

# THE EFFECTIVENESS OF CEFTRIAXONE AND MEROPENEM IN THE TREATMENT OF ENTERIC FEVER IN CHILDREN- EXPERIENCE IN A TERTIARY CARE HOSPITAL IN PAKISTAN

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## ABSTRACT

**Objectives:** To determine the effectiveness of ceftriaxone and Meropenem in the treatment of Enteric Fever in the Paediatric Department of Khyber Teaching Hospital Peshawar.

**MATERIALS AND METHODS:** This cross-sectional descriptive study was conducted at the Department of Child Health Khyber Teaching Hospital Peshawar Pakistan from June 2020 to June 2022. The sample size included 392 patients. Keeping in view 392 blood samples were taken and sent for blood culture. Both positive and negative cultures were incorporated in the study. The patients were started empirically on ceftriaxone and then in case of no response, the patients were shifted to Meropenem based on the sensitivity of the culture report. The response was defined as when the patient is afebrile for 72 hours after the treatment and the absence of complications like peritonitis, intestinal hemorrhage, and obtundation. Data was analyzed using SPSS version 21.0.

**RESULTS:** In our study, out of 392 patients, 64% were males while 36% were females. Among blood cultures sent, 16.8% were positive and 83.2% were negative. Among the culture positive, 10.5% of patients were sensitive to Meropenem, 3.6% were sensitive to ceftriaxone and 2.8% were sensitive to other drugs. 60.7% of patients responded to Meropenem. Ceftriaxone-responsive patients were 11.7%, while 27.6% showed a response to other drugs.

**CONCLUSION:** The efficacy of Meropenem was significantly high (in 2/3rd patients) while Ceftriaxone showed 11.73% efficacy.

**KEYWORDS:** Enteric fever, Ceftriaxone, Meropenem

**This article may be cited as:** Afridi JM, Amir S, Pervez S, Rahman SKU. The Effectiveness of Ceftriaxone and Meropenem in the treatment of enteric fever in children- experience in a tertiary care hospital in Pakistan. *J Med Sci* 2023 October;31(4):330-334

## INTRODUCTION

Enteric fever also called typhoid fever caused by the rod-shaped gram-negative bacteria *Salmonella enterica* serovar Typhi is a life-threatening systemic infection. The presentation of enteric fever differs in children from that in adults.<sup>1</sup> Children present with fever, abdominal pain, diarrhea, vomiting, hepatosplenomegaly, anaemia, and thrombocytopenia.<sup>2,3</sup> *S typhi* is frequently cultured during the first week of illness in blood. It is important to diagnose the infection clinically and via blood culture as soon as possible and to institute appropriate therapy to minimize the risk of adverse outcomes and mortality associated with the disease.

According to WHO, about 11 to 21 million cases of Typhoid Fever are reported annually and the death toll ranges from 12,8000 to 161,000 annually.<sup>4</sup> South Asia has been the focal point where maximum numbers of typhoid fever cases have been found and resistant bacterial strains have become a serious issue.<sup>5</sup> For the developing countries it poses a major problem because of poor sanitation and public health standards.<sup>6</sup> Antibiotics are prescribed indiscriminately for all febrile illnesses. This misuse has led to the emergence of antibiotic-resistant strains.<sup>7</sup>

In the last 20 years, multiple outbreaks of multi-drug-resistant *S. typhi* of the HS8 genotype have occurred in different parts of the world.<sup>8,9</sup> These organisms are resistant to ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole, which are regarded as 1<sup>st</sup> line antimicrobials for typhoid fever. Similarly, the strains resistant to fluoroquinolones have also emerged.<sup>10,11</sup>

Ceftriaxone and Meropenem are two commonly used antibiotics used these days in the treatment of enteric fever. Ceftriaxone is a 3<sup>rd</sup> generation cephalosporin while Meropenem is a carbapenem antibiotic.<sup>12,13</sup> One common subject of interest regarding the treatment of en-

