

RESEARCH ARTICLE

AN INSIGHT ON THE SUSCEPTIBILITY PATTERN OF URINARY ISOLATES OF ESCHERICHIA COLI AND KLEBSIELLA PNEUMONIAE AGAINST FLUOROQUINOLONES WITH SPECIAL **REFERENCE TO PRULIFLOXACIN**

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Abstract

..... Introduction: The most prevalent infections in outpatient and inpatient settings are urinary tract infections (UTIs), which can be treated with a variety of antibiotics. Fluoroquinolones are the preferred antibiotic class and Prulifloxacin is one of these agents. It can be tested in vitro for its activity against urinary isolates of the bacteria Escherichia coli(E. coli) and Klebsiella pneumoniae (K. pneumoniae) for the purpose of surveillance, along with other fluoroquinolones.

Objective: Evaluation of the fluoroquinolone susceptibility of urine isolates of K. pneumoniae and E. coli with a focus on Prulifloxacin.

Results: 877 urine samples processed, 257 showed positive cultures, satisfying the Kass concept/Significant bacteriuria. Of these, 106 (41.2%) contained E. coli and K. pneumoniae, of which 92 (87%) were E. coli and 14 (13%) were K. pneumoniae. E. coli exhibited the highest susceptibility to Levofloxacin (61.9%), followed by Prulifloxacin (58.6%) where as to K. pneumoniae Levofloxacin (42.8%) and Prulifloxacin (50%).

Conclusion: Levofloxacin is thought to be a drug reserved for the treatment of multi-drug resistant tuberculosis (MDR-TB), the study provides insight into the susceptibility patterns of urinary isolates of E. coli and K. pneumoniae against Prulifloxacin, which can be preferred as the drug of choice for the treatment of UTIs.

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Introduction:-

Urinary tract infections (UTIs) are the most common infections where nearly 150 million UTIs occur yearly worldwide^{1,2} in outpatients as well as hospitalized patients. UTI is defined as a disease caused by microbial invasion of the genitourinary tract that extends from the renal cortex of kidney to the urethral meatus. UTIs are classified by the site of infection as lower UTI involving the bladder (cystitis) and urethra (urethritis) and upper UTI

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involving ureters (urethritis) and kidneys (pyelonephritis). UTI can also be classified as asymptomatic and symptomatic based on a spectrum of symptoms ranging from dysuria, frequency, urgency, pyrexia and suprapubic tenderness to severe urosepsis characterized by UTI along with 2 or more of the following signs like temperature $> 38^{\circ}$ C or $< 36^{\circ}$ C heart rate > 90 bpm, respiratory rate > 20/min, WBC count > 12000/mm³ or < 4000/mm³. UTIs also can be classified as complicated UTIs which refers to infection seen in the urinary tract with many kinds of structural or functional abnormalities and also seen in patients with indwelling catheters and renal calculi whereas uncomplicated UTIs refers to infections in structurally and neurologically normal urinary tract^{3,4}.

Microbiologically to indicate UTI there must be significant bacteriuria which means that there should be the growth of more than 10^5 colony forming units /ml in a clean catch midstream urine. There can be growth of the smaller number of bacteria (10^2-10^4 colony forming units/ml) especially in specimens from suprapubic aspiration, catheter specimens and also specimens from immunocompromised patients⁵ or in patients in whom antibiotic therapy was already started. Although UTIs are caused by many species of microorganisms, the most common cause is Uropathogenic Escherichia coli (70-95%) followed by Klebsiella species especially Klebsiella pneumoniae (5%)^{3,6}.

UTIs can be treated with various broad-spectrum antibiotics like β -lactams, Carbapenems, Aminoglycosides, etc. especially for Gram negative organisms. But Fluoroquinolones which were introduced in 1962 are being considered as drugs of choice because of their broad spectrum activity. They act by inhibiting DNA synthesis^{1,2}. Acquired bacterial resistance to these compounds has been reported not only mainly in the members of Enterobacteriaceae but also other Gram negative isolates which may be due to mutations in the chromosome leading to alteration of target enzymes DNA Gyrase, DNA Topoisomerase⁴, or due to activation of efflux systems³. These compounds are being regularly used in clinical practice. Due to better understanding of the structural and functional relationships of the Fluoroquinolones, compounds with better pharmacokinetics and better antimicrobial spectrum³ were developed.

