Multidrug-Resistant Organisms in Catheter-Associated Urinary Tract Infection

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ABSTRACT

Objective

To assess the multidrug-resistant organisms (MDROs) in catheter-associated urinary tract infections (CAUTI) in a tertiary care hospital.

Methodology

10-15ml of midstream urine was collected directly from the indwelling catheters of 52 catheterized patients at allied hospitals of Peshawar Medical College from November 2021 to March 2022 and was processed at the Microbiology Laboratory Peshawar Medical College. Wet preparations were examined under a light microscope for pus cells, red blood cells, and bacteria and the findings were recorded. The standard loop technique was used to inoculate urine specimens on MacConkey and blood agar plates and were incubated for 24 hours at 37°C. A colony count of 10^5 cfu/ml was thought to be significant. Gram staining of the colonies was performed. A number of biochemical tests were performed on API 10S system for bacterial identification. The Kirby-Bauer disc diffusion method was next used to test antibiotic susceptibility on Mueller-Hinton agar according to CLSI guidelines. For statistical analysis, statistical software for the social sciences (SPSS) version 20.0 was utilized.

Results

Out of a total of 52 urine samples 86.5% samples had positive microbial growth. In vitro Nitrofurantoin was the most effective oral antibiotic (65% of MDROs were sensitive), whereas Meropenem and Gentamycin were the most effective parenteral antibiotics (77.7% and 64.4% of MDROs were sensitive, respectively).

Conclusion

Surprisingly, only nitrofurantoin was found to be advised orally as a suitable drug for the treatment of CAUTIs among the 13 commonly used antibiotics.

Key words: MDRO, CAUTI, antibiotic susceptibility.

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INTRODUCTION

Urinary catheters have been in use to relieve urinary retention in men since 3000 B.C. In Greek language, the word catheter comes from the term "kathie´nai", which means ''to thrust into''. Initially the catheters were rigid and used as per requirement. In 18th century urinary catheters were prepared from rubber material. Later on, indwelling catheters were introduced and the rubber material was replaced by latex, polyurethane and later silicone.[1] Although the use of urinary catheters has favourably transformed healthcare by improving the quality of life of chronically debilitated patients, but it has also increased the risk of urinary tract infections (UTIs) in such patients.[2] Catheterization is one of the major causes of hospital-acquired UTIs (HA-UTIs). As around 25% of hospital admissions have an indwelling catheter, approximately 70-80% of HA-UTIs are catheter-related. Not only are catheterized patients at risk for CAUTI, but they also have a bleak prognosis.[3]

Catheter-associated urinary tract infection (CAUTI) is a UTI that develops after 48 hours of insertion of an indwelling urinary catheter.[4] Studies have shown that indwelling urinary catheterization elicits histological and immunological changes in the urinary bladder, which leads to robust inflammatory response, edema and mucosal lesions of the bladder epithelium and even affects the kidneys.[5] It is also understood that CAUTI is due to a mix of internal microbiota and external pathogens during insertion of the catheter when aseptic conditions are not met.[6]

Prolonged use of antibiotics in UTIs leads to damage to periurethral flora and colonization by uropathogens. The main issue related to UTI treatment is the development and spread of multidrug-resistant organisms (MDROs), leaving limited therapeutic alternatives for clinicians. [7,8] The spread of MDROs is now becoming a global health issue, prevailing in both community

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and hospital-acquired infections. Widespread use of cephalosporins and quinolones, especially in developing countries, has contributed greatly to the spread of MDROs.[9]

MDROs were formally defined in 2010, as those bacteria that show in vitro resistance to two or more classes of antimicrobials.[10] It is currently defined as in vitro resistance to at least one antimicrobial in three or more antibiotic classes. High levels of antibiotic resistance has been reported for Gram-negative bacteria in communities where no restrictions are in place on the purchase and injudicious use of antibiotics, leading to emergence of drug resistance and therapeutic failures.[11] It is of special concern in patients with some underlying conditions such as weakened immune system, prolonged hospitalization, intensive care units (ICUs), chronic diseases, and catheterization.[12-14]

Irrational use of antibiotics, unethical healthcare practices, and improper prescription in selection of antibiotics, unreasonable duration and inadequate dosage in empirical treatment, mostly in developing countries, expedites emergence of MDROs.[15] The global spread of bacterial resistance to last-line antibiotics such as carbapenems is increasing the risk of resurgence of pre-antibiotic era. As the development of new effective drug usually takes a decade, it is important to optimize the use of currently available repertoire of antibiotics.[16]

METHODOLOGY

It was a Cross-sectional study. Ethical approval was sought from and granted by the Institutional Review Board of the Prime Foundation. The urine samples of patients having an indwelling urinary catheter in place for at least 48 hours were collected. While the patients having an indwelling catheter for less than 48 hours or who have already started antibiotics were excluded from the study. Samples were collected from Prime teaching hospital, Mercy teaching hospital, and Kuwait teaching hospital. The samples were processed at the Microbiology laboratory of Peshawar Medical College. A total of 52 samples were collected fulfilling the inclusion and exclusion criteria. Non-probability convenience sampling was performed. Further, 10-15ml of urine was collected in a priorly labeled sterile container directly from the Foley catheter.

