International Journal of Allied Medical Sciences and Clinical Research (IJAMSCR)

ISSN: 2347-6567 IJAMSCR |Volume 2 | Issue 1 | Jan-Mar - 2014

www.ijamscr.com

Research article

Comparision of *in vitro* antibacterial activity of cefoperazone and levofloxacin against different clinical isolates.

Mehwish Rizvi[1], Zeb-Un-Nisa[1], Maqsood Ahmed[1], Baqar Naqvi[2], *Atta Abbas[1,3], Arif Sabah[1].

[1]Faculty of Pharmacy, Ziauddin University & Hospitals Karachi, Sindh, Pakistan.

[2]Faculty of Pharmacy, Hamdard University, Karachi, Sindh, Pakistan.

[3]Department of Pharmacy, Health and Well Being, University of Sunderland, England, United Kingdom.

ABSTRACT

Cefoperazone (a third generation cephalosporin) has effective *in vitro* activity against majority of pathogens. Levofloxacin (a flouroquinolone) is one which prescribed more due to its increased antibacterial activity against Gram-positive, Gram-negative, and atypical bacteria. Microbial resistance to antibiotics is now prevalent and poses a serious clinical threat. An attempt has been made to evaluate sensitivity of cefoperazone and levofloxacin against *Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa* and *Salmonella typhi*.

A total of 120 isolates were collected from different pathological laboratories and medical centers in Karachi, Pakistan. The above stated clinical isolates were extracted from urine/stool, skin, blood and sputum samples.

Results show least resistance of levofloxacin as compared to cefoperazone against *Escherichia coli* (32.5% and 42.5%) and *Pseudomonas aeruginosa (*36% and 48%) while *Staphylococcus aureus* is still susceptible towards cefoperazone and least sensitive to levofloxacin by showing 26.6% and 50% resistance respectively. Study concluded that the prevalent pathogens are still susceptible towards levofloxacin and cefoperazone but the gradual increase in resistance is alarming to the general practice of prescribing antibiotic which require routine evaluation and surveillance to ensure the effectiveness of the antibacterial agents.

Key words: In vitro; Cefoperazone; Levofloxacin; Antibacterial activity; Clinical Isolates.

INTRODUCTION

In recent years, the level of resistance of *S. pneumoniae* to beta-lactam and/or macrolides has increased around the world. Because of this resistance, it is necessary to test the therapeutic alternatives for treating this pathogen, including the newer quinolones[1].

Levofloxacin **(**a fluoroquinolone**)**, the levorotatory isomer of ofloxacin, possessed antibacterial activity[2]. Fluoroquinolones inhibit the α sub-unit of DNA gyrase and topoisomerase IV, the enzyme which catalyze the negative super coiling of DNA in bacteria[3]. Levofloxacin rated superior in antibacterial activity when compared with ofloxacin, particularly against pathogens isolated from respiratory tract infections[4]. In clinical practice levofloxacin is one which prescribed more due to its antibacterial activity against Gram-positive, Gram-negative, and atypical bacteria[5].On comparison with non-fluoroquinolone used for respiratory tract infections, Levofloxacin has lower rate of adverse effects[6]. The changes in DNA gyrase can confirm a high degree of resistance specific to the fluoroquinolone [7].

Cefoperazone is highly active against the *Enterobacteriaceae*. Its activity against *Staphylococcus aureus* is comparable to that of the other newer cephem antibiotics. Synergy studies with cefoperazone plus β-lactamase inhibitors or aminoglycosides against *Enterobacteriaceae* and *Pseudomonas aeruginosa* show enhanced killing[8]. Cefoperazone was found to be most effective

*** Corresponding author: Atta Abbas**

E-mail address: bg33bd@student.sunderland.ac.uk

(74%) against *Pseudomonas aeruginosa*[9]. Resistance of Gram-negative bacteria to cephalosporins, is due to outer-membrane permeability, affinity and stability to beta-lactamases, and their activity against target sites (penicillin-binding proteins)[10]. Cefoperazone /sulbactam showed effective *in vitro* activity against majority of pathogens and may be considered as a potential drug of choice for empiric therapy of sepsis[11].

The objective of the study was to determine invitro susceptibility of levofloxacin and cefoperazone against different gram negative and gram positive isolates by disc diffusion method.

