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Poster Session VI
MDR Gram-negatives - clinical observations

DEVELOPING AND IMPLEMENTING ANTIMICROBIAL TREATMENT STRATEGIES AGAINST EXTENSIVELY DRUG-RESISTANT ACINETOBACTER BAUMANNII (XDR-AB) INFECTIONS

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Objectives. Extensively drug-resistant *Acinetobacter baumannii* (XDR-Ab) infections have emerged worldwide, but optimal treatment regimens are unknown. In 2009, we instituted a systemic approach to develop institution-specific treatment strategies against XDR-Ab infections. In this abstract, we report our experience.

Methods. Our approach consisted of several steps: 1) Type institutional XDR-Ab strains and identify resistance mechanisms; 2) Measure responses to antimicrobial combinations *in vitro*; 3) Introduce treatment regimens based on *in vitro* data; 4) Measure patient outcomes. XDR-Ab was defined by resistance to all agents with the tigecycline (TGC) and polymyxins (colistin; COL).

Results. Over 50 randomly-selected XDR-Ab strains from our biorepository were demonstrated to be clonal by PFGE and carry OXA-23 carbapenemase. Despite clonality, strains differed in antimicrobial MIC ranges. Doripenem (DOR, 8 μg/mL) and COL (0.25 μg/mL) exerted no activity or were bacteriostatic, respectively, during TKA against 20 strains. The DOR-COL combination was synergistic and bactericidal against each strain. DOR-COL responses were comparable to DOR-sulbactam (S, 4 μg/mL), and superior to other combinations of TGC, rifampin, DOR, COL and S. We recommended DOR 1g every 8-h (4-h infusion, if possible) and COL 5 mg/kg per day (divided in 2–4 doses) as the regimen of choice for the treatment of OXA-23–producing XDR-Ab infections at our center, since COL (unlike S) had some activity by itself. We also recommended inhaled COL (150 mg twice a day) for patients with pneumonia. We studied outcomes among 41 solid organ transplant (SOT) recipients in 2006-11. XDR-Ab infections were significantly more common among cardiothoracic than abdominal SOT recipients (p=0.0004). 98% (40/41) of patients had respiratory tract infections, most commonly ventilator-associated pneumonia (VAP; 88% [36/41]). Clinical responses and 28-d survival was significantly better for patients treated with carbapenem (usually DOR)-COL (78% and 81%) than monotherapy (0%) or other combinations (9% and 31%; all p≤0.009). Carbapenem-COL treatment was the only factor independently associated with survival (p=0.01). 100% (3/11) of isolates collected from patients who received TGC-COL developed COL resistance compared to 18% (2/11) from patients who received carbapenem-COL (p=0.03). 44% of patients who responded at 28-d relapsed within 3 mos; all were successfully treated with DOR-COL or DOR-COL-Ampicillin/S. DOR-COL was significantly less active against relapse than initial strains during TKA (mean log-kill -2.88 vs. -5.74; p=0.01). DOR-COL-S restored bactericidal activity against COL-resistant, relapse strains (-5.65 vs -2.43; p=0.04).

Conclusions. Our strategy for identifying institution-specific treatment strategies against XDR-Ab infections identified an antimicrobial combination (carbapenem-COL) that resulted in improved clinical responses and survival compared to other regimens, and limited the emergence of COL resistance. TKA and clinical data also suggested that the addition of Ampicillin/S may be useful for XDR-Ab infections that relapse after an initial response to carbapenem-COL.