Mechanisms of Imipenem Resistance in Acinetobacter baumannii Isolate from Taiwan

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ABSTRACT

Acinetobacter baumannii is a common human bacterium which has recently emerged as a primary nosocomial pathogen in hospital outbreaks. A. baumannii clinical isolates were routinely collected from Chang Gung Children ’ s Hospital during 2004 and 2006. Among them, 33 isolates were tested as multidrug resistant. In this research, these multidrug-resistant A. baumannii isolates were further investigated by PCR, metallo- β -lactamase test, one-dimensional and two-dimensional electrophoresis, Southern blotting and E-test analysis were also employed in order to determine the underlying resistance mechanisms. Sixteen strains analyzed by E-test showed imipenem-resistant, in which 7 isolates with MIC>32 μ g/ml all carried resistant gene blaIMP-1. The rest of 9 isolates with MIC between 8~32 μ g/ml exhibited inducible resistance to imipenem due to those inner clear zones scattered with satellite colonies. Through PCR gene confirming tests of these nine isolates, the results indicated that none of the following resistance genes bla VIM, blaOXA23 or blaOXA24 was present. Metallo- β -lactamase tests turned out negative either. When cultures of three imipenem-inducible resistant strains were supplemented with different concentrations of imipenem (0, 16 and 32 μ g/ml), higher production of AmpC was observed at higher concentration of imipenem supplement via MALDI-TOF MS analysis. Through sequence analysis, this novel blaAmpC belongs to blaADC-1 group, named blaADC-29. Up to 85% of imipenem-inducible resistant isolates do carry ISAba1, which is located upstream of blaADC-29, indicating the strong correlation between ISAba1 and overexpression of blaADC-29. Furthermore, Southern blotting analysis showed blaIMP-1was carried on a large communicable plasmid while blaAmpC located on the chromosome. In addition, real-time quantitative PCR analysis revealed that the expression of blaADC-29 and ompA were positively correlated with the imipenem supplement, and the similar results were also observed in MALDI-TOF MS analysis. However, the expression of efflux pump-related adeB remained constant. These studies indicated that the co-existance of blaADC-29 and its upstream gene ISAba1 could play important roles in inducible imipenem.resistance in A. baumannii. Therefore, overusing imipenem clinically might provoke inducible-resistance in A. baumannii. According to the surveillance of Chang Gung Memorial Hospital, the imipenem treatment duration of bacteremia against imiperem-susceptible (SS) and imiperem-nonsusceptible (SR and RR) A. baumannii were shown significantly statistical variations.

Keywords : multidrug-resistant Acinetobacter baumannii (MDRAB) ; β -lactamase ; inducible resistance ; imipenem

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