Pattern of antimicrobial sensitivity in Enterococcus in case of urinary tract infection, 5 years experiences in a tertiary care hospital

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Abstract
Introduction: Urinary tract infection is very common in our community mostly in females and enterococcal infection is very frequent. There is gradual development of resistance against this organism thus narrowing the spectrum of susceptibility.
Aims: So, the aim of this study to detect the spectrum of sensitivity pattern in case of enterococcus in case of urinary tract infection.
Materials and Methods: In this retrospective cross sectional study, morning midstream clean-catch urine form total 1550 symptomatic patients was studied for the spectrum of antibiotic susceptibility according to Clinical & laboratory Standard Institute (CLSI) guideline.
Results: Total 189 patients were infected with enterococci. They showed sensitivity to Vancomycin (87.83%), Teicoplanin (85.18%), Lenazolid (84.12%) and nitrofurantoin (74.07%), and moderate degree of sensitivity in piperacillin-tazobactam (67.19%), imipenem (64.60%) and gentamicin (46.56%) and Amoxycillin-clavulanic acid (54.49%).
Conclusion: Proper antibiotic-stewardship is ultimate requirement to prevent the development of bacterial resistance. So, regular surveillance as well as monitoring is very much necessary to update the knowledge about the susceptibility pattern of urinary pathogens which will guide the therapy.

Keyword: Enterococcus, Symptomatic urinary tract infections, Culture and sensitivity, Tertiary medical centre.

Introduction

Urinary tract infection (UTI) is one of the most common infection in case community as well as hospital settings worldwide.[1-3] It is most common in females but in case of elderly its incidence is equal in both men and women.[4-6] The factors responsible frequency of UTI in females are due to shorter urethra, close proximity to anus and lack of bacteriostatic properties of prostatic secretion. Again, female genital tract is very close to urethra which may lead to spread of infection from one tract to the other.[7] UTI may be complicated or uncomplicated. Uncomplicated UTI may be asymptomatic bacteriuria, or it may be cystitis, pyelonephritis in case of men and nonpregnant women. Complicated UTI may be due to above causes when there is associated comorbidity, like, diabetes, immunocompromized or any anatomical barrier, pregnancy. Some organisms will be more virulent in glucose environment so history diabetes is very important in case UTI. Symptoms are usually burning sensation during in micturition, frequency or urgency in micturition, hematuria, suprapubic pain or loin pain. Anatomical barrier may be prostate related, foreign body, tumor or stone in urinary tract, obstructed catheter usually hinder the free flow of urine leading to accumulation of urine and it will imbibe the infection. Again after therapy there may be reinfection or relapse of infection. Relapse is due to infection with the same organism by which the patient was infected as it persisted even after treatment. On the other hand reinfection is due the new organism. The organisms responsible for UTI are Escherichia coli, Enterococcus, Klebsiella, Pseudomonas, Streptococci, Staphylococcus Epidemidis, Proteus, Gram Negative Staphylococci, Serratia, Gram Negative Enteric Bacteria and Yeast.[6,8,9] Now annual incidence of urinary tract infection is nearly 25 million

worldwide and 30% of total UTI is hospital acquired.[10] Traditionally 7—10 courses of antibiotics are recommended for UTI in males short courses for 3 days even single dose therapy are for females as they mainly suffer from cystitis. Short course of B-lactam is not properly investigated as compared to trimethoprim or nitrofurantoin so it requires extensive studies.[11] Again in case of hospital acquired acute pyelonephritis, the organisms are resistant to common antibiotics. So, in those cases, broad spectrum antibiotics should be given to start with after sending the urine for culture. Catheter induced UTI is fairly common which may lead to asymptomatic bacteriuria but it can be resolved by removal of catheter.[12] But now-a-days novel catheters have been introduced because in these catheters bacteria will not be able to adhere which will decrease the incidence of asymptomatic or symptomatic bacteriuria. The catheter may be of silver alloys based or incorporated with rifampicin and minocycline.[13,14] But from the costing point of view silver-alloyed catheter is usually used when it is absolutely necessary to keep the catheter for more than months.[15] In case of pregnancy, nearly 5% suffer from asymptomatic bacteriuria and again few of these patients enter into pyelonephritis and these are usually responsible for low-birth weight babies, pre mature delivery, preeclampsia or hypertension. So, repeated urinary culture to detect asymptomatic bacteriuria should be done and follow-up antibiotic treatment should be done to reduce the incidence of UTI and complications during pregnancy.[16,17] Following measures can be taken to reduce the incidence of UTI, like, antiseptic use after intercourse, cranberry or blueberries juice containing tannis as it decrease the incidence of pathogens to the uroepithellium, regular cleaning of the urethral opening, intravaginal application of topical estrogen and long courses of low-dose antibiotics. But now-a-days

