Susceptibility of *Pseudomonas aeruginosa* (P.a.) to biocides among clinical isolates collected from Intensive Care Units (ICU) patients with nosocomial pneumonia in 5 Belgian teaching hospitals during the 2004-2008 period

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Abstract (revised)

Background: Increasing reports point to the emergence of common resistance mechanisms to antibiotics (AB) and biocides in nosocomial pathogens. We have examined whether this pattern could develop for P.a. collected from ICU patients.
Methods: Strains: 137 first, non-duplicate isolates collected between 2004 and 2008 from patients with confirmed nosocomial pneumonia in ICU of 5 teaching hospitals, and stratified as (i) fully susceptible and (ii) with decreased susceptibility to FEP or AMK (taken as example for beta-lactams and aminoglycosides). Biocides MICs were determined by geometric microdilution in cation-adjusted Muller-Hinton broth (following CLSI guidelines as proposed for ABs).
Results: All isolates were susceptible to ethanol at concentrations of 3 % or higher. Data for other biocides are shown in the Table.

Susceptibility of P.a. to common biocides and dilution safety factor (DSF)

Biocides (concentrations) [a]	MIC_{50} / MIC_{90} (g/L)		DSF [b]
	fully suscept. (n = 60)	decreased suscept. (n = 78) [c]	
Eosin (2 %) [d]	> 10	> 10	< 1
Eosin / Thiomersal (2 % / 0.04 g/L) [e]	1.25 / 2.5	2.5 / 10	2
Thiomersal (0.04 g/L)	0.0025 / 0.005	0.0025 / 0.02	2
Chlorhexidine (0.05 – 2 %)	0.016 / 0.016	0.032 / 0.032	15.6 / 625
Polyvinylpyrolidone (80 g/L) [f]	5 / 5	5 / 5	16

[a] concentrations observed in most common commercial hospital solutions
[b] ratio of the concentration of the commercial solution to **MIC_{90}** of AB-resistant isolates
[c] increase of 2 – 4 mm in diameters (disk-diffusion) for FEP and AMK compared to wild-type
[d] commercial pure eosin solution (Sigma-Aldrich)
[e] commercial mixture of both agents (Medgenix®)
[f] commercial solution of Polyvinylpyrolidone (Betadine®)

Eosin (alone) is ineffective for most isolates. Thiomersal and chlorhexidine MICs are higher in isolates with reduc. suscept., and close to those of the commercial solution for thiomersal. Polyvinylpyrolidone is unaffected by AB-resistance but is DSF is lower than that of chlorhexidine.
Conclusions: Although MICs of biocides other than eosin remain low, dilution of these agents may markedly reduce their effectiveness. Common resistance mechanisms with AB are likely for chlorhexidine and thiomersal.

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Introduction

Nosocomial pneumonia in intensive care units (ICU) is a common complication of critical illness and is associated with significant attributable morbidity and mortality, including prolongation of mechanical ventilation and increased risk of death of patient [1-2]. *Pseudomonas aeruginosa* (P.a.) is a major cause of nosocomial pneumonia in ICU. P.a. develops many mechanisms of resistance to widely used antipseudomonal antibiotics such as amikacin (AMK) or cefepime (FEP) [3-4]. The use of antimicrobial chemicals (biocides) in general practice and in domestic, clinical and industrial settings may be a contributory factor to development and selection of antibiotic resistant isolates [3]. This triggered us to evaluate the level of resistance of P.a. to 5 biocides used in ICU (eosine, thiomersal, chlorhexidine [CHX], polyvinylpyrolidone [PVI, Betadine®] and ethanol 96 %) in isolates collected from ICU patients with nosocomial pneumonia in 2004-2008.

