International Journal of Research in Medical Sciences
Vasundhara Devi P et al. Int J Res Med Sci. 2015 Jun;3(6):1368-1371
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: 10.18203/2320-6012.ijrms20150149

Research Article

Incidence of carbapenem resistant nonfermenting gram negative bacilli from patients with respiratory tract infections among intensive care units

P. Vasundhara Devi*, P. Sreenivasulu Reddy, Maria Sindhura John

Department of Microbiology, Narayana Medical College, Nellore, Andhra Pradesh, India

Received: 28 March 2015
Revised: 01 April 2015
Accepted: 07 May 2015

***Correspondence:**
Dr. P. Vasundhara Devi,
E-mail: dr.pvasundhara@gmail.com

ABSTRACT

Background: Non fermenting gram negative bacilli that were considered to be contaminants in the past have now emerged as important healthcare- associated pathogens. Pseudomonas aeruginosa and Acinetobacter species are now known to be the common nosocomial pathogens. Carbapenems are one of the essential antibiotics in the armamentarium against, serious nosocomial infections. Development of resistance against these is a cause of concern. Misuse and inappropriate duration of antibiotic therapy helps in development of resistance.
Methods: A total of 200 endo tracheal aspirates and sputum samples were collected from patients of all age groups with clinical evidence of lower respiratory tract infection from Medical, surgical, pediatric ICUS. Non fermenting gram negative bacilli isolated and identified according to CLSI guidelines and antibiotic sensitivity test was performed by Kirby Bauer disc diffusion method.
Results: Out of 200 samples 50 Acinetobacter spp. and 38 Pseudomonas aeruginosa were isolated. Among 38 Pseudomonas isolates (42%) 16 were resistant to imipenem and 11 (29%) were resistant to meropenem. Among 50 Acinetobacter isolates 14 (28%) were resistant to imipenem and 12 (24%) were resistant to meropenem.
Conclusions: Our study documents an increase in the carbapenem resistance. Reduction in antimicrobial resistance in the ICUS has been a goal for all ICUS as it improves outcome and cost of patient care. Carbapenem must be used judiciously to prevent further resistance or else this would erode the strength of life saving antibiotics.

Keywords: Carbapenem resistance, NFGNB, Nosocomial, Kirby Bauer disk diffusion

INTRODUCTION

Non fermenting gram- negative bacilli (NFGNB) are a taxonomically diverse group of aerobic, non sporing, bacilli that do not utilize glucose as a source of energy or utilize it oxidatively.[1] They occur as saprophytes in the environment and some are also found as commensals in the human gut.[2,3] Non fermenting gram negative bacilli, normally a saprophyte, cause serious infections in immuno compromised and hospitalized patients especially those admitted in Intensive Care Units (ICU).[4]

Lower respiratory tract infections are the most common bacterial infections among patients in intensive care units occurring in 10-25% of all ICU patients and resulting in high overall mortality, which may range from 22.71%.[5,6] Most common bacterial agents of LRTI in the ICU are Pseudomonas, Acinetobacter, Klebsiella, Citrobacter, Escherichia coli[7-9] which are multi drug resistant, and limiting the therapeutic options.[4] Carbapenems which were introduced first in 1980 are now frequently used as the last choice in treating serious infections caused by multidrug resistant, gram negative bacilli which are stable to β-lactamases including the Extended Spectrum β-

Lactamases (ESBLS) and Ampc.[10-12] NFGNB are known to produce ESBLs and metallo β-lactamases.[3,13] Pseudomonas aeruginosa and Acinetobacter species in particular are most often associated with carbapenem resistance. This is of significance since NFGNB can cause fatal, LRTIS in patients admitted to ICU.[14] Carbapenem resistance appears to be due to metallo-β-Lactamases and this can be transferred to other species like Escherichia coli, Enterobacter spp. and Klebsiella spp. posing serious problem[15] due to lack of therapeutic options. Chromosomal Ampc β-Lactamases can slowly hydrolyze imipenem. When expression of an Ampc enzyme is coupled with an additional mechanism of resistance, frank carbapenem resistance can result. The combination of porin loss and class c β-lactamase expression is an important cause of imipenem resistance in P. aeruginosa[16] and Acinetobacter baumanii.[17]

METHODS

A total of 200 samples were collected from patients of all age groups with clinical evidence of lower respiratory tract infection admitted to medical, surgical, neuro and pediatric ICU'S of Narayana General Hospital, Nellore during April, 2013 to April 2014. A general history of diabetes, hypertension and personal history of smoking, alcoholism, chewing tobacco were collected. Specimens were collected before antibiotic administration. Samples collected were Endotrracheal aspirates from suction tips of patients on ventilators and sputum samples from others in sterile universal containers. Endotracheal aspirates were collected by using sterile 12 gauge endotracheal suction catheter tube connected to suction pump passed through endotracheal tube. Samples were transported immediately within 15 minutes to microbiology laboratory and processed.

