Background: Two polymyxin agents, colistin (COL) and polymyxin B (PB), are available for clinical use worldwide and clinical laboratories may not be able to susceptibility test both compounds appropriately. We evaluated the correlation between COL and PB MIC values on a large collection of Gram-negative bacilli (GNB), including Acinetobacter spp., Pseudomonas aeruginosa (PA), and Enterobacteriaceae.

Methods: 15,377 clinical GNB, including PA, E. coli (EC), K. pneumoniae (KP), Enterobacter (E), S. marcescens (SM), and P. aeruginosa (PA), were tested for susceptibility against COL and PB by CLSI broth microdilution methods using commercial Sensititre® dry-form panels. The isolates were collected worldwide in 2013.

Results: Percentages of strains inhibited ≤2 µg/ml of COL were 96.8/96.8/99.8% for CA, KP, and EC, respectively, and 95.8/95.9/99.9% for KP and 99.6/99.6/99.6% for EC. Among PA and ASP, COL and PB MIC values were within ±1 doubling dilution for >99.0% of strains, and identical MIC values were observed for >98.9% of PA and PB MIC values of ≤2 µg/ml. However, differences in potency varied when testing 15,377 strains collected worldwide in 2013.

Differences in Potency and Categorical Agreement between Colistin and Polymyxin B when Testing 15,377 Strains Collected Worldwide

• Percentages of strains inhibited ≤2 µg/ml of colistin (MIC ≤2 µg/ml) were lower compared to polymyxin B (MIC ≤4 µg/ml) for clinical isolates. 97.29/97.29/97.29% for Acinetobacter spp., 95.8/95.8/95.8% for Klebsiella spp., and 96.9/96.9/96.9% for E. coli (data not shown).

• Among P. aeruginosa and Acinetobacter spp., colistin and polymyxin B MIC values were within ±1 doubling dilution for >99.0% of strains, and identical MIC values were observed for >98.9% of PA and PB MIC values of ≤2 µg/ml. (Table 1).

• When CLSI breakpoints were applied, i.e. susceptible at ≤2 µg/ml for both colistin and polymyxin B for PA and Acinetobacter spp., and resistant at ≥25 µg/ml for PA and polymyxin B and ≥4 µg/ml for Acinetobacter spp., categorical agreement (CA) was 99.8% for PA, 98.9% for PB, and 99.8% for Acinetobacter spp. (Table 1 and Figures 1 and 2).

• Among Klebsiella spp. and E. coli, 55.0 and 52.3% of strains displayed a colistin MIC one dilution lower than polymyxin B, respectively. However, differences in potency varied according to the degree of polymyxin susceptibility (Table 1 and Figures 1 and 2).

MATERIALS AND METHODS

Diversity Collection: A total of 15,377 clinical isolates of Gram-negative bacilli were included in this investigation, including 3,821 P. aeruginosa, 1,056 Acinetobacter spp., 4,177 Klebsiella spp., and 6,311 E. coli were tested for susceptibility against colistin and polymyxin B by CLSI broth microdilution methods. The isolates were collected through the SENTRY Antimicrobial Surveillance Program from January to December 2013.

Susceptibility Testing: Antimicrobial susceptibility testing of isolates was performed by validated broth microdilution method using commercial (Sensititre® dry-form) and panels following the Clinical and Laboratory Standards Institute (CLSI) recommendations. The results were interpreted according to the CLSI and European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoint criteria, when available. Quality control was performed by testing E. coli ATCC 25922 and P. aeruginosa ATCC 27853, with all results within published ranges.

REFERENCES


ABSTRACT

The polymyxins are polypeptide antibiotics with a basic structure consisting of a protein-like ring composed of 8 to 10 amino acids. These antibiotics are cationic detergents that disrupt cell membrane lipids, causing leakage of cytoplasmic contents. The polymyxins are active against a wide variety of Gram-negative bacilli, and are not active against Gram-positive organisms or non-fertile species. However, Gram-negative species are intrinsically resistant to the polymyxins.

