Objective

We evaluated the bactericidal and synergistic activity of double-carbapenem regimen in three patients with bloodstream infections due to carbapenem and colistin resistant *Klebsiella pneumoniae* successfully treated with meropenem plus ertapenem.

**Case 1.** A 63-year-old man underwent aortic endoprosthesis placement for aorta abdominal aneurysm. One year later, endoprosthesis was replaced for infection. He developed fever and three blood cultures were positive for carbapenem and colistin resistant *Klebsiella pneumoniae*. Fosfomycin and tigecycline were given with no response. Meropenem 2 g every 8h plus ertapenem 1 g every 24h were administered for 21 days with clinical response.

**Case 2.** A 71-year-old man underwent aorto-bisiliac graft placement because of aortic aneurysm. Six months later, he developed fever and three blood cultures were positive for carbapenem and colistin resistant *Klebsiella pneumoniae*. Meropenem and daptomycin were given without response. Six days later, ertapenem 500 mg every 24h and meropenem 1g every 12h were started according to creatinine clearance. The patient became afebrile after 48h of treatment and blood cultures were sterile. He died two days later for acute heart failure.

**Case 3.** A 54-year-old man was hospitalized because of left renal hematoma. After 48 hours, the patient had fever and blood cultures were positive for *Klebsiella pneumoniae*; meropenem and tigecycline were given with partial response. Meropenem 2 g every 8h plus ertapenem 1 g every 24h were administered for 24 days with clinical success.

Methods.

Minimal inhibitory concentration (MIC) of ertapenem and meropenem were determined by broth macrodilution method in cation-adjusted Mueller Hinton broth. The activity of meropenem alone and plusertapenem was investigated by time-kill studies. Bactericidal activity was defined as ≥99.9% reduction of the initial bacterial count at each time point. Synergy was defined as a ≥100-fold decrease in CFU/mL between the combination and its most active constituent after 24h.

Results

Ertapenem MICs were 128, 256 and 256mcg/ml for patient 1, 2 and 3, respectively. Meropenem MICs were 256, 256 and 128 mcg/ml for patient 1, 2 and 3, respectively.

In patients 1 and 2, bactericidal and synergistic activity were achieved at time 4, 6, 8 and maintained at 24h at different concentrations of meropenem and ertapenem (Figure 1A, 1B). In patient 3, bactericidal effect was present at time 8 whereas a regrowth was observed at 24h (Figure 1C).

Conclusion

Our *in vitro* analyses confirmed the efficacy of double-carbapenem regimen which might be considered as a valid and safe option in carbapenemase-producing *Klebsiella pneumoniae* infections,
especially in patients who experienced colistin failure because of either resistance or toxicity.