ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

SHORT COMMUNICATION

Zinc and Meropenem Induced Expression of Cryptic Metallo Beta Lactamase In *Pseudomonas Aeruginosa*

Debasrita Chakraborty, Saikat Basu, Moutusi Saha, Satadal Das

Department of Microbiology and Serology, Peerless Hospital and B. K. Roy Research Centre, 360 Panchasayar, Kolkata- 700094, India.

The emergence of metallo beta lactamase (MBL) in *Pseudomonas aeruginosa* is becoming a threat in treatment procedure as these bacteria posses resistance genes against new generation cephalosporins and carbapenems [1]. MBL use zinc ions at their active sites to catalyze the hydrolysis of all classes of beta lactam antibiotics, including carbapenems . As no known inhibitor is there for MBLs, it is very important to understand their mechanism of action and hence we gave emphasis on the role of di-nuclear Zn (II) complexes (Zinc sulfate) in the hydrolysis of carbapenem antibiotic (Meropenem).

According to CLSI guideline, MIC breakpoint for meropenem susceptibility is 4mg/L and strains that grow at $\geq$16 mg/L are considered as meropenem resistant or MBL producing. Our experiment was carried out with some MBL producing and MBL non-producing *Pseudomona aeruginosa* (Screened by E-test, DDST and combined disc test), grown in Mueller Hinton broth, equivalent to 0.5 McFarland standard. Changes in absorbance of meropenem solution in spectrophotometric assay with MBL producing and MBL non producing bacteria were performed in presence of different concentrations of zinc sulphate (1- 1000 µM) [2] with fixed very high concentration of meropenem (0.1 mg/mL), in 96 microtitre well plate. In each row of wells in the left to right direction zinc sulfate had been diluted serially and after addition of meropenem and different bacteria OD values were measured at 620 nm in Micronaut multiskan system (Germany) after 24 hours of incubation at 35^{o}C.

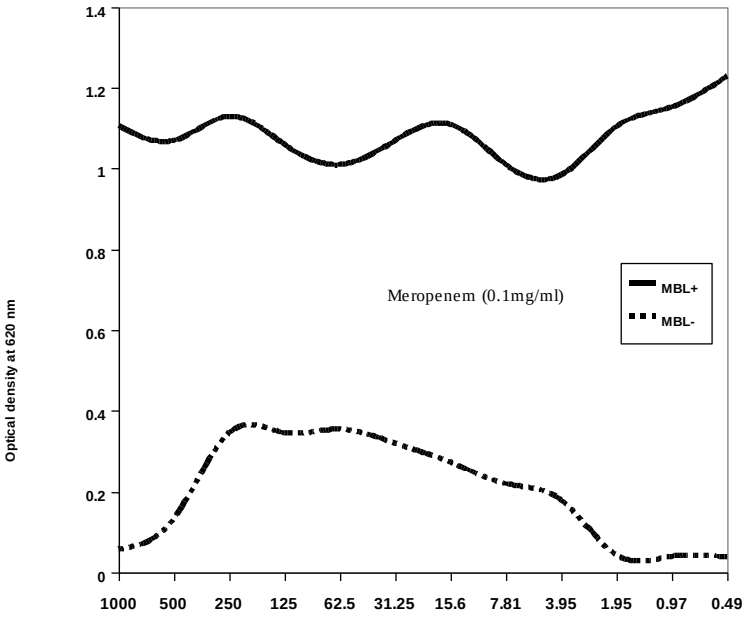
With this selection procedure under very high concentration of meropenem, only 25% of MBL producing *P. aeruginosa* could grow while the most interesting finding was that 30% of MBL negative bacteria could also grow particularly in between 2- 500 µM concentrations of zinc sulfate with an optimum growth at 62.5 µM concentration of zinc sulfate (Graph). However a maximum of 30% growth could be achieved in MBL non-producing bacteria in comparison to the growths which were obtained in MBL producing bacteria.

Corresponding author

ISSN: 0975-8585

P. aeruginosa is known to cause a variety of infections, is now emerging as MBL producer [3] and is spreading the gene in a horizontal way to members of Enterobacteriaceae. The overuse of carbapenems has extended the incidence of MBL production in community as well. In this study the most interesting observation was that known MBL negative *P. aeruginosa* became MBL producing by activating the suppressed or cryptic resistance gene that could express the MBL gene under selection pressure of 2-500 µM concentration of zinc sulfate and very high concentration (0.1 mg/mL) of meropenem. Thus we should monitor these group of bacteria because they may transfer this resistance gene to other microorganisms. This fact needs to caution our clinicians and draw their attention towards rational use of carbapenems [4].

Graph: Average growth patterns of some MBL positive and MBL negative Pseudomonas aeruginosa under selection pressure of Zn and Meropenem



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