In vitro activity of ceftolozane/tazobactam against contemporary extended-spectrum cephalosporin resistant Enterobacteriaceae and multi-drug resistant Pseudomonas aeruginosa clinical isolates of Argentina

Fernando Pasteran*, Melina Rapoport, Ezequiel Albornoz, Alberto Carena, Pablo Scapellato, Walter Vasen, Pedro Pessacq, Paola Ceriana, Ceftolozane Argentina Group, Fabian Herrera, Alejandra Corso

1Centro de Educación Médica e Investigaciones Clínicas, CEMIC, Argentina, 2Hospital de Gastroenterología “Dr. B. Udaondo”, Argentina, 3Hospital Rodolfo Rossi, La Plata, Argentina, 4Laboratorio Nacional de Referencia en Antimicrobianos, INEI-ANLIS “Dr. Carlos Malbrán”, 5ceftolozane group, Argentina, 6Hospital Donación “F. Santojanni”, Argentina, 7Hospital Italiano, Buenos Aires, La Plata, Argentina

Background: The global increase in the prevalence of multidrug-resistant (MDR) pathogens, such as extended-spectrum cephalosporin-resistant Enterobacteriaceae (EEE) and MDR Pseudomonas aeruginosa (PA), is a challenge for health systems. A new antimicrobial to treat infections caused by these pathogens, ceftolozane/tazobactam (C/T), has been approved by the FDA/EMA. Objective: to evaluate the in vitro activity of C/T in comparison with other antimicrobial agents against a representative EEE/MDR-PA collection.

Materials/methods: We included 113 EEE and 180 MDR-PA unique clinical isolates (59 hospitals), recovered from: 1) adult patients with complicated intra-abdominal infection undergoing surgical focus control procedure. 2) infections of the urinary tract (adults). 3) bacteremia in cancer and hematopoietic stem cell transplantation adult patients. 4) extreme-drug resistant isolates (mainly PA) submitted to the NRL. Carbapenemase producers were excluded. The MIC of C/T was determined by gradient strips (Liofilchem), susceptibility to other agents by micro-dilution (Sensititre) or disk diffusion and the results were interpreted with CLSI criteria. The molecular characterization of β-lactamases and mcr genes was carried out by PCR/sequencing. The bacterial identification was confirmed with MALDI-TOF (Bruker). The Chi2 test (Yates correction) was used to compare the activity of C/T vs piperacillin/tazobactam.

Results: Fig.

a) Enterobacter cloacae, 5 Serratia marcescens, 3 Salmonella, 2 Citrobacter freundii, 2 Proteus mirabilis, 1 Providencia stuartii, 1 Klebsiella oxytoca. b) EEE-ESBLs: 41%CTX-M-1/15, 20%CTX-M-2, 13%CTX-M unassigned variant, 8%CTX-M-9/14, 4%OXA-1/31, 1%CTX-M-8/24, 1%CTX-M-1/15+CTX-M-9/14, 1%PER, 1%CTX-M-2+PER, 8% uncharacterized ESBL. c) Plasmidic AmpC: DHA. d) PA-ESBLs: 75%OXA-1/31, 16%GES-1, 3%CTX-M-1/15, 3%CTX-M unassigned variant, 3%PER. High level resistance to C/T (MIC >48mg/L) was observed mainly among GES-1-producing PA. C/T was significantly more active than PTZ among MDR-PA (p<0.01) and only the Klebsiella subgroup within the EEEs (p<0.01).
**Conclusions:** A uniform sensitivity of C/T was observed among EEE, although differences were detected by bacterial species but not by the type of CTX-M produced. C/T was the most active β-lactam assayed against MDR-PA. C/T could be a potential alternative for the treatment of infections in adult patients such as those caused by EEE and MDR-PA circulating in Argentina.