Developing a score to shorten the time to initiation of appropriate therapy for extensively drug resistant Gram-negative bacilli and avoid unnecessary use of polymixins

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Introduction

•In regions where extensively drug resistant (XDR) Gram-negative bacilli (GNB) pathogens are endemic, and when nosocomial bloodstream infection (BSI) is suspected, clinicians must choose between empiric therapy with broad-spectrum β-lactam agents (including carbapenems) for multi-drug resistant (MDR)-GNB, or polymyxins, for XDR-GNB. Due to toxicity and concerns pertaining to emergence of resistance, prescribers are reluctant to use polymixins empirically, and as a result, the median time to initiation of appropriate therapy in patients with XDR-GNB BSI is over 100 hours.

•Delays in initiation of appropriate antibiotic therapy (DAAT) is the strongest independent modifiable predictor for in-hospital mortality.

•Creative measures are needed in order to reduce DAAT in these circumstances, because MDR and XDR GNBs share several epidemiological features.

•The aim of this study was to differentiate BSIs due to MDR-GNBs from those due to XDR-GNBs.

Materials and Methods

•Unique adult patients with monomicrobial BSI due to MDR-GNB or XDR-GNB, isolated >72 hours after hospitalization, were enrolled at Assaf Harofeh hospital from 01/2007 to 05/2012.

•For the purposes of this submission, and based of published criteria, MDR-GNBs were defined as: 1) extended-spectrum β-lactamase producing Enterobacteriaceae; 2) ceftazidime-resistant carbapenem-susceptible *Pseudomonas aeruginosa*; and 3) ceftazidime-resistant carbapenem-susceptible *Acinetobacter baumannii*.

•XDR-GNBs included: 1) carbapenem-resistant Enterobacteriaceae; 2) ceftazidime-resistant carbapenem non-susceptible *P. aeruginosa*; and 3) ceftazidime-resistant carbapenem non-susceptible *A. baumannii*.

Results

•There were 109 patients with nosocomial MDR-GNB and 152 with XDR-GNB BSI enrolled.

•Parameters with significant ($p \leq 0.05$) association with XDR-GNB included ICU stay (OR=6.2, p<0.001), mechanical ventilation (OR=1.8, p=0.03), carbapenem exposure in the past 90 days (OR=4.1, p<0.001), and penicillins (including penicillins combined with β-lactamases inhibitors) exposure in the past 90 days (OR=2.2, p=0.002).

•In multivariable analysis, only ICU stay (OR=5, p<0.001) and carbapenem exposure (OR=3.3, p<0.001) remained significant predictors XDR-GNB BSI.

Characteristics	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Current ICU stay	92% (89%, 95%)	35% (29%, 41%)	66% (61%, 72%)	76% (71%, 81%)
Carbapenems in previous 90 days	50% (44%, 56%)	81% (76%, 85%)	78% (73%, 83%)	53% (47%, 59%)
Current ICU stay AND carbapenems in previous 90 days	93% (90%, 96%)	29% (34%, 35%)	65% (59%, 70%)	74% (69%, 80%)
Current ICU stay AND carbapenems in previous 90 days AND ventilated at illness	94% (91%, 97%)	16% (11%, 20%)	61% (55%, 67%)	65% (60%, 71%)

Conclusions

•ICU stay and recent exposure to carbapenems are two factors that can be used to develop future score to differentiate XDR and MDR-GNB.

•A reliable simple score can potentially be used to reduce DAAT and mortality associated with BSI due to XDR-GNB and also limit toxicity and resistance due to unnecessary empiric polymyxin use.