Activity of Colistin against Asian *Pseudomonas aeruginosa* from the TEST Study: 2009-2010

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Revised Abstract

Background: Successful treatment of infections due to *Pseudomonas aeruginosa* has become problematical due to widespread resistance to currently available therapies. As many isolates exhibit resistance to multiple antimicrobial agents, older agents, such as colistin (polymyxin E), are being reexamined for their treatment potential. This study investigated the activity of colistin against Asian clinical isolates of *P. aeruginosa* collected during 2009 - 2010. **Methods:** 94 isolates collected from 7 Asian countries (China, Singapore, Malaysia, India, South Korea, Taiwan, and Thailand) during the 2009-2010 Tigecycline Evaluation and Surveillance Trial (TEST) program from various infection sources were included in this study. MICs were performed following CLSI guidelines and interpreted according to CLSI breakpoints. **Results:**

	MIC_{50}(mcg/ml)	MIC_{90}(mcg/ml)	%S[a]	%I	%R
Colistin	2	4	72.3	17.1	10.6
Meropenem	1	>16	66.3	11.6	22.1
PipTazo	16	>128	66.3	--[b]	33.7
Imipenem	2	16	61.1	9.4	29.5
Cefepime	4	32	57.9	21.1	21.1
Levofloxacin	1	>8	57.9	3.2	38.9
Ceftazidime	8	>32	56.8	5.3	37.9

[a]Interpretive criteria are defined according to CLSI breakpoints (M100-S21, 2011); [b]No defined breakpoint

Conclusions: Colistin was the most active agent *in vitro*, with 72.3 of the Asian *P. aeruginosa* isolates, including multi-drug resistant strains, susceptible by CLSI criteria. Colistin represents a potential addition to the treatment of drug-resistant *P. aeruginosa*. As usage of this agent increases, careful monitoring of the incidence of resistance is warranted.

Introduction

Pseudomonas aeruginosa is a gram-negative bacillus that is ubiquitous in the environment. In humans, it is responsible for chronic lung infections in patients with cystic fibrosis as well as serious acute infections in immunocompromised individuals, and is a common cause of ventilator-associated pneumonia and septic burn wounds [1]. Worldwide, *P. aeruginosa* is the third leading cause of nosocomial infections [2]. Successful treatment of infections due to *Pseudomonas aeruginosa* has become problematic due to widespread resistance to currently available therapies. As many isolates exhibit resistance to multiple antimicrobial agents, older agents, such as colistin (polymyxin E), are being reexamined for their treatment potential [3-5]. This study investigated the activity of colistin against Asian clinical isolates of *P. aeruginosa* collected in the T.E.S.T study during 2009 - 2010.

Materials & Methods

- All TEST study isolates were derived from blood, respiratory tract, urine, skin, wound, body fluids and other defined sources. Only one isolate per patient was accepted into the study. Clinical isolates were collected between 2009 and 2010 from hospitals from seven Asian countries (China, India, Malaysia, Singapore, South Korea, Taiwan, and Thailand).
- Organism collection, transport, confirmation of organism identification, as well as development and management of a centralized database was coordinated by Laboratories International for Microbiology Studies (LIMS), a division of International Health Management Associates, Inc. (IHMA) located in Schaumburg, IL, USA.
- All organisms were deemed clinically significant by local participant criteria. Isolate inclusion was independent of medical history, antimicrobial use, age or gender. All sites identified each study isolate utilizing local laboratory site criteria.
- Minimum inhibitory concentrations (MICs) were determined by the CLSI recommended broth microdilution testing method [6] on panels produced at IHMA. MIC interpretive criteria followed published guidelines established by the Clinical and Laboratory Standards Institute [7].
- Quality controls (QC) were performed by each testing site on each day of testing using the corresponding ATCC control strains *E. coli* ATCC 25922, *E. coli* ATCC 35218, and *Pseudomonas aeruginosa* ATCC 2785. Results were included in the analysis only when corresponding QC isolates tested within the acceptable range according to CLSI guidelines [7].

References

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Acknowledgements

We gratefully acknowledge the contributions of the investigators, laboratory personnel, and all members of the Tigecycline Evaluation Surveillance Trial program group. This study was sponsored by Pfizer Inc.

Results

Table 1. *In vitro* activity of colistin and comparators against 94 *P. aeruginosa* from Asia, 2009-2010.

