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Emergence of In-Vitro Colistin and/or Tigecycline resistance among Carbapenemase producing Gram negative Bacteria in nosocomial set up

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ABSTRACT: Resistance to Tigecycline and/or Colistin among nosocomial pathogens is an emerging problem. Objective of the study was to record the drug susceptibility pattern of carbapenemase producing gram negative bacteria causing various nosocomial infections. This study was performed over six months from January to June- 2013 with 167 nonrepeat culture isolates causing various nosocomial infections.Antimicrobial Susceptibility testing was performed as per CLSI guidelines (2013) in Modified Kirby-Bauer technique. Carbapenemase production was Phenotypically confirmed by Modified Hodge test. Out of total isolated 37 Carbapenemase producers, 6 were resistant to Tigecycline but sensitive to Colistin (16.21%) and 2 were sensitive to Tigecycline but resistant to Colistin (5.04%). Four isolates were resistant to both the drugs (10.81%). As a whole, 12 strains were resistant to Tigecycline whereas 6 were resistant to Colistin. Out of 17 Carbapenemase producing Klebsiella pneumoniae, 4 were resistant to Tigecycline (23.8%). All of them were susceptible to Colistin. Isolated Klebsiella oxytoca was resistant to Tigecycline but susceptible to Colistin. Isolated E.coli were susceptible to Tigecycline and resistant to Colistin All of the Carbapenemase producing Acinetobacter were sensitive to both Tigecycline and Colistin. Four Pseudomonal isolates were resistant to both Colistin and Tigecycline and one was resistant to Tigecycline but susceptible to Colistin. Out of total 12 Tigecycline resistant isolates, 4 (33.33%) were susceptible to aminoglycosides. All isolates were susceptible to Polymyxin-B, the only reliable therapeutic option.

I. INTRODUCTION

Colistin (polymyxin E) is a polymyxin antibiotic produced by certain strains of *Bacillus polymyxa* var. *colistinus*. Colistin is a mixture of cyclic polypeptides colistin A and B. Colistin is bactericidal agent acting on cell membrane of most Gram-negative bacilli and is used as a polypeptide antibiotic[1].

On the other hand, Tigecycline is a bacteriostatic drug and is a protein synthesis inhibitor by binding to the 30S ribosomal subunit of bacteria and thereby blocking entry of Aminoacyl-tRNA into the A site of the ribosome during prokaryotic translation[2].

These two drugs are the last-resort antibiotics for multidrug-resistant *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Acinetobacter*. Carbapenemase producer Enterobacteriaceae have also shown susceptibility to them [1,3].

Gram negative bacteria resistant to Carbapenem antibiotics are often treated with combination with Colistin and Tigecycline because Colistin is notorious for nephrotoxicity. Thus combination therapy allows dose reduction of Colistin.

II. OBJECTIVE

Emergence of Drug resistance to one or both of the above drugs leaves behind very few therapeutic options to fight out Carbapenem resistant GNB s. Our objective was to study the drug susceptibility pattern of Multidrug resistant carbapenemase producing gram negative bacteria causing various nosocomial infections.
Materials and Methods:

This study was performed over six months from January 2013 to June 2013 with 167 nonrepeat culture isolates from various nosocomial infections. Antimicrobial Susceptibility testing was performed as per CLSI guidelines (2013) in disc diffusion method by Modified Kirby-Bauer technique.

Antibiotic discs (eg,10 µg Imipenem or Meropenem discs,15µg Tigecycline discs, 10µg Colistin and 300unit PolymyxinB discs) supplied by Hi Media, Mumbai, India. *E.coli* ATCC25922 was used as control strain. After placing the antibiotic discs on lawn culture of test organisms which were already been inoculated

on Muller Hinton Agar from 0.5 MacFarland unit turbid broth, were incubated at 37 °c for overnight. Next day, the zone diameters surrounding the discs were interpretated as per standard guideline.

Carbapenemase production was screened by zone diameter surrounding the Meropenem disc<21mm and phenotypically confirmed by Modified Hodge test.

III. RESULTS

Out of167 culture isolates, 37 were Carbapenemase producers (22%), of which17 strains were *Klebsiella pneumoniae*, 11 were *Pseudomonas aeruginosa*, 6 were *Acinatobacter baumannii* , 2 were *Escherichia coli* and 1 was *Klebsiella oxytoca.*

Out of total isolated 37 Carbapenemase producers, 6 were resistant to Tigecycline but sensitive to Colistin (16.21%) and only 2 isolates were reverse i.e. sensitive to Tigecycline but resistant to Colistin (5.04%). Four isolates were resistant to both the drugs (10.81%). As a whole, 12 strains were resistant to Tigecycline whereas exactly the half i.e. 6 were resistant to Colistin.

