Section: Microbiology

Original Research Article

ASSESSMENT OF ANTIMICROBIAL ACTIVITY OF FOSFOMYCIN ON ESBL POSITIVE AND NEGATIVE E COLI ISOLATES

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Abstract

Background: Assessment of antimicrobial activity of fosfomycin on ESBL Positive and Negative E Coli isolates. **Material and Methods**: The urine samples were collected using the clean catch mid-stream technique using aseptic protocols to minimize contamination. A total of 330 midstream urine samples were collected from individuals, including inpatients and outpatients, who were suspected of having urinary tract infections. The urine samples were inoculated over Cystine–Lactose–Electrolyte-Deficient (CLED) agar using calibrated loop method. The culture medium was then transferred to a 37 °C incubator for a period of 24 hours. **Results:** Our research indicates that Escherichia coli was the predominant bacteria linked to urinary tract infections. Out of the total of 330 isolates 191 of them were isolates of E. coli, accounting for 57.88%. The majority of ESBL-producing E.coli strains exhibited sensitivity in 181 cases (98.8%), whereas resistance was seen in 8 cases (4.2%), and intermediate susceptibility was observed in 2 cases (1%). The efficacy of fosfomycin against ESBL-positive E. coli isolates- ESBL-positive E. coli exhibited a sensitivity rate of 94.9% (75 cases) and a resistance rate of 5.1% (4 cases). The efficacy of fosfomycin against ESBL-negative E. coli isolates-The ESBL-negative E. coli showed a sensitivity rate of 94.6% (106 cases), a resistance rate of 3.6% (4 cases), and an intermediate rate of 1.8% (2 cases). **Conclusion:** The current investigation found that fosfomycin exhibited a significant level of susceptibility against Escherichia coli isolates that produce extended-spectrum beta-lactamases (ESBLs). Our research indicates that fosfomycin is one of the most effective choice for treating urinary infections caused by ESBL-producing Escherichia coli isolates.

INTRODUCTION

Escherichia coli is a prevalent pathogen in both community-acquired and nosocomial urinary tract infections (UTIs), biliary tract infections, and severe intraabdominal infections. Statistically around 33% of adult women gets urinary tract infections (UTIs), with E. coli being responsible for over 50% of these cases.[1,2] Despite E. coli's natural susceptibility to several antimicrobial drugs, there has been a growing prevalence of antimicrobial resistance caused by extended-spectrum β-lactamases (ESBLs), carbapenemases, plasmid-mediated quinolone resistance, and mcr genes which leads to colistin resistance.[3] The rise of antimicrobial resistance in E. coli results in a decrease in effective therapeutic drugs and extends the duration of hospitalization owing to the lack of effective oral medications. ESBL-producing E. coli causing urinary tract infections are showing an increase in trend Infections caused by these pathogens have limited treatment options. . The emergence and spread of MDR gram-negative bacteria associated with UTIs is increasing worldwide, both in hospitals and in the community. Presence of these pathogens in urinary tract infections need ongoing surveillance to provide suitable empirical therapy. Treatment should be administered based on susceptibility test results to prevent the emergence of resistant mutants or incomplete cures.[6] The treatment of bacterial infections is negatively impacted by the widespread presence of multidrug-resistant (MDR) pathogens. Fosfomycin, an oral bactericidal antimicrobial agent similar to phosphonic acid in chemical structure, is active against most uropathogens. It has a wide range of action against both Gram-positive and Gram-negative infections and is especially potent against bacteria that are resistant to many drugs, such as ESBL-producing Escherichia coli.[7] .

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Fosfomycin functions as a phosphoenolypyruvate analog that hinders the first step of cell wall formation by inhibiting the MurA enzyme (UDP-N-acetylglucosamine enolpyruvyl-transferase). This enzyme is responsible for catalyzing the initial stage of N-acetylmuramic acid and peptidoglycan biosynthesis, ultimately resulting in the death of bacterial cells. The current prevalence of E. coli resistant to fosfomycin is believed to be less than 5% globally, and less than 10% among extended spectrum β-lactamase (ESBL) producers. Fosfomycin has excellent tolerability, with adverse events occurring in around 1% to 5% of patients.[8-10] The global presence of the ESBL-producers in Enterobacteriaceae family has been identified, and the risk factors associated with it may be linked to hospitalization or the use of antibiotics.

MATERIALS AND METHODS

The research was carried out at the microbiology laboratory. A total of 330 individuals who were qualified for participation in the study had undergone a bacteriological analysis of urine and had not taken any antimicrobial medications in the two weeks before. This eligibility criterion was based on the requirement that the antibiotics should have hindered or eradicated the disease-causing microorganisms. Non-compliant UTI patients were omitted from this research.

