(RESEARCH ARTICLE)

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Clinical Experience on the Use of Faropenem in Indian Patients with Urinary Tract Infections

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Abstract

Background: Urinary tract infections (UTIs) are a common infectious disorders affecting both men and women. India has the highest rate of extended-spectrum beta-lactamase (ESBL)-producing microbes worldwide. Faropenem (FRPM) is a suitable antibiotic, belonging to the penem group of β-lactam antibiotics that can be taken orally. Faropenem has little practical clinical experience at the urologists level and lacks real-world evidence.

Methods: A questionnaire-based survey was conducted from Indian urologists. The study collects data to understand the appropriate use of FRPM in Indian patients with UTIs in the real-world setting in India. The study focuses on the utility of FRPM in UTI; prevalence of UTI with other comorbidities such as type 2 diabetes mellitus (T2DM) and benign prostate hypertrophy (BPH), prescription trends among urologists for UTIs, other antibiotics along with FRPM, response to stepdown therapy in UTI and response in elderly patients with UTI.

Result: A total of 49 urologists participated in the study and a surveillance form with 16 structured questions was formulated. Data from their responses showed that of the 10 patients treated with FRPM, largest proportion (46.94%) of patients had history recent recurrent UTI and 40 physicians agreeing than more than 3 (81.63%) out of 10 patients treated with FRPM had UTI and diabetes. E. coli was the most prevalent pathogen in causing UTI as per past lab reports (73.47%) Significant majority were treated with other antibiotics before seeking FRPM and specifically fluoroquinolones (44.90%) were the preferred antibiotics prior to prescribing FRPM. 97.96% of respondents indicated of using FRPM as sequential therapy during step-down treatment after imipenem cilastatin or meropenem in hospitalized patients and they continued to be asymptomatic and infection resolved completely after step-down therapy with oral FRPM. A higher percentage (44.90%) of respondents could be ESBL producers and more than half of them indicated of prescribing FRPM as the first drug of choice. Vast majority (93.88%) of elderly patients tolerated FRPM well and overall, 38.77% indicated patient underwent complete cure with FRPM.

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Conclusion: Faropenem is well tolerated and clinically effective in treating UTIs even in elderly patients and as a step-down therapy. Several urologists use it in complicated UTIs or in cases when other antibiotics fail to treat the infection. It can be considered as a first choice after the susceptibility data is analyzed.

Keywords: Questionnaire-Based Study; Complicated Urinary Tract Infection; Step-Down Therapy; Benign Prostate Hypertrophy; Extended-Spectrum Beta-Lactamase (ESBL) Producers

1. Introduction

Antimicrobial resistance has become a major healthcare concern in both the treatment and prevention of infections worldwide. The microbiomes develop resistance over a period of time, causing an increase in the treatment cycle, longer hospital stays and an increase in the mortality and morbidity rates [1]. The possible causes for the development of resistance could be excessive or inadequate use of antimicrobial drugs, inadequate patient care and an increase in the adverse effects [2]. Out of the available β-lactam antibiotics, carbapenems offer the broadest spectrum of activity against gram-positive and gram-negative microbiomes. This makes it a preferred choice in treating severe, resistant bacterial infections or critical infections with high mortality. Carbapenem is used as an IV formulation in treating severe respiratory, urinary and skin infections. Faropenem, an oral penem, is an alternative to intravenous carbapenem and has a broad antimicrobial activity against gram-positive, gram-negative and anaerobic bacteria.

UTI is a major infectious disease in India and is chiefly caused due to E-coli, Klebsiella, Proteus, Pseudomonas, Staphylococcus and other bacteria. In India, Faropenem (FRPM) has been approved for the treatment of urinary tract, respiratory, skin and gynecological infections and in certain scenarios, it has been used in invasive ESBL-producing Enterobacteriaceae infections. Though it has been reported that FRPM had good efficacy (overall efficacy rate: 82.0%) in patients with complicated UTI, it has not been frequently used for UTI patients. FRPM has pronounced beta-lactamase stability as compared to other cephalosporins and imipenem [3] . It has a concentration in urine which is more than 4-fold higher than the minimum inhibitory concentration (MIC) required to inhibit the growth of 90% of ESBL-E. coli [4]. There is an unmet need to evaluate its use in real-world clinical experience, analyzing the level of satisfaction and challenges of the urologists while using this drug. Hence, the present survey aims to collect and assess the responses of Indian urologists with the use of Faropenem in treating UTIs.