Among Enterobcteriaceae, out of 17 Carbapenemase producing *Klebsiella pneumoniae*, 4 were resistant to Tigecycline (23.8%). All of them were susceptible to Colistin in-vitro. Similarly, the only isolate of *Klebsiella oxytoca* also was resistant to Tigecycline but susceptible to Colistin. Antimicrobial susceptibility pattern of *E.coli* was just reverse two Klebsiella isolates. All of the isolated *E.coli* was susceptible to Tigecycline and resistant to Colistin.

Among nonenterobacteriaceae, surprisingly, all of the Carbapenemase producing Acinetobacter were found to be sensitive to both Tigecycline and Colistin while four Pseudomonal isolates were resistant to both Colistin and Tigecycline and one was resistant to Tigecycline but susceptible to Colistin. Tigecycline resistance was highest among *Pseudomonas aeruginosa* (45.45%).

All of the above 37 Carbapenemase producer nosocomial pathogens were susceptible to Polymyxin-B. Out of total 12 Tigecycline resistant isolates, 4 (33.33%) were susceptible to Amikacin and Gentamicin (in-vitro susceptibility).

IV. DISCUSSION

Klebsiella, Pseudomonas and Acinetobacter are very notorious for causing nosocomial infections, they are also well known for their multidrug resistance pattern. In a study by other workers, total of 150 nonduplicate *A. baumannii* clinical isolates were tested, including 89 colistin-susceptible isolates (randomly selected) and 61 colistin-resistant isolates(4). On the contrary, in our study, we have found no Tigeycline or Colistin resistance among *A. Baumannii.* By Msyuki Nigo et al, a nested case-control (ratio 1:4) study was done on the emergence of tigecycline-resistant (TR) multidrug-resistant *Klebsiella pneumoniae* (MDRKP) among patients who initially presented with a tigecycline-susceptible MDRKP. Out of 260 patients, 24 (9%) had a subsequent clinical culture positive for a TR-MDRKP within the 90-day follow-up period. On logistic regression analyses, receipt of tigecycline (adjusted OR 5.06, 95% CI 1.80 to 14.23; P=0.002) was the only independent predictor of subsequent isolation of a TR strain(5) but in our study, about 24% Klebsiella isolates were Tigecycline resistant and about 36.36% Pseudomonal strains were resistant to both Colistin and Tigecycline. This high prevalence of resistance among the nosocomial isolates are really a worrisome fact.

V. CONCLUSION

Emerging resistance to Colistin and/or Tigecycline is very high among Pseudomonas along with Klebsiella in nosocomial setup. Polymyxin-B is the only reliable drug to treat the nosocomial infections caused by Colistin and/or Tigecycline-resistant Carbapenemase producers according to in-vitro antimicrobial susceptibility pattern.

REFERENCES

[1]. Falagas, ME, Grammatikos, AP, Michalopoulos, A. Potential of old-generation antibiotics to address current need for new antibiotics. *Expert review of anti-infective therapy* 2008;**6** (5): 593–600.

[2]. Scheinfeld, N. Tigecycline: a review of a new glycylcycline antibiotic. *Journal of Dermatological Treatment* 2005; **16** (4): 207–12.

[3]. Kumarasamy *et al.*; Toleman, Mark A; Walsh, Timothy R; Bagaria, Jay; Butt, Fafhana; Balakrishnan, Ravikumar; Chaudhary, Uma; Doumith, Michel et al.. Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study. *The Lancet Infectious Diseases* 2010; **10** (9): 597–602.

[4]. Luis A. Arroyo, Ingeborg Mateos, Verónica González, Javier Aznar. In Vitro Activities of Tigecycline, Minocycline, and Colistin-Tigecycline Combination against Multi- and Pandrug-Resistant Clinical Isolates of *Acinetobacter baumannii* Group. *Antimicrob Agents Chemother*. 2009; 53(3): 1295–1296.

[5]. Masayuki Nigo, Catalina Salinas Cevallos, Krystina Woods,Vicente Maco Flores,Gweneth Francis,David Perlman,Manuel Revuelta, Donna Mildvan,Mary Waldron,Tessa, Gomez,Sanjana Koshy,Tomasz Jodlowski,William RileyJörg Ruhe. Emergence of tigecycline resistance among multidrug-resistant Klebsiella pneumoniae: A nested case-control study . *Antimicrobial agents and Chemotherapy* 2013 Published ahead of print 26 August 2013, doi: 10.1128/AAC.00827-13 AAC.00827-13