

Original Article

Bacterial Isolate Profile in Gram-Negative Urinary Isolates: Role of Nitrofurantoin

Meghna Sharma¹, Sapna Soneja², Loveena Oberoi³, Anuradha Malhotra², Kamaldeep Singh⁴, Babica Mahindroo⁴

Abstract

Background: In current times epidemic drug resistance has renewed interest in drugs belonging to the yesteryears, most importantly Nitrofurantoin for urinary tract infections. Studies have reported that more than 90% of urinary tract infections are due to enteric Gram-negative organisms, of which more than 80% are *E.coli*. **Objectives:** To study bacterial profile in Gram-negative urinary isolates and evaluate the role of nitrofurantoin. **Methods:** We retrospectively evaluated 500 consecutive Gram-negative bacterial isolates for bacteriological profile and nitrofurantoin sensitivity of patients of urinary tract infections at a tertiary care facility in Indiabetween January and June of 2022. **Results:** We had a total of 500 Gram- negative urinary isolates. 383 (76.6%) of these were found to be susceptible to nitrofurantoin. *E. coli* alone constituted 343 (68.6%) of total 500 Gram-negative isolates, 264 (76.96%) of which were sensitive to nitrofurantoin. 20 (4%) *Proteus* and 05 (1%) *Citrobacter species* were isolated and found to be resistant to nitrofurantoin. 12 (80%) out of the 15 *Acinetobacter* isolates were resistant to nitrofurantoin. All 12 (100%) *Pseudomonas* isolates tested resistant to nitrofurantoin. **Conclusion:** *E. coli* is the most common of uropathogens and despite rise in antibiotic resistance, it continues to be sensitive to nitrofurantoin. Resistance to nitrofurantoin is also being reported and this calls for judicious further use of this drug based on culture reports and local prevalence data.

Keywords: Nitrofurantoin, urinary tract infection, uropathogens, *E. coli*, drug resistance

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Introduction

In current times drug resistance has reached epidemic proportions and has thrown a new challenge before the medical and scientific fraternity.¹ The menace of drug resistance has even rendered the reserve drugs ineffective.² Presently, clinicians are struggling with urinary pathogens resistant to most of the oral drugs available like sulfonamides, flouro quinolones, cephalosporins and even the newer drugs like Faropenem.³ Times have seen an increased incidence of extended spectrum beta lactamase (ESBL) producing bacteria.⁴ Studies have reported that more than

90% of urinary tract infections are due to enteric Gram-negative organisms, of which more than 80% are *E.coli*.⁵

In this age of multi drug resistance, there is a renewed interest in drugs belonging to the yesteryears, most importantly nitrofurantoin for lower urinary tract infections.⁶ Nitrofurantoin hits bacteria at multiple levels blocking bacterial enzymes involved in carbohydrate and protein synthesis, and subsequently at higher concentrations inhibits RNA and DNA formation by its action on bacterial ribosomes.⁷ Nitrofurantoin gets activated by the bacterial

1. Resident, Department of Microbiology, Government Medical College, Amritsar, India.
2. Associate Professor, Department of Microbiology, Government Medical College, Amritsar, India.
3. Professor, Department of Microbiology, Government Medical College, Amritsar, India.
4. Assistant Professor, Department of Microbiology, Government Medical College, Amritsar, India.

Correspondence to: Dr.Sapna Soneja, Associate Professor, Department of Microbiology, Government Medical College, Amritsar, India. Email: drsapnabatra@gmail.com

reductases to form highly reactive electrophilic intermediates that damage bacterial ribosomal proteins.⁸ Nitrofurantoin has an oral bioavailability of 50% and is excreted primarily through the kidneys. This results in a high concentration in the urinary pathways though the plasma levels may be much lower.⁹ A landmark study in Uppsala University Sweden, 2014, had demonstrated 100% efficacy of nitrofurantoin in terminating ESBL and non-ESBL *E. coli*. Same study also demonstrated 99% efficacy in killing of Vancomycin resistant and non-vancomycin resistant Enterococci.¹⁰

Nitrofurantoin has thus emerged as a cost-effective oral alternative in current era of antibiotic resistance. The susceptibility of uropathogens is known to vary in different geographical regions and even in same geographical region.¹¹ Most urinary tract infections are being treated empirically. In this retrospective study we aim to observe the prevalence of nitrofurantoin resistance in the Gram-negative uropathogen isolates. The aim of the present study was to observe bacterial profile in Gram-negative urinary isolates and evaluate the role of Nitrofurantoin against those isolates.

Methods

In this study, we retrospectively evaluated 500 consecutive Gram-negative bacterial isolates for bacteriological profile and nitrofurantoin sensitivity of patients of urinary tract infections at our tertiary care facility in Amritsar, India, between January and June of 2022. Antimicrobial susceptibility was performed using Kirby-Bauer disk diffusion method on Mueller Hinton agar and finding interpreted with CLSI M100-S-31. Normally distributed continuous variables were recorded as mean and categorical variables were expressed as percentage.