2. Methods

2.1. Study design

This questionnaire-based study was conducted among Indian urologists and their responses were obtained. Participation in the study was completely voluntary, and the study process, along with the data analysis, ensured the confidentiality and anonymity of the HCPs.

2.2. Study questionnaire

A surveillance form was designed based on existing literature, guidelines, and expert opinions. It included a total of 16 structured questions having multiple choice responses that focused on the utility of Faropenem in UTI; along with other comorbidities such as type 2 DM, BPH, prescription trends, other antibiotics along with Faropenem, response to stepdown therapy in UTI and response in elderly patients with UTI. The study protocol was approved by the independent ethics committee (ACEAS-Independent Ethics Committee, Ahmedabad, Date of approval: 30 July 2024).

2.3. Inclusion and exclusion criteria

The study included participants with urinary tract infections. Patients with T2DM and BPH, elderly patients, can be included in the study.

2.4. Data collection

Urologists participating in the study were provided with a concise overview of the study's nature and the process for completing the questionnaire. The questionnaire was given to them either in person, via phone calls, or through online platforms, at their convenience.

2.5. Data analysis

The responses of urologists were entered into Microsoft Excel and descriptive statistics, such as frequencies and percentages, were employed to present data.

3. Results

A total of 49 urologists were included in this study. Data from their responses showed that of the 10 patients treated with FRPM, the largest proportion (46.94%) of patients had a history recent recurrent UTI and 40 physicians agreed that more than 3 (81.63%) out of 10 patients treated with FRPM had UTI and diabetes. Of all the physicians, 73.47% responded that Escherichia coli has been the most prevalent pathogen in causing UTI as per past lab reports and more than half (51.02%) of the respondents reported treating UTI and BPH. A significant majority of respondents indicated more than 3 out of 10 patients were treated with other antibiotics before seeking FRPM and the majority of them responded that fluoroquinolones (44.90%) were the preferred antibiotics prior to prescribing FRPM. A vast majority (97.96%) of respondents indicated using FRPM as sequential therapy during step-down treatment after imipenem cilastatin or meropenem in hospitalized patients when they were to be switched over to oral antibiotics. A larger number of respondents (57.14%) observed that patients continued to be asymptomatic and infection resolved completely after step-down therapy with oral FRPM. The majority (63.26%) of respondents suggested that more than 3 out of 10 patients were prescribed step-down therapy and a significant (67.35%) urologists rated the efficacy of step-down therapy with FRPM as excellent. A higher percentage (44.90%) of respondents indicated that 2 out of 10 patients could be ESBL producers and more than half of them indicated of prescribing FRPM as the first drug of choice for 2/10 patients. Over two-thirds of respondents (67.35%) suggested of prescribing FRPM to patients with renal stones. More than half (55.10%) of respondents reported that more than 3 out of 10 patients treated with other antibiotics were elderly (more than 60 years). The vast majority (93.88%) of elderly patients tolerated FRPM well. An equal number of respondents (38.77%) indicated that 8 out 10 and 9 out 10 patients underwent complete cure with FRPM.

Table 1 Surveillance questionnaire

Questions	Options	Response (N=49)
Out of the 10 patients you treated with FRPM what was the patient's profile which as associated with UTI?	Newly diagnosed case of UTI	08 (16.33)
	H/o recent recurrent UTI	23 (46.94)
	T2DM with UTI	18 (36.73)
Out of the 10 patients you treated with FRPM how many patients had UTI and diabetes?	1/10 patients	05 (10.20)
	2/10 patients	04 (08.16)
	>3 patients	40 (81.63)
What are the pathogens implicated in causing UTI in your hospital / clinic as per past lab reports?	Proteus mirabilis	08 (16.33)
	Klebsiella pneumonia	05 (10.20)
	Escherichia coli	36 (73.47)
Out of the 10 patients you treated with FRPM how many patients had UTI and BPH?	1/10	07 (14.28)
	2/10	25 (51.02)
	>3/10	17 (34.70)
Out of the 10 patients you treated with FRPM, how many of them had been treated with other antibiotics before they visited you for treatment?	1/10 patients	1 (02.04)
	2/10 patients	12 (24.49)
	>3 patients	36 (73.47)
Which antibiotics had the patients been treated with before you prescribed FRPM for UTI management?	Amoxycillin	9 (18.37)
	Cephalosporins	18 (36.73)
	Fluroquinolones	22 (44.90)
	Yes	48 (97.96)