MATERIALS AND METHODS

Clinical isolates were collected from different pathological laboratories located in Karachi. Isolates were identified as *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Salmonella typhi* and segregated from pus, sputum, blood, urine and stool tabulated in table 1.1. Standard discs of levofloxacin (5µg) and cefoperazone (75µg) were purchased from local market (Oxoid, UK).Mueller Hinton Agar (Merck) and Broth (Merck) were prepared under the guidelines of CLSI[12]. Mcfarland turbidity standard (0.5) was used and prepared[13]. With the help of sterile forceps the antimicrobial discs of levofloxacin and cefoperazone were placed on the dry inoculated streaked agar plates with light pressure to ensure its contact with the agar. The plates were then incubated at 37^{o}C for 24 hours. After incubation period the plates were examine for the zone of inhibition and measured in mm. The zones of inhibition for *E.coli a*nd *P.aeruginosa* were set as resistant (≤13), intermediate resistant (14-16mm), and sensitive (≥17mm). Whereas the zones for *S.aureus* were resistant (≤15mm), intermediate resistant (16-18mm), and sensitive (≥19mm) [12, 14]

RESULTS

The resistance pattern of *Escherichia coli* (32.5% and 42.5%), *Pseudomonas aeruginosa* (36% and 48%), *Staphylococcus aureus* (50% and 26.6%) and *Salmonella typhi* (20% and 16%) towards levofloxacin and cefoperazone respectively. Levofloxacin is found to be more effective against *E.coli* and *P.aeruginosa* as compared to cefoperazone. In table 1.2 isolates referred as resistant are those which are not inhibited by normal dose of the anti-microbial agent or show insignificant zone of inhibition around experimental disc, intermediately resistant isolates are with smaller diameter zones around the experimental disc and require higher doses for the treatment of infections and susceptible isolates show significant zone around the experimental disc, normal dose is sufficient for their killing.

TABLE 1.1 SOURCES OF CLINICAL ISOLATES

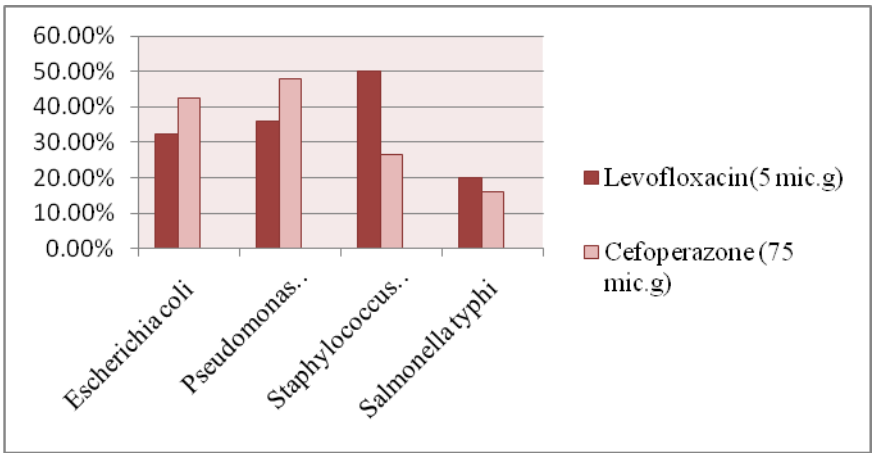
S.No	Pathogens	Sources				
		Blood	Stool/ Urine	Skin pus	Sputum	Sample size (N)
1.	*Escherichia Coli*	-	40	-	-	40
2.	*Pseudomonas Aeruginosa*	-	-	15	10	25
3.	*Staphylo-coccus Aureus*	-	-	15	15	30
4.	*Salmonella Typhi*	25	-	-	-	25

TABLE 1.2 SENSITIVITY OF LEVOFLOXACIN AGAINST CLINICAL ISOLATES

Pathogens	Levofloxacin			Cefoperazone		
	R	IR	Sensitive	R	IR	Sensitive
Eschrichia coli	8	5	27	16	1	23
Pseudomonas aeruginosa	5	4	16	8	4	13
Staphylococcus aureus	8	7	15	4	4	22
Salmonella typhi	0	5	20	2	2	21

Legend
R - Resistance
IR - Intermediate Resistance

Graph 1.1 Resistance pattern of different clinical isolates against levofloxacin and cefoperazone.



DISCUSSION

Microbial resistance to antibiotics is now prevalent and poses a serious clinical threat. The responsible factors of bacterial resistance to antimicrobial agents are: over prescription of antibiotics, use of under dose, prescriber's irrational attitudes, patient's demands, inappropriate advertisements and use of antibiotics in agriculture[15]. In recent years, the level of resistance to beta-lactam and/or macrolides has increased around the world, because of this resistance, it is necessary to test the therapeutic alternatives[2]. In the present study the antibacterial activity of levofloxacin and cefoperazone were tested against *Escherichia coli* (n=40), *Staphylococcus aureus* (n=30), *Pseudomonas aeruginosa* (n=25) and *Salmonella typhi* (n=25).

