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IN VITRO COMPARATIVE EFFICACY OF CIPROFLOXACIN AND CO-TRIMOXAZOLE AGAINST ESCHERICHIA COLI IN URINARY TRACT INFECTIONS

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ABSTRACT

Background: *Although majority of the UTIs in adults are uncomplicated infections and are treated with antibiotic empirically, but it is still a major issue for the health system due to antibiotic resistance.*

Objective: *To determine in vitro comparative efficacy of ciprofloxacin and co-trimoxazole against Escherichia coli individuals with UTI*

Methodology: *This Randomized controlled trial was carried out in the Dept. of medicine, Saidu Group of Teaching Hospital (SGTH), Saidu Medical College (SMC) Saidu Sharif Swat, Pakistan from July 01, 2022 – December 31, 2022. Two groups of 97 individuals each were randomly selected from a total of 194 patients who had been diagnosed with an E. Coli urinary tract infection. Following the 48th hour of therapy, all of the enrolled patients were monitored, and the outcomes were documented. SPSS version 24 was used to analyze all of the data.*

Results: *Participants in group A had an average age of 48.4 + 11.1 years, whereas those in group B had an average age of 48.2 + 11.5 years (p value 0.913). Group B had 80.4% males and 19.6% females, whereas group A had 69.1% males and 30.9% females (p value 0.069). Groups A and B had effectiveness rates of 79.3% and 50.5%, correspondingly, after 48 hours after end therapy (p value 0.000).*

Conclusion: *Our research work concludes that ciprofloxacin is more effective than co-trimoxazole in the treatment of UTIs due to E.Coli. Although, literature suggested growing resistance of E Coli to commonly used antibiotics, we would recommend in vitro studies for antibiotic sensitivity testing before making future recommendations.*

Keywords: *Urinary tract infection, Escherechia Coli, Ciprofloxacin, Co-Trimaxazole, Trimethoprin, Sulphamethaxazole, Urine culture.*

INTRODUCTION

Infection of urinary tract by pathogenic bacteria is termed as Urinary Tract Infection (UTI); which includes symptomatic patients having cystitis, prostatitis and pyelonephritis. UTI's may be uncomplicated or complicated. Uncomplicated UTI represent those UTI cases which are acute and without any co-morbid conditions such as, acute pyelonephritis or cystitis, females without pregnancy or anatomic abnormalities,

outpatient male, or without instrumentation of the urinary tract; complicated UTI is a catch-all term that includes all other types of UTI.[1] Now-a-days, it encompass one of the most prevalent diseases globally, averaging about 150 million newly diagnosed cases annually and people of all ages are prone to UTI.[2] The UTIs occur more in elderly patients with a prevalence of 51.04% than in pediatric patients and affects women more commonly (66.66%).[3] UTIs are mostly not life threatening and does not result in any irreversible damage. However, when pyelonephritis occurs, there is a greater risk of irreparable tissue damage with a higher risk of leading to bacteremia.[4]

Fluoroquinolones (Ciprofloxacin) has been considered as an ideal drug for the treatment of UTIs, since their diverse mechanisms of action seem prevent resistance by the E. coli. Ciprofloxacin is also potent against large number of E. coli strains compared to other commonly used drugs.[2, 5] Moreover; ciprofloxacin is comparatively least expensive too.[6]

The resistance of all UTI isolates, especially E. Coli, to ciprofloxacin was found to be 46% by Manikandan S. et al (Hence 54% Efficacy), and this resistance was observed to increase continuously.[2] Hooton TM demonstrated on the criteria by Infectious Diseases Society of America (IDSA),[6,7] ciprofloxacin (250 mg BID for 3 days) for acute uncomplicated cystitis is about 90% effective and is 96% effective in 500 mg BID for 7 days dosage, in Acute Uncomplicated Pyelonephritis.[6]

Materials and methods:

This Randomized controlled trial was carried out in the Dept. of medicine, Saidu Group of Teaching Hospital (SGTH), Saidu Medical College (SMC) Saidu Sharif Swat, Pakistan from July 01, 2022 – December 31, 2022. Two groups of 97 individuals each were randomly selected from a total of 194 patients who had been diagnosed with an E. Coli urinary tract infection. Following the 48th hour of therapy, all of the enrolled patients were monitored, and the outcomes were documented.

Inclusion Criteria:

1. Patients with uncomplicated UTI[1] due to E. Coli on urine culture and has given consent.
2. Patients of either gender with age $\geq$ 18 years.

