

European Journal of Biotechnology and Bioscience

Volume: 3, Issue: 4, 22-24
April 2015
www.biosciencejournals.com
ISSN: 2321-9122
Impact Factor: 3.742

Syed Bilal Tanvir
House Officer, Department
of Surgery, Dr Ziauddin
Medical University, Karachi
Department of Medicine,
Sindh, Karachi, Pakistan

Kanaan Mansoor
MD, Causality Medical
Officer, Department of
Emergency Medicine, Dr
Ziauddin Medical University
Hospital, Sindh Karachi,
Pakistan

Ali Shariq
Assistant Professor
Microbiology department, Dr
Ziauddin Medical University
Hospital, Sindh, Karachi,
Pakistan

Heba Shariq
Senior Resident Microbiology
department, Dr Ziauddin
Medical University Hospital,
Sindh, Karachi, P.O Box
75600, Pakistan

Arif Hussain
Professor, Director Clinical
Laboratories, Dr Ziauddin
University Hospital,
Sindh, Karachi, Pakistan

Badar Jahan Farooqi
Professor, Head of
Department Medical
Microbiology, Dr Ziauddin
University Hospital,
Sindh, Karachi, Pakistan

Roofia Tanvir
3rd year M.B, B.S student at
Ziauddin Medical University,
Sindh, Karachi, Pakistan

Correspondence:
Syed Bilal Tanvir
House Officer, Department
of Surgery, Dr Ziauddin
Medical University, Karachi
Department of Medicine,
Sindh, Karachi, Pakistan

Emerging resistance to meropenem in *Pseudomonas aeruginosa* Isolates among patients of a tertiary care hospital of Pakistan

Syed Bilal Tanvir, Kanaan Mansoor, Ali Shariq, Heba Shariq, Arif Hussain, Badar Jahan Farooqi, Roofia Tanvir

Abstract

Background: To discern the prevalence of *P. aeruginosa* isolates from tracheal and bronchial aspirates and compare its emerging resistance pattern to meropenem with previous studies.

Methods: A cross-sectional study was performed for a time frame of 2 years from January 2013 to January 2015 in 200 bedded tertiary care private hospital in Karachi. The isolates were cultured on chocolate and MacConkey agar. Meropenem sensitivity profile of *P. aeruginosa* isolates were deduced by utilizing Kirby Bauer Disc diffusion method on Mueller Hinton Agar.

Results: A total of 634 isolates of *P. aeruginosa* from tracheal and bronchial aspirates during a study time frame of January 2013 to January 2015 were cultured. Positive cultures were most commonly observed in male samples who were above 50 years of age. 66.1% of the isolates were sensitive to Meropenem while 33.9% of the isolates were resistant.

Conclusions: *P. aeruginosa* isolates from samples of tracheal aspirate, Pus, Urine, Blood, Body fluids and Bronchoalveolar lavage were collected and their prevalence was deduced. The increased resistance pattern of isolates to meropenem and its causes were also discerned.

Keywords: *P. aeruginosa*; Meropenem; Resistance; Prevalence; tracheal aspirates

1. Introduction

Pseudomonas aeruginosa is a gram negative rod and it is a clinically recognized pathogen which is associated with a large number of nosocomial infection. Most of these infections are life threatening and often difficult to treat.¹

Mostly *Pseudomonas aeruginosa* is associated with lung diseases in cystic fibrosis patient² and wound infection and septicemia in burns patient³ followed by UTI and respiratory tract infection.⁴ Recently multi drug resistant pseudomonas have also emerged mostly due to selective pressure by the non-judicious use of antipseudomonal antibiotics.⁴

Chronic infections with *Pseudomonas aeruginosa*, particularly with lung infections are associated with shortening the lifespan of affected patient.⁵ Due to intrinsic multiple drug resistance as well as acquired antimicrobial resistance the therapeutic options for treating *Pseudomonas aeruginosa* infection has been limited.⁶ Resistance to most antipseudomonal drugs has increased upto greater than twenty percent over the last decade.⁷

Meropenem belongs to the carbapenem group of antimicrobials. It was approved by US FDA in July 1996. Meropenem is used to treat serious life threatening infections by *Pseudomonas aeruginosa*, particularly as one of the last resort, when the organism is resistant to other primary therapeutic agents. Various studies have suggested that meropenem is an effective antimicrobial drug which can be used to treat *Pseudomonas aeruginosa*.⁵ Unfortunately *Pseudomonas aeruginosa* is acquiring resistance to carbapenems which will further limit the therapeutic options.⁸ We have studied the invitro meropenem susceptibility of *Pseudomonas aeruginosa* strains isolated from various clinical samples, collected from a 200 bedded tertiary care hospital, Karachi, Pakistan.