Intracellular bacteria are responsible for the relapsing and refractory infections which can be treated by levofloxacin as it have increased bactericidal activity against intracellular bacteria[7]. It is reported that levofloxacin is a good antibiotic against *Escherichia coli* and is supported by the published reports[16,17,18] however the current study showed that levofloxacin has started producing resistance (32.5%). Fluoroquinolones have good activity against many Gram-negative microorganisms, including *Pseudomonas aeruginosa*[19] however; resistance to these antibiotics had been also reported in recent years[20] as well as in the present study where 36% resistance showed by *Pseudomonas aeruginosa* against levofloxacin. Levofloxacin causes enhanced killing of cell associated *Pseudomonas aeruginosa* and *Staphylococcus aureus*[2] and is more bactericidal as compare to ofloxacin against all strains of *Staphylococcus aureus* which were tested[21] but in the current study 50% antibacterial activity of *staphylococcus aureus* against levofloxacin were observed. The resistance is produced by multiple resistance mechanisms against fluoriquinolones[22].

Studies showed that cefoperazone produce more eradication of *Escherichia coli* as compared to *Pseudomonas aeruginosa*[23] however cefoperazone /salbactum was found to be highly effective against *Pseudomonas aeruginosa* in wound infections[9].

In US 1% resistance of cefoperazone reported among 652 isolates of *Escherichia coli*[24], whereas the documented range of susceptibility of cefoperazone is (63.9% to 99.1% against nosocomial gram negative bacilli including *Escherichia coli* and *Pseudomonas aeruginosa*[25] however the present study showed 42.5% and 48% resistance respectively. These results describe the increasing pattern of resistance of mentioned clinical isolates against cefoperazone and levofloxacin and make the clinical practioners to realize that the choice of antibiotics is not only based on its antibacterial activity but also on its potential to select resistance[26]**.** Microbial resistance to antibiotics can be minimized through proper enlightenment, more rational antibiotic selection during treatment and proper legislation[15].

CONCLUSION

The current study revealed that levofloxacin is comparatively more susceptible to the infections cause by *Escherichia coli* and *Pseudomonas aeruginosa* while the other antibiotic cefoperazone is found to be effective against *Staphylococcus aureus* and *Salmonella typhi.* Authors suggested

that the periodic surveillance of commonly prescribed antibiotics must be done to evaluate the status of resistance against prevalent microbes.

SOURCE OF FUNDING
None.

CONTRIBUTION OF THE AUTHORS
All authors contributed equally in all aspects of the study.

CONFLICT OF INTERESTS
The authors declare no conflict of interests exists.

REFERENCES

[1] Nicodemo A.C., M. C. M. F., Oplustil C.P. And Sinto S. In vitro Activity of Fluoroquinolones (Gatifloxacin, Levofloxacin and Trovafloxacin) and Seven Other Antibiotics against Streptococcus. *Brazilian Journal of Infectious Diseases.* 2001. (5).

[2] Raymond P. Smitha, B, Aldona L. Baltcha,B, Mary A. Frankea, Phyllis B. Michelsena and Lawrence H. Boppa. Levofloxacin penetrates human monocytes and enhances intracellular killing of *Staphylococcus aureus* and *Pseudomonas aeruginosa*. *Journal of antimicrobial chemotherapy.* 2000. (45) 83-88 P.

[3] Fish DN. Gatifloxacin: An Advanced 8-Methoxy Fluoroquinolone. *Pharmacotherapy.* 2001. 21(1): 35-59 P.

[4] C.-J. Soussy, M. C., M.-C. Ploy, M.-D. Kitzis, C. Morel,A.Bryskier, And P. Courvalin. Invitro antibacterial activity of levofloxacin against hospital isolates a multicentre study. *journal of antimicrobial chemotherapy.* 1999. (43)**,** 43-50 P.

[5] Vadlamudi, R. S. M., MPH; Smalligan, Roger D. MD, MPH; Ismail, Hassan M. MD, MPH, July. Interaction between Warfarin and Levofloxacin. *Southern Medical Journal.* 2007. (100**)** 720-724 P.

[6] Acar, J. F. A Comparison of Side Effects of Levofloxacin to Other Agents Concerning the Ecological and Microbiological Effects on Normal Human Flora. *International journal of experimental and clinical chemotherapy*. 2001. (47) 15-23 P.

[7] Cambau E, G. L. Mechanisms of resistance to quinolones. *pubmed. US national library of medicine National institute of health.* 1993. (45**)** 15-23 P.

[8] Jones, R. N. A Review of Its Antimicrobial Spectrum, β-Lactamase Stability, Enzyme Inhibition, and Other in Vitro Characteristics. *Oxford Journal.* 1983. (5) 108-126 P.

[9] Shampa Aunupurba, A. B., Atul Garg, Malay Ranjan Sen,. Antimicrobial susceptibility of *Pseudomonas aeruginosa* isolated from wound infections. *Indian journal of dermatology.* 2007. (51**)** 286-288 P.