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Date received: 19/07/2023

Date reviewed: 28/09/2023

Date accepted: 20/10/2023

enteric fever in children that existed among medical professionals for several years is the efficacy of ceftriaxone and Meropenem. <sup>14</sup> Both antibiotics seem to be efficacious in the treatment of disease, but the optimal choice of antibiotics in children remains unclear. <sup>15</sup> Several studies have been run in children to study the effectiveness of ceftriaxone and Meropenem. <sup>16</sup>

The results depended upon the patient's age, severity of illness, and resistance patterns of bacteria. All these factors were taken into consideration. <sup>12</sup> To find out the best treatment option for children with enteric fever more research is required, furthermore, this disease needs continued monitoring regarding the efficacy of ceftriaxone and Meropenem. <sup>13</sup>

This study was conducted to see the effectiveness of ceftriaxone and Meropenem in enteric fever based on clinical and microbiological remission, shortened hospital stay, and lower chances of relapse. This will help us to formulate a standardised protocol to treat enteric fever thus preventing further antimicrobial resistance in the best interest of the patients.

**MATERIALS AND METHODS**

This cross-sectional descriptive study was conducted at the Department of Paediatric, Khyber Teaching Hospital Peshawar, Pakistan from June 2020 to June 2022. The sample size included 392 patients. Patients

aged more than 6 months and less than 15 years of both genders and those cases presenting with signs and symptoms of enteric fever such as fever, vomiting, and abdominal pain were included. Both positive and negative cultures were incorporated in the study. The patients were started empirically on ceftriaxone and then in case of no response or on the basis of drug sensitivity in the culture report were shifted to Meropenem.

A nonprobability consecutive sampling technique was used for sample taking. Data was entered and analyzed using SPSS version 21.0. Percentages were calculated for categorical variables. A chi-square test was employed where needed. P value < 0.05 was taken as significant.

**RESULTS**

Table 1 shows the demographic characteristics, clinical presentation, and antibiotic sensitivity of salmonella to Ceftriaxone and Meropenem.

Gender and age-wise percentages with association to drug response have been shown in Table 2. In those with a positive blood culture, 14.3% were sensitive to ceftriaxone, while 80.5% were sensitive to Meropenem, and 12.2 % were sensitive to other drugs. Overall, 7.6% responded to ceftriaxone, 56.1% responded to Meropenem, and 36.4% responded to other drugs. In those with a negative blood culture, 12.6% responded to ceftriaxone,

**Table 1: Baseline characteristics of the participants**

Demographics		Subgroups	N	%
		Male	251	64.0%
		Female	141	36.0%
		1 - 5 Years	123	31.4%
		6 -10 Years	202	51.5%
		11 - 15 Years	67	17.1%
Symptoms	Fever		392	100.0%
	Vomiting		172	43.9%
	Abdominal Pain		114	29.1%
	Diarrhea		42	10.7%
	Constipation		25	6.4%
	Toxicity		45	11.5%
	Headache		34	8.7%
	Obtundation		4	1.0%
Drug Sensitivity and Response to Treatment	Blood Culture	Positive	66	16.8%
		Negative	326	83.2%
	Sensitive	Ceftriaxone	14	3.6%
		Meropenem	41	10.5%
		Others	11	2.8%
	Response	Ceftriaxone	46	11.7%
		Meropenem	238	60.7%
			108	27.6%

**Table 2: Demographics with association to drug Response**

Variables	Subgroups	Drug response						P-value
		Ceftriaxone		Meropenem		Others		
		n	%	n	%	N	%	
Gender	Male	27	10.8%	149	59.4%	75	29.9%	0.341
	Female	19	13.5%	89	63.1%	33	23.4%	
Age in Years	1 - 5 Years	15	12.2%	85	69.1%	23	18.7%	0.052
	6 -10 Years	22	10.9%	120	59.4%	60	29.7%	
	11 - 15 Years	9	13.4%	33	49.3%	25	37.3%	

**Table 3 Blood Culture Sensitivity to Different Drugs**

Variables	Subgroups	Ceftriaxone		Drug response				p-value
				Meropenem		Others		
		n	%	N	%	n	%	
Blood Culture	Positive	5	7.6%	37	56.1%	24	36.4%	0.158
	Negative	41	12.6%	201	61.7%	84	25.8%	
Sensitivity	Ceftriaxone	2	14.3%	4	28.6%	8	57.1%	0.000
	Meropenem	3	7.3%	33	80.5%	5	12.2%	
	Others	0	0.0%	0	0.0%	11	100.0%	

