



INDUS JOURNAL OF BIOSCIENCE RESEARCH

<https://induspublishers.com/IJBR>

ISSN: 2960-2793/ 2960-2807



Preferences of Pakistani Doctors in Selection of Antibiotics for the Treatment of Uncomplicated Enteric Fever: Ciprofloxacin vs. Meropenem

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ARTICLE INFO

Keywords

Doctors, Preferences, Enteric Fever, S. Typhi, Ciprofloxacin, Meropenem.

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Declaration

Author's Contributions: All authors contributed to the study and approved the final manuscript.

Conflict of Interest: The authors declare no conflict of interest.

Funding: No funding received.

Article History

Received: 06-10-2024

Revised: 22-10-2024

Accepted: 26-10-2024

ABSTRACT

Background: The field of enteric fever therapy has undergone a significant transformation due to the advent of antibiotic resistance (AMR). Amoxicillin, trimethoprim-sulfamethoxazole, and chloramphenicol were once the first-line therapies. However, these choices are no longer as successful due to the emergence of multidrug-resistant (MDR) bacteria. ciprofloxacin, have been the recommended option in recent years because of their oral absorption and potency against vulnerable bacteria. Unfortunately, a reassessment of treatment procedures has been necessitated by reports of significant incidence of fluoroquinolone resistance, particularly in South Asia. The move toward meropenem is indicative of the pressing need for efficient treatments given the rise in resistance. Meropenem is recommended by the World Health Organization to treat severe infections brought on by XDR S. typhi, highlighting its significance in modern treatment protocols.

Methodology: It was a cross sectional study conducted at a tertiary care hospital of Karachi. The calculated sample size was n=64. All the doctors working in medicine ward and working residents who were in third and fourth year of their residency in medicine were included. A preformed questionnaire was administered to them to identify their preferences. Frequencies and percentages of responses were assessed and compared with chi square and t-test analysis. P-value less than 0.05 was considered as significant.

Results: Participants of all the groups responded that they have examined the patients with enteric fever (p-0.001), there was disparity in advising blood test for diagnosis (p-0.098), most of them mentioned they initiate therapy on clinical examination. When asked for the preference between ciprofloxacin and meropenem majority responded in the favor of ciprofloxacin (p-0.001).

Conclusion: The doctors preferred choosing ciprofloxacin for uncomplicated enteric fever which is positive indication to preserve the last resort antibiotics such as meropenem.

INTRODUCTION

Abdominal discomfort, gastrointestinal symptoms, and a persistent fever are the hallmarks of enteric fever, a systemic illness. Pakistan is among the most impacted countries, as it is prevalent in many low- and middle-income nations¹. Because of its high rates of morbidity and death, the illness presents a serious threat to public

health and is mostly spread through contaminated food and water². An estimated 14 million incidences of enteric fever occur each year, with roughly 136,000 fatalities from the illness, most of which occur in underdeveloped nations. The field of enteric fever therapy has undergone a significant transformation due

to the advent of antibiotic resistance (AMR)³. Amoxicillin, trimethoprim-sulfamethoxazole, and chloramphenicol were once the first-line therapies. However, these choices are no longer as successful due to the emergence of multidrug-resistant (MDR) bacteria^{4, 5}.

Fluoroquinolones, especially ciprofloxacin, have been the recommended option in recent years because of their oral absorption and potency against vulnerable bacteria. Unfortunately, a reassessment of treatment procedures has been necessitated by reports of significant incidence of fluoroquinolone resistance, particularly in South Asia^{6, 7}. However, a possible substitute for treating complex instances of enteric fever, especially those brought on by extensively drug-resistant (XDR) bacteria, is the carbapenem antibiotic meropenem. The move toward meropenem is indicative of the pressing need for efficient treatments given the rise in resistance. Meropenem is recommended by the World Health Organization to treat severe infections brought on by XDR *S. typhi*, highlighting its significance in modern treatment protocols^{2, 8}.

In Pakistan, the management of uncomplicated enteric fever necessitates a close examination of the changing pattern of antibiotic resistance as well as the therapeutic effectiveness of currently prescribed medications⁹. The inclinations of Pakistani physicians when choosing between ciprofloxacin and meropenem will be critical in guaranteeing efficient patient care when resistance trends change. Gaining insight into these choices will help shape future recommendations and enhance the quality of care received by people dealing with this important public health concern. thus, it is important to look more closely at Pakistani physicians' preferences when it comes to using ciprofloxacin against meropenem.

