INCREASING INCIDENCE OF BACTERIAL RESISTANCE TO ANTIBIOTICS BY ISOLATES FROM THE URINARY TRACT

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ABSTRACT

This is a prospective study to determine the prevalence of antibiotic resistance among organisms causing urinary tract infections in a Teaching Hospital between August 2003 and July 2004 and to compare them with an earlier study in 1993.

A total of 1,104 urine samples were collected in sterile universal containers from patients attending University of Nigeria Teaching Hospital and studied. All samples showing significant bacteriuria were studied and isolates identified using standard bacteriogical methods. Antibiotic sensitivity testing was performed on sensitivity test agar (Biotec, UK) using the disc diffusion method in accordance with the National Committee for Clinical Laboratory Standards (5). The results were compared with a previous study in 1993.

A total of 336 urinary isolates were identified, with the coliforms being the most predominant (51.2%), followed by *Staphylococcus aureus* and Proteus species (28.9% and 7.1%) respectively. Compared to the earlier study, a significant increase in the resistance of the urinary pathogens to ofloxacin, ciprofloxacin and nalidixic acid was observed, however there was a decrease in the resistance to nitrofurantoin (p<0.05) using chi-square test.

The results of this study should now alert doctors about the increasing possibility of treatment failures, when ciprofloxacin, ofloxacin and nalidixic acid are used for the treatment of urinary tract infections without laboratory testing. A multi-faceted approach including continued and improved surveillance, a reduction in the unnecessary use of antibiotics and infection control are necessary.

Key Words: Resistance. Antibiotics. Urinary tract.

INTRODUCTION

For the treatment of urinary tract infections, the clinician requires information about the patient, the infecting organism and the drugs available.[1] Knowledge of the sensitivity pattern of the causative organism is also of most vital importance for a successful therapy. Resistance to antibiotics however has undermined the idealistic hope that bacterial infection would cease to be an important cause of death and disease.[2] Emergence of bacterial resistance to both the newer and older drugs is an alarming problem and the spectrum of antibiotic resistance is changing continuously.[3] Indeed antibiotic resistance increasingly compromises the outcome of many infections including those of the urinary tract that were until recently treatable and remain the most common diseases in Africa.

Much of the antibiotic therapy in our locality is not based on laboratory sensitivity pattern and therefore results in empirical antibiotic prescription, with resistance being detected only by therapeutic failure. Thus, this study was undertaken to examine the resistance patterns of organisms causing urinary tract

infections to drugs used in treating them at the University of Nigeria Teaching Hospital and to compare them with an earlier study in the same center.

MATERIALS AND METHOD

This is a prospective study of 336 urinary pathogens isolated from 1,104 urine specimens sent to the medical microbiology department from August 2003 to July 2004. The patients comprised both inpatients and out patients. Various urine samples (Midstream, catheter, etc) were collected in sterile universal bottles and examined within two hours of collection. A urine sample is regarded as showing significant bacteriuria, if it contains more than 100,000 organisms per ml of a single type, using blood agar and Cysteine – lactose electrolyte deficient agar (CLED). The isolates were identified using standard bacteriological techniques.[5] Antibiotic sensitivity testing was done on sensitivity test agar (Biotec) using the disc diffusion method in accordance with the National Committee for Clinical Laboratory Standards[6] *Staphylococcus aureus* (ATCC 29213) and *E.coli* (ATCC 35218) were included in all test as control.

The results of the antibiotic sensitivity tests were then compared with a previous study carried out in 1993[6] using the chi-square method.

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RESULTS

A total of 336 urinary isolates were identified and their sensitivities determined. The types and numbers of organisims isolated are presented in table I. Coliforms as a group were the most common, (51.2%), followed by *Staphylococcus aureus* and Proteus species (28.9% and 7.1%) espectively (table I).

Resistance of the urinary pathogens to antimicrobials is presented in table II, together with their ranking. The proportion of resistant organisms varied from antimicrobial to antimicrobial with the lowest rates of resistance being shown to Ofloxacin, Ciprofloxacin and Nitrofurantoin (23.6%, 26.4% and 26.7%) respectively. Compared to an earlier study (table II), a significant increase in the resistance of the urinary pathogens to Ofloxacin, Ciprofloxacin and Nalidixic acid was observed, while there was a decrease in the resistance of the pathogens to nitrofurantoin ($P<O.05$) using chi-square test.

