Isolates were collected as part of the CANWARD 2014 studies occurring between January 2014 and December 2014. 15 Canadian hospitals in 8 provinces contributed clinically relevant isolates. Enterobacteriaceae (Escherichia coli, Klebsiella pneumoniae, Enterobacter aerogenes, Acinetobacter species and P. aeruginosa) were included in this study. Colistin MICs for 962 Enterobacteriaceae and 350 P. aeruginosa were determined with and without 0.02% FS-P8 using M100-S24 and CLSI M7-A10 CLSI susceptibility (6.7). ECOFs were calculated using standard statistical methods (8).

For the determination of probability of target attainment (PTA), published Monte-Carlo simulations were used to define the PK profiles of colistin dosed at 5 μg/kg. Colistin MICs for 962 Enterobacteriaceae and 350 P. aeruginosa from Canadian hospitals were determined with and without 0.02% FS-P8 using M100-S24 CLSI recommendations. ECOFs were calculated using standard statistical methods. Various PTA were calculated from both methods.

Results: See Table 1.

Conclusions: The current ART method (M100-S25; 15) provides MICs compatible with target attainment with permissive PK/PD targets. Although the current 0.02% FS-P8 provides MICs that appear more compatible with PK/PD targets that predict positive clinical outcomes, however, clinical susceptibility breakpoints would need to be reconsidered if 0.02% FS-P8 is used for in vitro susceptibility testing.

Efficacy MICs without FS-P8 are higher than the expected mean free serum concentrations of colistin using 5 μg/kg dosing, strongly suggesting that true MIC values are over-estimated. Integrating population MIC values for Enterobacteriaceae (excluding the genus Pseudomonas, Providencia, and Morganella), Pseudomonas aeruginosa and Acinetobacter species with PK/PD models of colistin dosing suggests the addition of FS-P8 would provide MIC values more compatible with PK/PD target attainment, the probability of target colistin dosing while permissive PK/PD is unlikely to be unattainable using MIC values without FS-P8. Adding FS-P8 provides MIC values that greatly signify significantly higher PTAs across a range of target and PTA remains relatively high with AUC/MIC target values similar to better studied antimicrobials where AUC/MIC is the PK parameter that predicts outcomes (e.g. AUC/MIC > 120 for imipenem).

If FS-P8 were to be routinely added to colistin microbroth panels, susceptibility breakpoints would need to be reconsidered and truly lowered. Although widely used and not having thought of significant antibacterial activity, reports of synergism between FS-P8 and colistin need to be fully investigated prior to changing susceptibility methodology.

ACKNOWLEDGMENTS

We acknowledge the contributions of the directors and technologies of the contributing microbiology laboratories.

This study was supported in part Abbott Laboratories Ltd, Annifel, Atslius, AstraZeneca, Carex/Forest, Cubist, Merck Canada, Pfizer, Sunovion, and The Medicines Company.

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