

Sensitivity Pattern of Levofloxacin and Nitrofurantoin in Patients of Urinary Tract Infection in a Tertiary Care Hospital, Jaipur

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ABSTRACT

Background: There has been upsurge in the antibiotic resistance mechanisms in the uropathogens over the years. Fluoroquinolones have gained popularity over time and are being used to treat a number of infections. This study was undertaken to assess the distribution patterns of uropathogens and their sensitivity towards levofloxacin and nitrofurantoin.

Method: A total of 628 urinary pathogens were isolated from the month of June 2018 to December 2018. A semi quantitative method was taken on for the primary isolation of organisms using a calibrated loop which delivers 0.01 ml of urine onto Blood agar and MacConkey agar media plates. The plates were then incubated at 37°C overnight. Samples with a colony count of $\geq 10^5$ cfu/ml were considered with significant bacteriuria. The final identification of the organism and its antibiotic susceptibility testing was done on Vitek 2 Compact™ (Biomerieux, France).

Result: In this study we isolated 73.5% (462) Gram Negative Bacilli, while 13.69% (86) were Gram Positive Cocci isolates and 12.7% (80) were *Candida* isolates. *E. coli* was the predominantly isolated organism (48.40%) followed by *Klebsiella pneumoniae* (10.82%) and *Enterococcus faecalis* (5.73%). Levofloxacin was found to be 20.98% sensitive for Gram Negative Bacilli while it was sensitive for 20.93% of the Gram Positive Cocci isolates. Nitrofurantoin showed a sensitivity rate of 65.70% for Gram Negative Bacilli and 72.09% for Gram Positive Cocci isolates.

Conclusion: Increasing prescription of fluoroquinolones has resulted in the drugs like levofloxacin and nitrofurantoin losing their effectiveness. The data in this study shows high resistance pattern to second generation

fluoroquinolones and increasing resistance to nitrofurantoin.

Keywords: Fluoroquinolones, levofloxacin, nitrofurantoin, Uropathogens, E.coli

INTRODUCTION

The American National Institute for Health and Clinical Excellence (NICE) defines UTI as a combination of clinical features (urinary tract symptoms) and the presence of bacteria in urine. ⁽¹⁾ Urinary tract infections can be classified into complicated or uncomplicated and acute or recurrent. The symptoms of UTI vary from mild asymptomatic cystitis to pyelonephritis and septicemia. Infections of the urinary tract are among the most common bacterial infections and have become increasingly common occurring in people of all ages as well as in all ethnic groups affecting approximately 150 million people every year throughout the world. Among the UTI cases, approximately, 35% are nosocomial infections in origin. ⁽²⁾

One of the major barriers to medical management of UTIs is the increasing rate of multidrug resistance. Therefore, empirical antibiotics should be selected based on the knowledge of the prevailing local resistance pattern from time to time in the given region. ⁽³⁾

Gram-negative organisms are the most common pathogens involved in UTI, but almost all known pathogens have been incriminated as possible causative agents. ⁽⁴⁾ The distribution of uropathogens and their susceptibility pattern to antibiotics vary

regionally with time. The most prevalent facultative gram-negative bacillus involved in causation of UTIs is *Escherichia coli*. It usually inhabits the colon as an innocuous commensal and is incriminated as being the principal pathogen both in the community as well as in the hospital. (5) Fluoroquinolones (FQs) are broad spectrum antibiotics widely used for the treatment of numerous diseases and has broad acceptance in hospitalized and community patients. They are also commonly prescribed for empirical treatment of UTI because of high bactericidal rates as well as low rates of resistance among uropathogens Over-prescription of the drug has led to their increasing resistance worldwide in recent years, especially in gram-negative bacteria. (6) The resistance in their mechanism of action occurs through multiple mechanisms including chromosomal point mutations in the genes encoding DNA gyrase and/or topoisomerase iv, mutations that cause decreased expression of outer membrane proteins (OMPs), alterations in the lipopolysaccharide (LPS) component of the cell envelope, and enhanced fluoroquinolone efflux by efflux pumps such as AcrAB.

Nitrofurantoin is a synthetic antibacterial, nitrofuran derivative available since World War II that has been categorized as a grade A-I antibiotic in the treatment of UTIs as per the IDSA guidelines. The major strength of nitrofurantoin is its action at multiple sites and levels which helps the drug in maintaining an excellent level of sensitivity over the years besides being well tolerated for the treatment of acute uncomplicated cystitis. (7)

The drug has natural resistance towards *Morganella sp.*, *Proteus spp.* And *Providencia spp.* (8)

Levofloxacin, belonging to the secondary generation fluoroquinolone, is a widely prescribed fluoroquinolone approved for the treatment of complicated urinary tract infections and acute pyelonephritis. The activity profile of levofloxacin is broad

spectrum demonstrating excellent in vitro activity against most aerobic Gram-positive and Gram-negative pathogens.

MATERIALS AND METHODS

Mid stream clean catch fresh samples were collected through aseptic measures in a sterile, wide mouth, leak proof, labeled universal container. A semi quantitative method was taken on for the primary isolation of organisms by using a calibrated loop with diameter of 4 mm, delivering 0.01 ml of urine. Samples were then cultured on Blood agar and MacConkey agar media plates and incubated at 37°C overnight.