Exclusion Criteria:

1. Patients who have taken antibiotics in last five days at the time of presentation.
2. Immunocompromised patients.
3. Patients with impaired renal functions.
4. Patients with urinary tract anatomical abnormalities and urinary tract calculi.

Data Collection Procedure:

The institution's research and ethics committee gave its ethical clearance prior to this investigation. All outpatient department patients who met the study's inclusion requirements were enrolled. After obtaining written informed permission, the patient was recruited. To meet the exclusion criteria, the selected patients will go through standard testing such as a complete blood count, a urinary system ultrasound, renal function tests, and a random blood sugar test. Following that, the patients were randomly assigned to one of two groups: "Group-A" for Ciprofloxacin 500 mg BD and "Group-B" for Co-Trimoxazole 960 mg BD. Both groups were treated for ten days. Every patient that was recruited had a complete medical history and assessment. The criteria mentioned above were used to diagnose UTIs. A urine sample was collected in a sterile container and then subjected to bacterial growth using CLED or MacConkey agar, which was incubated for 24 hours at 37°C in a hospital laboratory.

Data Analysis Procedure:

SPSS latest version software (SPSS. 24) was used to analyze all the collected data from patients. Continuous variable such as age were expressed as Mean ± SD. Efficacy and gender were categorical variables that were

represented using percentages and frequencies. The effectiveness of the two medicines was compared using the Chi-Square test, with a P value of less than 0.05 being regarded as significant.

Results:

Participants in group A had an average age of 48.4 + 11.1 years, whereas those in group B had an average age of 48.2 + 11.5 years (p value 0.913). Group B had 80.4% males and 19.6% females, whereas group A had 69.1% males and 30.9% females (p value 0.069). (Table 1)

Patients of both groups (group A and B) were also further distributed in 4 age categories i.e. ≤40 years, 40.01-50 years, 50.01-60 years and ≥60.01 years. This distribution reflected that age has no relationship with UTI due to E Coli however, slightly more patients were observed in age group above 50 years as evident from tables. Also, we used chi square test to see the difference between patient distribution with regards to age in between group A and B (P value 0.288) (Table 2)

ON follow up, urine culture was performed to detect the presence or absence of infection. It was observed that in group A, 77 (79.3%) patients had negative culture and in group B 49 (50.5%) patients had culture negative report of urine at 48th hour of treatment and overall, in the whole study population (194), negative culture was found in 126 (63.9%) of the patients (Table 3)

Culture negativity at 48th hour of treatment was considered efficacy for the treatment. According to this, efficacy in group A was recorded in 77 (79.3%) of patients while in group B it was recorded in 49 (50.5%) of patients (p value of 0.000)

TABLE NO: 1: GENDER BASED DISTRIBUTION OF PATIENTS IN BOTH GROUPS (n=97 in each)

		Group		Total	P value
		Group A (CIPRO)	Group B (CO TRI)		0.069
Gender	Male	67	78	145	
	Female	30	19	49	
Total		97	97	194	

TABLE NO: 2: AGE GROUP DISTRIBUTION OF PATIENTS IN BOTH GROUPS (n=97 in each)

		Group		Total	P value
		Group A (CIPRO)	Group B (CO TRI)		0.288
Age Groups	≤ 40.00 yrs	29	29	58	
	40.01-50.00 yrs	19	29	48	
	50.01-60.00 yrs	29	20	49	
	≥60.1 yrs	20	19	39	
Total		97	97	194	

TABLE NO. 3:CULTURE REPORT AFTER 48HOURS OF END OF TREATMENT IN BOTH GROUPS (n = 97 each)

		Group		Total
		Group A (CIPRO)	Group B (CO TRI)	
Urine Culture result after 48 hours	Negative	77	49	126
	Positive	20	48	68
Total		97	97	194

TABLE NO. 4: COMPARISON OF EFFICACY BETWEEN BOTH GROUPS (n = 97 each)

		Group		Total	P value
		Group A (CIPRO)	Group B (CO TRI)		0.000
Efficacy of the Drug	Yes	77	49	126	
	No	20	48	68	
Total		97	97	194	

Discussion:

