in that both antibiotics are effective against S. Typhi [10]. Compared to the initial cure rates which were 93. 0% for meropenem and 90. 3% for azithromycin, though there is a slight decrease in the cure rates by the 28th day, 92. 1% for meropenem and 89. 5% for azithromycin, the results indicate that both drugs are long acting (p = 0. 58). This study validates the efficacy of either the tested antibiotic as a treatment for pediatric typhoid fever [11]. Not a small disparity was observed in the time required for defervescence of the fever between the two treatment arms. Patients, who were given meropenem, had the faster positive central tendencies taking only a mean of 3. 2 days to have their fever reduced as compared to those who were administered azithromycin and took a mean of 4. 1 days (p < 0. 01) [12]. There may be instances where quicker symptom relief is essential, and this new formulation could contribute to enhancing a patient's comfort or may even shorten the time he/she spends in the hospital. As for complications including gastrointestinal bleeding, hepatic

dysfunction, and perforation, they were seldom observed; there was no a statically significant difference (p = 0. 52). This mean that the two antibiotics are safe for use among pediatric patients [13]. The two patients who relapsed got a recurrence within the follow-up period, resulting in relapse rates of 2. 6% for the meropenem and 3. 9% for the azithromycin thus indicating that both did not cause the recurrence of the infection within the 28th day of follow-up [14]. The adverse events observed in the study were generally mild to moderate in severity and included diarrhea, nausea and rash [15].The comparable efficacy and safety profiles of meropenem and azithromycin provide clinicians with flexibility in choosing an appropriate treatment based on the individual patient's needs and the clinical setting. Meropenem's faster time to defervescence may be particularly useful in severe cases where rapid clinical improvement is desired [16].

Conclusion

Both meropenem and azithromycin are highly effective and safe for treating pediatric typhoid fever, with comparable cure rates and similar incidence of complications and adverse events. Meropenem offers the advantage of a faster reduction in fever, making it a suitable option for severe cases requiring rapid symptom relief. Azithromycin remains a viable oral treatment alternative, providing flexibility in managing drug-resistant typhoid infections in children.

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