P0306

Paper Poster Session II

Focus: Acinetobacter, Pseudomonas and other nonfermenters

Temocillin is not substrate for OprD2 porin from *Pseudomonas aeruginosa*

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Objectives: Resistance to beta-lactams in *P. aeruginosa* can be mediated by a decreased bacterial outer membrane permeability (e.g., loss or modification of the OprD2 porin or overexpression of efflux pumps), associated or not with overproduction of AmpC cephalosporinases, extended-spectrum beta-lactamases (ESBLs) or carbapenemases. Temocillin (TMO; 6-alpha-methoxy-ticarcillin), a beta-lactam stable against most beta-lactamases (including most ESBLs, AmpC and KPC-type carbapenemases), is proposed as a sparing drug for carbapenems. Temocillin, however, is, considered as inactive on *P. aeruginosa,* due to active efflux by the constitutively-expressed MexAB-OprM pump (JAC 2012, 67:771-75). Yet, we showed that a subset of strains (~ 20 %) collected from cystic fibrosis (CF) patients harbored natural mutations in *mexA* or *mexB* genes, which restored their susceptibility to TMO, suggesting a potential therapeutic interest in this specific population (ESCMID Conference on Reviving Old Antibiotics 2014; P02). In order to further document this interest, we aimed now at determining whether TMO was substrate for the OprD2 porin, for which mutations or loss of expression are known to confer high resistance to carbapenems in *Pa*.

Methods: MICs were determined by microdilution in Muller Hinton broth, according to CLSI guidelines, using as test organisms (a) *Pa* PA14 and its OprD2 defective mutant (PA14DOprD2) and (b) a porin-deficient *E.coli (K-12 W3110: ΔompFΔompC)* transformed with either a pB22 empty vector or a pB22-OprD2 construct coding for the *Pa* OprD2 under the control of the P_{BAD} promoter of the arabinose operon.

Results: The table shows that the MICs of carbapenems were higher in PA14DOprD2 than in PA14 and lower in K-12 W3110 expressing OprD2 than in the strain transformed by the empty vector. On the contrary, MICs of carboxypenicillins, including TMO, were the same, whether *oprD2* was expressed or not.

Conclusions: TMO, as other carboxypenicillins, is not substrate for OprD. Testing susceptibility to this drug, including in carbapenem-resistant strains (including those with mutations or loss of expression of OprD2 porin) isolated from CF patients, could be useful.

Strains	Antibiotic MIC (mg/L)					
MEM	IPM	DOR	TIC	CAR	TMO	
PA14 wild type	0.5	0.25	0.25	32	64	256
PA14 DOprD2	8	2	2	32	64	256
K-12 W3110 + pB22 empty	1	0.25	0.5	>2048	>2048	32
K-12 W3110 + pB22-OprD2	0.125	0.032	0.064	>2048	>2048	32