[10] PA, R. D. Bacterial resistance to cephalosporins as a function of outer membrane permeability and access to their target. *Journal of antimicrobial chemotherapy.* 1996. (8**)** 37-47 P.

[11] L.Stratchounski, I. E., A. Narezkina, M. Edelstein, M. Pimkin. In vitro activity of cefoperazone/sulbactam vs amoxicillin/clavulanic acid and piperacillin/tazobactam against extended spectrum beta-lactamase (ESBL)-producing strains of *Escherichia coli* and *Klebsiella pneumoniae*. *12th European Congress of Clinical Microbiology and Infectious Diseases,* Poster # P1413. 2006

[12] Performance Standards for Antimicrobial susceptibility Testings , Clinical and Laboratory Standard Institute 2012.

[13] Bushra R, Rizvi M,Ahmed M, Alam S ,Bano N. In-vitro Susceptibility of Levofloxacin against Different Clinical Isolates. *Pakistan Journal of Medicine and Dentistry.* 2013. 2(03): 8-12 P.

[14] Nasiri MI, Naqvi SBS, Zaidi AA, Saeed R, Raza G. Report - Comparative study on resistant pattern of clinical isolates against Levofloxacin and Cefepime. Pakistan *Journal of Pharmaceutical Sciences*. 2013. 26(2):415-419 P.

[15] Chinedum, I. E. Microbial resistance to antibiotics. *African Journal of Biotechnology.* 2005. (4): 1606-1611 P.

[16] Drago L, De Vecchi E, Mombelli B, Nicola L, Valli M and Gismondo MR. Activity of levofloxacin and ciprofloxacin against urinary pathogens. *J.Antimicrob. Chemother.,* 2001. 48(1): 37-45 P.

[17] Weber P, Dip C, Durand C and Moniot-ville N.Evaluation of levofloxacin susceptibility against strains isolated from lower urinary tract infections in the community. *Patho. Biol.* 2005. 53(2): 125 P.

[18] Matsuzaki K, Koyama H, Chiba A, Omika K, Harada S,Sato Y, Hasegawa M, Kobayashi I, Kaneko A and Sasaki J. *In vitro* activities of levofloxacin and other antibiotics against fresh clinical isolates.*Jpn.J.Antibiot.* 1999. 52(9): 571-584 P.

[19] Algun U, Arisoy A, Gunduz T and Ozbakkaloglu B(2004). The resistance of pseudomonas aeruginosa strains to fluoroquinolone group of antibiotics. *Int. J.Med. Microbiol*. 2004. 22(2): 112-114 P.

[20] Polk RE, Johnson CK, McClish D, Wenzel RP and Edmond MB. Predicting Hospital Rates of Fluoroquinolone-Resistant *Pseudomonas aeruginosa* from Fluoroquinolone use in US Hospitals and their surrounding communities. *Clin. Infect Dis.* 2004. (39): 497-503 P.

[21] Muller-Serieys C, Decré D, Benoit C, Bigot C, Maubert B, Carbon C. Levofloxacin: serum bactericidal activity against methicillin-resistant Staphylococcus aureus isolates. *J Antimicrob Chemother*. 1999. (43) Suppl C:67-70 P.

[22] Beatriz Guerra, Burkhard Malorny, Andreas Schroeter and Reiner Helmuth. Multiple Resistance Mechanisms in Fluoroquinolone-Resistant *Salmonella* Isolates from Germany. *Antimicrob.Agents Chemother*. 2003. 47(6): 2059 P.

[23] Thomas M. File Jr. James S. Tan, Ian Baird, James W. Simon and Jack L. Summers. Evaluation of cefoperazone in the therapy of urinary tract infections. *J. Antimicrob. Chemother.* 1982. 9(3): 223-230 P.

[24] R Cooksey, J Swenson, N Clark , E Gay and C Thornsberry. Patterns and mechanisms of beta-lactam resistance among isolates of Escherichia coli from hospitals in the United States. 1990.

[25] Hui Wang, Minjun Chen, Yuxing Ni,Yudong Liu,Hongli Sun,Yunsong Yu, Xiujuan Yu,Min Liu,Ziyong Sun,Yunzhuo Chu,Zhidong Hu, Xinhong Huang. Antimicrobial resistance among clinical isolates from the Chinese Meropenem Surveillance Study (CMSS), 2003–2008. *International Journal of Antimicrobial Agents*. 2010. 35(3): 227–234 P.

[26] Wai C. Chana, R. C. L.,Julia M. Lingb, Augustine F. Chengb And Jerome J. Schentagc. Markedly different rates and resistance profiles exhibited by seven commonly used and newer β-lactams on the selection of resistant variants of Enterobacter cloacae. *J. Antimicrob. Chemother.* 1999. (43)**:** 55-60 P.

****