Original Research Article

Nitrofurantoin Susceptibility in Urinary Tract Infections (UTIs) in an Era of Drug Resistance

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ABSTRACT

UTI are the most common bacterial infections that account for significant morbidity and health care cost world-wide. The most profound advance in the management of UTIs has been the introduction of antimicrobial agents. An old drug Nitrofurantoin has increased as a solution to the ever increasing menace of antimicrobial resistance. In this study, we studied the susceptibility pattern of Nitrofurantoin to the common uropathogens. Study was conducted from January 2015 to December 2015 in VIMS hospital Ballari. All the urine isolates are subjected to susceptibility for Nitrofurantoin and results were interrupted. Among 1372 urinary isolates, 86.7% of E.Coli, 89.9% of S.aureus, 92.3% of Enterobacter spp, 88.6% of Klebsiella spp, 90% of Enterococcus were susceptible to Nitrofurantoin. Overall Nitrofurantoin showed 89.3% of susceptibility and 10.7% of resistance in urinary isolates. In this study nitrofurantoin showed 89.3% of susceptibility to the most common urinary isolates. Nitrofurantoin should be considered as an acceptable treatment for uncomplicated UTIs and should be considered the first line treatment.

Keywords
Urinary tract infection(UTI), Nitrofurantoin, antimicrobial susceptibility pattern, uropathogens, antimicrobial resistance.

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Introduction

UTI are one of the most common bacterial infections among the community and hospital acquired infections (Alicem Tekin et al., 2012). Worldwide about 150 million people are being diagnosed with urinary tract infection every year (Manikandan et al., 2011). Approximately 95% cases of UTIs are bacterial in origin (Bonadio et al., 2001). Today inappropriate use of antibiotics has led to increasing resistance rates of Gram negative bacteria against standard antibiotics (Alicem Tekin et al., 2012). With the ever increasing menace of antimicrobial resistance, an old drug Nitrofurantoin has increased as a solution. Among susceptible uropathogens after extensive use worldwide for >50 years, there has been virtually no acquired resistance to Nitrofurantoin (Rizvi et al., 2011).

Treatment of uncomplicated UTI is not usually problematic, but alarmingly, in the
recent years, the incidence of multi-drug resistant uropathogens has been undergoing a steady and rapid increase (Rizvi et al., 2011). High concentration is achievable in urine makes it an ideal choice for treatment of urinary tract infection (UTI). Nitrofurantoin can be hypothesized to be the best choice for first line empirical treatment. In this study we aim to analyze the susceptibility pattern of most common urinary isolates in patient with UTI.

**Objectives**

To determine the antibiotic susceptibility pattern of Nitrofurantoin among urinary isolates.

**Materials and Methods**

All the urine isolates are subjected to susceptibility for Nitrofurantoin.

Among all the patients in whom urine culture was performed in our laboratory, those showing significant bacteriuria (more than 1,00,000 colony forming units per ml of urine) were included in this study.

The urine cultures were performed from mid stream specimens of urine that were sent to clinical microbiology laboratory. The mid stream specimens of urine were obtained from patients with a preliminary diagnosis of UTIs. The urine specimens were inoculated quantitatively onto 5% sheep blood agar and McConkey agar. Then, media plates were incubated aerobically at 35±2°C for 18-24 hours (Colle et al., 1996).

Antimicrobial susceptibility testing was done by Kirby- Bauer disc diffusion method on Mueller Hinton Starch Casein Hydrolysate Agar. The antibiotic discs were supplied by Hi-Media laboratories Pvt. Ltd. Mumbai, India. The antibiotics used and susceptibility test results were interpreted according to the Clinical Laboratory Standard Institute (CLSI) 2016 guidelines.

**Results and Discussion**

Total number of urine samples tested in the study period were 3251, out of which 1372(42.2%) showed growth of bacteria with significant count. *E.coli*(69.3%) was the commonest organism isolated followed by *Klebsiella spp*(14.2%), *S.aureus*(9.3%), *Enterobacter* (7.6%), *Enterococcus*(4.5%) and others.

Among 1372 urinary isolates, 86.7% of *E.Coli*, 89.9% of *S.aureus*, 92.3% of *Enterobacter spp*, 88.6% of *Klebsiella spp*, 90% of *Enterococcus* were susceptible to Nitrofurantoin.

Overall Nitrofurantoin showed 89.3% of susceptibility and 10.7% of resistance in urinary isolates.

Nitrofurantoin is a broad-spectrum bactericidal antibiotic. Since its discovery in 1952, and its use for more than four decades no clinically significant resistance has developed, as seen with other commonly used antibiotics. This is probably because Nitrofurantoin has multiple sites and levels of action in contrast to antibiotics that attack a single target like ampicillin or two targets like cotrimoxazole. Bacterial nitroreductase enzyme converts nitrofurantoin to highly reactive electrophilic intermediates which non-specifically attack bacterial ribosomal proteins resulting in complete inhibition of protein synthesis (McOsker et al., 1994) and cause single-strand breaks in DNA (McCalla et al., 1970).
Nitrofurantoin is usually well tolerated. Side-effects occur at rates <0.001% (Munoz-Davila, 2014). Nitrofurantoin is active against most common uropathogens including *E. coli, Citrobacter* spp., *Staphylococcus saprophyticus*, and *Enterococcus* spp. whereas, *Enterobacter* spp. and *Klebsiella* spp. are only moderately inhibited, *Proteus* spp., *Providencia* spp., *Morganella morgannii*, *Serratia* spp., *Pseudomonas* spp., and *Acinetobacter* spp. are mostly resistant to nitrofurantoin. Sandegren *et al.* found the mutation frequency to be approximately 10−7/cell for *E. coli*. Mutations in the genes encoding bacterial nitroreductase *nfsA* and *nfsB* were responsible for high-level nitrofurantoin resistance (median MIC of 96 μg/mL) (Sandegren *et al.*, 2008; Whiteway *et al.*, 1998).

Nitrofurantoin is recommended as the first choice for the treatment of uncomplicated cystitis and pyelonephritis in women by Infectious Disease Society of America and the European Society for Microbiology and Infectious Disease (Gupta *et al.*, 2011).

In conclusion, in this study nitrofurantoin showed 89.3% of susceptibility to the most common urinary isolates. Nitrofurantoin should be considered as an acceptable treatment for uncomplicated UTIs and
should be considered the first line treatment. To provide optimum use and to avoid misuse and overuse of this drug, culture and susceptibility testing is the need of the hour.

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