Uropathogen isolation & identification:

Urine microscopy for pus cells, red blood cells, and bacteria was performed after centrifugation of the urine samples. The standard loop technique was used for inoculation of urine on MacConkey and Blood agar plates and were incubated at 37^{o}C for 24 hrs. A colony count of ≥10_5cfu/ml was considered significant.[17] Gram staining of the colonies was performed. The biochemical tests such as oxidase, citrate, urease, indole, methyl red, and Voges Proskauer tests were conducted on API 10S.

Antibiotic susceptibility:

The Kirby-Bauer disc diffusion method was used to test antibiotic susceptibility on Mueller-Hinton agar. Nitrofurantoin, ciprofloxacin, levofloxacin, ceftriaxone, ceftazidime, cefepime, cefotaxime, gentamycin, meropenem, trimethoprim sulfamethazine, amoxicillin/clavulanic, aztreonam, and penicillin sensitivity discs (provided by Becton, Dickinson and Company) were used for the determination of antibiotic susceptibility according to Clinical and Laboratory Standards Institute (CLSI: M100) 2021 guidelines.

The statistical program for the social sciences (SPSS) version 20.0 was used for the analysis. A Fisher's Exact test was applied. P-value<0.05 was taken as significant.

RESULTS

Table1 shows the distribution of CAUTI patients with respect to age and gender. The mean age in males was 44.5±15.5 and the mean age for females was 40.4±11.8. Among 52 catheterized patients, 18 were male patients and 34 were female patients. The frequency of UTIs in female patients was more as compared to males.

Gender	Mean age (years) with Standard deviation	Frequency
Male	44.5±15.5	18 (34.6%)
Female	40.4±11.8	34 (65.4%)
Total	41.9 ± 12.8	52 (100%)

Table 1 Demographic characteristics of CAUTI patients according to gender and age.

Figure 1 (A) shows the culture growth and MDRO status in catheterized patient urine sample cultures. Out of 52 catheterized patients, 45 patients had positive culture growth. Out of 45 positive culture growth cases; 42 (93.30%) were MDRO and 3 (6.70%) were non-MDRO. The MDRO cases were more than the non-MDRO cases with a p-value of 0.017 (Fischer Exact Test) which is < 0.05 and is statistically significant. Figure 2 shows the antibiotic susceptibility pattern by disc diffusion method showing the zone of inhibition in cases of sensitive antibiotics. Figure 1 (B) shows the multidrug resistance pattern by the disc diffusion method showing no zone of inhibition around the antibiotic disc. Table 2 shows antibiotic susceptibility (sensitivity) in isolated organisms.

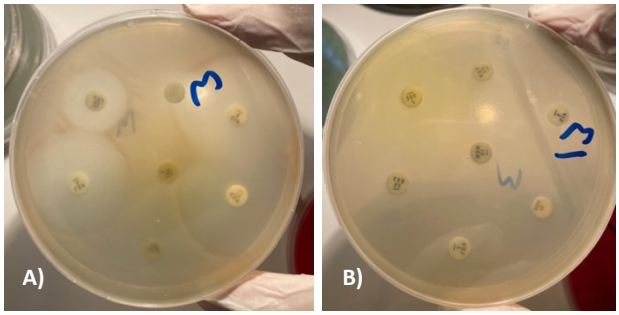

Figure 1 A) Antibiotic susceptibility pattern by disc diffusion method. B) Multidrug resistance pattern by disc diffusion method

DISCUSSION

The introduction of indwelling urinary catheters served as a big step forward in the management of debilitated patients and eased the life of such patients, however; at the same time it introduced another issue of increased risk of urinary tract infections (UTIs) in catheterized patients.[2] Currently about 70-80% of HA-UTIs are

DRUGS	E.coli n=30	Enterobacter n=2	Klebsiella oxytoca n=3	Klebsiella pneumoniae n=5	Serratia marcescens n=1	Serratia odorifera n=1	Pseudomonas aeruginosa n=3
Nitrofurantoin	21 (70%)	1 (50%)	1 (33.3%)	3 (60%)	0 (0%)	1 (100%)	*-
Trimethoprim sulfamethoxazole	8 (26.6%)	0 (0%)	0 (0%)	1 (20%)	0 (0%)	1 (100%)	*-
Ciprofloxacin	15 (50%)	1 (50%)	2 (66.6%)	2 (40%)	1 (100%)	1 (100%)	2 (66.7%)
Levofloxacin	15 (50%)	1 (50%)	2 (66.6%)	2 (40%)	1 (100%)	1 (100%)	2 (66.7%)
Ceftriaxone	7 (23.4%)	0 (0%)	0 (0%)	1 (20%)	0 (0%)	1 (100%)	*-
Cefotaxime	7 (23.7%)	0 (0%)	0 (0%)	1 (20%)	0 (0%)	1 (100%)	*-
Ceftazidime	5 (16.6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (100%)	1 (33.3%)
Cefepime	8 (26.6%)	0 (0%)	0 (0%)	1 (20%)	0 (0%)	1 (100%)	0 (0%)
Aztreonam	1 (3.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Meropenem	26 (86.6%)	1 (50%)	1 (33.3%)	4 (80%)	0 (0%)	1 (100%)	2 (66.7%)
Amoxicillin/clavulanic	11 (36.6%)	1 (50%)	1 (33.3%)	1 (20%)	0 (0%)	1 (100%)	*-
Gentamycin	21 (70%)	1 (50%)	1 (33.3%)	3 (60%)	1 (100%)	1 (10%)	1 (33.3%)
Penicillin	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Table 2. Antibiotic susceptibility in isolated organisms