Processing of samples: Smears were prepared on clean microscopic glass slides and gram staining was done for gram reaction, size, shape, arrangement of organisms, pus cells, squamous epithelial cells and yeast cells. Samples were inoculated onto nutrient agar, blood agar and Macconkey agar and incubated at 37°C for 18-24 hours. Isolates were identified according to CLSI guidelines. Non fermenting gram negative bacilli were subjected to antimicrobial susceptibility testing using Kirby Bauer disc diffusion method with ampicillin (10 µg), imipenem (10 µg) meropenem (10 µg), gentamicin (10 µg) cefotaxime (30 µg), ceftazidime (30 µg) cefpirome (30 µg) and amikacin (30 µg).

RESULTS

Out of 200 samples processed 168 (84%) yielded growth and in 32. Samples there was no growth. Maximum number of samples were collected from 31-40 age group individuals i.e. 42 (21%) (Table 1). Among the 200 samples collected 87 (43.5%) were sputum and 113 (56.5%) were Endotrracheal, Aspirates (Table 3). Among the total isolates (286) Pseudomonas spp. were 38 (22.61%) and Acinetobacter spp. were 50(29.76%) which are the non-fermenting gram negative bacilli (Table 2). Among the 88 (30.76%) NFGNB 33 (11.53%) were isolated from sputum and 55 (19.23%) from ET aspirates (Table 3). Antimicrobial resistance pattern of pseudomonas isolates, reference to imipenem and meropenem (Table 4). Antimicrobial resistant pattern of Acinitobacter showing resistance to carbapenems (Table 5). Among the 38 Pseudomonas isolated 16 (42%) were resistant to imipenem and 11(29%) were resistant to meropenem (Table 6). 14(28%) and 12 (24%) of Acinetobacter spp. showed resistance to imipenem and meropenem respectively (Table 7).

Table 1: Age wise distribution of total samples.

Age	No. of samples	Percentage
0-10	03	1.5
11-20	21	10.5
21-30	25	12.5
31-40	**42**	**21**
41-50	36	18
51-60	34	17
61-70	31	15.5
71-80	06	3
81-90	02	1
Total	200	100

Table 2: Prevalence of NFGNB and other isolates in the total No. of positive samples.

Isolates	No. of isolates (286)	Percentage
Klebsiella spp.	81	48.21
Escherichia coli	28	16.66
Pseudomonas spp.	**38**	**22.61**
Acinetobacter spp.	**50**	**29.76**
Citrobacter spp.	09	5.35
Proteus spp.	10	5.95
Enterobacter spp.	05	2.97
Streptococcus spp.	32	19.04
Moraxella spp.	12	7.14
Staphylococcus aureus	07	4.16
CONS	05	2.97
Candida	09	5.35

Table 3: Prevalence of NFGNB in different samples.

Sample	Number of isolates	Pseudomonas	Acinetobacter
Sputum (81)	33 (11.53%)	15 (5.24%)	18 (6.29%)
ET Aspirates (87)	55 (19.23%)	23(8.04%)	32 (11.19%)
Total	88 (30.76%)	38 (13.28%)	50 (17.48%)

Table 4: Antimicrobial resistance profiles of Pseudomonas isolates by disk-diffusion method (n=38).

Antibiotics	Resistance	Percentage
Ampicillin	32	84
Cefotaxime	27	71
Ceftazidime	37	97
Cefpirome	29	76
Gentamicin	27	71
Amikacin	21	55
Imipenem	**16**	**42**
Meropenem	**11**	**29**

Table 5: Antimicrobial resistance profiles of Acinetobacter isolates by disk-diffusion method (n=50).

Antibiotics	Resistance	Percentage
Ampicillin	45	90
Cefotaxime	31	62
Ceftazidime	45	90
Cefpirome	45	90
Gentamicin	45	90
Amikacin	36	72
Imipenem	**14**	**28**
Meropenem	**12**	**24**

Table 6: Prevalence of carbapenem resistance among Pseudomonas isolates by disk-diffusion method (n=38).