61.7% responded to Meropenem and 25.8% responded to other drugs. (table 3)

## DISCUSSION

Enteric fever also called typhoid fever caused by rod-shaped gram-negative bacteria. Salmonella is a life-threatening systemic infection. Children present with fever, abdominal pain, diarrhea, vomiting, hepatosplenomegaly, anaemia, and thrombocytopenia. Typhoid fever is treated with antibiotics, antipyretics, and IV fluids. Commonly used antibiotics include Fluoroquinolones, Cephalosporins, and carbapenems. Ceftriaxone is a third-generation Cephalosporin antibiotic while Meropenem is a carbapenem antibiotic. Both antibiotics seem to be efficacious in the treatment of disease, but the optimal choice of antibiotics in children remains unclear.

Resistance to third-generation Cephalosporins emerged in 2016, during the epidemic of enteric fever in Karachi and Interior Sindh in Pakistan.<sup>17</sup> Currently, Meropenem and Azithromycin are the most commonly prescribed drugs for the treatment of extensive drug-resistant enteric fever.

A study was conducted in Lahore where blood culture showed positivity for Salmonella in 62 (25.2%) patients, and negativity in 184 (74.8%) patients among 246 children.<sup>18</sup> In our study, 392 patients were enrolled. The mean age of children was 8 ranging between 1 to 15 years. Among them, 141 (36%) were females and 251 (64%) were males. Out of 392 patients' blood cultures showed positivity in 66 (16.8%) patients and negativity in 326 (83.2%). In our study decreased culture positivity

rate was due to frequent antibiotic prescriptions already taken by our patients prescribed either by quacks or taken by themselves. A study conducted in Karachi Pakistan showed a culture-positive rate of 22%.<sup>19</sup>

Data derived from population-based research in Vietnam, Delhi, and Egypt showed a blood culture positivity of 8.5%, 5%, and 4.2% respectively in febrile cases.<sup>20</sup> In our study 16.8% of patients were blood culture positive while 83.2% were blood culture negative in febrile patients. A challenge in countries with limited resources like Pakistan is the emergence of resistant strains causing enteric fever. It is endemic in South-East Asia including Pakistan, Nepal, Bangladesh, and India.<sup>21</sup>

In a study conducted in Lahore, ceftriaxone had a sensitivity of 38.7%, which was not comparable with research from central Asia in which ceftriaxone had a sensitivity of 100%. Meropenem was found sensitive in all patients and up till now no resistance has been seen to this drug.<sup>18, 22</sup>

In our study, the response to Ceftriaxone was 11.7% while the response to Meropenem was 60.7% and the response to other drugs was 27.6%. The sensitivity pattern to ceftriaxone was 3.6%, to Meropenem was 10.5%, and 2.8% to other drugs.

In a study conducted in Korea, the efficacy of Ceftriaxone and Meropenem in the treatment of enteric fever in children was 53.6% vs 63.9%.<sup>23-25</sup> This is comparable to our study in which the efficacy of ceftriaxone is 11.73% while the efficacy of Meropenem is 68.79%.

Some of the limitations of this study include a small

sample size and the cross-sectional nature of the study. The study was restricted to one hospital only. Multicentre studies are needed before general guidelines for antibiotic prescription can be made.

## CONCLUSION

The emergence of resistant organisms causing enteric fever is on the rise and there is very high resistance to the majority of antibiotics. Ceftriaxone showed 11.73% efficacy in response to enteric fever while Meropenem showed 68.79% efficacy.

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**CONFLICT OF INTEREST:** Authors declare no conflict of interest

**GRANT SUPPORT AND FINANCIAL DISCLOSURE:** NIL

#### AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

**Afridi JM:** Concept, Critical appraisal, and Discussion Writing

**Amir S:** Data collection, compilation of results, formatting of the article

**Pervez S:** Data Collection, Manuscript writing

**Rahman SKU:** Manuscript Writing, Bibliography

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.



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