Samples with a colony count of $\geq 10^5$ cfu/ml were considered with significant bacteriuria. (9)

The primary identification was made with basic microbiological methods using colony morphology and Gram staining. The final identification of the organism and antibiotic sensitivity pattern were done on an auto-analyzer system (bioMérieux, VITEK 2 Compact™).

Nitrofurantoin is not included in the Non Fermenter panel of Vitek 2 AST Card (AST N364, Vitek 2 Compact™, Biomerieux)

RESULTS

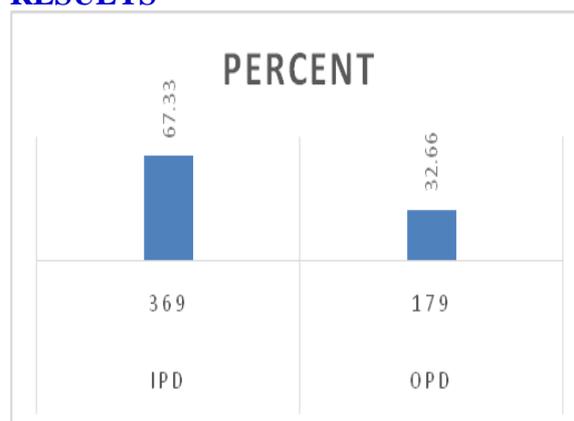


Fig 1: Location wise distribution

A total number of 628 positive urine culture were included in the present study, out of which 67.33% were IPD patients and 32.66% were isolated from OPD (Fig 1). During the study period, 48.09% of the patients were male and 51.09% were female

(Fig 2). 462 (73.5%) of the isolates were Gram Negative Bacilli, 86 (13.69%) were Gram Positive Cocci while 80 (12.7%) of the isolates were Candida (Fig 3). *E. coli* was the predominantly isolated organism (48.40%) followed by *Klebsiella pneumoniae* (10.82%) and *Enterococcus faecalis* (5.73%).

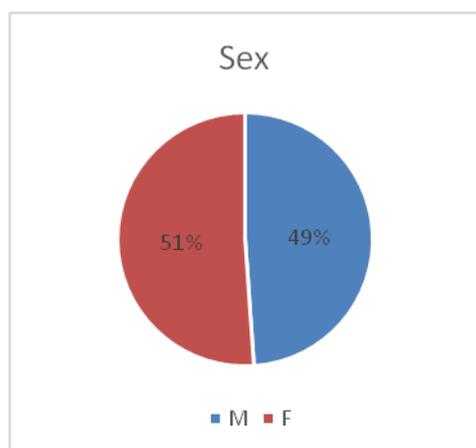


Fig 2: Sex wise distribution

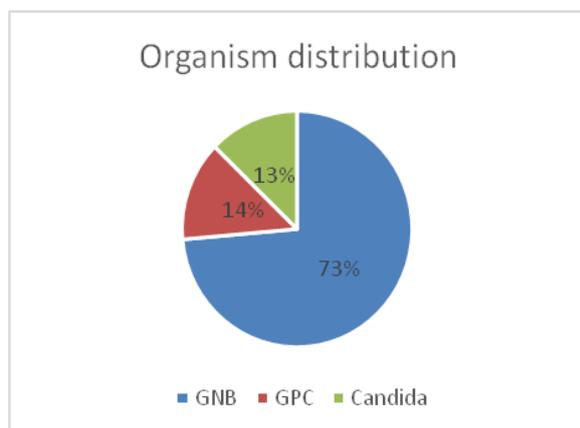


Fig 3: Organism group wise distribution

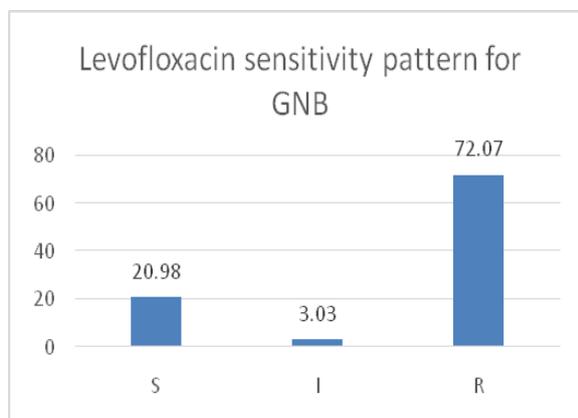


Fig 4: Levofloxacin sensitivity for Gram negative bacilli

Levofloxacin was sensitive for 20.98% of the Gram Negative Bacilli (Fig 4) and 20.93% of the Gram Positive Cocci (Fig 5). Nitrofurantoin was observed to be sensitive for 65.70% of Gram Negative Bacilli (Fig 6) and 72.09% (Fig 7) of the Gram Positive Cocci. 2.55% and 14.34% fell into the intermediate category for levofloxacin and nitrofurantoin respectively.

