Comparison of In vitro Bactericidal Activity between Carbapenem and Combination of Beta-lactam/beta-lactamase Inhibitor against ESBL-producing Organism

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Abstract

Carbapenems are the treatment of choice for ESBL infection. However, widespread use of this agent subsequently contributes to emergence of carbapenem resistant organism. Thus, an alternative is needed to limit carbapenem usage particularly in non-bacteraemic cases such as urinary tract infection. This study was performed to evaluate the in vitro bactericidal activity of ertapenem, piperacillin/tazobactam, and ceftolozane/tazobactam against ESBL-producing organism by time-kill assays. Strains of ESBL producing organism isolated from urine sample were randomly selected. ESBL were confirm phenotypically by disc diffusion and further confirmed for detection of ESBL gene by conventional PCR. Minimum inhibitory concentration (MIC) was determined by broth microdilution method. Time kill assay were performed in triplicate for ertapenem (1 µg/ml), piperacillin/tazobactam (32 µg/ml), and ceftolozane/tazobactam (4 µg/ml) by using standard inoculum. Two strains of ESBL producing organism which expressed ESBL gene were selected. *Klebsiella pneumoniae* strains which expressed SHV and TEM genes has MIC of ertapenem 0.125 µg/ml (sensitive), piperacillin/tazobactam 16 µg/ml (sensitive) and ceftolozane/tazobactam 8 µg/ml (resistant). *Escherichia coli* strain which expressed TEM gene only has MIC of ertapenem 0.125 µg/ml (sensitive), piperacillin/tazobactam 8 µg/ml (sensitive) and ceftolozane/tazobactam 4 µg/ml (intermediate). In time kill study, ertapenem exhibited rapid and sustained bactericidal effect against both strains. Piperacillin/tazobactam was initially bactericidal against both strains, however regrowth was demonstrated after 8 hours. Ceftolozane/tazobactam was initially bactericidal against *E. coli* strain, however regrowth occurred after 4 hours. No activity was observed against *K. pneumoniae* strain. Carbapenem exhibited rapid and maintain bactericidal killing over 24 hours and hence, is superior to combination of beta-lactam/beta-lactamase inhibitor for treatment of ESBL infection.

Keywords: ESBL, time kill assay, carbapenem, beta-lactam/beta-lactamase inhibitor

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