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In vitro susceptibility of amikacin against Gram-negative respiratory and blood isolates from US hospitals

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Background: Nosocomial pneumonia caused by *P. aeruginosa* continues to pose significant challenges in US hospitals due to increasing antimicrobial resistance. Yet more challenging is delivering effective antibiotic concentrations to the lung as many parenteral therapies have poor penetration including amikacin. To overcome this challenge, the administration of amikacin by inhalation (Amikacin Inhale, BAY41-6551) is currently under phase III study as an adjunctive therapy to IV antibiotics for the treatment of Gram-negative pneumonia in intubated and mechanical ventilated patients. Our objective was to define the potency of amikacin against a US collection of *P. aeruginosa* nosocomial isolates and relate these data to achievable lung concentrations.

Material/methods: 34 US hospitals provided non-duplicate nosocomial blood and respiratory isolates of *P. aeruginosa* from adult inpatients. MICs were determined using Clinical Laboratory Standards Institute (CLSI) defined broth microdilution methods for ceftolozane/tazobactam, cefepime, ceftazidime, ciprofloxacin, colistin, aztreonam, imipenem, piperacillin/tazobactam, meropenem, tobramycin and amikacin. CLSI and FDA breakpoints were used to define susceptibility.

Results: Hospitals provided 516 nosocomial blood and respiratory isolates of *P. aeruginosa*. Rank order % susceptibility (MIC_{90}, mg/L) was as follows: ceftolozane/tazobactam 96% (4), amikacin 96% (16), colistin 95% (2), tobramycin 91% (4), meropenem 73% (16), cefepime 72% (32), ceftazidime 72% (64), ciprofloxacin 71% (16), piperacillin/tazobactam 67% (256), and imipenem 66% (16). For amikacin 96% of these organisms had MICs ≤ 16 mg/L, 1% = 32 mg/L, 2% = 64 mg/L and 1% = ≥128 mg/L. Comparing amikacin against meropenem resistant isolates (n=104), 91% of these organisms had MICs ≤16 mg/L, 8% = 32-64 mg/L and 1% = ≥128 mg/L. Comparing amikacin against cefepime resistant isolates (n=71), 86% of these organisms had MICs ≤16 mg/L, 13% = 32-64 mg/L and 1% = ≥128 mg/L. Comparing amikacin against piperacillin/tazobactam resistant isolates (n=93), 92% of these organisms had MICs ≤16 mg/L, 3% = 32 mg/L, and 5% = 64 mg/L.

Conclusions: In this study we defined the phenotypic profile of amikacin for blood and respiratory nosocomial isolates implicated in ICU based pulmonary infections. When considering the MIC_{90}, only ceftolozane/tazobactam, colistin, tobramycin and amikacin had values at or below their respective breakpoints. Despite resistance to other β-lactams, amikacin maintained high susceptibility. For amikacin 96% of organisms had a MIC of ≤16 mg/L, moreover nearly all (99%) organisms have MICs ≤64 mg/L which is well below the achievable lung concentrations of approximately 5000 mg/L with the administration of Amikacin Inhale. These data highlight the enhanced potency of amikacin and suggest that the achievable lung concentrations after inhalation will exceed the MICs typically observed for *P. aeruginosa* in the hospital setting.