Results

We had a total of 500 Gram negative urinary isolates. 383 (76.6%) of these were found to

be susceptible to nitrofurantoin. *E. coli* alone constituted 343 (68.6%) of total 500 Gram negative isolates, 264 (76.96%) of which were sensitive to nitrofurantoin. 20 (4%) *Proteus* and 05 (1%) *Citrobacter* species were isolated and found to be resistant to nitrofurantoin. 12 (80%) out of the 15 *Acinetobacter* isolates were resistant to nitrofurantoin. All 12 (100%) *Pseudomonas* isolates tested resistant to nitrofurantoin.

Table 1: Sensitivity to nitrofurantoin of Gram-negative uropathogens

Staining	Sensitive to Nitrofurantoin	Resistant to Nitrofurantoin	Total
Gram negative	383	117	500
Percentage	76.6%	23.4%	100

Table 2: Gram negative isolate profile

Gram negative Isolate	Frequency	Percentage
<i>E. coli</i>	343	68.6%
<i>Klebsiella</i> sp.	105	21%
<i>Proteus</i>	20	4%
<i>Citrobacter</i>	5	1%
<i>Acinetobacter</i>	15	3%
<i>Pseudomonas</i>	12	2.4%
Total	500	100%

Discussion

Urinary tract infections are one of the commonest infective pathologies affecting communities at large and are commoner in females because of anatomical reasons. Irrational antibiotic use has contributed to the emergence of multi drug resistant uropathogens, forcing clinicians to go back to old generation of drugs like nitrofurantoin. Shaifali et al. in their study on antibiotic susceptibility pattern of urinary pathogens found nitrofurantoin to be most effective drug against *E. coli* was the commonest uropathogen.¹² Our

Table 3: Isolate Sensitivity pattern to nitrofurantoin

Isolate	<i>E. coli</i>	<i>Klebsiella</i>	<i>Proteus</i>	<i>Citrobacter</i>	<i>Acinetobacter</i>	<i>Pseudomonas</i>
Sensitive	264 (76.96%)	77 (73.33%)		-	3 (20%)	-
Resistant	79 (23.04)	28 (26.66%)	20 (100%)	5 (100%)	12 (80%)	12 (100%)
Total	343	105	20	5	15	12

study has shown similar patterns. Kothari et al. too observed E. coli to be the commonest pathogen causing urinary infections and nitrofurantoin to be the most effective drug against it. They also highlighted poor activity of nitrofurantoin against Proteus sp. Our study revealed that Proteus isolates were resistant to nitrofurantoin, while they found 24.4% of E. coli isolates to be resistant to nitrofurantoin, that is marginally higher than the 23.04% observed in our study.¹³ Kulkarni and associates studied the susceptibility pattern of E. coli to various antibiotics and found E. coli to be the commonest of uropathogens. They also showed 92.41% sensitivity of E. coli to Nitrofurantoin.¹⁴

Singh and fellows studied the resistance pattern of uropathogens to nitrofurantoin and found alarming levels of resistance amongst Enterobacteriaceae. They found highest level of resistance (92.30%) to nitrofurantoin in Klebsiella sp. that is much higher than the 26.6% observed in our study. They found nitrofurantoin to be effective against 69.9% of E. coli isolates.¹⁵

Sood et al. studied antibiotic resistance in various uropathogens and found E. coli to account for 61.84% isolates. They found nitrofurantoin resistance in only 5-6% E. coli isolates.¹⁶

Biswas et al. studied choice of antibiotics for empirical therapy of acute cystitis and found 9.3% resistance of E. coli to nitrofurantoin against 23.04% E. coli resistance observed in our study. They also found that more than 80% isolates resistant to fluoroquinolones are sensitive to

nitrofurantoin.¹⁷

Tanweer et al. studied urinary infections in renal transplant patients and found E. coli in 51% isolates. They reported 76% of the organisms to be sensitive to antibiotics, 7% isolates were multi drug resistant while remaining were partially sensitive. They also found Pseudomonas to be the commonest multi drug resistant organism in post-transplant urinary infections. In our study we have 2.4% Pseudomonas isolates, all of which are resistant to nitrofurantoin.¹⁸

Conclusion

To conclude, E. coli is the most common of uropathogens and despite the recent rise in antibiotic resistance, it continues to be sensitive to nitrofurantoin. Resistance to nitrofurantoin is also being reported and this calls for judicious use of this drug based on culture reports and local prevalence data.

Conflict of interest: None to declare.

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Ethical approval: The study was approved by the REB of Government Medical College, Amritsar, India.

Authors' contribution: Meghna Sharma was involved in conception and design of the study. All authors were equally involved in data collection, analysis, manuscript preparation, revision and finalization.

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