Have you prescribed FRPM as sequential therapy after imipenem cilastatin or meropenem in hospitalized patients when they were to be switched over to oral antibiotics (STEP DOWN therapy) ?	No	1 (02.04)
What was the response of the patients after stepdown therapy from IV carbapenems to oral FRPM?	No recurrent UTI	12 (24.49)
	No relapse of UTI	9 (18.37)
	Patient continued to be asymptomatic and infection resolved completely	28 (57.14)
How many out of these 10 patients were prescribed STEP DOWN therapy?	1/10	3 (06.12)
	2/10	15 (30.61)
	>3/10	31 (63.26)
How would you rate the efficacy of STEP DOWN therapy with FRPM in your patients?	Excellent	33 (67.35)
	Good	15 (30.61)
	Fair	1 (02.04)
	Poor	0
Out of these 10 patients who had been treated with other antibiotics earlier how many of them could be ESBL producers which resulted in resistance to other antibiotics?	1/10	9 (18.37)
	2/10	22 (44.90)
	>3/10	18 (36.73)
In how many patients with UTI did you prescribe FRPM as the first drug of choice?	1/10	11 (22.45)
	2/10	25 (51.02)
	>3/10	13 (26.53)
Have you prescribed FRPM in any of these 10 patients with renal stones?	Yes	33 (67.35)
	No	16 (32.65)
Out of these 10 patients who had been treated with other antibiotics how many of these patients were elderly (greater than 60 years of age)?	1/10	4 (8.16)
	2/10	18 (36.73)
	>3/10	27 (55.10)
Was FRPM well tolerated in these elderly patients?	Yes	46 (93.88)
	No	3 (6.12)
Out of these 10 patients treated with FRPM how many of them underwent complete clinical cure?	10/10	7 (14.28)
	9/10	19 (38.77)
	8/10	19 (38.77)
	<8/10	4 (8.16)
Data presented as n (%). FRPM, Faropenem: UTI, urinary tract infection; BPH, Benign Prostate hypertrophy: ESBL, extended spectrum β lactamse:IV, intravenous: T2DM: type 2 diabetes mellitus		

4. Discussion

Recurrent and complicated UTI is a major concern among clinicians and India happens to have the largest number of ESBL-generating microbes. E. coli is the commonest cause of UTI, with 95% prevalence and Klebsiella, Enterobacter, Pseudomonas, Staphylococcus and other bacteria also cause UTI. UTIs pose a major burden both medically and financially. There has been an increased prevalence of UTIs caused by drug-resistant microbes, specifically ESBL-positive E. Coli, posing challenges in treating these UTIs [5]. The availability of an oral penem is essential since it is easy

to administer and is suitable for patients discharged from hospitals. FRPM is a potent penem with a structure similar to carbapenem and is a hybrid of penem (penicillin) and cepham (cephalosporin) nuclei. FRPM has pronounced beta-lactamase stability as compared to other cephalosporins and imipenem [3].

The responses from the present survey indicate that FRPM is chiefly utilized for managing recurrent UTIs (46.94%) and UTIs in diabetic patients (36.73%), highlighting its role in treating cases where first-line antibiotics may be ineffective or contraindicated. Recurrent UTI in T2DM poses a major risk of renal injury and these patients are more susceptible to resistant strains, including ESBL [6]. This could be due to the use of multiple causes, such as the use of multiple antibiotics for mild or asymptomatic cases or increase in hospital-acquired UTI, or due to catheter use. The low responses for newly diagnosed cases (16.33%) reflect its position as a second-line or specialized treatment option. These findings suggest that clinicians consider FRPM a reliable option for treating complicated UTIs, particularly in patients with comorbidities or recurrent infections. E. coli is one of the most common causative pathogens in causing UTI in hospital/clinic settings. And the survey findings are also in favor of this statement, as 73.47% urologist stated the same. P. mirabilis (16.33%) and Klebsiella pneumonia (10.20%) accounted for a smaller percentage, which could be in catheterized patients or in cases of recurrent infections. It is effective against E. coli strains resistant to other antibiotics, fluoroquinolones and cephalosporins [7].

Identifying the exact pathogen is crucial while treating UTI for selecting specific antimicrobial therapy for effective management.