Although majority of the adults with UTI are uncomplicated infections and are treated with antibiotic empirically, but it is still a major issue for the health system, more specifically in women, where, each year 62-5/1000 of the hospital visit are for bladder or other urinary tract infection.[8] Rarely, UTI results in grave and long lasting renal damage in those patients harboring any associated abnormalities such as renal tract anomalies, ,diabetes mellitus or pregnancy.[9] UTI is rare in young males who haven't had any instrumentation of the genitourinary tract, but common in homosexuals. However, it is not uncommon in males with age of 50 or more especially due to prostatic gland complications. 20-50% females and 5-20% in institutionalized care had reported asymptomatic bacteriuria.[10, 11]

10% of urinary tract infections are caused by saprophytic staphylococci in sexually active women. Community acquired pathogens are usually responsive to commonly used antimicrobial drugs. On the other hand, E coli results in only half of the nosocomial infections while the rest are caused by *P.aeruginosa, klebsiella, staphylococci, serratia, proteus, enterococci, yeasts*, etc.[12]

25-35% of E. coli in cystitis are resitant to ampicillin and sulfonamide in vitro, [13, 14] and trimethoprim resistance is also on the rise in different regions of the world.[15] Therefore, alternative therapeutic drugs are the need of the day in order to cure such cases. The fluoroquinolone group is one of the antimicrobial agents which are currently evaluated for UTI treatment. The more recently developed drugs in this group i-e, norfloxacin, [17] ciprofloxacin, and ofloxacin, [16] are effective for all kinds of UTIs when used for a period of 7-10 days. We also confirmed that ciprofloxacin is as potent compared to prescribed regimen of trimethoprim-sulfamethoxazole used for UTI caused by E. Coli. The cure rates at 48th hour after treatment in terms of culture of urine observed here with CIPRO are higher than conventional regime of trimethoprim-sulfamethoxazole in this study.

According to IDSA 1999 guidelines trimethoprim-sulfamethoxazole, one tablet per oral route in double dose, BID for 3 days, is recommended for any uncomplicated case of UTIs and effectively covers almost 95% such cases.[18] While One-day course, due to its lower coverage(almost 85%) and is not advised as primary treatment.[34] Compared to amoxicillin and cephalexin(β-lactam antibiotics), Trimethoprim-sulfamethoxazole are advantageous. Firstly, trimethoprim-sulfamethoxazole has a higher cure rate, even when resistance to the drug is noncontributory. Second, it prevents recurrent UTI over the next few months, which is mainly due to the fact that this drug also kill enterobacteriaceae.[19]

The IDSA recommendation states that when in a community there is 10-20% resistance to trimethoprim sulfamethoxazole then other drugs, such as fluoroquinolones should be used for empirical treatment, having the highest efficacy. Analysis by Le and Miller[20] demonstrated that fluoroquinolones are cost effective to trimethoprim-sulfamethoxazole in more than 22 % resistance; primarily due to failed treatment, hospital revisits, and laboratory expenses. Other studies showed similar results with cost effectiveness of floroquinolones compared to trimethoprim-sulfamethoxazole at 19-21%. Resistance[21]

Henry DC et al, in their study used ciprofloxacin in two combinations one in QD and the other in BID. His results concluded 94.5% bacterial eradication in the former and 93.7% in later group (95% CI, −3.5 to 5.1) resulting in clinically cured 95.5% in QD and 92.7% in BID group (95% CI:1.6-7.1). The follow up results were in agreement with the test-of-cure findings.[22] In another research work by Williams AH et al. in hospital admitted elderly patients with indwelling cathethers associated UTI were subjected to oral ciprofloxacin 100mg BID and 250mg BID and co-trimoxazole 960 mg, where P. aeruginosa caused 24% infections. At 28 days follow up, the successfully cured cases were 94 percent, 88 percent and 87 percent, respectively. There were minimal side effects. Even in complicated UTIs ciprofloxacin is a safe drug when

administered orally[23]. However, in a study by Goettsch WG et al,[24] treatment with trimethoprim and nitrofurantoin showed 14.4% treatment failure rate in patients and with floroquinolones it was 9.6%. Multivariate researches stat that five and seven days treatment with trimethoprim and nitrofurantoin better than three day course. Age, the year of treatment and previous hospitalizations are some factors which can affect treatment.

Conclusion:

Our research work concludes that ciprofloxacin is more effective than co-trimoxazole in the treatment of UTIs due to *E.coli*. Although, literature suggested growing resistance of E Coli to commonly used antibiotics, we would recommend in vitro studies for antibiotic sensitivity testing before making future recommendations. Also, we didn't consider the adverse effects of the drug under test so we recommend randomized controlled trial comparing not only efficacy but also the safety of the drugs

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