Bloodstream Infections caused by *Enterobacteriaceae* isolates co-harboring NDM-1 and KPC-2.

Taniela Bes, MD[1,2], Debora Nagano, B.Sc.[2], Roberta Martins, PhD[2], Ana Paula Marchi, MPH[2], Lauro Perdigão Neto, MD[1,2,3], Hermes Higashino, MD[1], Gladys Prado, MD[2], Thais Guimaraes, MD, PhD[1,3], Anna Levin, MD, PhD[1,2,3] and Silvia Costa, MD, PhD[1,2,3]

(1)Infectious Diseases Division, Hospital das Clínicas da Universidade de São Paulo, São Paulo, Brazil

(2)Instituto de Medicina Tropical da Universidade de São Paulo, São Paulo, Brazil

(3)Infection Control, Hospital das Clinicas Faculdade de Medicina da Universidade de Sao Paulo, Sao Paulo, Brazil

Abstract

Background: Carbapenem-resistant *Enterobacteriaceae* is a worldwide health problem, mainly due to production of carbapenemases (class A serine carbapenemase, such as KPC, and class B metallo-beta-lactamase, as NDM), however isolates carrying both *bla*$_{KPC-2}$ and *bla*$_{NDM-1}$ are unusual. The aim of this study was to describe microbiological and clinical characteristics of five cases of bloodstream infections caused by carbapenem-resistant *Klebsiella pneumoniae* (KP) and *Serratia marcescens* (SM) co-harboring KPC-2 and NDM-1.

Methods: KP and SM carbapenem-resistant clinical isolates from Hospital das Clinicas, Sao Paulo, Brazil, isolated from 2012 to 2014 and co-harboring *bla*$_{KPC-2}$ and *bla*$_{NDM-1}$ were involved in this study. Carbapenemases codifying genes were detected by PCR and confirmed by Sanger sequencing (SS) and Whole Genome Sequencing (WGS). Phenotypical assay using the disk diffusion (DD) method: meropenem was tested with EDTA and/or Phenylboronic Acid (PBA).

Results: The blood culture isolates: three from hematopoietic stem cell transplant, one from a kidney transplant patient and one surgical patient whose lived in poor neighborhoods in the Sao Paulo area, with no history of international travel. Despite antibiotic treatment, almost all with colistin and tigecycline, and four of the patients died (Table 1). Subsequently, the phenotypic analyzes shows that Meropenem added with either EDTA, PA or both showed increased zone of inhibition in comparison to Meropenem alone (Figure 1). Molecular tests indicated KPC-2 and NDM-1, respectively.

Conclusion: In summary, this study shows the high difficulty characterizing isolates co-harboring these two mechanisms however seems like phenotypic analyzes using meropenem added with either EDTA and PA at the primary level and Sanger sequencing to confirm the gene presence.

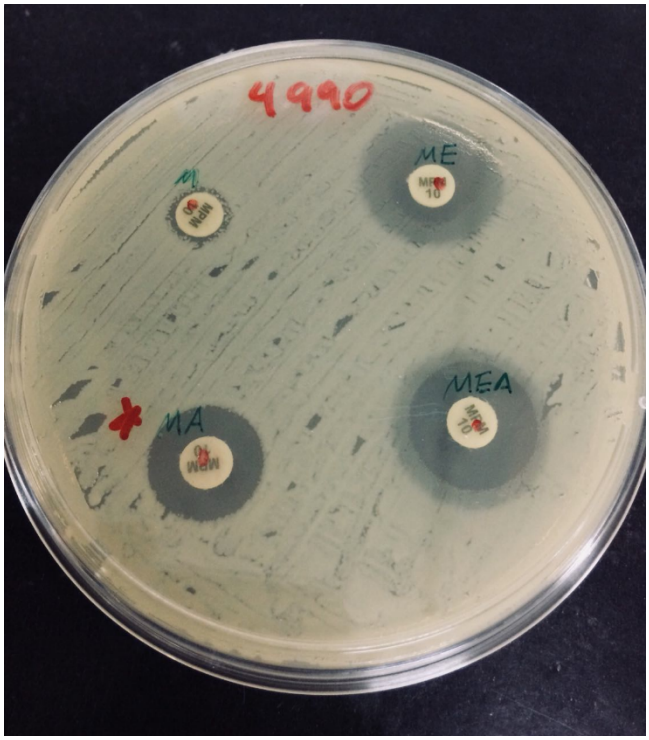
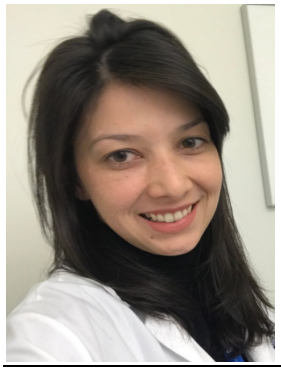


Figure 1: Phenotypic test M: Meropenem ME: Meropenem + EDTA MA: Meropenem + Phenylboronic Acid MEA: Meropenem + EDTA + Phenylboronic Acid

Blood culture	Lenght of stay to positive blood culture	Agent	Underlying diseases	Approach	Leukocytes / Neutrophils	Treatment	Outcome 14 day death
10/19/2012	10/21/12	*K. pneumoniae (1411)*	Myelodysplastic syndrome	Allogeneic BMT (10/11/2012)	100/0	Meropenem + Colistin tempo tratamento	Death 10/21/12
12/14/2012	12/16/12	*K. pneumoniae (1581)*	Severe aplastic anemia	Not related allogeneic TCTH (12/09/2012)	100/0	Meropenem + Colistin	Death 12/16/12
10/16/2014		*K. pneumoniae (4301)*	Peripheral T-cell lymphoma	Autologous BMT 9/17/2014	3,33/2,43	Meropenem + Colistin	Discharge from hospital 11/08/14
6/14/2013	06/25/13	*S. marcescens (1756)*	Necrotizing fasciitis	Amputation of the right arm (05/31/13) Complication: Ischemic cecum perforation (6/07/2013)	10,42/8,02	Tigecycline + Fosfomycin	Death 06/25/13
10/21/16	11/30/16	*K. pneumoniae (4990)*	Kidney transplant	Urinary tract infection (10/20/16) Graft Nephrectomy (11/23/16)	9,64/7,23	Ceftazidime + Avibactam	Death 11/30/16

Table 1: Demographic, clinical characteristics and outcome of bloodstream infection caused by *K. pneumoniae* and *S. marscencens* co-harboring KPC and NDM



Taniela Bes has her expertise in basic and epidemiological research, she has been working with aptamers technology against MDR gram-negative rods. She was graduated from Medical School in December 2012 and completed her Infectious Diseases medical residence teenier in 2018. During her training she worked as volunteer in the microbiology research laboratory, focus on MRSA and MDR gram-negative, as well as bioinformatic techniques. Currently she is involved in a PhD project focus on Antibiotics resistance using aptamers. Beside the research carrier, she has a strong background with medical science, she has been working with clinical patients has been 7 years, since 2012. Due her clinical experience, she has the capacity to focus the research findings on the clinical necessities.

Email: taniela.bes@usp.br

- Full Name: Taniela Marli Bes
- Personal Email: tanielabes@gmail.com
- Mobile Number: +5519996011254
- Linked In: https://www.linkedin.com/in/taniela-bes-79359b176/
- Facebook: https://www.facebook.com/tanielabes
- Session Name/ number:
- Category: Oral presentation
- Date of Birth: 02/24/1985
- Postal Address:
  - 470, Dr Eneas Carvalho de Aguiar
  - Cerqueira Cesar, São Paulo/SP - Brasil
  - Zip: 05403000