Material and methods

From January 2013 to January 2015 this cross sectional study was conducted at Microbiology Department of Ziauddin Medical university hospital Karachi, Pakistan. For over a time frame of two years inpatients who were admitted ICU and HDU of Hospital had their samples of

Tracheal aspirate, Pus, Urine, Blood, Body fluids and Bronchoalveolar lavage collected. Included patients were of all age groups. The samples were cultured on Chocolate, and MacConkey agar and incubated at 37C for a period of 18 hours. Isolates were identified according to standard microbiological methods (Koneman et al., 2006) *P. aeruginosa* by its colony morphology, on gram staining pleomorphic gram negative rod, non lactose fermentation on MacConkey, pigment production with characteristics grape like odor, Oxidase positivity, nonmotile along with its ability to reduce nitrate to nitrite and arginine decarboxylase and gelatin liquefaction. Api 20 NE was used for confirmation of isolates.

Antibiotic sensitivity patterns of these isolates were studied by using Kirby Bauer Disc Diffusion method on Mueller – Hinton agar, by following CLSI 2014 Guidelines [6A], by using Hi-media antibiotic discs. Antibiotic which was tested included meropenem (10mcg). Strains which had the similar types of resistance patterns (antibiotype) were deduced to be from the same clone. For quality control *Pseudomonas aeruginosa* ATCC 27853 strain was utilized for in this study. disc Diffusion criteria mentioned in CLSI was used for interpretation of Antibiotic susceptibility zone.

SPSS version 17 was used for statistical analysis. Frequency of percentage of resistant antibiotics were calculated

Results and Discussion

Table I depicts the relationship of age and gender of *Pseudomonas Aeruginosa* isolates. Males (58.2%) to some extent outweighed the total number of female (41.8%) patients. Roughly 60.4% of the patients were less than 50 years of age out of which 37.1% were males and 23.3% were females. Even in patients less than 50 years of age 21.1% were males while 18.5% of the patients were females.

The resistance and sensitivity pattern of *P. aeruginosa* isolates to carbenem(meropenem) is portrayed in table II. It reveals that 33.9%(215) of the isolates were resistant to meropenem whereas 66.1%(419) of the isolates were sensitive to it, which is a considerably high resistance pattern to meropenem as compared to the previous researches which were conducted.

Pseudomonas aeruginosa is non-fermenter gram negative pleomorphic bacteria. Among the organisms which cause nosocomial infections *Pseudomonas aeruginosa* stands as one of the leading cause. It is a ubiquitous organism, which means that it is present in a large area of hospital environment, which includes critical care devices such as ventilator, nebulizers and antiseptic solutions.⁹ Environmental sources have a significant role in transmission of *pseudomonas aeruginosa* in hospitalized patients.⁴ Various outbreaks caused by Multiple drug resistant *pseudomonas aeruginosa* are reported in a variety of nosocomial settings mostly in intensive care units. The risk for acquiring *Pseudomonas aeruginosa* is related to various factors which include a number of carriers in the same ward as well as individual risk factors. For example immunocompromised patients, use of invasive devices and antibiotic treatment.

Table 1: Age and Gender relationship with isolates n=634

Age (years)	Male %	Female %	Total %
> 50	37.1%	23.3%	60.4%
< 50	21.1%	18.5%	39.6%
Total	58.2%	41.8%	100%

Table 2: Sensitivity pattern of isolates to Meropenem

Pattern	Frequency	Percent	Valid Percent
Resistant	215	33.9%	33.9%
Sensitive	419	66.1%	66.1%
Total	634	100.0%	100.0%

Meropenem is a broad spectrum injectable antibiotic belonging to carbapenem class of antibiotics with minimal side effects and antipseudomonal activity. Its penetration in body tissue and fluids is very well including CSF, bile and peritoneal fluid.¹⁰

According to a study conducted by Fink.MP et al. it showed 10.9% resistance to meropenem among *Pseudomonas aeruginosa* isolates.⁸ Another research carried out by Christenson JC et al. in department of Pediatrics division of Infectious diseases and Geographic Medicine, University Utah school of Medicine revealed that 6% of the isolates were resistant to meropenem and 92.5% of the isolates were sensitive.¹¹ While another study performed by Indu Baswal et al. illustrated that 79.3% of the isolates were sensitive to meropenem while only 8% of the isolates were resistant.³ Research carried out by Songara.P et al. also rendered that the resistance of *P. aeruginosa* isolates to meropenem was 27%.¹²