METHODOLOGY

It was a cross sectional study conducted at tertiary care hospital of Karachi. The calculated sample size was $n=64$ at 50% proportion of doctors present in a tertiary care hospital at 95% confidence interval and keeping the power of beta at 80. All the doctors working in medicine ward of tertiary care hospital were approached to participate in the study to complete the sample size

working residents who were in third year of their residency in medicine were also approached. A written informed consent was taken and they were informed about the study objectives and outcome. Following this a preformed questionnaire was administered to them to identify their preferences. The questionnaire was self-developed and pre assessed by a small group of participants. The obtained data was entered in SPSS version 20. Frequencies and percentages of responses were assessed and compared with chi square and t-test analysis. P-value less than 0.05 was considered as significant.

RESULTS

The calculated sample size was 64 however the sample size was raised to 70 and data was analyzed. The mean age of the study participants was 34.1 ± 5.3 , among them 31 (44.29%) were male and 39 (55.71%) were females. Figure 1 shows the distribution of participants. Participants of all the groups responded that they have examined the patients with enteric fever ($p=0.001$), there was disparity in advising blood test for diagnosis ($p=0.098$), most of them mentioned they initiate therapy on clinical examination, there was no consensus on advising culture and sensitivity report, among residents many of them asked that they do not know about the concept of antibiotic stewardship table 1 highlights the general concepts of antibiotic prescription among doctors of a tertiary care hospital. When asked for the preference between ciprofloxacin and meropenem majority responded in the favor of ciprofloxacin ($p=0.001$) (Table 2).

Figure 1
Distribution of Participants

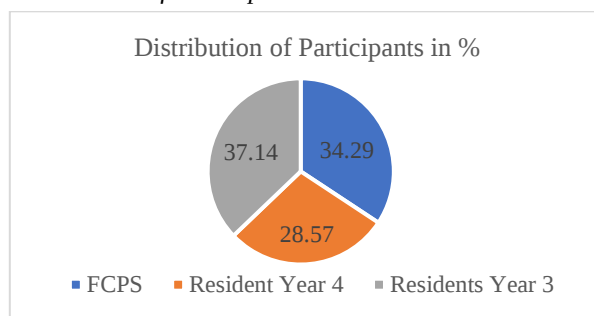


Table 1
General concepts of study participants regarding antibiotic prescription

Questions	Residents (Year 3) n=26		Residents (Year 4) n=20		FCPS consultants n=24		p-value
	Yes	NO	Yes	No	Yes	NO	
Do you examine patients with enteric fever?	23 (88.4%)	3 (11.6%)	19 (95%)	1 (5%)	23 (95.8%)	1 (4.1%)	0.001*

Do you advice blood report for diagnosis?	12 (46.2%)	14 (53.8%)	12 (60%)	8 (40%)	20 (873.4%)	4 (16.6%)	0.095
Do you initiate the therapy on clinical examination?	24 (92.3%)	2 (7.7%)	19 (95%)	1 (5%)	22 (91.6%)	2 (8.4%)	0.041*
Do you advice culture and sensitivity analysis?	10 (38.5%)	16 (61.5%)	7 (35%)	13 (65%)	10 (841.6%)	14 (58.4%)	0.521
Do your hospital policy endorse getting culture and sensitivity report before prescription of antibiotics?	4 (15.4%)	22 (84.6%)	3 (15%)	17 (85%)	2 (8.4%)	22 (91.6%)	0.001*
Do you follow any guidelines for antibiotics prescriptions?	2 (7.7%)	24 (92.3%)	5 (25%)	15 (75%)	18 (75%)	6 (25%)	0.033*
Do you know the concept of antibiotic steward ship?	1 (3.8%)	25 (96.2%)	8 (40%)	12 (60%)	23 (95.8%)	1 (4.1%)	0.141

Table 2*Preference of doctors in choosing antibiotic for uncomplicated enteric fever*