Fluoroquinolones generally used in case of UTI are Norfloxacin, Ofloxacin, Ciprofloxacin, Levofloxacin and the latest used among them is Prulifloxacin. Prulifloxacin is a Thiazeto quinolone, a prodrug of Ulifloxacin metabolized after oral administration in the small intestine by esterases mainly Paraoxonase. And this drug shows a good activity at a dose of 600mg once daily for 10 days where elimination t $\frac{1}{2}$ is approximately 9-12 hrs and indicated in both complicated UTIs^{7,8}.

In this study, we would like to report the susceptibility pattern of urinary isolates of Escherichia coli and Klebsiella pneumoniae against regularly used Fluoroquinolones with special reference to Prulifloxacin. This serves the purpose as a surveillance study from different parts of the world which shows the acquired resistance pattern to Fluoroquinolones which generates data that will be useful in clinical management of empirical as well as confirmed treatment in cases of UTI.

Materials And Methods:-

This is a cross-sectional observational study which was carried out during a period of eight months after Institutional Ethics committee (IEC) approval was obtained. A total of 106 urinary isolates of Escherichia coli, Klebsiella pneumoniae from clean catch midstream urine samples and satisfying the concept of significant bacteriuria were collected. Antibiotic susceptibility testing was done by using Kirby Bauer disc diffusion method using Mueller Hinton agar plates according to CLSI guidelines against Norfloxacin (10 μ g), Ofloxacin (5 μ g), Ciprofloxacin (5 μ g), Levofloxacin (5 μ g), Prulifloxacin (5 μ g), (Himedia labs Mumbai). The susceptibility zones were interpretated as Sensitive (S), Intermediate(I), Resistance(R) according to CLSI guidelines 2022¹¹.

Results:-

In the study period of eight months, a total of 877 urine samples were processed and among them, 257 were culture positive. (Table-1)

Table 1:- Showing culture positives among total urine samples.

Total No of samples	Culture positive	Culture negative
877	257 (29.3%)	620 (70.6%)

 Table 2:- Showing total Escherichia coli and Klebsiella pneumoniae isolates.

Culture positive	Escherichia coli and Klebsiella pneumoniae
257	106 (41.2%)

Table 3:- Showing number of Escherichia coli and Klebsiella pneumoniae isolates.

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Total	Escherichia coli	Klebsiella pneumoniae
106	92 (87%)	14 (13%)

Among the 92 Escherichia coli isolates tested, 57 (61.9%) were sensitive to Levofloxacin and 54 (58.6%) were sensitive to Prulifloxacin followed by other fluoroquinolones.

Among the 14 Klebsiella pneumoniae isolates, 7 (50%) were sensitive to Prulifloxacin followed by other Fluoroquinolones.

Among the Fluoroquinolones tested Levofloxacin showed the highest sensitivity followed by Prulifloxacin.

Table 4 Fluoroquinoiones susceptionity among Eschericina con, Ricostena pileunomae urmary isolates.						
Organism/Drugs	Ofloxacin	Norfloxacin	Ciprofloxacin	Levofloxacin	Prulifloxacin	
Escherichia coli	38(41.3%)	39(42.3%)	42(45.6%)	57(61.9%)	54(58.6%)	
(92)						
Klebsiella	6(42.8%)	6(42.8%)	6(42.8%)	6(42.8%)	7(50%)	
pneumoniae (14)						
Total (106)	44(41.5%)	45(42.4%)	48(45.2%)	63(59.4%)	61(57.5%)	

 Table 4:- Fluoroquinolones susceptibility among Escherichia coli, Klebsiella pneumoniae urinary isolates.

Discussion:-

In the present study, we sought to determine invitro antibiotic susceptibility pattern against Fluoroquinolones with special reference to Prulifloxacin in urinary isolates of Escherichia coli and Klebsiella pneumoniae. Escherichia coli isolates showed higher susceptibility to Levofloxacin (61.9%) correlating with findings of Abdu et al, Rolf Nyah-tuku Nzalie et al and Bhattacharya et al. ^{5,12,13} followed by Prulifloxacin (58.6%) correlating with findings of Durga devi B followed by Ciprofloxacin (45.6%), Norfloxacin (42.3%), Ofloxacin (41.3%) correlating with findings of Abdu et al, Olorunmola et al. ^{5,14}

Among Klebsiella pneumoniae isolates higher susceptibility was observed for Prulifloxacin (50%) correlating with findings of Bhattacharya et al ¹³ followed by Levofloxacin, Ciprofloxacin, Norfloxacin, Ofloxacin 42.8% each correlating with findings of Ashis Kumar Saha et al¹⁵.

