RESEARCH ARTICLE

A hospital-based descriptive cross-sectional study in Eastern India to estimate the effect of nitrofurantoin, an age-old therapeutic option, in uncomplicated urinary tract infection

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ABSTRACT

Background: Urinary pathogens develop lesser resistance against Nitrofurantoin than other antimicrobials such as Fluoroquinolones, Cotrimoxazole, and Carbapenems. Aim and Objective: The objective of this study was to estimate the sensitivity pattern of the urinary isolates against Nitrofurantoin in uncomplicated Urinary tract infection (UTI).

Materials and Methods: The descriptive cross-sectional study was performed from January 1, 2020, to June 30, 2020, with 759 cases with signs and symptoms of uncomplicated UTI. Aseptically collected midstream urine was inoculated on Nutrient Agar Media, MacConkey’s Agar media, and Blood Agar media for bacterial isolation. Antimicrobial susceptibility testing was done by disk diffusion technique on Mueller Hinton Agar (Kirby Bauer technique) as per Clinical Laboratory Standards Institute guidelines.

Results: Out of total of 759 urine samples, in 165 cases bacterial pathogens were isolated (21.73%). Only 17 were resistant to Nitrofurantoin (10.30%) whereas resistance to Fluoroquinolone (Ciprofloxacin) was in 58 isolates (35.15%) and Cotrimoxazole, in 37 isolates (22.42%). Resistance against Carbapenem antibiotics (Imipenem and Meropenem) was found in 29 isolates (17.57%). All the Nitrofurantoin resistant isolates were Gram-negative. Majority of the Nitrofurantoin resistant isolates were Klebsiella pneumonia (8 out of 17, i.e, 47.05%). All Nitrofurantoin resistant isolates were sensitive to Colistin and Tigecycline. Five out of 17 Nitrofurantoin resistant isolates were sensitive to Meropenem and Imipenem (29.41%). The Fischer exact test reveals that Nitrofurantoin is effective against the isolates resistant to Fluoroquinolones, Cotrimoxazole, and Carbapenems. Conclusion: Nitrofurantoin, even today, remains a good choice for empirical therapy for uncomplicated UTI.

KEY WORDS: Nitrofurantoin; Urinary Tract Infection; Empirical

INTRODUCTION

Urinary tract infection (UTI) is a commonly encountered health problem in the community as well as in nosocomial set up in India.[¹] However, Nitrofurantoin is a classical drug to treat uncomplicated UTI.[²] It damages Deoxy Ribonucleic Acid of both Gram Positive and Gram-Negative Bacteria since a highly reactive reduced form is produced. Minimum Inhibitory Concentration is 32 µg/mL or less for Nitrofurantoin susceptibility. It is bacteriostatic at concentrations less than 32 µg/mL. The concentration of nitrofurantoin in blood, following an oral dose of 100 mg, is achieved less than 1 µg/mL. Nitrofurantoin is bacteriocidal when drug concentration is achieved >100 µg/mL in urine.[³,⁴] Nitrofurantoin and the Quinolones and Nitrofurantoin show antagonism in vitro, hence, the
combination is not recommended. Currently, different standards are emphasizing on the use of fluoroquinolones and cotrimoxazole to treat UTI. Again, beta-lactam antimicrobials including Carbapenems have also been recommended by several schools. However, this study reveals the fact that bacterial isolates developed lesser resistance against Nitrofurantoin than other antimicrobials such as Fluoroquinolones, Cotrimoxazole, and Carbapenems.

Objective
The objective of this study was to estimate the sensitivity pattern of the urinary isolates against Nitrofurantoin in uncomplicated UTI.

MATERIALS AND METHODS
The descriptive cross-sectional study was performed from January 01, 2020 to June, 2020 with 759 cases with signs and symptoms of uncomplicated UTI. Inclusion criteria were fixed as per clinical, demographic, geographical, and temporal compliance. Pyrexia, urinary hesitancy, urgency, increased frequency of and burning sensation during micturition were the symptoms to satisfy the inclusion criteria. Patients who had a probability to get lost during follow-up or had complications, vulnerability, or severe morbidity were excluded from the study. Mid-stream urine was collected in proper aseptic manner for microbiological culture to isolate and identify the bacterial pathogen. Urine samples were inoculated on Nutrient Agar Media, MacConkey’s Agar media, and Blood Agar media for bacterial isolation. Antimicrobial susceptibility testing was done by disk diffusion technique on Mueller Hinton Agar (Kirby Bauer technique) as per Clinical Laboratory Standards Institute guidelines. Human subject autonomy, rights, and welfare were protected as per standard ethical guidelines. There was no objection from the institutional review board.

RESULTS
Out of total of 759 urine samples, in 165 cases bacterial pathogens were isolated (21.73%). Among these 165 isolates, only 17 were resistant to Nitrofurantoin (10.30%), whereas resistance to Fluoroquinolone (Ciprofloxacin) was in 58 isolates (35.15%) and cotrimoxazole, in 37 isolates (22.42%). Resistance against Carbapenem antibiotics (Imipenem and Meropenem) was found in 29 isolates (17.57%). All the Nitrofurantoin resistant isolates were sensitive to Meropenem and Imipenem (29.41%). There were no other therapeutic options such as Fluoroquinolones or Cotrimoxazole to manage the Nitrofurantoin resistant isolates as all seventeen of them were also resistant to those antimicrobials [Tables 1-3].

