Abstract:
Urinary Tract Infection (UTI) is the third most common cause of hospital visits in our country. The emergence of drug resistance among uropathogens is constantly increasing. The antimicrobial agent, Nitrofurantoin was used extensively to treat the UTIs. The use of this drug has gradually declined in recent years, not because of treatment failure but because of lack of interest and the development of many newer drugs in treating UTIs. So the aim of the study is to determine the sensitivity profile of Nitrofurantoin among urinary isolates of UTI in indoor and outdoor patients at CMCH, Coimbatore, to find out the commonest isolates causing UTI and to assess the role of Nitrofurantoin in the treatment of UTI.

MATERIALS AND METHODS
Three hundred and twenty six clean catch mid stream urine samples received in diagnostic Microbiology laboratory, CMCH were taken and processed for this study over a period of three months (June 2011 August 2011). RESULTS The most common bacterial isolates were E.coli (52) followed by Coagulase negative staphylococci - Staphylococcus saprophyticus (25), the overall sensitivity profile of Nitrofurantoin among urinary isolates was 83.3. E.coli and CONS showed sensitivity to Nitrofurantoin of 98.5 and 100 respectively.

CONCLUSION Nitrofurantoin showed highest in vitro sensitivity among most commonly isolated uropathogens. Being the cheapest drug with minimal side effects, showing good safety profile and highest sensitivity profile in almost all age groups including pregnant women and children with UTI, Nitrofurantoin can be prescribed for the empirical treatment of UTI in place of other drugs such as cotrimoxazole, ciprofloxacin and cephalaxin.

Keyword: UTI, NITROFURANTOIN

INTRODUCTION:
Urinary tract infection represents one of the most common diseases encountered in medical practice today and occurring from the neonate to the geriatric age group. The incidence of UTI is greater in women as compared to men who may be either due to
Anatomical predisposition or urothelial mucosa adherence to the mucopolysaccharide lining or other host factors. It is estimated that about 20 - 30% of adult women experience UTI once during their life time. Escherichia coli is the most frequent urinary tract pathogen isolated from 50 to 90% of all uncomplicated urinary tract infections. UTIs may involve only the lower urinary tract or may involve both the upper and lower tract (Akram et al., 2007). Antibiotic resistance may develop in uropathogen due to frequent misuse of antibiotics. Factors such as the patients’ population, extensive use of antimicrobial agents, could contribute to change in microbial profile of urinary tract isolates (Gales et al., 2005). Since pattern of antibiotic resistance in a wide variety of pathogenic organisms may vary, periodic evaluation of antibacterial activity is needed to update information (Gupta et al., 2002).

Nitrofurantoin belongs to the family Nitrofurans. Chemically it contains 5 nitro 2 furaldehyde derivative in which the 5 nitro group is responsible for the antimicrobial activity. Nitrofurantoin is a yellow coloured compound which is highly active at acid pH and in undissociated form. The drug is converted into highly reactive intermediates within bacterial cells by reductases. Nowadays, the majority pathogens isolated from urine are resistant to commonly used antibiotics and the first choice of an antimicrobial agent for empiric treatment of paediatric urinary tract infections (UTIs) is not well established (Tseng et al., 2008). Antibiotics are usually prescribed empirically before the laboratory results of urine culture are available. For better decision-making, physicians need more information about local susceptibility pattern of uropathogens. Therefore the aim of this study is to determine the etiologic agents of (UTIs), their antibiotic susceptibility pattern with special reference to Nitrofurantoin in outpatients and inpatients in CMCH, Coimbatore and to assess the role of Nitrofurantoin in the treatment of UTI.

MATERIALS AND METHODS:
Three hundred and twenty six clean catch mid stream urine samples of outpatients and inpatients from all age group and both sexes were taken for this study over a period of three months (June 2011 – August 2011) at diagnostic Microbiology laboratory, CMCH, Coimbatore.

With standard calibrated loop delivering 0.01 ml of urine was inoculated on MacConkey agar plate, blood agar plate and incubated aerobically at 37°C for 18-24 h. After incubation, if the CFU is more than 10^5, it was considered as significant bacteriuria and such urine samples further processed for identification and antibiogram of bacterial pathogen. Identification of bacterial pathogens was made on the basis of gram reactions, morphology and biochemical characteristics. Isolates were tested for antimicrobial susceptibility pattern of Nitrofurantoin by disc diffusion technique on Mueller Hinton agar (CLSI method, 2007) using the ready made antibiotic disc (300 µg) supplied by Hi-media Ltd, Mumbai.