Our study reveals that overall sensitivity is high for Levofloxacin (59.4%) followed by Prulifloxacin (57.5%) against urinary isolates of Escherichia coli and Klebsiella pneumoniae. Prulifloxacin can be preferred over Levofloxacin for the treatment of urinary tract infection, as Levofloxacin is considered as reserved drug for the treatment of multidrug resistant tuberculosis (MDR-TB) cases.

Conclusion:-

Our results indicate similar rates of susceptibility in urinary isolates of Escherichia coli and Klebsiella pneumoniae to Levofloxacin followed by Prulifloxacin compared to other Fluoroquinolones like Ciprofloxacin, Ofloxacin and Norfloxacin. However, Prulifloxacin can be considered as an appropriate drug of choice for the treatment of such urinary tract infections with the above mentioned organisms in the study area as Levofloxacin is to be considered as reserved drug for the treatment of multi drug resistant tuberculosis (MDR-TB). However further studies and periodic monitoring of susceptibility pattern against fluoroquinolones in uropathogens are warranted.

Conflict of interest:-

The authors declare no conflict of intrest regarding the publication of this paper

References:-

1. Durka Devi B, Kennedy kumar P, Sridharan K S, et al. A comparative study of efficacy of purlifloxacin with other quinolones and fluroquinolones among the Escherichia coli isolates from various clinical specimens. 2016.

2. Lyonga EE, Toukam M, Nkenfou C, et al. Resistance pattern of enterobacteriaceae isolates from urinary tract infections to selected quinolones in Yaoundé. Pan African Medical Journal. 2015;21(1).

3. Jack D.Sobel, Donald Kaye, Gerald L.Mandell, et al. Principles and practice of infectious diseases: urinary tract infections.7th edition. Elsevier.2010;957-986.

4. Cao D, Shen Y, Huang Y, et al. Levofloxacin versus ciprofloxacin in the treatment of urinary tract infections: Evidence-based analysis. Frontiers in pharmacology. 2021;12:551.

5. Abdu A, Kachallah M, Bolus DY. Antibiotic susceptibility patterns of Uropathogenic Escherichia coli among patients with urinary tract infections in a tertiary care hospital in Maiduguri, North Eastern, Nigeria. J Biosci Biotechnol Discov. 2018;3:14-24.

6. Drago L, Nicola L, Mattina R, et al. In vitro selection of resistance in Escherichia coli and Klebsiella spp. at in vivo fluoroquinolone concentrations. BMC microbiology. 2010;10(1):1-7.

7. Locatelli M, Cifelli R, Carlucci G, et al. Stability study of Prulifloxacin and Ulifloxacin in human plasma by HPLC–DAD. Journal of enzyme inhibition and medicinal chemistry. 2016;31(1):106-11.

8. Tellone V, Coppola P, Ammendola M, et al. New Insights on the Pharmacokinetics of Ulifloxacin After Administration of Prulifloxacin in Patients with Mild, Moderate and Severe Renal Impairment. Drugs in R&D. 2018;18(3):237-45.

9. Patricia M. Tille. Bailey & Scotts Diagnostic Microbiology. Infections of the urinary tract. 14th edition. Elsevier.2017;987-998.

10. Gary w. procop, Deirdre L. Church, Geraldine S.Hall et al. Konemans Color atlas and Textbook of Diagnostic Microbiology. Urinary tract infections. 7th edition. Wolters kluwer.2017;80-84.

11. Wayne PA.Clinical and laboratory standards institute. Performance standards for antimicrobial susceptibility testing.M-100.32 ed.2022.

12. Nzalie RN, Gonsu HK, Koulla-Shiro S. Bacterial etiology and antibiotic resistance profile of communityacquired urinary tract infections in a Cameroonian city. International journal of Microbiology.2016:1-6.

13. Bhattacharyya S, Kumari S, Sarfraz A, et al. Comparative efficacy of Levofloxacin and Prulifloxacin against Uropathogenic Escherichia coli and Klebsiella spp. from a tertiary care hospital and their correlation with expression of lipase and lecithinase. Eastern Journal of Medical Sciences. 2016;1:1-3.

14. Olorunmola FO, Kolawole DO, Lamikanra A. Antibiotic resistance and virulence properties in Escherichia coli strains from cases of urinary tract infections. African journal of infectious diseases. 2013;7(1):1-7.

15. Saha AK. Pattern of antimicrobial susceptibility of Klebsiella pneumoniae isolated from urinary samples in urinary tract infection in a tertiary care hospital, Kishanganj, Bihar. International Journal of Contemporary Medical Research . 2019;6(12):125-128.