Methodology

The urine samples were collected using the clean catch mid-stream technique, using aseptic protocols to minimize contamination. A total of 330 midstream urine samples were collected from individuals, including inpatients and outpatients, who were suspected of having urinary tract infections. The specimens were obtained in aseptic universal containers. The specimens were accurately labeled and processed following collection.. The urine cultures that showed the presence of bacteria other than E. coli were excluded from the study.

The urine samples were inoculated into Cystine–Lactose–Electrolyte-Deficient (CLED) agar using calibrated loop techniques. The culture medium was then transferred to a 37 °C incubator for a period of 18 to 24 hours.

Identification and Antimicrobial Susceptibility Testing

Organisms were identified by conventional microbiological methods. Antimicrobial Susceptibility Testing was performed on Muller Hinton agar using Kirby-Bauer disk diffusion method and interpreted according to Clinical Laboratory Standards Institute(CLSI). Identification of ESBL production was performed using phenotypic testing based on the Clinical and Laboratory Standards Institute's (CLSI) guideline

Data Analysis and Processing

The data were gathered and examined using the SPSS Version 25.0. A p-value below 0.05 was deemed to be statistically significant.

RESULTS

Our research indicates that Escherichia coli was the predominant bacteria associated with urinary tract infections. Out of the total of 330 bacteria 191 of them were isolates of E. coli, accounting for 57.88%. Table 1 demonstrates that the majority of ESBL-producing E.coli strains exhibited sensitivity in 181 cases (98.8%), whereas resistance was seen in 8 cases (4.2%), and intermediate susceptibility was observed in 2 cases (1%). [Table 1]

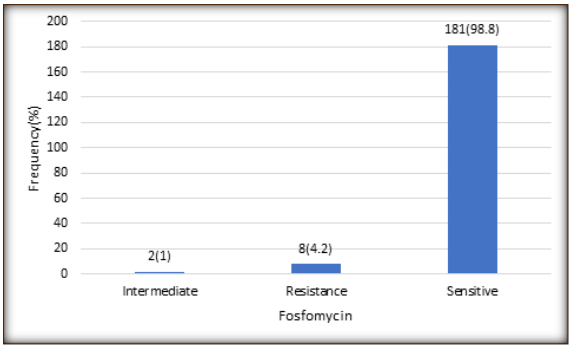

Figure 1

Table 2 show that out of 191, Positive ESBL was 79 (41.4%) and Negative ESBL was 112 (58.6%).

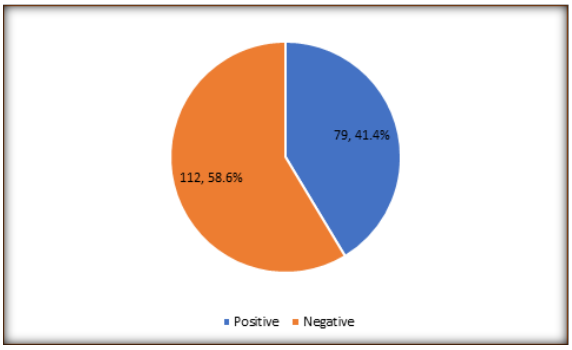

Figure 2

Table 3 demonstrates the efficacy of fosfomycin against ESBL-positive E. coli isolates. ESBL-positive E. coli exhibited a sensitivity rate of 94.9% (75 cases) and a resistance rate of 5.1% (4 cases). [Table 3]

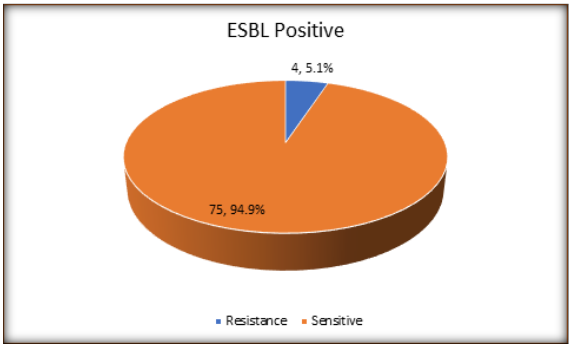

Figure 3

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Table 4 demonstrates the efficacy of fosfomycin against ESBL-negative E. coli isolates. The ESBL-negative E. coli showed a sensitivity rate of 94.6% (106 cases), a resistance rate of 3.6% (4 cases), and an intermediate rate of 1.8% (2 cases). [Table 4]