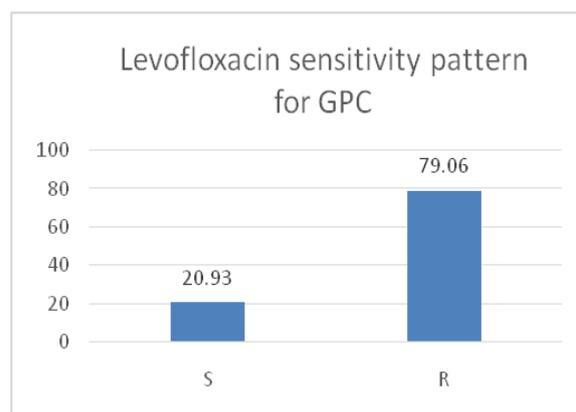


Fig 5: Levofloxacin sensitivity pattern for Gram positive cocci

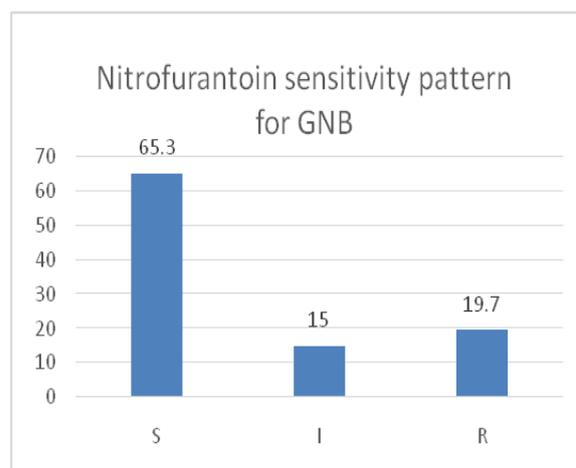


Fig 6: Nitrofurantoin sensitivity pattern for Gram negative bacilli

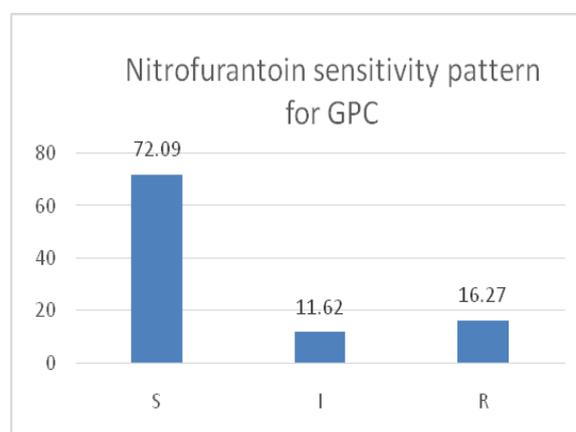


Fig 7: Nitrofurantoin sensitivity pattern for Gram positive cocci

DISCUSSION

UTI is a recurrent problem that continues to present a problem due to changes in aetiology and antibiotic susceptibility patterns over the years.

Gram Negative Bacilli are the most commonly isolated urinary pathogens accounting for significant morbidity and increased healthcare costs. (10)

Even though fluoroquinolones are considered among the most effective drugs in the treatment of UTI, there has been a notable increase in resistance with patient age because of decreased immune function and overall more frequent fluoroquinolones exposure as compared to the younger patients. Milan et al noted the abusive and anarchic use of fluoroquinolone as the probable leading factor for the high percentage of resistance. (11)

Among monomicrobial growths with significant bacteriuria, the predominantly isolate to be identified was *E.coli* constituting 48.40% in the present study. The incidence of *E. coli* as a causative pathogen in India varies from 48% to 65% as reported by studies conducted by Farrell et al and Hasan et al. (12, 13)

Following this was *Klebsiella pneumoniae*, constituting 10.82% of the isolates. Similar rates of *Klebsiella spp* were isolated in urine sample of patients from many developing countries in studies conducted by Chen et al and Lina et al. (14, 15)

10.94% of the isolates from this study were not tested for Nitrofurantoin. These included *Pseudomonas spp.* and *Acinetobacter spp.* amongst others.

In this study we observed a resistance rate of 73.17% for levofloxacin. The findings were similar to that done by T. Gururaju et al. (16) and Lehasab W et al. (17)

Nitrofurantoin has proved to be a cost effective oral drug with good patient compliance. The advantage with nitrofurantoin is that it is both bactericidal and bacteriostatic and does not offer any cross resistance with other antibiotics. Hence, the development of resistance or

resistant mutants is comparatively slower. According to our study, nitrofurantoin has better antimicrobial properties in Gram Positive Cocci than in Gram Negative Bacilli. We observed an overall sensitivity of 63.70%. This is unlike other studies that have been conducted previously by Shanthi et al and Mariraj et al (18, 19) where 80-90% sensitivity to nitrofurantoin has been observed.

CONCLUSION

A constant surveillance is essential to monitor resistance mechanisms to the commonly used antibiotics for these organisms. A conscientious and methodical knowledge of the prevalence of these uropathogens and resistance patterns is required to decide on an empirical therapy for the same.

Conflict of interest: NA

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