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Combination antibiotic susceptibility of biofilm-grown Burkholderia cepacia and Pseudomonas aeruginosa isolated from patients with pulmonary exacerbations of cystic fibrosis.

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Abstract

We identified double and triple antibiotic combinations effective against biofilm-grown *Burkholderia cepacia* and *Pseudomonas aeruginosa* sampled from cystic fibrosis (CF) patients undergoing acute pulmonary exacerbations. Sputum bacteria from 110 CF patients were grown as biofilms. Combination antibiotic susceptibility testing was used to test 94 double and triple antibiotic combinations. Biofilm-grown bacterial isolates were less susceptible to antibiotic combinations compared to the same bacterial isolates grown planktonically ($P < 0.001$). Fifty-nine percent of biofilm-grown *B. cepacia* isolates and 29% of *P. aeruginosa* isolates were resistant to all double antibiotic combinations tested. Triple antibiotic combinations were more effective than double antibiotic combinations against biofilms ($P < 0.0001$). For *P. aeruginosa* biofilms, the addition of azithromycin or rifampin to otherwise effective antibiotic combinations was frequently associated with antagonism. Bacterial biofilms of CF organisms are highly resistant to antibiotics. This study identified potentially effective antibiotic combinations to guide the empirical treatment of CF pulmonary exacerbations.

Table 1: Inhibitory activity of the most effective double and triple antibiotic combinations against *pseudomonas aeruginosa* biofilm-grown isolates.

Most effective double antibiotic combinations against *P. aeruginosa*		Most effective triple antibiotic combinations against *P. aeruginosa*	
Antibiotic combination	% of isolates inhibited	Antibiotic combination	% of isolates inhibited
$Tobramycin_{200}$/meropenem	56	$Tobramycin_{200}$/meropenem/ceftazidime	68
$Tobramycin_{200}$/ceftazidime	50	$Tobramycin_{200}$/meropenem/amikacin	68
$Tobramycin_{200}$/ciprofloxacin	45	$Tobramycin_{200}$/meropenem/sulfamethoxazole/trimethoprim	66
Meropenem/amikacin	33	$Tobramycin_{200}$/meropenem/ciprofloxacin	63
$Tobramycin_{200}$/meropenem	28	$Tobramycin_{200}$/meropenem/piperacillin-tazobactam	57
Meropenem/ceftazidime	28	$Tobramycin_{200}$/ciprofloxacin/piperacillin	53
Meropenem/ciprofloxacin	27	$Tobramycin_{200}$/piperacillin-tazobactam/ceftazidime	53
Meropenem/sulfamethoxazole-trimethoprim	20	$Tobramycin_{200}$/meropenem/chloramphenicol	53
Ceftazidime/ciprofloxacin	20	Rifampin/$tobramycin_{200}$/ceftazidime	52
Azithromycin/meropenem	20	$Tobramycin_{200}$/sulfamethoxazole/trimethoprim/ceftazidime	51

Table 2: Inhibitory activity of the most effective double and triple antibiotic combinations against *Burkholderia cepacia* biofilm-grown isolates

Most effective double antibiotic combinations against *B. cepacia*		Most effective triple antibiotic combinations against *B. cepacia*	
Antibiotic combination	% of isolates inhibited	Antibiotic combination	% of isolates inhibited
$Tobramycin_{200}$/meropenem	35	$Tobramycin_{200}$/meropenem/piperacillin-tazobactam	53
Meropenem/amikacin	26	$Tobramycin_{200}$/meropenem/sulfamethoxazole/trimethoprim	51
$Tobramycin_{200}$/ceftazidime	22	$Tobramycin_{200}$/meropenem/amikacin	50
Meropenem/ciprofloxacin	18	$Tobramycin_{200}$/meropenem/ceftazidime	49
$Tobramycin_{200}$/meropenem	16	$Tobramycin_{200}$/sulfamethoxazole/trimethoprim/ceftazidime	43
Meropenem/ceftazidime	14	$Tobramycin_{200}$/meropenem/ciprofloxacin	42
Amikacin/ceftazidime	14	$Tobramycin_{200}$/amikacin/ceftazidime	36
Azithromycin/meropenem	14	$Tobramycin_{200}$/meropenem/chloramphenicol	36
$Tobramycin_{200}$/ciprofloxacin	12	$Tobramycin_{200}$/ceftazidime/azithromycin	35
Meropenem/sulfamethoxazole-trimethoprim	12	$Tobramycin_{200}$/ceftazidime/ciprofloxacin	35