American Journal of Microbiology 3 (2): 34-36, 2012
ISSN: 1948-982x

doi:10.3844/ajmsp.2012.34.36 Published Online 3 (2) 2012 (http://www.thescipub.com/ajm.toc)

In Vitro Activity of Tigecycline in the Era of NDM-1

Dorairajan Sureshkumar, Ram Gopalakrishnan and M.A. Thirunarayan

Department of Infectious Disease, Apollo Hospitals, Chennai, 600 006, India

ABSTRACT

In the current era of New Delhi Metallo-betalactamase-1 (NDM-1) infections and a dry antibiotic pipeline, managing infections caused by Multi-Drug Resistant Gram-Negative Bacterial infections (MDR-GNBs) presents a great challenge to physicians in the developing world. Tigecycline, a broad spectrum glycylcycline is a one among the few treatment options against MDR-GNBs. However it has been studied mostly in the western world, where the prevalence of MDR-GNB infections is less than the developing world. In this study, we report the *in vitro* activities of tigecycline and selected antimicrobials against gram-negative bacterial isolates. We evaluated the *in vitro* activity of tigecycline against 80 gram-negative bacterial isolates and compared its susceptibility against Cefoperazone-Sulbactam (CS), imipenem and colistin in a tertiary care hospital in South India. Tigecycline showed 100% activity against *E.coli*, similar to colistin and better than impenem and cefoperazone-sulbactam. However only 80% of *Klebsiella pneumoniae* isolates remained susceptible to tigecycline and colistin had higher *in vitro* activity against *Acinetobacter*. Tigecycline is a good option for the management of MDR *E.coli* and an alternative option against *Acinetobacter* infections in India. However the decline in susceptibility of tigecycline against *K.pneumoniae* is a worrisome phenomenon.

Keywords: Tigecycline, *In Vitro*, Antibiotic Susceptibility

1. INTRODUCTION

Increasing rates of antimicrobial resistance and specifically multiple drug resistance among gram-negative bacteria limit our armamentarium of potentially active agents (Falagas and Bliziotis, 2007; Gopalakrishnan and Sureshkumar, 2010). The emergence and spread of carbapenem resistance, including New Delhi metallo-betalactamase (Walsh *et al*., 2011), has complicated the treatment of infections caused by these microorganisms. There is an urgent need for the development of new antimicrobial agents to keep in pace with the resistant gram-negative bacteria.

Tigecycline, a member of glycylcycline class of antibiotics, provides activity against a broad range of gram-positive and gram-negative bacterial isolates with the exception of *Pseudomonas aeurginosa*, *Proteus mirabilis* and the indole-positive Proteus species (Livermore, 2005). Tigecycline has shown to evade common mechanisms of tetracycline resistance such as those conferred by efflux pumps. The role of tigecycline for the treatment of infections caused by Enterobacteriaceae and *Acinetobacter* species has not been adequately evaluated in India after the emergence of carbapenemase producing bacteria.

1.1. Aim

We evaluated the *in vitro* efficacy of tigecycline against *Escherichia coli*, *Klebsiella pneumoniae* and *Acinetobacter baumannii* and compared its activity against other commonly used antimicrobials.

2. MATERIALS AND METHODS

Our hospital is a 600 bed tertiary care hospital located in Chennai, South India.

Corresponding Author: Dorairajan Sureshkumar, Department of Infectious Disease, Apollo Hospitals, Chennai, 600 006, India

Table 1. Susceptibility and comparison data of tigecycline

	Cefoperazone-sulbactum-susceptible isolates N (%)	Imipenem-susceptible isolates N (%)	Colistin-susceptible isolates N (%)	Tigecycline-susceptible isolates N (%)
E.coli (T-33)	26 (78.78%)	31 (93.93%)	33 (100%)	33 (100%)
K.pneumoniae (T-30)	20 (66.66%)	25 (83.33%)	30 (100%)	24 (80%)
A.baumannii (T-17)	9 (52.94%)	6 (35.29%)	17 (100%)	15 (88.23%)

A total of 80 blood stream isolates of *Escherichia coli* (*E.coli*-33), *Klebsiella pneumoniae* (*K.pneumoniae*-30) and *Acinetobacter baumannii* (*A.baumannii*-17) isolated using standard microbiological techniques between January 2011 and July 2011 were analyzed.

Antimicrobial susceptibility testing was determined by using Vitek 2 (BioMerieux, Hazelwood, France) commercial micro dilution system and CLSI breakpoints (CLSI, 2008) were applied in interpreting the susceptibility results. Only one isolate per patient was included in the study.

3. RESULTS

A total of 80 isolates were evaluated in the study. As shown in **Table 1**, tigecycline demonstrated 100% activity against *E. coli*, similar to colistin and was substantially higher than cefoperazone-sulbactam (78.78%-26/33) and better than imipenem (93.93%-31/33). Against *Klebsiella* tigecycline was active in 80% (24/30), inferior to both colistin (100%-30/30) and imipenem (83.33%-25/30). Tigecycline (88.23%-15/17) was the second best option after colistin (100%-17/17) against *A. baumannii* and better than cefoperazone-sulbactam (52.94%-9/17) and imipenem (35.29%-6/17).

