P0217
Poster Session I
Antibacterial drug activity and interactions in Gram-negative bacteria

FOSFOMYCIN SYNERGY ACTIVITY AGAINST MULTI-DRUG RESISTANT ACINETOBACTER BAUMANNII STRAINS.

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Background and aim: The emergence and rapid spreading of multidrug-resistant *Acinetobacter baumannii* isolates have become a serious health threat worldwide and therapeutic options for treatment of infections caused by these pathogens are limited.

The aim of this study was evaluated 'in vitro' the effect of combination of fosfomycin with colistin, imipenem, tigecycline, vancomycin, amikacin, rifampicin, gentamycin and meropenem against twenty *A. baumannii* clinical isolated being 7 colistin resistant and 13 carbapenem resistant.

Methods: Minimal inhibitory concentration (MIC) was determined by broth microdilution, synergy was investigated by using checkerboard microbroth using two interpretation methods (FICI and 2 Well). Synergistic interaction was confirmed by time-kill assay. PCR for carbapenemase genes and outer membrane proteins of the isolates were performed as well as outer membrane protein analysis by SDS-PAGE. Clonality was evaluated by pulsed-field gel electrophoresis.

Results: Tigecycline resistance was present in 1 (5%) of isolates, colistin 7 (35%), gentamycin 13 (60%), imipenem 19 (95%), amikacin 19 (95%), rifampicin 20 (100%), meropenen 20 (100%), phosphomycin 20 (100%). Ten isolates harboring OXA-23; 7 isolates OXA-143 and 3 co-harboring OXA-23 and OXA-143. All isolates showed lost or diminished of outer-membrane proteins (29KDa; 33-36kDa and 43kDa). The 7 isolates colistin resistant belonged to the same clone. Time-kill analysis confirmed the synergistic interaction. Antagonism was not observed for any combination against any of the strains tested, the other results are shown in table 1.

Table 1. Synergistic effect 'in vitro' of fosfomycin combinations against 20 isolates of multi-drug resistant *Acinetobacter baumannii*. USP, São Paulo-Brazil, 2013.

Antibiotic	Antibiotic tested in combination	Carbapenem Resistant (n13)				Colistin Resistant (n7)			
		Synergy (%)		Indifference (%)		Synergy (%)		Indifference (%)	
		FICI	2Well	FICI	2Well	FICI	2Well	FICI	2Well
Fosfomycin	Colistin	0	**53,8**	100	46,2	0	0	100	100
	Imipenem	0	23,1	100	76,9	0	14,3	100	85,7
	Tigecycline	0	0	100	100	0	0	100	100
	Gentamycin	0	**76,9**	100	23,1	0	42,9	100	57,1
	Amikacin	0	**100**	100	0	0	**71,4**	100	28,6
	Meropenem	0	23,1	100	76,9	0	28,6	100	71,4
	Vancomycin	0	23,1	100	76,9	0	14,3	100	85,7
	Rifampicim	0	38,5	100	61,5	0	0	100	100

Conclusion: These findings showed that fosfomycin combined with amikacin followed by fosfomycin with gentamycin or with colistin are the best option to treat infection due to carbapenem-resistant *A. baumannii* multidrug resistant at our hospital. The combination of fosfomycin with colistin was indifferent against colistin-resistant isolates. Thus, the synergy result probably depends on the mechanism of resistance and clonality of isolates.