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Antimicrobials: Mechanisms of action and resistance

Carbapenemase-producing *Klebsiella pneumoniae* isolates: a three-year study of mechanisms of carbapenem resistance

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Objectives: Dissemination of carbapenemase-producing *Klebsiella pneumoniae* clinical isolates is a major public health concern. The aim of the present study was to determine the mechanisms of carbapenem resistance among multi-drug resistant Klebsiella pneumoniae in a tertiary hospital

Methods: During a 3 year period (01/11/10-31/10/13), 733 carbapenem resistant K. pneumoniae isolates were tested for the detection of KPC-carbapenemase and metallo beta –lactamase (MBL) production. K. pneumoniae clinical isolates were collected mainly from blood (188), urine (149), pus (246), catheters (39) and bronchial secretions (98) cultures of patients hospitalized in different wards of our hospital (332 out of 733 isolates recovered from ICU patients' samples). All isolates had meropenem and/or imipenem MICs > 1mg/ml. The identification and susceptibility testing was performed via the Vitek II automated system (Biomerieux, France), and when necessary susceptibility results were confirmed with the use of E-test strips (AB Biodisc, Sweden) according to CLSI guidelines. Metallo-β-lactamase (MBL) production was evaluated using disks containing meropenem with and without EDTA, and KPC-production with boronic acid combined-disk tests, using disks containing meropenem with and without boronic acid

Results: All *K. pneumoniae* isolates were carbapenem resistant, being resistant as well to other agents such as beta-lactams, aminoglycosides, fluoroquinolones and trimethoprim/sulfamethoxazole. The majority of the isolates were susceptible to gentamicin (23.2 % of isolates were found non susceptible to gentamicin). As for tigecycline and colistin, 36.7% isolates were found non susceptible to tigecycline and 38.2% to colistin. Of 733 isolates, 24.8 % were MBL producers, 73.5 % were KPC producers and the rest 1.7 % were producing both MBL and KPC. Correlating the three year periods (first year period from 01/11/10 to 31/10/11, second year period from 01/11/11 to 31/10/12 and third year period from 01/11/12 to 31/10/13), a switch was observed in the presence of MBL producing strains. The reduction from 23 % in the first period to 18% in the second, was followed by an increase of 33% in the third period, while the percentage of KPC producing strains for those periods was 77%, 82% and 62% respectively. In the third period strains producing both MBL and KPC were observed for the first time (5%)

Conclusion: The worldwide spread of multidrug resistant K. pneumoniae isolates, that produce different carbapenemases, pose a most serious therapeutic problem. Carbepenem resistant isolates, even those with low carbapenem MICs, should be routinely tested for the presence of the two predominant types of carbapenemases, and timely identify other emerging types