Meropenem is included as one of the last resorts in treating life threatening pseudomonal infection. Our results demonstrate that 33.9% of *Pseudomonas aeruginosa* strains are resistant to meropenem. The resistance to meropenem is due to various mechanisms, which includes production of extended spectrum beta-lactamases, efflux pumps due to reduced expression of OprD as well as porin channel mutations.¹³ Expression of the MexAB-OprM and the MexEF OprN.⁶

This increase in meropenem resistance is an alarming situation which can lead to an increase in morbidity, mortality as well as treatment costs and duration of stay in hospital. One of the most leading factors associated with this increased antibiotic resistance is non-judicious and over the counter selling of antibiotics in this region of the world. Judicious use, strict regulations and continuous surveillance along with educating healthcare staff are key factors to halt this situation. Culture and antimicrobial susceptibility should be performed before starting therapy. Infection control team of hospital should implement strict policies in order to prevent the spread and transmission of organism.

Typing of strains of multi drug resistant *pseudomonas* is also essential in order to determine the epidemiology in designing strategies for controlling nosocomial *Pseudomonas aeruginosa* strains.

Finally more clinical research studies are needed to identify factors and mechanisms associated with antimicrobial resistance in order to counteract them.

Conclusion

In conclusion there should be strict implementation of infection control policies along with judicious usage of antibiotics and antibiotic stewardship should be specifically tailored to the needs of each institution. New antipseudomonal therapeutic agents with fewer side effects and costs are needed on priority basis. Additional attention to disinfection of hospital environment to limit the transfer of *Pseudomonas aeruginosa* should also be highlighted.

References

1. Brewer SC, Wunderick RG, Jones CB, Leeper KV, Ventilator-associated pneumonia due to *Pseudomonas aeruginosa*. *Chest* 1996;109(4):1019-29
2. Gilligan, P.H, Microbiology of airway diseases in patients with cystic fibrosis. *Clin Microbiol Rev*, 1991;4(1): 35–51.
3. Biswal I, Arora BS, Kasana D, Neetushree, Incidence of multidrug resistant *Pseudomonas aeruginosa* isolated from burn patients and environment of teaching institution, *J Clin Diagn Res*, 2014,8(5):26-29
4. Mahmoud AB, Zahran WA, Hindawi GR, Labib AZ, Galal R, Prevalence of Multidrug-Resistant *Pseudomonas aeruginosa* in Patients with Nosocomial Infections at a University Hospital in Egypt, with Special Reference to Typing Methods, *J. Virol Microbiol*, Feb;2013:10-13..
5. Webb A.K, The treatment of pulmonary infection in cystic fibrosis, *Scand J Infect Dis. Suppl.*, 1995;96:24-7.
6. Pai H, Kim J-W, Kim J, Lee JH, Choe KW, Gotoh N. Carbapenem Resistance Mechanisms in *Pseudomonas aeruginosa* Clinical Isolates. *Antimicrob. Agents Chemother.* 2001;45(2):480-84
7. Jung R, Fish DN, Obritsch MD, Maclaren R, Surveillance of multi-drug resistant *Pseudomonas aeruginosa* in an urban tertiary-care teaching hospital, *J Hosp Infect*, 2004;57(2):105-11
8. Fink MP, Snyderman DR, Niederman MS, et al. Treatment of severe pneumonia in hospitalized patients: results of a multicenter, randomized, double-blind trial comparing intravenous ciprofloxacin with imipenem-cilastatin. The Severe Pneumonia Study Group. *Antimicrob. Agents Chemother.* 1994;38(3):547-57.
9. Weber DJ, Rutala WA, Sickbert-Bennett EE. Outbreaks Associated with Contaminated Antiseptics and Disinfectants, *Antimicrob. Agents Chemother.* 2007; 51(12):4217-24.
10. AHFS Drug Information (2006 ed.). American Society of Health-System Pharmacists. 2006, available at <http://www.ahfsdruginformation.com/>
11. Christenson JC, Korgenski EK, Daly JA, In vitro activity of meropenem, imipenem, cefepime and ceftazidime against *Pseudomonas aeruginosa* isolates from cystic fibrosis patients, *J Antimicrob Chemother*, 2000;45(6):899-901
12. Songara.P, Neema.S, Kothari.V, Sachdeva.R, Dev.R., Antibiotic Resistance Pattern in *Pseudomonas Aeruginosa* Species Isolated at Indore (M.P.). *J Evol Med Dent Sci*, 2014; 3(1):109-14.
13. Rodríguez-Martínez JM, Poirel L, Nordmann P. Molecular Epidemiology and Mechanisms of Carbapenem Resistance in *Pseudomonas aeruginosa*, *Antimicrob. Agents Chemother* 2009;53(11):4783-88