indiscriminate and improper use of antibiotics, inadequate dose, inadequate duration, frequent change of antibiotic usually lead to resistance of many organisms to many broad spectrum antibiotics and there is change in the pattern of sensitivity of many organisms to different antibiotics. This sensitivity pattern again varies in different geographical areas depending upon the use of antibiotics. Therefore, the aim of this study was to know the pattern of sensitivity of enterococcus against different antibiotics in this geographical area so that it can be used as guideline for proper treatment of all types of patients.

Materials and Methods

The study was started after getting permission from the local ethical committee of our hospital. This is a cross sectional retrospective study of five years from our medical college. Total 1550 patients with suggestive symptoms of UTI were taken in this study. Morning midstream clean catch urine specimen were collected for microbial analysis. No mixed infections were encountered. Urine specimen was inoculated by pre calibrated platinum loop in MacConkey agar and 5% sheep blood agar media to deliver a measured quantity (1.0 μl) to detect the growth of the susceptable bacteria. Enterococcus was detected on brain-heart infusion agar (Becton Dickinson Microbiology systems, Cockeysville, MD, USA) supplemented with 2000 mg/L streptomycin as well as 500 mg/L gentamicin. At 37° C for 48 hours colony forming unit (CFU) count of 10^5/ml was considered as positive. Then, antibiotic susceptibility was tested by using Kirby-Bauer disk diffusion method following CLSI guideline. For this commercial antibiotics were used for sensitivity test. Following antibiotic disc were taken from the manufacturers, Becton Dickinson and Company, USA, Oxoid Ltd. UK: Imipenem (10 μg), amikacin (30 μg), nitrofurantoin (300 μg), gentamicin (30 μg), tobramycin (30 μg), ceftazidime (30 μg), ceftriaxone (30 μg), ciprofloxacin (5 μg), amoxicillin-clavulanic acid (20/10 μg), ampicillin (25 μg), Vancomycin (30 μg), linezolid (30 μg), piperacillin-tazobactam (100/10 μg), Teicoplanin (30 μg), azithromycin (15 μg), cephalexin (30 μg) were used. Staphylococcus aureus (ATCC 25923), Pseudomonas aeruginosa (ATCC 27853) and E. coli (ATCC 25922) were used as control strains.

Statistical method

Obtained data were entered in the STATISTICAL PACKAGE SOCIAL SCIENCES version 17 for proper evaluation for calculation of percentage for different susceptibility pattern.

Result

Total number of patients included was 1550 and total number of affected patients with enterococcus was 189 (12.19%).

Table 1: Pattern of antimicrobial Sensitivity pattern of Enterococcus fecalis infection of urinary tract (n=189)

Antibiotic	Sensitivity	Percentage
Amoxycillin	53	28.04
Amoxycillin-Clavulanic acid	103	**54.49**
Piperacillin-Tazobactam	127	**67.19**
Cefoparazone-Tazobactam	2	1.05
Cefuroxime	1	0.53
Cefotaxime	1	0.53
Cefoxitin	1	0.53
Ceftazidime	1	0.53
Ceftriaxone	1	0.53
Cefepime	0	0
Azithromycin	0	0
Aztreonam	2	1.05
Ertapenem	3	1.58
Imipenem	124	**65.60**
Meropenem	13	6.87
Gentamicin	88	**46.56**
Tobramycin	10	5.29
Netilmicin	26	13.75
Amikacin	16	8.46
Norfloxacin	42	22.22
Ciprofloxacin	60	31.74
Ofloxacin	53	28.04
Levofloxacin	66	34.92
Cotrimoxazole	6	3.17
Chloramphenicol	5	2.64
Tetracycline	6	3.17
Tigicycline	4	2.11
Vancomycin	166	**87.83**
Teicoplanin	161	**85.18**
Lenazolid	159	**84.12**
Polymyxin B	11	5.82
Colistin	11	5.82
Ticarcillin	4	2.11
Nitrofurantoin	140	**74.07**

