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The search for inhibitors of Gram-negative bacteria's metallo-β-lactamase in a model systemAnna Afinogenova¹, Gennady E Afinogenov¹ and Tatiana M Voroshilova²¹St. Petersburg Pasteur Institute, Russia²The Nikiforov Russian Center of Emergency and Radiation Medicine, Russia

Aim: The study aims to assess the possibility of clodronic acid to inhibit the standard reagent of *P. aeruginosa* Metallo-β-Lactamase (MβL)/Sigma, USA/ and to prevent the acquisition of resistance by Gram-negative bacteria that were previously susceptible to carbapenems.

Method: The final load of sensitive to Meropenem (MIC 2 µg/ml) reference strains of *P. aeruginosa* ATCC 27853, *A. baumannii* ATCC BAA-747, *K. pneumoniae* ATCC 70603 was 5×10⁴ CFU in 200 µl, exposure 24 hours. Checkerboard array was used to determine the enzyme activity against Meropenem (MIC 2-512 µg/ml) as well as to evaluate the possibility of clodronic acid sub-bactericidal doses to inhibit the standard reagent of *P. aeruginosa* MβL and to prevent the acquisition of resistance to carbapenems by previously sensitive strains. Suppression of the MβL by clodronic acid and as a result, the lack of growth of the test strains were confirmed in microcells, as well as on the ELx800 reader (Bio-Tek Instruments Inc., USA).

Result: A dose-dependent effect of acquiring resistance to Meropenem in Gram-negative bacteria (increasing MIC) in the presence of various amounts of the standard reagent of the enzyme MβL at an exposure of 24 hours was revealed. At the same time, *P. aeruginosa* MβL reagent leads to the emergence of resistance in other types of Gram-negative microorganisms previously sensitive to carbapenems. Sub-bactericidal doses of clodronic acid do not affect the growth of intact sensitive test strains, but at the same time its ½ MIC and ¼ MIC completely inhibit the activity of the standard *P. aeruginosa* MβL reagent and prevent the acquisition of resistance of previously sensitive to carbapenems Gram-negative bacteria.

Conclusion: Using this method will simplify the search for perspective inhibitors of MβL.

Biography

Anna Afinogenova is a Pharmacist, Microbiologist and the Doctor of Biological Science since 2011, specialized in Clinical Microbiology. She is the Head of Laboratory Centre of Saint Petersburg Pasteur Institute and Professor of Saint Petersburg State University. She has published more than 30 papers in profile journals and has 17 patents to her credit. She is the Member of European Wound Management Association since 2010.

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