O2 COMPARATIVE IN-VITRO STUDY OF KILLING ACTIVITIES AND MORPHOLOGICAL CHANGES OF CEFPIROME, CEFEPIME, IMIPENEM AND MEROPENEM ALONE AND IN COMBINATION AGAINST GRAM NEGATIVE BACTERIA

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ABSTRACT

The β-lactam antibiotics are generally regarded as the bactericidal agents. The mechanism of action is inhibiting of the enzymes in the late stage of peptidoglycan synthesis namely Penicillin binding proteins (PBPs). The inhibitions of PBPs cause morphological changes leads to bacteriolysis and cell death. The relationship among PBPs, morphological changes and bactericidal activities by the β-lactam antibiotics has been evaluated in this research. Cefpirome, Cefepime, Imipenem and Meropenem were tested against susceptible strain of *P. aeruginosa*, *E. cloacae* and *E. coli* by time kill method. Cefpirome and Cefepime have demonstrated bactericidal properties in *E. coli* above concentration 4MIC, whereas *E. cloacae* have shown regrowth to both drugs concentration range from ¼MIC-128MIC after 24 hours of exposure. For morphological changes, both drugs have established filamentous cells in both Enterobacteriaceae, which related to PBP3 binding as primary target of cephalosporins. Interestingly, Cefepime above 32MIC has established filamentous with bulge cells that correlated to PBP2 and 3 binding with an increase of bactericidal property. Imipenem and Meropenem have manifested bactericidal properties in *E. coli* above concentration 1MIC, whereas *P. aeruginosa* required concentration up to 4MIC for this property after 24 hours of exposure. For morphological changes, both drugs have established ovoid cells that related to PBP2 binding as primary target of carbapenems while Meropenem required concentration above 4MIC to established the filamentous with bulge cells that correlated to PBP2 and 3 binding in *E. coli*. For synergy testing, the combination between Cefpirome (PBP3 attacker) and Imipenem (PBP2 attacker) at 1/4MIC and 2 MIC was done in *E. coli*. The synergism has been detected in 1/4MIC combination, whereas the regrowth was observed in both combinations after 24 hours of exposure. Conclusion, drugs/concentrations that attack to many types of essential PBPs can increase bactericidal properties and morphological changes of the susceptible bacteria, which may be the useful data to eradicate bacteria for clinical application.

Key words : PBPs, bactericidal activity, morphological change and gram negative bacteria