Table I: **Organisms Isolated From the Urinary Tract**

Organism	No.	%
Coliforms	172	51.2
Staphylococcus aurens	97	28.9
Proteus	24	7.1
Streptococcus faecalis	4	1.2
Other Streptococcus species	20	6.0
Pseudomonas aeruginosa	9	2.7
Coagulase negative staphylococci	10	2.9
TOTAL	**336**	**100**

Table II: **Resistance to Various Antibiotics Comparison between the Current Study and the Previous (1993) Study**

Antibiotics	% Resistant (Current Study)	% Resistant (Previous Study)	P Value	X^2
Ampicillin	89.6(1)	90.6	0.8094	0.06
Cotrimoxazole	88.1(2)	91.8	0.345	0.89
*Nalidixic acid	67.1(5)	20.4	0.0000	44.94
*Nitrofurantoin	26.7(8)	42.0	0.0256	4.98
Tetracycline	79.4(3)	84.4	0.362	0.83
Gentamycin	34.6(7)	33.9	0.881	0.02
*Ciprofloxacin	26.4(9)	0.6	0.000002	26.76
*Ofloxacin	23.6(10)	2.2	0.0000037	21.4
Augmentin	37.7(6)	-	-	-
Amoxicillin	69.2(4)	-	-	-
Pefloxacine	39.8	-	-	-

*$P<O.05$ = statistically significant using chi-square
Figures in parenthesis indicate ranking

Table III: **Percentage Coliforms Resistant To Various Antibiotics**

Antibiotic	% Resistant Current Study	% Resistant Previous Study	Pvalue	X^2
Ampicillin	93.5 (1)	93.5	-	-
Cotrimoxazole	89.0 (2)	92.3	.	.
*Nalidixic acid	57.7 (6)	19.8	0.00000	30.35
Nitrofurantoin	26.7 (11)	36.7	0.129	2.50
Tetracycline	88.6 (3)	85.1		..
Gentamycin	52.8 (7)	22.0	.	-
*Ciprofloxacin	39.0 (9)	6.5	0.000001	28.93
*Ofloxacin	29.9 (10)	6.5	0.000028	17.54
Augmentin	58.1 (5)	-	..	..
Amoxycillin	88.3 (4)	-		
Pefloxacine	45.9 (8)	-	-	-

*$P<O.05$ = Statistically significant using chi-square test. Figures in parenthesis indicate ranking.

DISCUSSION

The coliform group was the most predominant organisms accounting for 51.2%, followed by *Staphylococcus aureus* and proteus species. 28.9% and 7.1% respectively. These results confirm an earlier report from our center, where these organisms were among the four most important bacterial pathogens of urinary tract infections[6]. These bacteria are also important pathogens of the urinary tract in other centres in Nigeria, as well as other parts of the world[7,8] In all, Gram negative bacilli were more prevalent than Gram positive bacteria, similar to reports from other Nigerian centers.[7,8]

The continued surveillance of hospital bacteria and their resistance pattern is important in the management of nosocomial infections.[9] Even when not available for individualized patient care, surveillance susceptibility testing is a valuable tool for cost-effective customization of empiric antibotic therapy.[10,11] A choice made solely on the basis of antimicrobial sensitivity in this study, would rank the drugs in decreasing order of preference as follows: ofloxacin, ciprofloxacin, nitrofurantoin, gentamycin, augmentin, nalidixic acid, amoxicillin, tetracycline, cotrimoxazole and ampicillin. Compared to the previous study,[6] there was only a slight, change in the order of preference, although three antibiotic discs namely augmentin, amoxicillin and pefloxacin were not available in 1993.

Three antibiotics named ofloxacin, ciprofloxacin and nalidixic acid were significantly more resistant compared to the previous study ($P<O.05$). This increase in resistance to the flouroquinolones, ofloxacin and ciprofloxacin has been observed from other centers.[12] There has been an increasing dependence on the flouroquinolones, ofloxacin and ciprofloxacin for the treatment of infections including

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urinary tract infections in Nigeria, because of the narrow choice of antibiotics available to the clinician in Nigeria and increasing resistance to other commonly used antibiotics.[6] Unfortunately, studies in other parts of the world, where flouroquinolones are more commonly employed, have revealed that routine use of these drugs is often associated with a rapid increase in the proportion of resistant strains.[13] Many doctors in Nigeria, also do not bother to carry out sensitivity testing before administering antibiotics, leading to misuse of antibiotics. For example, many prescribers use antibiotics that are no longer effective due to the increased prevalence of resistance, eventually requiring multiple chemo-therapeutic courses to effect a cure. Conversely expensive agents that are employed in life threatening situations may be substituted for cheaper agents, if local susceptibilities are known.[10,11] There was a significant decrease in the resistance of the urinary pathogens to nitrofurantoin compared to the earlier study. Resistance to nitrofurantoin, like nalidixic acid is not plasmid mediated but with much increased resistance (36.7%) observed earlier on,[6] a restriction in its use, led to a reduction in resistance observed in the current study. Resistance to ampicillin, cotrimoxazole and tetracycline was very high as was also observed from other centers.[7,8] These drugs cannot therefore be used as an initial choice for the treatment of urinary tract infections without susceptibility testing.

They are the most commonly abused and misused drugs and are easily available from chemists' shops without doctors prescriptions. The increased resistance of strains to ciprofloxacin, ofloxacin and nalidixic acid has complicated treatment options and increased the likelihood of treatment failures. Thus, doctors in Enugu and Nigeria as a whole should be aware that there is now an increasing possibility of treatment failures when ciprofloxacin, ofloxacin and nalidixic acid are used for the treatment of urinary tract infections without susceptibility testing. To stem the tide of rising resistance will require a multi-faceted approach, including continued and improved surveillance, a reduction in the unnecessary use of antibiotics and infection control.

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