4. DISCUSSION

Tigecycline is a recently introduced antibiotic in India for severe community as well as nosocomial infections where MDR pathogens are suspected (Pankey, 2005). Constant monitoring of its sensitivity patterns is of paramount importance in the era of carbapenem resistance.

In our study tigecycline remains an important option against the management of *E.coli* infections by retaining 100% *in vitro* activity against *E.coli* isolates. However the activity of tigecycline against *Klebsiella pneumoaie* in this study was only 80%, a worrisome phenomenon when compared to previous studies conducted in India by (Tellis *et al*., 2012; Behera *et al*., 2009; Manoharan *et al*. (2010), who all demonstrated 100% activity. The difference could possibly be explained by increasing use of tigecycline in our centre in the management of serious MDR-GNB infections when compared to other centers.

Tigecycline is very active against *Acinetobacter* spp (Souli *et al*., 2006). In our study 88.23% (15/17) of the *Acinetobacter* isolates were susceptible. Previous studies in India showed high prevalence of tigecycline resistance in *Acinetobacter* spp (Behera *et al*., 2009). About 70% of *Acinetobacter* in India is sensitive.

The Tigecycline Evaluation Test (TEST), a global programme (Curcio and Fernandez, 2007), showed only 2% of *Acinetobacter* isolates showing high MIC (>2 microgram/ml). The difference in the susceptibility may be due to different methodologies used in the susceptibility testing like disc diffusion, E-test and VITEK 2 system (Pillar *et al*., 2008). More agreement on methodology of tigecycline in-vitro susceptibility testing is needed to determine the true magnitude of tigecycline resistance against *Acinetobacter* spp.

5. CONCLUSION

Tigecycline is a promising antibiotic that currently plays a key role in the management of *E.coli* and *Acinetobacter* spp infections. The declining susceptibility of *Klebsiella* should be confirmed in large multicenter studies and there is an urgent need for an ongoing multi-center monitoring program to determine antimicrobial susceptibilities on a longitudinal basis.

6. REFERENCES

Behera, B., A. Das, P. Mathur, A. Kapil and R. Gadepalli *et al*., 2009. Tigecycline susceptibility report from an Indian tertiary care hospital. Ind. J. Med. Res., 129: 446-450.

CLSI, 2008. Performance standards for antimicrobial susceptibility testing: CLSI document M100-S18. Clinical and Laboratory Standards Institute, Wayne, PA.

Curcio, D. and F. Fernandez, 2007. *Acinetobacter* spp. susceptibility to tigecycline: A worldwide perspective. J. Antimicrob. Chemother., 60: 449-450. PMID: 17561503

Falagas, M.E. and I.A. Bliziotis, 2007. Pandrug-resistant Gram-negative bacteria: The dawn of the post-antibiotic era? Int. J. Antimicrob. Agents, 29: 630-636. PMID: 17306965

Gopalakrishnan, R. and D. Sureshkumar, 2010. Changing trends in antimicrobial susceptibility and hospital acquired infections over an 8 year period in a tertiary care hospital in relation to introduction of an infection control programme. J. Assoc. Phys. Ind., 58: 25-31. PMID: 21563610

Livermore, D.M., 2005. Tigecycline: What is it and where should it be used? J. Antimictrpb. Chemother., 56: 611-614. DOI: 10.1093/jac/dki291

Manoharan, A., S. Chateerji, S. Madhan and D. Mathai, 2010. Evaluation of tigecycline activity in clinical isolates among Indian medical centers. Ind. J. Patho. Microbiol., 53: 734-737.

Pankey, G.A., 2005. Tigecycline. J. Antimicrob. Chemother., 56: 470-480. DOI: 10.1093/jac/dki248

Pillar, C.M., D.C. Draghi, M.J. Dowzicky and D.F. Sahm, 2008. *In vitro* activity of tigecycline against gram-positive and gram-negative pathogens as evaluated by broth microdilution and etest. J. Clin. Microbiol., 46: 2862-2867. PMID: 18596149

Souli, M., V.K. Flora, K. Evangeos, A. Anastasia and G. Efthimia *et al*., 2006. *In vitro* activity of tigecycline against multiple-drug-resistant, including pan-resistant, gram-negative and gram-positive clinical isolates from greek hospitals. Antimicrob. Agents Chemother., 50: 3166-3669.

Tellis, R., S. Rao and A. Lobo, 2012. An in-vitro study of tigecycline susceptibility among multidrug resistant bacteria in a tertiary care hospital. Int. J. Biomed. Res., 3: 192-195.

Walsh, T.R., J. Weeks, D.M. Livermore and M.A. Toleman, 2011. Dissemination of NDM-1 positive bacteria in the New Delhi environment and its implications for human health: An environmental point prevalence study. Lancet Infect. Dis., 11: 355-362. DOI: 10.1016/S1473-3099(11)70059-7