catheter-relate. This issue of CAUTI is further compounded by the emergence of MDROs and moreover, in the setting of other co-morbidities the patient's prognosis becomes dismal.[3]

The main issue related to UTI treatment is the development and spread of MDROs, leaving limited therapeutic alternatives for clinicians.[7,8] The spread of MDROs is now becoming a global health issue, prevailing in both community and hospital-acquired settings. In our study, it was shown that CAUTI is more common in females 65.4% than in males 34.6%. A similar study was conducted in Lady reading hospital Peshawar determined that the prevalence of CAUTI in females was 63.4% and 36.36% in males.[18] The prevalence of MDR in catheterized patients was 42/45 (93.3%) (Table 2). One study from a Tertiary hospital in Somalia reported MDRO to be 47% from a 3-year retrospective study of CAUTI. The MDRO in our study was high compared to this study because of the study design; large sample volume (their 779 samples vs our 52 samples), duration of study (their 3 year vs our 4 months) and the most important difference was culture-positive samples (their 99/779 – 12.7% vs our 45/52 – 86.5%), inclusion and exclusion criteria and differences in the traits of bacterial strains from various regions. The infection control department estimated the CAUTI based on catheter-associated UTI/catheter days X 1000 days of catheterization in a specified time period (typically one month) of all catheterized patients in all hospital units. MDRO is primarily determined by catheter days and the use of a bundle strategy for the insertion and management of catheters and numerous medicines.[19]

Most of our uropathogenic E. coli (UPECs) 73.4% were resistant to trimethoprim-sulfamethoxazole and only 26.6% were sensitive, which is an effective drug for treating CAUTIs (table 3). Ali et al. also found a significant increase in frequency of trimethoprim-sulfamethoxazole resistance (82%) in UPECs isolated in Pakistan.[20] More than 70% of UPECs in Mexican research were resistant to trimethoprim-sulfamethoxazole.[7] This frequency was 66% in another study conducted in Mexico.[21] Furthermore, there was a considerable increase in the prevalence of trimethoprim-sulfamethoxazole resistance in uropathogenic E. coli isolates among US outpatients from 2000 to 2010. As a result, the use of this drug in the management of UTIs may indeed be restricted.[20,22] Quinolones are widely prescribed for the treatment of simple pyelonephritis and complex UTIs; nevertheless, UPEC resistance to these antibiotics is critical. In our research, 50% of the isolates were quinolone-resistant. This matched the findings of a Mexican research.[7] In another study, E. coil resistance to ciprofloxacin was found to be 23.9 % and in other strains of the same species showed resistance to this quinolone of 54.1%.[23] The growing resistance to quinolones may be related to the overuse of these antibiotics. According to our results the average resistance rates

to the tested cephalosporins in UPECs, were about 77% while sensitivity was only 23%. Antimicrobial resistance rates in UPEC isolates from various parts of Iran as well as other countries such as Pakistan, Turkey, Mexico, Saudi Arabia, Brazil, Mongolia, and others have been discovered to be relatively comparable or different. As a result, without a regional and even case-by-case review of the antimicrobial susceptibilities of infected E. coli, cephalosporins should not be used as an empirical medicine for the treatment of UTIs.[20]

According to sensitivity profile in our study it was observed that most sensitive oral antimicrobial in uropathogens was nitrofurantoin 65% and lowest sensitivity was observed in cefepime 20% (table 3). Another study reported sensitivity rate up to 90%. According to these experts, nitrofurantoin should be used as the first-line treatment for UTIs in regions where resistance to this antibiotic is less than 20%, citing the European Association of Urology (EAU) and the Infectious Diseases Society of America (IDSA).[24-26] In comparison of our results with the above studies, we noted that resistance to nitrofurantoin is on the rise due to inadvertent prescriptions and the use of drugs in our society.

CONCLUSION

The MDRO in CAUTIs was as high as 93.3% in the current research. Nitrofurantoin could be suggested orally as an acceptable medicine for the treatment of CAUTIs. Regular testing for antimicrobial susceptibility should be done to choose the right antibiotic or create new treatment plans, particularly in developing countries due to differences in the traits of bacterial strains from various regions and their changes over time.

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