sion and that the use of antimicrobial drugs selected the resistant strain, which was then transmitted to the second patient. Unfortunately, none of the patients was screened for VRE colonization at the time of ICU admission, and thus we cannot support or exclude the possibility that the patients already carried the isolates before admission.

Emerging linezolid resistance is a fact. Therefore, one could suggest that clinical laboratories should be routinely testing linezolid susceptibility in all clinically significant enterococci. Worldwide surveillance programmes should closely monitor all linezolid resistance reports in order to trace any trends in the development of resistance.

References


Effect of subinhibitory concentrations of azithromycin on adherence of Pseudomonas aeruginosa to bronchial mucins collected from cystic fibrosis patients

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Sir,

Pseudomonas aeruginosa, an opportunistic pathogen, is the major pathogen in the airways of patients with cystic fibrosis (CF) and is currently associated with the morbidity and mortality seen in this disease. Macrolides, such as azithromycin, are normally not included in the anti-pseudomonal therapeutic arsenal because of the absence of bactericidal or bacteriostatic activity. However, several previous investigators have reported that long-term administration of azithromycin is effective in patients with pulmonary P. aeruginosa infections.1 The clinical benefits achieved could include the effects of an anti-inflammatory2 and/or modulation of the production of virulence factors of P. aeruginosa, such as bacterial exoproducts,3 the formation of biofilm,4 or the synthesis of flagella5 and some outer membrane proteins.6 Adherence of P. aeruginosa to respiratory mucins plays an important role in the colonization of the airways of these patients. This adherence process involves flagella and several non-pili adhesins localized on the outer membrane of P. aeruginosa. Supporting the clinical observations, adherence of this organism to human salivary or airway mucins has been demonstrated in vitro using liquid- or solid-phase adherence assays.6

In order to investigate the action of azithromycin on the pathogenesis of P. aeruginosa, we evaluated—in a solid-phase adherence assay—the action of subinhibitory concentrations of the macrolide on the adherence of different bacterial strains to respiratory mucins of CF patients.
patients. The reference strain PAO-1, and 13 strains (five mucoid and eight non-mucoid strains) freshly isolated from the sputum of CF patients known to be infected by different strains and who were not treated with azithromycin, were tested. MICs of azithromycin were determined by an agar dilution method, following the recommendations of the NCCLS (2002), with powdered azithromycin suspension of MICs, which varied from 64 to >1024 mg/L, but they were compatible at 2 and 4 mg/L. These concentrations were much lower than the 7.8% for non-mucoid clinical strains and 6.2% for mucoid strains.

bronchial mucins in our assays, with a mean rate of adherence of the action of azithromycin on adherence was efficient for the non-mucoid clinical strains. Since it was observed especially with azithromycin 2 mg/L, whereas that of mucoid isolates was low or even non-existent with azithromycin 2 mg/L, but obvious with azithromycin 4 mg/L. This observation agreed with numerous studies that describe a decrease in antibiotic susceptibility of mucoid strains. However, we could not establish whether the inhibition of adherence was dose-dependent, since only two concentrations of azithromycin were analysed. For the PAO-1 strain, an increase in the inhibition of adherence was observed between azithromycin 2 and 4 mg/L, whereas it was not confirmed for the non-mucoid clinical strains. The inhibition of the adherence properties of bacteria were in agreement generally with low MICs, but it was difficult to show an absolute correlation between low MICs of azithromycin and the effect of the macrolide on adherence of bacterial cells to mucins. Thus, no decrease was observed in one strain (strain mucoid 2) with an MIC of 128 mg/L, whereas an effect was seen in another (strain non-mucoid 6) for which the MIC was 1024 mg/L.

In conclusion, the decrease of adherence by azithromycin is a strain-dependent event, partially but not absolutely correlated to the MIC of azithromycin. Concentrations necessary for this action are compatible to therapeutic diffusion of azithromycin in mucus, even if this action requires a two-fold higher concentration when strains are mucoid. Since adherence to mucins is one of the first lines of colonization, azithromycin administration might be beneficial in the early stages of P. aeruginosa infection. This work provides an additional argument for the use of azithromycin in CF patients.

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References