Table 1 showed highest dgree of sensitivity in case of Vancomycin (87.83%), Teicoplanin (85.18%), Lenazolid (84.12%) and nitrofurantoin (74.07%), and moderate degree in piperacillin-tazobactam (67.19%), imipenem (64.60%) and gentamicin (46.56%) and Amoxycillin-clavulanic acid (54.49%). Table 1 also demonstrated 100% resistance to cefepime and azithromycin, less than 5% sensitivity to other fourth generation of cephalosporin, aztreonam, ertapenem, ticarcillin, Cotrimoxazole, chloramphenicol, tetracycline, Tigicycline. Fluoroquinolones demonstrated mild degree of sensitivity (lowest was the Norfloxacin 22.22% and highest was levofloxacin 34.92%).

Discussion

Since bacterial infection of the urinary tract is most common in our community hence it needs urgent attention.[18] So identification of the organism is of prime importance as it detects the susceptibility of the organism to the specific

antibiotic which can cure the patient. Empirical use and improper duration of the antibiotic administration will lead to resistance to that antibiotics which may be responsible for the emergence of multidrug resistant organism in the community as well as in the hospital settings. This resistance may be due to development of spontaneous mutation, development in the enteric bacteria by R plasmids which is responsible multidrug resistance. Similarly, another study demonstrated 100% sensitivity to vancomycin, lenazolid.[19] Sharifi et al. demonstrated 18.6% resistance against enterococcus as compared to this present study.[20] One study from South India demonstrated 81% sensitivity for vancomycin to enterococcus.[21] Antibiotic resistance cannot explain the virulence of enterococci. Because any infection in the body follows a common sequence of events, like, colonization followed by adhesion to host tissues, invasion of the host tissues and resistance to the host defense mechanism. Now the pathogen directly infects the urinary tract by toxin production or indirectly by producing inflammation produces for pathological changes.[22]

In the antibiogram of Khan IU et al, in the year 2014 enterococcus was susceptible to Lenazolid, vancomycin and Teicoplanin are 100% sensitive and nitrofurantoin was 92.3% sensitive which was very similar to this present study where this organism are highly susceptable to these drugs (vancomycin 87.83%, Teicoplanin 85.18%, Lenazolid 84.12% and nitrofurantoin 74.07%).[23] On the other hand, the present study demonstrated 65.60% sensitivity to imipenem whereas the study of Khan IU et al. it was nearly 92%.

This study showed that only 12.19% patient was affected by enterococcus related urinary tract infection. It is nearly same in the study done by Setu SK et al.in 2016 (268 out of total number affected 2287, 11.67%).[24]

Significant resistance was observed in case of most commonly used antibiotics, like, fluoroquinolones for their broad-spectrum action, bacterial potency, well tolerance to the patients, good oral bioavailability and excellent post antibiotic effect. But due to progressively development of resistance enterococcus in this present study demonstrated low sensitivity (31.74% -- 34.92%) as shown in the study done by Setu et al.[24]

Conclusion

Due to empiric use of antibiotics in inadequate dose for improper duration without proper culture and sensitivity lead to development of multidrug resistant bacteria. Thus, there is gradual narrowing of the spectrum of antibiotic sensitivity for any bacteria which ultimately increases the mortality of the patient. So, proper antibiotic-stewardship is the ultimate requirement to prevent the development of bacterial resistance. So, regular surveillance as well as monitoring is very much necessary to update the knowledge about the susceptibility pattern of urinary pathogens which will guide the therapy.

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