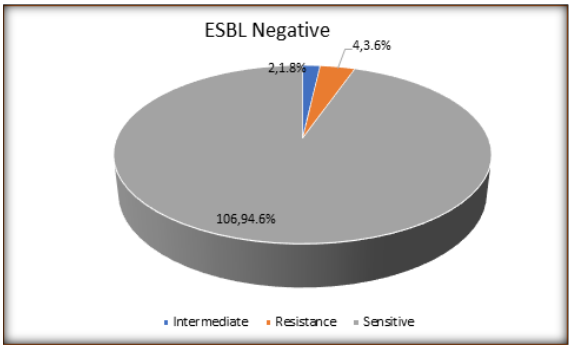

Figure 4

Table 1: Sensitivity and resistance of Fosfomycin

Fosfomycin	Frequency	Percentage
Intermediate	2	1
Resistance	8	4.2
Sensitive	181	98.8
Total	191	100

Table 2: ESBL Positive and Negative

ESBL	Frequency	Percentage
Positive	79	41.4
Negative	112	58.6
Total	191	100

Table 3: fosfomycin sensitive and resistance on ESBL Positive E Coli isolates

Fosfomycin	Frequency	Percentage
Resistance	4	5.1
Sensitive	75	94.9
Total	79	100

Table 4: fosfomycin sensitive and resistance on ESBL Negative E Coli isolates

Fosfomycin	Frequency	Percentage
Intermediate	2	1.8
Resistance	4	3.6
Sensitive	106	94.6
Total	112	100

DISCUSSION

Urinary tract infection (UTIs) is one of the most frequent infections among hospital-acquired or community-acquired infections.Currently the rise of antibiotic resistance has severely restricted the available treatment options for urinary tract infections (UTIs). Therefore, it is imperative to develop and use novel antimicrobials to address this need. However, there are only a limited therapeutic options. Fosfomycin, a previously used antibiotic, has regained its effectiveness in treating urinary tract infections (UTIs). Fosfomycin disrupts the building of bacterial cell walls by blocking formation of cell wall precursors . It has a wide range of antibacterial action against uropathogens. Furthermore, the oral availability of this medication, is very convenient for the treatment of urinary tract infections in outpatient settings.[11]

The drug resistance of ESBLs is attributed to their ability to enzymatically hydrolyze penicillins, cephalosporins, and monobactams. ESBLs are also accountable for the development of resistance to co-trimoxazole, fluoroquinolones, and amino glycosides. ESBL-producing bacteria often provide significant challenges in the treatment of urinary tract infections (UTIs) due to the aforementioned causes.[12-15].The Escherichia coli strains in our investigation that produced ESBLs exhibited a modest level of resistance to fosfomycin, with a rate of 4.2%. The reported zero resistance rate in other regions, such as Sri Lanka in 2019,[16] Morocco in 2021,[12] and India in 2022,[17] is lower than the current finding. Nevertheless, in 2019, other extensive investigations conducted at both single-center and multi-center facilities revealed a fosfomycin resistance rate of 3%.[18] Similarly, in 2021, another study indicated a resistance rate of 4.6%.[13]Fosfomycin is one of the preferred therapeutic options for urinary tract infections in individuals caused by ESBL-producing E. coli isolates It has excellent tissue penetration and impairs adherence to the urogenital mucosa, and it is excreted in urine in high concentrations. Fosfomycin is available as an oral tablet that may be taken as a single dosage with good safety profile. Fosfomycin has no detrimental impact on the gut flora as shown by several clinical studies. Consequently, this antibiotic has been found to be very successful in treating urinary infections, surpassing the efficacy of

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other primary antibiotics.[19-21] It is noteworthy that this antibiotic was added to the list of antibiotics recommended as first line treatments for urinary infections in European nations.[22] Furthermore fosfomycin is included in the most recent roster of primary antibiotics for the management of urinary tract infections as advised by the European Association of Urology.[23-25] In France, fosfomycin is recommended as the first line oral therapy for cystitis, with a single dosage being sufficient.[26]The findings from our investigation regarding the efficacy of fosfomycin against ESBL-producing E. coli validate the results established by earlier researchers.[27,28] Our findings revealed that a significant proportion of ESBL-producing E. coli isolates (up to 95.8%) exhibited sensitivity to fosfomycin. This indicates that fosfomycin is very effective against multidrug-resistant Escherichia coli isolates.. Despite being used for many decades, fosfomycin remains susceptible to ESBL-producing E. coli isolates. Additional factors contributing to the low prevalence of resistance to fosfomycin in ESBL-producing Escherichia coli isolates may include the antibiotic's quick exposure to the isolates and its efficient excretion via urine in its active state.[30]

CONCLUSION

The current investigation found that fosfomycin exhibited a significant level of sensitivity against Escherichia coli isolates that produce extended-spectrum beta-lactamases (ESBLs). Our research indicates that fosfomycin is one of the most effective choice for treating urinary tract infections caused by ESBL-producing Escherichia coli isolates. Undoubtedly, fosfomycin is quickly absorbed and does not have any adverse effects on the microbiota. Furthermore, it is excreted in urine in high concentrations, in its active state.

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