DISCUSSION
In this descriptive cross-sectional study, out of total of 759 urine samples, in 165 cases bacterial pathogens were isolated (21.73%). Only 17 were resistant to nitrofurantoin (10.30%) whereas resistance to fluoroquinolone (Ciprofloxacin) was in 58 isolates (35.15%) and cotrimoxazole, in 37 isolates (22.42%). Resistance against Carbapenem antibiotics (Imipenem and Meropenem) was found in 29 isolates (17.57%). All the Nitrofurantoin resistant isolates were sensitive to Meropenem and Imipenem (29.41%). There were no other therapeutic options such as Fluoroquinolones or Cotrimoxazole to manage the Nitrofurantoin resistant isolates as all seventeen of them were also resistant to those antimicrobials [Tables 1-3].

### Table 1: The Fischer exact test to show nitrofurantoin susceptibility amongst fluoroquinolone-resistant isolates

<table>
<thead>
<tr>
<th>Variables</th>
<th>Fluoroquinolone resistant</th>
<th>Fluoroquinolone sensitive</th>
<th>Marginal row totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrofurantoin resistant</td>
<td>17</td>
<td>0</td>
<td>17</td>
</tr>
<tr>
<td>Nitrofurantoin sensitive</td>
<td>41</td>
<td>107</td>
<td>148</td>
</tr>
<tr>
<td>Marginal column totals</td>
<td>58</td>
<td>107</td>
<td>165 (Grand Total)</td>
</tr>
</tbody>
</table>

The Fischer exact test statistic value is <0.00001. The result is significant at $P < 0.05$.

### Table 2: The Fischer exact test to show nitrofurantoin susceptibility among cotrimoxazole resistant isolates

<table>
<thead>
<tr>
<th>Variables</th>
<th>Cotrimoxazole resistant</th>
<th>Cotrimoxazole sensitive</th>
<th>Marginal row totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrofurantoin resistant</td>
<td>17</td>
<td>0</td>
<td>17</td>
</tr>
<tr>
<td>Nitrofurantoin sensitive</td>
<td>37</td>
<td>128</td>
<td>165</td>
</tr>
<tr>
<td>Marginal column totals</td>
<td>54</td>
<td>128</td>
<td>182 (Grand Total)</td>
</tr>
</tbody>
</table>

The Fischer exact test statistic value is <0.00001. The result is significant at $P < 0.05$.

### Table 3: The fischer exact test to show nitrofurantoin susceptibility amongst carbapenem-resistant isolates

<table>
<thead>
<tr>
<th>Variables</th>
<th>Carbapenem resistant</th>
<th>Carbapenem sensitive</th>
<th>Marginal row totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrofurantoin resistant</td>
<td>12</td>
<td>5</td>
<td>17</td>
</tr>
<tr>
<td>Nitrofurantoin sensitive</td>
<td>17</td>
<td>148</td>
<td>165</td>
</tr>
<tr>
<td>Marginal column totals</td>
<td>29</td>
<td>153</td>
<td>182 (Grand Total)</td>
</tr>
</tbody>
</table>

The fischer exact test statistic value is <0.00001. The result is significant at $P < 0.05$.  

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Gram-Negative. Majority of the nitrofurantoin-resistant isolates were Klebsiella pneumonia (8 out of 17, i.e., 47.05%). All nitrofurantoin resistant isolates were sensitive to Colistin and Tigecycline. 5 out of 17 Nitrofurantoin resistant isolates were sensitive to Meropenem and Imipenem (29.41%). The Fischer exact test reveals that Nitrofurantoin is effective against the isolates resistant to Fluoroquinolones, Cotrimoxazole, and Carbapenems.

Nitrofurantoin is a cost-effective treatment option for uncomplicated UTI. It is an oral drug which can even be used in pregnancy especially in the first trimester. However, it is contraindicated against Proteae group of bacteria and not very much effective against urease-positive bacteria as they are urinary alkalizer. The present study establishes the fact that the majority of the organisms causing uncomplicated UTI are sensitive to Nitrofurantoin. Among 165 isolates, only 17 were resistant to Nitrofurantoin (10.30%) and resistance to quinolone (Ciprofloxacin) was in 58 isolates (35.15%). Resistance against Cotrimoxazole was in 37 isolates (22.42%) and Resistance against Carbapenem antibiotics (Meropenem) was found in 29 isolates (17.57%). In this study, all of the Nitrofurantoin resistant bacteria were Gram-negative and Klebsiella pneumoniae was found to be most commonly resistant (47.05%). The Fischer exact test reveals the fact that in statistically significant level, Nitrofurantoin is effective in vitro against the isolates resistant to Fluoroquinolones, Cotrimoxazole and Carbapenems. All these findings in our antimicrobial resistogram corroborate with the work of Awari et al. (2013). In a study conducted by Razak et al. (2012) in south India, it has been reported that most of the uropathogens are susceptible to Nitrofurantoin, i.e. 81.92% of isolated E. coli were sensitive to Nitrofurantoin.

There is a scarcity of data in medical literature about the sensitivity of Gram-positive organisms to Nitrofurantoin. However in the study of Bhattacharyya et al. in Kolkata, no Nitrofurantoin resistant Enterococcus spp. was reported and two intermediately sensitive Enterococcus spp. were detected (determined by VITEK 2-AES system).

The study is a descriptive cross-sectional one which lacks temporality as well as analytical and comparative aspects. Moreover, all the findings are based on in vitro testing. Randomized control trial would provide stronger evidences with in vivo findings. However, this study is one of a kind to reevaluate an age-old yet cost-effective drug to manage one of the common infectious syndromes.

CONCLUSION

Hence, this study estimates the fact that nitrofurantoin, although an older option to manage uncomplicated UTI, is quite effective till date. Thus nitrofurantoin may be preferred as the drug of choice over fluoroquinolones or cotrimoxazole for empirical therapy to treat uncomplicated UTI even today. There was no conflict of interest.

REFERENCES


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