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Poster Session IV
Molecular epidemiology of MDR Enterobacteriaceae

CHARACTERIZATION OF OUTER-MEMBRANE PROTEINS AND CARBAPENEMASE IN CARBAPENEM-RESISTANT ENTEROBACTER AEROGENES AND ENTEROBACTER CLOACAE

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Carbapenem resistance in *Enterobacter* spp. has increased significantly in recent years. Few studies, however, assessed the mechanisms involved with carbapenem resistance in this pathogen.
Objectives: The aim of this study was to evaluate the presence of carbapenemase, alteration of outer membrane proteins, and clonality of clinical isolates of *E. aerogenes* and *E. cloacae* isolated in 03 Brazilian hospitals from 2005 to 2012.
Methods: The inhibitory concentration of the following antimicrobials: imipenem, meropenem, ertapenem, fosfomycin, tigecycline, and polymyxin B was performed by microdilution according to the CLSI. PCR of genes of carbapenemase (KPC, VIM, SPM, IMP, NDM, NMC/SME, Oxa-48), outer membrane proteins (OMP35-36) was achieved for all the isolates. The clonality of the isolates was evaluated by PFGE and isolates with different clonal profiles were selected for SDS analysis. Hydrolysis of imipenem was evaluated for the isolates that did not show any of carbapenemase searched.
Results: 105 isolates *E. aerogenes* and 25 isolates of *E. cloacae* totaling 130 isolates were evaluated, of which 44 and 9 were respectively resistant to carbapenem. Of the 44 isolates of *E. aerogenes* carbapenem- resistant 44 (100%) showed resistance to imipenem, 36 (65.5%) to ertapenem and 35 (79.5%) to meropenem. The 9 isolates of *E. cloacae* were resistant to all carbapenem. Surgical infection was the most frequent site of infection (23 of 53) followed by blood (14 of 53). KPC-2 was the only carbapenemase identified and the most frequent mechanism of resistance identified in 33 of 44 isolates of *E. aerogenes* and in 6 of 9 isolates of *E. cloacae*.
Eleven isolates with imipenem MIC that ranged from 8 ug/mL to 32 ug/mL and meropenem from 2 ug/mL to 16 ug/mL exhibited more than a mechanism of resistance as KPC, absence of genes of Porin (35-36Kda) and decrease and or absence of outer membrane proteins (35-36Kda and 39 and 42 Kda) by SDS. Among these isolates all *E. aerogenes* belonged to the predominant clone named clone A, except to that belonged to clone B and all *E. cloacae* to clone D. Lost of protein of 39Kda was associated with high imipenem MIC, lost of protein of 42Kda and diminished of OMP35 and 36 with isolates imipenem resistant and meropenem susceptible. Seventeen isolates did not present any of carbapenemases evaluated, however, 5 showed hydrolysis of imipenem, of which 2 were screening test of metallo-beta-lactamase with EDTA positive, exploring the possibility of the presence of a new carbapenemase.
Conclusions: KPC was the most frequent mechanism of resistance identified, which alerts to the potential rapid spread of resistance in this genus. High imipenem MIC and difference in carbapenem susceptibility profile (imipenem resistance and meropenem susceptibility) was associated with alteration of outer-membrane protein.