Methods

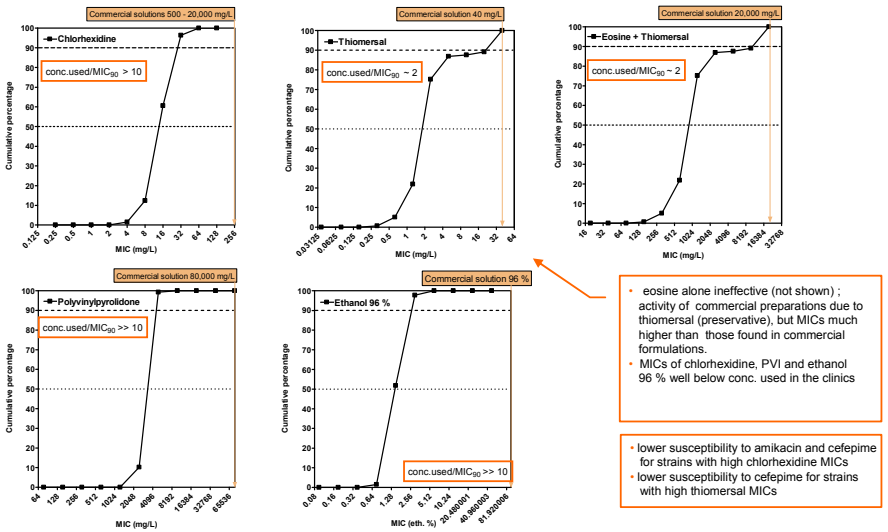
Bacteria: 137 strains of *P. aeruginosa* collected from patients admitted in ICU with a diagnosis of nosocomial pneumonia (confirmed by analysis of clinical and radiological data) in 5 Belgian hospitals.

Susceptibility testing: MICs determined by geometric microdilution in cation-adjusted Mueller-Hinton broth following the general methods of CLSI. *P. aeruginosa* ATCC 27853 and PAO1 were used as a quality control.

Assessment of the "clinical" efficacy: Ratio of the concentration of the commercial solution to the MIC_{90} (values > 1 suggest efficacy if used undiluted)

Results

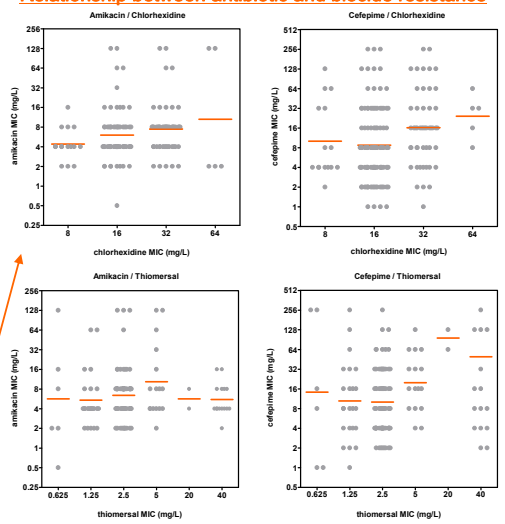
Cumulative distribution of MICs for biocides in 137 isolates of *P. aeruginosa*



- eosine alone ineffective (not shown) ; activity of commercial preparations due to thiomersal (preservative), but MICs much higher than those found in commercial formulations.
- MICs of chlorhexidine, PVI and ethanol 96 % well below conc. used in the clinics

- lower susceptibility to amikacin and cefepime for strains with high chlorhexidine MICs
- lower susceptibility to cefepime for strains with high thiomersal MICs

Relationship between antibiotic and biocide resistance



Conclusions

No resistance was detected for chlorhexidine, PVI and ethanol 96 %. Eosin alone is ineffective (the marginal activity of commercial formulations is due to the presence of thiomersal). Chlorhexidine MICs however spread over a broad range of values, suggesting the presence of low level resistance mechanisms.
Worryingly enough, strains that are less susceptible to chlorhexidine (and to thiomersal to a lesser degree) also show higher MICs to antipseudomonal antibiotics, suggesting possible common mechanisms of resistance related to permeability. This raises questions about the best way to decontaminate ICU from multidrug resistant strains.

References

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