Background: Carbapenem-resistant Acinetobacter baumannii (CR-Ab) infections are associated with high morbidity and mortality, since therapeutic options are limited. The antibacterial properties of N-acetylcysteine (NAC), a mucolytic agent usually co-administered with antibiotics in case of lower respiratory tract infections, have been recently investigated.

The aim of the study was to evaluate the activity of NAC, alone and in combination with different antimicrobials, against clinical strains of CR-Ab.

Materials/methods: Over a 6-months period, 8 CR-Ab strains were collected from hospitalized patients at Sapienza University of Rome. MICs50/90 of meropenem (MEM), ampicillin/sulbactam (A/S), colistin (COL), rifampin (RIF) and tigecycline (TIG) were determined by broth macrodilution method (BMD) and checkerboard method was used to evaluate the synergistic activity of the tested combinations. Synergism was defined as FIC index ≤0.5. Additionally, killing curves evaluating the activity of NAC alone and in combination with beta-lactams were performed.

Results: The CR-Ab strains were OXA producers. MICs50/90 were 128/512 µg/mL (MEM), 64/256 µg/mL (A/S), 0.25/4 µg/mL (COL), 2/4 µg/mL (RIF), 0.5/1 µg/mL (TIG), 2.5/5 mg/mL (NAC). Synergism was observed in 87.5% (MEM+NAC), in 75% (A/S+NAC), in 62.5% (RIF+NAC), whereas for COL+NAC and TIG+NAC only additivity was found (87.5% and 62.5%, respectively). Given the high activity of NAC plus beta lactams, these combinations were tested in killing experiments.

In the killing curves, NAC alone exhibited a full bactericidal activity in the first 2h at 5 mg/ml. When tested at sub-inhibitory concentrations in combination with concentrations obtainable in the serum of MEM and A/S, a high bactericidal and synergistic activity at 24h was observed (Figure 1A-1B-1C).

Conclusions: NAC exhibited a remarkable synergistic and bactericidal activity in combination with beta-lactam antibiotics used in therapy to fight CR-Ab infections. The addition of NAC as a part of combination therapy against difficult-to-treat infections caused by CR-Ab might be considered a valid therapeutic option and deserves further investigations in the clinical practice.

Figure 1. Killing activity of NAC, alone (A) and in combination with MEM (B) and A/S (C), against CR Ab.
- 5 mg/ml
- 2.5 mg/ml
- 1.25 mg/ml
- Growth control
- Bactericidal line

Log10 CFU/ml

Time (h)