RESULTS:
A total of 326 urine samples were analyzed for isolation and identification of bacterial isolates as per standard methods. Out of 126 cultural isolates, the most common uropathogen was E.coli – 65 (51.6%), followed by CONS - 28 (22.2%). The less common isolates were Entebacter species- 1 (0.7%) and Pseudomonas aeruginosa – 3 (2.4%). The remaining isolates were Klebsiella pneumoniae 17 (13.5%), Proteus mirabilis 8 (5.6%) and Enterococci spp 4 (3.2%). (Table 1 & Figure 1.1)
The sensitivity profile for Nitrofurantoin is given in the Table 1. & Figure 1.2. The highest sensitivity was shown by the Gram positive isolates, the CONS 28/28 (100%) and Enterococci 4/4 (100%) followed by Gram negative isolates, E.coli 64/65 (98.5%) and Proteus mirabilis 4/8 (50%), accounted for 85% of the total isolates. The lowest sensitivity for Nitrofurantoin was shown by Pseudomonas aeruginosa 0/3 (0%), Enterobacter spp 0/1 (0%) and Klebsiella 5/17 (30%), accounted for 15% of total isolates.

**DISCUSSION:**

In the present study E.coli was found to be the most common isolate 65/126 (51.6%) among all uropathogens. This was similar to the study conducted by Biswas D et al (67.7%) 2006 at Dehradun, India and various other studies world wide.7,8,9 In Biswas D et al study the next common isolate was CONS (17.9%), followed by Klebsiella pneumoniae (7.8%). In this study also same results were obtained, the next common isolate was CONS 28/126 (22.2%) followed by Klebsiella pneumoniae 17/126 (13.6%). The remaining isolates were Proteus mirabilis 8 (5.6%), Enterococci spp 4 (3.2%), Enterobacter species- 1 (0.7%) and Pseudomonas aeruginosa – 3 (2.4%)

<table>
<thead>
<tr>
<th>ISOLATE</th>
<th>NUMBER (%)</th>
<th>NIT SENSITIVITY (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>E.coli</td>
<td>65 (51.6)</td>
<td>64 (98.5)</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>17 (13.5)</td>
<td>05 (30.0)</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>08 (05.6)</td>
<td>04 (60.0)</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>03 (02.4)</td>
<td>00 (00.0)</td>
</tr>
<tr>
<td>Enterobacter spp</td>
<td>01 (0.7)</td>
<td>00 (00.0)</td>
</tr>
<tr>
<td>CONS (Staph saprophyticus)</td>
<td>28 (22.2)</td>
<td>28 (100)</td>
</tr>
<tr>
<td>Enterococci</td>
<td>04 (03.2)</td>
<td>04 (100)</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>126 (38.7)</strong></td>
<td><strong>105 (83.3)</strong></td>
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</table>
In this study, among Gram negative isolates, E.coli showed the highest sensitivity pattern (98.5%) for Nitrofurantoin which was supported by all other studies carried out in various parts of the world where sensitivity rates ranging from 98.3% to 99.9% \(8, 9, 10, 11, 13, 14\). In the present study, Staphylococcus saprophyticus and Enterococcus species showed 100% sensitivity to Nitrofurantoin as had been observed by other studies (99.93% - 100%) \(8, 9, 13, 14\). The overall sensitivity of Nitrofurantoin among all the isolates was 85% which was similar to the Biswas D et al study (85.1%).

The most suited antibiotic for empirical therapy should have low resistance rates, achieve significant urinary concentrations, be cost-effective, be free of adverse effects and satisfy patient compliance. Regarding the acceptable resistance rates, the Infectious Diseases Society of America recommends an antibiotic for empirical therapy only if <10-20% of the urinary pathogens are resistant to it. \(13\) Here in this study, Nitrofurantoin fulfilled these criteria with resistance rate for all isolates about 15%.

Nitrofurantoin is bactericidal in urine at therapeutic doses, and its multiple mechanisms of action appear to have enabled it to retain potent activity against E. coli despite nearly 50 years of use \(17\). The consistent and high-level susceptibility of E. coli to Nitrofurantoin may be influenced by Nitrofurantoin's narrow spectrum of activity, limited indication (treatment of acute cystitis), narrow tissue distribution (low or undetectable serum concentrations), and limited contact with bacteria outside the urinary tract. \(10, 18\)

CONCLUSION:
In conclusion, the present study suggests that Nitrofurantoin would be a best alternative drug for empirical therapy for all forms of UTI in all age groups including pregnant women & children (except in <2 months of age group in children and in last few weeks of pregnancy where it may induce haemolysis). It is also a cost effective drug with low resistance rate, achieves high urinary concentration with limited tissue distribution (not distributed outside the urinary tract), satisfies patient compliance and to be considered as a better alternative for treatment of UTI in developing country like India. However, though most of the isolates from complicated UTI were also susceptible to the drug in vitro in this study, the in vivo sensitivity should be further studied in such cases of complicated UTIs.

REFERENCES:


