Effectiveness of Ciprofloxacin and Levofloxacin in treatment of Pseudomonas Aeruginosa infection

Imtiaz Ahmad¹, Wasil Khan², Aleem ur Rashid², Samiullah³, Abdul Ahad², Aminullah², S.M.Naeem⁴

ABSTRACT

Background: Pseudomonas aeruginosa is the most troublesome and feared pathogen in medical field. It is the sixth most common cause of hospital-acquired infections and the cause of ventilator-associated pneumonia. The most common multidrug-resistant gram-negative pathogen in Ventilated Assisted Patient. In our study in 100 patients culture and sensitivity report only 46% were sensitive to oral treatment while 54% of the pseudomonas were resistant to ciprofloxacin and 34% sensitive and 66% resistant to levofloxacin.

Objective: To find out resistance of pseudomonas to oral medication.

Material and Methods: A cross-sectional study, conducted in Saidu Group of Teaching Hospital from January 2018 to July 2019. 100 patient samples (tracheal aspirate, bronchial washing, sputum, pus, urine and blood) were cultured for pseudomonas and its sensitivity to oral medication ciprofloxacin and levofloxacin was recorded.

Results: Sensitivity to 46% were samples was observed to oral treatment while 54% of the pseudomonas were resistant to ciprofloxacin and 34% sensitive and 66% resistant to levofloxacin respectively.

Conclusion: It was found that 54% pseudomonas were resistant to Ciprofloxacin and 66% resistant to levofloxacin. So we should always consider for combination therapy.

Key words: Pseudomonas, oral medication, culture and sensitivity, resistance

This article may be cited as: Ahmad I, Khan W, Rashid UA, Samiullah, Ahad A, Aminullah, Naeem SM.
Effectiveness of Ciprofloxacin and Levofloxacin in treatment Pseudomonas Aeruginosa infection. J Saidu Med Coll Swat 2020;10(1):79-82

INTRODUCTION

Pseudomonas is a rod-shaped, aerobic, Gram-negative bacterium belonging to the family Pseudomonadaceae¹. Pseudomonas aeruginosa easily adapts to the environment it inhabits and can also colonize and invade a human host to cause serious infections^{2,3}. P. aeruginosa isolates that cause infections are thought to express various virulence factors. This pathogen is one of the most common causes of pneumonia^{4,5}.

Risk factors for the development of infections caused by Pseudomonas include neutropenia, cystic fibrosis, severe burns, and foreign device installations^{2,3}. The general human population is refractory against infections caused by Pseudomonas species, but Pseudomonas species are physiologically highly flexible and able to act as opportunistic pathogens in humans with weakened immune systems⁶. P. aeruginosa causes life-threatening community-acquired pneumonia, nosocomial infections such as pneumonia, urinary tract infections, bacteremia and chronic lung infections in patients with cystic

fibrosis⁷. The identification of the microbiological cause of a case of pneumonia is especially important for preservation of the sensitivity of bacteria to antibiotics and for regulation of drug therapy⁷.

One of the most important challenges for physicians is the adequate treatment of infections due to Gram-negative pathogens because of the increasing antimicrobial resistance in the healthcare setting⁸. Among infections caused by Gram-negative rods, Pseudomonas aeruginosa has a leading role⁹, especially in critically ill and immunocompromised patients. Antimicrobial resistance has led to a serious restriction in treatment options for P. aeruginosa infections, which has become a critical and deadly issue causing a total of 51,000 healthcare infections in the USA per year^{10,11}.

According to data reported to the National Healthcare Safety Network (NHSN) in the United States from 2011 to 2014, P. aeruginosa is¹². The sixth most common cause of hospital-acquired infections in general (7.3 percent) The second most common cause of ventilator-associated pneumonia (VAP; 16.5 percent) and the most common multidrug-resistant gram-negative pathogen causing VAP. The third most common cause of catheter-associated urinary tract infections (10.3 percent). The fifth most common cause of surgical site infections (5.7 percent). It is also a common pathogen worldwide; it was the

1. Department of Pathology Saidu Medical College, Swat.

2. Department of Medicine Saidu Medical College, Swat.

3. Department of Nephrology, Saidu Medical College, Swat

4. Department of Biochemistry, Saidu Medical College, Swat.

Correspondence: Dr. Imtiaz Ahmad

Associate Professor of pathology, Saidu Medical College, Swat.

Email: imtiaz.ahmad71@gmail.com

Cell: 0345-8880737

Received October 28, 2019 Accepted March 2, 2020

third most common cause of intra-abdominal infections from 2002 to 2011 and the third most common cause of urinary tract infections from 2009 to 2011¹³.

MATERIAL AND METHODS

This cross-sectional study was conducted on one hundred (100) patients' in Saidu Group of Teaching Hospital from January 2018 to July 2019. Demographic details including age, gender, location and clinical features were recorded. The isolate were collected from tracheal aspirate, bronchial washing, sputum, pus, urine and blood specimens of patients' of different units including intensive care unit, pediatric, medical and gynecology units.

Clinical isolate were identified by standard methods. they were inoculated on Blood agar (Oxide), Mac Conkeys agar (Oxide) and Cystine lactose electrolyte deficient agar (Oxide). Isolate were identified on the basis of colony morphology, Gram Staining and biochemical tests including Catalase, Oxidase, Sulfide, Indole, Motility, Citrate, urea, TSI reaction, Pyocinin production and lactose. Mueller Hinton plates were seeded with 0.5 MacFarland suspension matched turbidity inocula and antibiotic Disc were placed on them.

Results were interpreted after 24 hours of incubation at 37°C by measuring zones of antibiotics around discs. Isolates that were not

identified on the basis of conventional methods was carried out by analytical Profile Index (API) 20 NE kit (BioMerieux, France).

Antibiotic susceptibility test was done by using the disc diffusion Kirby Bauer method. The antibiotics tested include Levofloxacin, Ciprofloxacin, Tazobactam/ Piperacillin 10/100Mcg, amikacin (30mcg), Gentamycin (10mcg), Ceftazidime 10mcg, cefepime (10mcg), meropenem (10mcg), imipenem (10mcg), ceftiofur/sulbactam and Colistin. Ps. Aeruginosa ATCC-27853 was used as reference strain.

RESULTS

In 100 patients' culture 46% were sensitive to ciprofloxacin and 54% were resistant while there is 34% sensitivity and 66% resistance to levofloxacin.

		Statistics			
		Ciprofloxacin		Levofloxacin	
N	Valid	100		100	
	Missing	0		0	

Ciprofloxacin					
Valid		Frequency	Percent	Valid Percent	Cumulative Percent
	Sensitive	46	46.0	46.0	46.0
	Resistant	54	54.0	54.0	100.0
	Total	100	100.0	100.0	

Levofloxacin					
Valid		Frequency	Percent	Valid Percent	Cumulative Percent
	Sensitive	34	34.0	34.0	34.0
	Resistant	66	66.0	66.0	100.0
	Total	100	100.0	100.0	

DISCUSSION

Pseudomonas aeruginosa is often an opportunistic pathogen, causing infections in patients with physical, phagocytic, or immunologic defects in host defense mechanisms. Historically, *P. aeruginosa* has been a major burn wound pathogen, a serious cause of bacteremia in neutropenic patients, and the most important pathogen in cystic fibrosis (CF) patients. However, these associations have undergone considerable change, with a shift in the spectrum of the hosts who are now commonly infected by *P. aeruginosa*.

In our study in 100 patients culture and sensitivity report only 46% were sensitive to oral treatment while 54% of the pseudomonas were resistant to ciprofloxacin and 34% sensitive and 66% resistant to levofloxacin. In Pakistan there is increase resistance to antibiotic because of irrational and over the counter use.

Better ways of administering antibiotics have been considered to overcome the increasing resistance patterns. In a pharmacodynamic analysis, high-dose, prolonged infusions of cefepime, ceftazidime, doripenem, and meropenem had the highest probabilities of achieving bactericidal exposure for *P. aeruginosa*¹⁴.

Acquired resistance, specifically, can result from mutation or acquisition of exogenous resistance determinants and can be mediated by a number of mechanisms, including degrading enzymes, reduced permeability, and active efflux^{15,16}.

Resistance to carbapenems, particularly imipenem, can arise by simple mutation resulting in the loss of a carbapenem-specific porin, OprD¹⁷.

Syed Maisam Ali et al have shown 39% resistance to ciprofloxacin¹⁸. A study conducted in Turkey in 1996, revealed only 94 % sensitivity of *Pseudomonas aeruginosa* to ciprofloxacin,¹⁹ while the resistance went higher to 100% of the isolates, showed resistance to ciprofloxacin²⁰.

Patterns of antibiotic resistance in *P. aeruginosa* evolve over time and vary geographically and by type of infection. This geographical variation highlights the importance of local epidemiological data when choosing empiric therapy.

As an example, in North America from 2005 to 2010, resistance to fluoroquinolones among intra-

abdominal and urinary tract infection isolates increased (from 22 to 33 percent), resistance to imipenem (20 percent) and other beta-lactams (piperacillin-tazobactam, cefepime, and ceftazidime; 23 to 26 percent) remained essentially unchanged, and resistance to amikacin declined (from 11 to 3 percent)⁷. Resistance patterns were different in other locations: in South Africa, resistance to piperacillin-tazobactam was 8 percent and to cefepime, ceftazidime, and imipenem was 25 to 26 percent; in China, resistance rates to amikacin and piperacillin-tazobactam were 12 and 8 percent, respectively.

In the United States specifically, surveillance suggests a trend towards declining rates of resistance, although rates still remain high⁶. Among catheter-related bloodstream infection, catheter-associated urinary tract infection, and ventilator associated pneumonia isolates, resistance ranged from 22 to 26 percent for extended-spectrum cephalosporins, 16 to 19 for piperacillin-tazobactam, 30 to 33 percent for fluoroquinolones, 24 to 28 percent for carbapenems, and 17 to 23 percent for aminoglycosides. Approximately 18 to 19 percent were multidrug-resistant. Rates of resistance were generally lower (4 to 11 percent) among surgical site infection isolates.

CONCLUSION

Pseudomonas Aeruginosa resistance is increasing day by day through different mechanism especially to oral antibiotic i.e. ciprofloxacin and levofloxacin.

RECOMMENDATIONS: Irrational use of antibiotic needs to be stopped. Over the counter antibiotic should be banned and should be only given according to Culture & Sensitivity. There should be check and balance of antibiotic use in veterinary and poultry industry by concern authorities as they are giving antibiotic and that also contributes in the development of resistance.

Further research should be made to establish the fact and develop new antibiotics, and combination of Intravenous antibiotics should be used for treatment and prevention of infection.

REFERENCES

1. Bentzmann S, Plésiat P. The *Pseudomonas aeruginosa* opportunistic pathogen and human infections. *Environ. Microbiol.* 2011; 13: 1655-1665.
2. Hardalo C, Edberg SC. *Pseudomonas aeruginosa*: assessment of risk from drinking water. *Crit. Rev. Microbiol.* 1997; 23: 47-75..
3. Mena KD, Gerba CP. Risk assessment of *Pseudomonas aeruginosa* in water. *Rev Environ Contam. Toxicol.* 2009 201, 711-15..
4. Zarb P, Coignard B, Griskeviciene J, Muller A, Vankerckhoven V, Weist K, et al. The European Centre for Disease Prevention and Control (ECDC) pilot point prevalence survey of healthcare-associated infections and antimicrobial use. *Euro Surveill.* 2012; 17: 203-16.
5. Kollef MH, Chastre J, Fagon JY, François B, Niederman MS, Rello J, et al. Global prospective epidemiologic and surveillance study of ventilator-associated pneumonia due to *Pseudomonas aeruginosa*. *Crit. Care Med.* 2014; 42:2178-87.
6. Bubonja-Sonje M, Matovina M, Skrobbonja I, Bedenic B, Abram M. Mechanisms of Carbapenem Resistance in Multidrug-Resistant Clinical Isolates of *Pseudomonas aeruginosa* from a Croatian Hospital. *Microb Drug Resist.* 2015;.
7. Tran CS, Rangel SM, Almlad H, Kierbel A, Givskov M, Tolker-Nielsen T, et al. The *Pseudomonas aeruginosa* type III translocon is required for biofilm formation at the epithelial barrier. *PLoS Pathog.* 2014; 10: 100447-9.
8. Pena C, Suarez C, Tubau F, Dominguez A, Sora M, Pujol M, Gudiol F, Ariza J. Carbapenem-resistant *Pseudomonas aeruginosa*: factors influencing multidrug-resistant acquisition in non-critically ill patients. *Eur J Clin Microbiol Infect Dis.* 2009;28(5):519-22.
9. El Zowalaty ME, Al Thani AA, Webster TJ, El Zowalaty AE, Schweizer HP, Nasrallah GK, Marei HE, Ashour HM. *Pseudomonas aeruginosa*: arsenal of resistance mechanisms, decades of changing resistance profiles, and future antimicrobial therapies. *Future Microbiol.* 2015;10(10):168370-6.
10. Fujii A, Seki M, Higashiguchi M, Tachibana I, Kumanogoh A, Tomono K. Community-acquired, hospital-acquired, and healthcare-associated pneumonia caused by *Pseudomonas aeruginosa*. *Respir Med Case Rep.* 2014;12:303.
11. Lund-Palau H, Turnbull AR, Bush A, Bardin E, Cameron L, Soren O, Wierre-Gore N, Alton EW, Bundy JG, Connett G, Faust SN, Filloux A, Freemont P, Jones A, Khoo V, Morales S, Murphy R, Pabary R, Simbo A, Schelenz S, Takats Z, Webb J, Williams HD, Davies JC. *Pseudomonas aeruginosa* infection in cystic fibrosis: pathophysiological mechanisms and therapeutic approaches. *Expert Rev Respir Med.* 2016;10(6):685-97.
12. Weiner LM, Webb AK, Limbago B, et al. Antimicrobial-Resistant Pathogens Associated With Healthcare-Associated Infections: Summary of Data Reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2011-2014. *Infect Control Hosp Epidemiol* 2016; 37:1288.
13. Morrissey I, Hackel M, Badal R,. A Review of Ten Years of the Study for Monitoring Antimicrobial Resistance Trends (SMART) from 2002 to 2011. *Pharmaceuticals (Basel)* 2013; 6:133-5.
14. Koomanachai P, Bulik CC, Kuti JL, Nicolau DP. Pharmacodynamic modeling of intravenous antibiotics against gram-negative bacteria collected in the United States. *Clin Ther* 2010; 32:766.
15. Livermore DM. Interplay of impermeability and chromosomal beta-lactamase activity in imipenem-resistant *Pseudomonas aeruginosa*. *Antimicrob Agents Chemother* 1992; 36:2046.
16. Yokoyama K, Doi Y, Yamane K, et al. Acquisition of 16S rRNA methylase gene in *Pseudomonas aeruginosa*. *Lancet* 2003; 362:1888.
17. Masuda N, Gotoh N, Ishii C. Interplay between chromosomal beta-lactamase and the MexAB-OprM efflux system in intrinsic resistance to beta-lactams in *Pseudomonas aeruginosa*. *Antimicrob Agents Chemother* 1999; 43:400.
18. Ali MS, Mahesar HJ, Shezad J, Zaman A, Shinwari W, Sajid T, Khatak KS. Spectrum of *Pseudomonas aeruginosa* sensitivity in chronic otitis media. *J Saidu Med Coll Swat* 2019;9(2): 191-4.
19. Altuntas A, Aslam A, Eren A, Unal A, Nalca Y. Susceptibility of microorganisms isolated from chronic otitis media to ciprofloxacin. *Eur Arch Otorinolaryngol.* 1996;253:364-6.
20. Jang CH, Park SY. Emergence of ciprofloxacin resistant *pseudomonas* in chronic suppurative otitis media. *Cli Otolaryngol.* 2004;29:321-3