Participants	Drug choice	F (P)	p-value
Residents (Year 3)	Ciprofloxacin	22 (84.6%)	0.001
	Meropenem	4 (15.4%)	
Residents (Year 4)	Ciprofloxacin	17 (85%)	0.001
	Meropenem	3 (15%)	
FCPS consultants	Ciprofloxacin	23 (95.8%)	0.001
	Meropenem	1 (4.1%)	

DISCUSSION

Since its initial discovery in late 2016, extensively drug-resistant typhoid fever (XDR-TF) has become a serious public health concern in Pakistan. Since its start in Karachi, in the province of Sindh, the outbreak has expanded throughout the area, with over 22,000 cases—including over 15,700 cases of the XDR strain—reported between 2016 and 2020^{10, 11}. The increase in incidence is highlighted in the results of current study as well, as most of the participants responded as yes when asked about examining a patient with enteric fever. Most of the doctors chose ciprofloxacin for the management of uncomplicated enteric fever. That can be influenced by the choice that most of them prescribe the antibiotic only on the basis of clinical examination and there is insignificant results regarding consensus on going for the culture and sensitivity analysis in routine hence the results are highlighting that if not proved or identified by culture and sensitivity they do not prescribe meropenem.

Because of its potency against *S. Typhi*, the fluoroquinolone antibiotic ciprofloxacin has been used extensively in the treatment of typhoid fever. Historically, ampicillin and chloramphenicol have been less effective against *S. Typhi* because to the rise of multidrug-resistant (MDR) strains of the infection¹¹. Fluoroquinolones thus emerged as the main therapeutic choice in several areas, including Pakistan, where typhoid fever is quite prevalent. Research has shown that ciprofloxacin, which is frequently considered to be 100% effective in clinical settings, has a high cure rate for typhoid fever¹². Ciprofloxacin is a practical option for both doctors and patients because of its efficacy, ease of administration by oral means, and brief course of therapy. Depending on the patient's reaction to therapy and the severity of the infection, a 500 mg twice day dose is usually prescribed for 7 to 14 days to treat typhoid fever¹³.

The evolution of fluoroquinolone resistance is a significant issue despite the drug's previous efficacy.

There have been reported examples of treatment failure in Pakistan, and reports suggest that ciprofloxacin resistance is rising¹⁴. One case study, for example, focused on a 14-year-old patient who, although taking ciprofloxacin, did not improve and finally needed to switch to ceftriaxone for therapy. This instance emphasizes how crucial it is to conduct continual monitoring and susceptibility testing in order to successfully guide antibiotic therapy¹⁵. Particularly since 2016, the prevalence of extensively drug-resistant (XDR) typhoid fever has increased, adding to the complexity of the treatment options. Because XDR strains are resistant to several medications, including fluoroquinolones, healthcare professionals in Pakistan face difficult hurdles. The dependence on ciprofloxacin may grow more troublesome as these resistant germs proliferate^{14, 16}.

There are several public health issues with the extensive use of ciprofloxacin for enteric fever in Pakistan. First, a review of treatment guidelines and the creation of substitute therapeutic approaches are required due to the growing resistance to fluoroquinolones¹⁷. To reduce the chance of resistance development, public health authorities need to give strong antimicrobial stewardship programs top priority¹⁸. Furthermore, the necessity of preventative interventions is underscored by the high prevalence of typhoid fever in Pakistan and the rise of resistant strains.

Campaigns to reduce disease burden and stop the development of resistant strains, like the introduction of the typhoid conjugate vaccine, are essential. To lower transmission rates, public education on safe food and water practices is also crucial^{18, 19}.

With 100% sensitivity in 2009 and 99% sensitivity in 2019, Pakistan's meropenem sensitivity trend has remained strong. But the advent of MDR and XDR *Salmonella enterica* serovar Typhi bacteria has made therapy with carbapenems, such as meropenem, more necessary²⁰.

The emergence of resistant forms of bacteria has been facilitated by the careless use of antibiotics. In ten-year research, 44% of the *S. Typhi* strains acquired prolonged resistance to first- and second-line medications. In Pakistan, meropenem is now only used as a last option to treat typhoid fever due of this concerning condition²¹.

CONCLUSION

The doctors preferred choosing ciprofloxacin for uncomplicated enteric fever which is positive indication to preserve the last resort antibiotics such as meropenem. However, practices of prescribing antibiotics and understanding the concepts of antibiotic stewardship need to be improved in residents of general medicine.

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