Antibiotic	Resistance	Percentage
Imipenem	16	42
Meropenem	11	29

Table 7: Prevalence of carbapenem resistance among Acinetobacter isolates by disk diffusion method (n=50).

Antibiotic	Resistance	Percentage
Imipenem	14	28
Meropenem	12	24

DISCUSSION

Carbapenems first introduced in 1980 are now frequently used as the last choice in treating serious infections caused by multidrug resistant, gram negative bacilli. These antibiotics are stable to β-lactamases including the extended spectrum β-lactamases (ESBL'S) and Amp c produced by gram negative bacilli. Unfortunately resistance to these antibiotics started emerging from 1990 and has been reported In Non-Fermenting Gram Negative Bacilli (NFGNB) world-wide over the years with varying frequencies Pseudomonas aeruginosa and Acinetobacter spp. in particular are most often associated with Carbapenem resistance causing fatal lower respiratory tract infections in ICU patients. Out study showed a higher prevalence of resistance among Pseudomonas aeruginosa (42.1%) than Acinetobacter spp. (24%) to meropenem. This is in accordance with Gladstone et al.[18] in 2005 reported 12.2% Carbapenem resistance among NFGNB, with higher prevalence in Pseudomonas (42.8%) than Acinetobacter (14.2%). Taneja et al.[14] reported 36.4% of non fermentors were resistant to imipenem and Navneeth et al.[7] reported a prevalence of 12% carbapenem resistance among 50 strains of Pseudomonas aeruginosa isolated from various clinical specimens spp. carbapenem resistance in Acinetobacter spp is an emerging problem and is a cause of concern as many nosocomial Acinetobacters are detected to be resistant to most other antibiotics. Taneja et al.[14] reported a high incidence of more than 20% carbapenem resistance among Acinetobacters. Corbella et al. found a high incidence (36%) of carbapenem resistance in Acinetobacter spp. among ICU patients[19] and Manikal et al. observed 50% carbapenem resistance among Acinetobacters in a New York hospital.[20]

Although there are specific tests to detect the underlying mechanism of Carbapenem resistance, Kirby Bauer disc diffusion test is a simple, easy to perform and cost effective test which can be conveniently used to screen carbapenem resistance. We found lesser incidence of resistance to meropenem than imipenem which is well-tolerated and offers several potential advantages, including greater in vitro activity against gram-negative pathogens and the option of bolus administration.

CONCLUSION

As our study documented an increase in carbapenem resistance unwarranted and unrestricted usage of antibiotics is associated with emergence of resistance in common nosocomial pathogens like Acinetobacter spp. Reduction in antimicrobial resistance in the ICUS has been a goal for all ICUS as it improves outcome and cost to the patients in terms of the expenses for costly antibiotics as well as prolonged ICU study. Measures to reduce antibiotic resistance include evidence-based selection of antibiotics, shorter courses of appropriately selected antibiotics with adequate dosages, surveillance for resistant organisms, cyclical usage of new antibiotics, education of consumers and prescribers about use and misuse of antibiotics or by potential use of probiotics. Steps need to be taken to prevent antimicrobial resistance or else this emerging menace would erode the strength of life- saving antibiotics, leave them with the negligible effect of placebo and put all significant resources allocated to research and treatment to waste in already resource poor countries.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