UTI is associated with an enlarged prostate due to incomplete emptying of the bladder, allowing the urine to stagnate and creating a favorable environment for the pathogens to grow [8]. The risk for UTI increases with benign prostate hypertrophy, causing higher post-void residual (PVR) urine volume [9]. The responses of the urologists also suggested UTI and BPH frequently occurred in patients treated with FRPM, with 51% responses of 2 out of 10 cases and 34.70% treating more than 3 out of 10 patients. This suggests a significant clinical burden of these co-existing conditions, potentially due to factors like age-related prostate enlargement or impaired urinary flow. The findings underscore the importance of targeting antimicrobial therapies to address both UTI and BPH effectively in this patient demographic. The survey also highlighted use of other antibiotics prior to be prescribed FRPM (73.47%). This underscores the potential role of FRPM in addressing infections that are either resistant to first-line antibiotics or in patients with a history of recurrent or unresolved infections. The findings emphasize the need for careful antibiotic stewardship and consideration of resistance patterns in selecting appropriate therapy. The responses indicate that fluoroquinolones (44.90%) and cephalosporins (36.73%) were the most frequently used antibiotics prior to FRPM for UTI management, with a notable failure or resistance rate. The limited reliance on Amoxicillin and Amoxicillin-Clavulanic Acid (19.23%) reflects their reduced efficacy in the current UTI resistance landscape. These findings underscore the importance of antibiotic stewardship and the need for agents like FRPM in cases where standard treatments fail. The overwhelmingly positive response (97.96%) demonstrates widespread use of FRPM in step-down therapy following potent IV carbapenems like imipenem-cilastatin or meropenem. This aligns with its efficacy, tolerability, and convenient oral formulation, making it a preferred choice for continuing therapy in hospitalized patients transitioning to outpatient care. Oral FRPM is a highly effective step-down therapy following IV carbapenem use, with over half of the patients achieving complete resolution of infection and remaining asymptomatic. The combined outcomes (no recurrence or relapse) further confirm its clinical utility in preventing UTI reemergence. These results underscore the role of FRPM in bridging IV to oral antibiotic therapy effectively. This step-down therapy with oral FRPM is widely utilized, suggesting the preference for transitioning a majority of patients to oral therapy after IV antibiotics, indicating its efficacy and safety in reducing hospital stays and improving treatment convenience.

Production of ESBLs signifies a resistance mechanism that impedes the antimicrobial treatment of infections caused by Enterobacteriaceae and can pose a serious threat to the available antibiotics. Data from studies have shown 29% prevalence of ESBLs in all gram-negative bacteria and 24% in E.coli [10]. While another study by Tande et al, 63% adults and 100% children were ESBL-producing Enterobacteriaceae showing resistance to antibiotics [11]. Data from a study conducted at a hospital in Iran showed 26.5% E.coli and 43% K. pneumoniae were ESBL producers, suggesting high prevalence in hospitalized patients [12]. Our survey findings are also in favor of the same, that ESBL producers are common in practice and it underlines the need for judicious antibiotic use after susceptibility testing. The data reveal that FRPM is moderately utilized as the first-line treatment for UTIs, with most clinicians reserving it for specific cases. The variability in its use reflects differing approaches influenced by local antibiotic resistance patterns, patient histories, or hospital protocols. This underscores the need for evidence-based guidelines to optimize its use as a first-choice antibiotic.

The proportion of nearly 50% of elderly patients were treated with other antibiotics in the survey, suggesting the effectiveness of other antibiotics might be influenced by age, with older patients potentially being more susceptible to

treatment failures. These findings are despite the response that 93.88% elderly patients tolerated FRPM well. The response to FRPM was variable in our study, which could be influenced by various factors, such as patient characteristics, severity of infection, or other medications being used.

5. Conclusion

There is limited real-world data available regarding the efficacy and utility of FRPM in patient population with UTI. The study highlights the gaining acceptance of FRPM in treating UTIs and complicated UTIs. In certain areas it was an alternative choice in cases where other antibiotics failed to treat the infection. Its tolerability in elderly patients makes it a suitable consideration. It has potential for the treatment of UTIs due to ESBL producers and other cephalosporin-resistant Enterobacteriaceae, but more such real-world data is required to emphasize its efficacy in UTI management.

Compliance with ethical standards

Disclosure of conflict of interest

All authors have no conflict of interest to declare

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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