	MIC_{50} (mcg/ml)	MIC_{90} (mcg/ml)	Range	%S[a]	%I	%R
Colistin	2	4	0.05 - >8	72.3	17.1	10.6
Meropenem	1	>16	≤0.12 - >8	66.3	11.6	22.1
PipTazo	16	>128	≤0.5 - >128	66.3	--[b]	33.7
Imipenem	2	16	≤0.5 - >16	61.1	9.4	29.5
Cefepime	4	32	1 - >32	57.9	21.1	21.1
Levofloxacin	1	>8	≤0.25 - >8	57.9	3.2	38.9
Ceftazidime	8	>32	2 - >32	56.8	5.3	37.9

[a]Interpretive criteria are defined according to CLSI breakpoints (M100-S21, 2011); [b]No defined breakpoint

Figure 1. Colistin susceptibility (%) for 94 isolates of *P. aeruginosa* from Asia categorized by country.

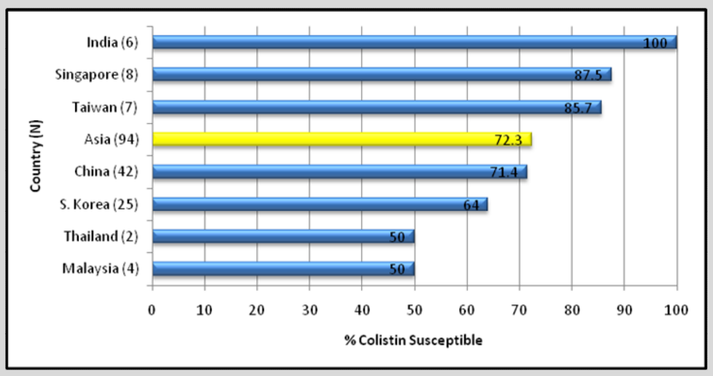


Table 2. *In vitro* activity of colistin and comparators against 30 multi-drug resistant[a] *P. aeruginosa* from Asia, 2009-2010.

	%S[b]	%I	%R
Colistin	80.0	10.0	10.0
Meropenem	6.7	26.7	66.7
PipTazo	20.0	--[c]	80.0
Imipenem	3.3	20.0	76.7
Cefepime	0	53.3	46.7
Levofloxacin	13.3	6.7	80.0
Ceftazidime	0	10.0	90.0

[a] Multi-drug resistance defined as resistant to 3 or more drug classes; [b] Interpretive criteria are defined according to CLSI breakpoints (M100-S21, 2011); [c] No defined breakpoint

Figure 2. Susceptibility (%) of *P. aeruginosa* from Asian Intensive Care Units (ICU; n = 33) and general medicine wards (n = 61).

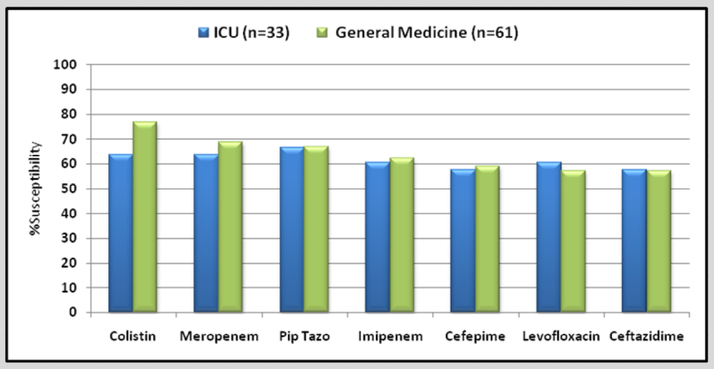
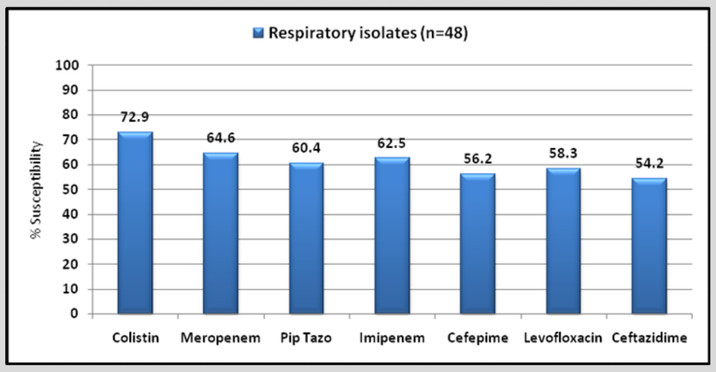


Figure 3. Susceptibility (%) of 48 respiratory isolates of *P. aeruginosa* from Asia.



Conclusions

- Colistin was the most active agent *in vitro*, with 72.3% of the Asian *P. aeruginosa* isolates, including multi-drug resistant strains, susceptible by CLSI criteria (MIC ≤2 mcg/ml).
- There were no significant differences between the colistin susceptibility of isolates from ICUs and general medicine wards (p=0.227), or between respiratory isolates versus isolates from other sources (p=1).
- While colistin represents a potential addition to the treatment of drug-resistant *P. aeruginosa*, careful monitoring of the incidence of resistance will be necessary as usage of this agent increases.