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P2797 *In vitro* activity of polymyxin B alone and in combination against colistin-resistant *Acinetobacter baumannii*

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Background: In the arsenal against multi-drug resistant *Acinetobacter baumannii,* antibiotics like polymyxins are the last line of defence. As polymyxin-resistances are emerging worldwide, combining a polymyxin with another antibiotic could be a solution. Colistin-resistant strains could be more susceptible to polymyxin B, being naïve to it. As colistin is administered as a prodrug while polymyxin B is administered as an active moiety to patients, making its pharmacokinetics easier to predict, it makes polymyxin B interesting to study. The objective of this study was to identify promising polymyxin B-based antibiotic combinations to use against colistin-resistant *A. baumannii*.

Materials/methods: Eleven *A. Baumannii* strains were tested including five colistin-resistant clinical isolates. MICs of colistin, polymyxin B, minocycline, rifampicin, aztreonam, chloramphenicol, fosfomycin and meropenem were determined for all strains according to EUCAST guidelines. Then, checkerboards evaluating the effect of these antibiotics combined with polymyxin B were performed on all strains.

Results: All strains showed high MICs for aztreonam, chloramphenicol and fosfomycin and 7/11 of the studied strains were resistant to meropenem. All strains were susceptible to minocycline, and 8/11 of the studied strains showed low rifampicin MICs. On all colistin-resistant strains, using clinical concentrations of minocycline restored their sensitivity to polymyxin B. Using clinical concentrations of rifampicin restored sensitivity to polymyxin B of 4 out of 5 colistin resistant strains.

	MIC (mg/L)		Checkerboard FICI						
	CST	PMB		MIN	RIF		PMB + MIN	PMB + RIF	
	(>2[+])	(>2[*])		(>8[*])	(n.d.)				
Strain		**Description**							
CR17		PmrA mutant	128	8		4	>512		0.2
062 D7		PmrB mutant	256	4		0.03	4		0.7
249 pmrB		PmrB mutant	128	4		0.5	2		0.4
347 pmrB		PmrB mutant	64	4		0.25	2		0.4
ABIsac_ColiR		PmrA mutant	128	1		0.25	>512		0.5

Clinical breakpoint for resistance according to: [*]CLSI, [+] EUCAST, n.d.: not determined. CST: colistin, PMB: polymyxin B, MIN: minocycline, RIF: rifampicin. Green cells are indicating synergy.

Conclusions: *A. baumannii* strains resistant to colistin can be susceptible to polymyxin B and combining polymyxin B with minocycline or rifampicin can be effective at clinically achievable concentrations of both antibiotics.