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Poster Session I
Antibiotic choices: clinical studies

OUTCOMES OF PATIENTS WITH BLOODSTREAM INFECTION (BSI) OF NON-URINARY SOURCE CAUSED BY EXTENDED-SPECTRUM BETA-LACTAMASE PRODUCING ENTEROBACTERIACEAE (ESBL): A MULTICENTER ANALYSIS COMPARING CARBAPENEMS TO PIPERACILLIN-TAZOBACTAM (PTZ)

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Objectives: Recent data suggest that β-lactam-β-lactamase inhibitors (BLBLI) are equivalent to carbapenems for treatment of ESBL-producing *Escherichia coli* BSIs. Urinary tract infections (UTIs) are the most frequent infection source for *E. coli* BSIs and are typically 'low inoculum' infectious syndromes. In addition, beta-lactamase inhibitors are excreted mostly unchanged in urine. Therefore, it is questionable whether this recent data could be generalized to all ESBL infections and truly contradict the known 'inoculum effect' theory associated with BLBLI usage in ESBL infections. The study aim was to compare the outcomes of patients treated with PTZ, versus those treated with a carbapenem, for documented ESBL-producing Enterobacteriaceae BSIs due to a non-urinary source.

Methods: Data for adult patients with monomicrobial ESBL-producing (*Klebsiella pneumoniae*, *K. oxytoca*, *E. coli*, *Proteus mirabilis*) BSIs due to non-urinary sources from 2010-2012 were abstracted at DMC (MI, USA), and from 2008-2012 at AHMC (Israel). Patients who received either ≥2 doses of a carbapenem or ≥2 doses of PTZ from 3 days prior to 14 days post culture were included (i.e. both empiric and main regimens were captured). Patients who received both types of agents were excluded. Appropriate therapy (including treatment with PTZ) was determined based on laboratory *in-vitro* reports. Patients who received PTZ for a PTZ non-susceptible isolate were excluded.

Results: Overall 98 patients were enrolled: 67 from AHMC and 31 from DMC. 86 patients were treated with a carbapenem and 12 with PTZ. Patients treated with PTZ were older (76±11 vs. 68±17 years, p=0.05), with higher Pitt bacteremia scores (p<0.001), but with lower Charlson's scores (p=0.001), and shorter time to initiation of appropriate therapy (p=0.05). There was an insignificant trend for increased in-hospital mortality among patients treated with PTZ vs. a carbapenem (6 of 12 [50%] vs. 32 of 86 [37%], respectively, OR=1.7, p=0.3). Among those who survived the index hospitalization, patients treated with PTZ experienced more frequent deterioration in their functional status (OR=3.3, p=0.12), and patients treated with carbapenems had prolonged length of stay (LOS; p=0.73) and prolonged ICU LOS (p=0.09), though none of these associations reached statistical significance. In multivariable model, after controlling for a propensity score measuring the likelihood of receiving a carbapenem, therapy with PTZ was still insignificantly associated with increased in-hospital mortality (OR=2.3, p=0.25).

Conclusion: Only insignificant trends towards reduced morbidity and mortality were noted with carbapenem usage. Costs (extrapolated from LOS) tended to be higher with carbapenem thearpy. There are difficulties in allocating patients with non-urinary originating ESBL BSI who are managed with PTZ and no carbapenems. Prospective randomized control trials are warranted in order to trial the assumption that BLBLI can be safely used to manage ESBL BSIs.