REFERENCES

1. Winn W Jr, Allen S, Janda W, Koneman E, Procop G, Schreckenberger P, et al. Nonfermenting Gram negative bacilli. In: Winn W Jr, Allen S, Janda W, Koneman E, Procop G, Schreckenberger P, et al., eds. Koneman's color Atlas and Textbook of Diagnostic Microbiology. 6th ed. USA: Lippincott Williams and Wilkins Company; 2006: 305-391.
2. Steinberg JP, Rio DC. Other Gram negative and Gram variable bacilli. In: Mardell GL, Bennett JE, Dolin R, eds. Principles and Practice of Infectious Diseases. 6th ed. Philadelphia, USA: Elsevier Publication; 2005: 2751-2768.
3. Gales AC, Jones RN, Forward KR, Linares, J, Sader HS, Verhoef J. Emerging importance of multi-drug resistant Acinetobacter species and Strenotrophomonas maltophilia as pathogen in seriously ill patients: Geographi patterns, Epidemiological features, and trends in the SENTRY antimicrobial surveillance program (1997-1999). Clin Infect Dis. 2001;32:104-13.
4. Goossens H. Susceptibility of multi-drug resistant Pseudomonas aeruginosa in intensive care units: results from the European MYSTIC study group. Clin Microbiol Infect. 2003;9:980-3.
5. Vincent JL, Bihari DJ, Suter PM, Bruining HA, White J, Nicolas MH, et al. The prevalence of nosocomial infection in intensive care units in Europe. JAMA. 1995;274:639-44.
6. Chastre J, Fagon JY. Ventilator-associated pneumonia. Am J Respit Crit Care Med. 2002;165:867-903.
7. Navaneeth BV, Belwadi MR. Antibiotic resistance among gram negative bacteria of lower respiratory tract secretion tract secretion in hospitalized patients. Indian J Chest Dis Allied Sci. 2002;44:173-6.
8. Gonlugur U, Bakici MZ, Akkurt I, Efeoglu T. Antibiotic susceptibility patterns among respiratory isolates of Gram negative bacilli in Turkish University Hospital. BMC Microbiol. 2004;4:32-4.
9. Mukhopadhyay C, Bhargava A, Ayyagari A. Role of mechanical ventilation and development of multidrug resistant organisms in hospital acquired pneumonia. Indian J Med Res. 2003;118:229-35.
10. Tognim MC, Andrade SS, Silbert S, Gales AC, Jones RN, Sader HS. Resistance trends of Acinetobacter spp. in Latin America and characterization of international dissemination of multi-drug resistant strains: five-year report of the SENTRY Antimicrobial Surveillance Program. Int J Infect Dis. 2004;8:284-9.
11. Deshpande LM, Fritsche TR, Jones RN. Molecular epidemiology of selected multidrug-resistant bacteria: a global report from the SENTRY Antimicrobial Surveillance Program. Diagn Microbiol Infect Dis. 2004;49:231-6.
12. Ouinn PJ. Clinical problems posed by multiresistant nonfermenting gram-negative pathogens. Clin Infect Dis. 1998;27:117-24.
13. Rubin SJ, Granato PA, Wasilauskas BL. Glucose nonfermenting Gram negative bacteria. In: Lennette EH, Balows A, Hausler WJ Jr, Shadomy HJ, eds. Manual of Clinical Microbiology. 4th ed. Washington, DC: American Society for Microbiology; 1985: 330-349.
14. Taneja N, Aharwal SM, Sharma M. Imipenem resistance in nonfermentors causing nosocomial urinary tract infections. Indian J Med Sci. 2003;57:294-9.
15. Spencer BA, Richard III JW, McCoy LF, Carino E, Washington J, Edgar P, et al. Antibiotic activity of meropenem on Multi-resistant gram-negative organisms. J Burns Surg. 2002;1:12-7.
16. Livermore DL. Interplay of impermeability and chromosomal betalactamases activity in imipenem-resistant Pseudomonas aeruginosa. Antimicrob Agents Chemother. 1992;36:2046-8.
17. Pai H, Kim JW, Lee JH, Choe KW, Gotch N. Carbapenem resistance mechanisms in Pseudomonas aeruginosa clinical isolates. Antimicrob Agents Chemother. 2001;45:480-4.
18. Gladstone P, Rajendran P, Brahmadathan KN. Incidence of carbapenem resistant nonfermenting gram negative bacilli from patients with respiratory tract infections in the intensive care units. Indian J Med Microbiol. 2005;23(3):189-91.
19. Corbella X, Montero A, Pujol M, Dominguez MA, Ayats J, Argerich MJ, et al. Emergence and rapid spread of carbapenem resistance during a large and sustained hospital outbreak of multiresistant Acinetobacter baumanii. J Clin Microbiol. 2000;38:4086-95.
20. Manikal VM, Landman D, Saurina G, Oydna E, Lal H, Quale J. Endemic carbepenem-resistant Acinetobacter species in Brooklyn, New York: citywide prevalence, inter-institutional spread and relation to antibiotic usage. Clin Infect Dis. 2000;31:101-6.

DOI: 10.18203/2320-6012.ijrms20150149
Cite this article as: Vasundhara Devi P, Sreenivasulu Reddy P, John MS. Incidence of carbapenem resistant nonfermenting gram negative bacilli from patients with respiratory tract infections among intensive care units. Int J Res Med Sci 2015;3:1368-71.