The Resistance Pattern of *Escherichia coli* to Trimethoprim in a tertiary care hospital

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**ABSTRACT**

To study the resistance pattern of *Escherichia coli* to trimethoprim. Culture and sensitivity reports enrolling 464 number of patients over a period of one year was studied at Bhaskar Medical College. Cases which were culture positive for *Escherichia coli* were identified and their resistance pattern to trimethoprim was assessed. Out of 44 strains of *Escherichia coli* which were isolated 43 were resistant to trimethoprim and only one strain was sensitive to trimethoprim. *Escherichia coli* is more resistant to trimethoprim than other drugs like Levofloxacin, Nitrofurantoin, Amikacin, Gentamicin.

**Keywords:** Escherichia coli, Resistance, Trimethoprim

**INTRODUCTION**

Trimethoprim belongs to the class of chemotherapeutic agents known as dihydrofolate reductase inhibitors. Trimethoprim is a bacteriostatic antibiotic mainly used in the prophylaxis and treatment of urinary tract infections. This drug was developed by George H. Hitchings and collaborators who shared the nobel prize for Medicine in 1988 for the discovery of antifolates.

Trimethoprim acts by interfering with the action of bacterial dihydrofolate reductase, inhibiting synthesis of tetrahydrofolic acid. Tetrahydrofolic acid is an essential precursor of DNA metabolite Thymidine triphosphate. Bacteria are unable to take up folic acid from the environment and are thus dependent on their own denovo synthesis. Inhibition of the enzyme starves the bacteria of nucleotides necessary for DNA replication causing, in certain circumstances, cell lethality due to thymineless death. Trimethoprim was commonly used in a 1:5 combination with sulfamethoxazole, a sulphonamide antibiotic, which inhibits an earlier step in the folate synthesis pathway.

This combination, also known as co-trimoxazole, TMP-sulfa, or TMP-SMX, results in an in vitro synergistic antibacterial effect by inhibiting successive steps in folate synthesis.[1,2]

The combination’s use has been declining due to reports of sulfamethoxazole bone marrow toxicity, resistance and lack of greater efficacy in treating common urine and chest infections, and side effects of antibacterial sulfonamides.[3,4] As a consequence, the use of co-trimoxazole was restricted in 1995 following the availability of trimethoprim.[5] Trimethoprim used as monotherapy, is indicated for the prophylaxis and treatment of urinary tract infections.
Trimethoprim can cause thrombocytopenia by lowering folic acid levels; this may also cause megaloblastic anemia. Trimethoprim antagonises the epithelial sodium channel in the distal tubule, thus acting like amiloride, which can cause hyperkalemia.

**MATERIAL AND METHODS**

The study was conducted for a duration of one year from March 2011 to February 2012 at Bhaskar Medical College, India. A total number of 464 patients were included in the study. The urine, pus or blood samples of these patients were collected. The urine and pus samples on reaching the laboratory were inoculated on Macconkey agar, Blood agar, and Nutrient agar to isolate the organisms.

The inoculated Blood agar and Nutrient agar plates were incubated aerobically at 37°C for 24 hours. After overnight incubation at 37 degrees C the Blood agar and Macconkey agar plates were examined for evidence of growth. The colony characters were studied, smears were stained by Grams' stain and examined under the 100X objective. The bacterial species then isolated were identified by morphology, cultural characteristics and biochemical reactions according to the standard techniques. The Gram negative bacilli identified were tested for motility by hanging drop and then they were subjected to biochemical and sugar fermentation tests. The tests were read after incubation at 37 degrees C at the end of 24 hrs and 48 hrs. Gram Negative lactose fermenting bacilli were classified on the basis of motility, fermentation of sugars, indole production, methyl-red reaction, and Voges--Proskauer test and utilisation of citrate in to Escherichia coli, Klebsiella.

*Escherichia coli* produced pink, smooth, irregular colonies on Macconkey agar
Klebsiella species produced pink, smooth and mucoid colonies.
44 strains of *Escherichia coli* were obtained comprising of 36 from urine samples, 5 from pus, and 3 from blood culture. The blood samples were inoculated in brain heart infusion broth.

**SENSITIVITY TESTS**

The sensitivity pattern was tested using Kirby Bauer disk diffusion method. The antibiotics used were amikacin, Levofoxacin, Nitrofurantoin, Gentamicin, Norfloxacin, Ciprofloxacin, Ofloxacin, Cefotaxime, Trimethoprim, Cefixime.

**RESULTS**

A total of 464 patients were included in the study. The Positive cultures for *Escherichia coli* were 44. Out of the 44 strains of *Escherichia coli* isolated 43 strains were resistant to trimethoprim, only one strain was found to be sensitive to trimethoprim.
DISCUSSION

Trimethoprim is used in the treatment of most genito urinary pathogens, enteropathogens, including enterotoxigenic Escherichia coli, shigella species and Salmonella typhi, in respiratory infection, in the prophylaxis and therapy of Pneumocystis carinii pneumonia (PCP) in immunosuppressed patients, particularly in those with HIV virus and in various miscellaneous infections like brucellosis, malaria, leishmaniasis and in CNS infection especially meningitis resulting from Streptococcus pneumoniae, Neisseria meningitides, and Haemophilus influenzae.

Clinically important trimethoprim resistance is uncommon, and development of resistance during therapy is rare. In hospitalized transplant patients receiving trimethoprim prophylaxis, 39% of the faecal isolates have proved resistant to the drug.[6]

Resistance depends on several potential mechanisms. The intrinsic resistance of bacteria may be related to the bacterial cell wall’s relative impermeability to trimethoprim.[7] Mutant organisms resistant to trimethoprim can be produced in a heavy inoculum in media that contain increasing trimethoprim concentrations. The addition of a sulphonamide sometimes prevents the development of trimethoprim resistance in this setting. Resistance can also be due mutants that have lost the capacity to synthesize thymidine and are dependent on exogenous sources of the nucleoside.[8] Perhaps the mechanism of greatest clinical importance is the production of plasmid-derived TMP-resistant forms of dihydrofolate reductase.[9]

REFERENCES


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