The emergence of multidrug-resistant (MDR) Pseudomonas aeruginosa, Acinetobacter spp., and Klebsiella pneumoniae has required the expanded systemic use of these antimicrobial agents. The polymyxins have the drugs of choice for treatment of serious infections caused by Caelyx-resistant-P. aeruginosa and Acinetobacter spp. isolates. In addition, polymyxins have also been evaluated as therapeutic options against Klebsiella pneumoniae carbapenemase (KPC)-producing K. pneumoniae infections. As polymyxins (colistin and polymyxin B) usage increases, the development of polymyxin resistance becomes a clinical concern. Thus, there is a need for standardization of antimicrobial agents testing these compounds. We evaluated the correlation between colistin and polymyxin B MIC values and compared these compounds, while polymyxin B was slightly more potent than colistin against strains with decreased susceptibility (MIC, ≥4 µg/ml) to the polymyxins.

INTRODUCTION

Susceptibility Testing: Antimicrobial susceptibility testing of isolates was performed by validated broth microdilution method using commercial (Sensititre® dry-form) and panels following the Clinical and Laboratory Standards Institute (CLSI) recommendations. The results were interpreted according to the CLSI and European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoint criteria, when available. Quality control was performed by testing E. coli ATCC 25922 and P. aeruginosa ATCC 27853, with all results within published ranges.

RESULTS

Table 1: Differences in MIC value between polymyxin B and colistin in selected MIC categories when testing 3,821 P. aeruginosa isolates collected worldwide in 2013.

Figure 1: Correlation between polymyxin B and colistin MIC values when testing 3,821 P. aeruginosa isolates collected worldwide in 2013a.

Figure 2: Correlation between polymyxin B and colistin MIC values when testing 1,056 Acinetobacter baumannii isolates collected worldwide in 2013a.

Figure 3: Correlation between polymyxin B and colistin MIC values when testing 611 E. coli isolates collected worldwide in 2013a.

CONCLUSIONS

• There was good correlation between colistin and polymyxin B MIC values when testing Acinetobacter spp. against P. aeruginosa and Acinetobacter spp. agreement when testing P. aeruginosa and Acinetobacter spp.

• Against Klebsiella spp. and E. coli, colistin exhibited slightly higher potency compared to polymyxin B, and polymyxin B was more potent than colistin against strains with decreased susceptibility (MIC, ≥4 µg/ml) to the polymyxins.

• Greater stickiness of polymyxin B to plastic compared to colistin caused problems with sub-MIC antibiotic recovery in agar plates. Confirmation of a compound among isolates more susceptible to colistin and polymyxin B MIC values is necessary to evaluate this hypothesis.

Table 1: Differences in MIC value between polymyxin B and colistin in selected MIC categories when testing 3,821 P. aeruginosa isolates collected worldwide in 2013.

<table>
<thead>
<tr>
<th>Organism Collection</th>
<th>Polymyxin B MIC (µg/ml)</th>
<th>Colistin MIC (µg/ml)</th>
<th>CA (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acinetobacter spp.</td>
<td>0.06 0.12 0.25 0.5 1 2 4 8 &gt;8</td>
<td>0.06 0.12 0.25 0.5 1 2 4 8 &gt;8</td>
<td>98.9/98.9/98.9</td>
</tr>
<tr>
<td>Klebsiella spp.</td>
<td>0.06 0.12 0.25 0.5 1 2 4 8 &gt;8</td>
<td>0.06 0.12 0.25 0.5 1 2 4 8 &gt;8</td>
<td>99.6/99.6/99.6</td>
</tr>
<tr>
<td>E. coli</td>
<td>0.06 0.12 0.25 0.5 1 2 4 8 &gt;8</td>
<td>0.06 0.12 0.25 0.5 1 2 4 8 &gt;8</td>
<td>99.8/99.8/99.8</td>
</tr>
</tbody>
</table>

• Differences in potency (MIC value) between polymyxin B and colistin were ≤2 µg/ml of COL ≤2 µg/ml and POLMIC ≥2 µg/ml for both compounds, with PB being slightly more potent than CA against strains with decreased susceptibility (MIC, ≥4 µg/ml) to the polymyxins.

DISCLAIMER

The contents of this article are solely the responsibility of the authors and do not necessarily represent the official views of the National Institutes of Health.