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Abstract (publication only)

Distribution and molecular characterisation of beta-lactamases in multidrug-resistant Enterobacteriaceae from the TEST study (2005-2011)

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Objectives: The Tigecycline Evaluation Surveillance Trial (TEST) has been monitoring antibiotic susceptibilities globally since 2005. Increasing rates of resistance to many antimicrobials due to extended-spectrum beta-lactamase (ESBL) production and other enzymatic mechanisms has necessitated the need to look for and evaluate these resistance factors. In this study we present the characterization of beta;-lactamases in a selection of multi-drug resistant isolates of Enterobacteriaceae obtained from the TEST during 2005-2011. Methods: 1980 Enterobacteriacae resistant to three or more antimicrobials were selected from isolates collected through the TEST global program from 2005 to 2011. From these, 225 E. coli, 292 K. pneumoniae and 14 K. oxytoca were positive for ESBL production by the CLSI disk diffusion confirmatory test and were selected for molecular ESBL characterization. Detection of blaSHV, blaTEM, blaCTX-M, blaNDM and blaKPC genes was done by the Check-Points technology and detection of blaIMP, blaVIM, and blaOXA-48 genes by multiplex-PCR. Specific variants were determined by PCR and sequencing. Results: 519 E. coli, K. pneumoniae and K. oxytoca were determined to be ESBL-positive. 398 produced CTX-M, 140 SHV and 17 TEM enzymes. Fifteen isolates produced AmpC enzymes (9 CMY-2, 4 DHA, 1 FOX, 1 CMY-1/MOX) and 49 produced carbapenemases (46 KPCs, 1 NDM, 1 VIM and 1 OXA-48-like). Among the ESBL-positive isolates, the most common variants found in this study, were blaCTX-M-15 (n=289, 56%), and blaSHV-12 (n=87, 17%). Among the carbapenemase-positive isolates, the most common variants were KPC-3 (n=29, 63%) and KPC-2 (n=17, 31%). Of the 519 ESBL-positive isolates tested, 488 (94%) were susceptible to tigecycline, and among the carbapenemase-positive isolates, 47 (96%) were susceptible to tigecycline (Tygacil®, 2010. Tigecycline FDA prescribing information). Conclusion: This evaluation of resistance mechanisms highlights the importance of surveillance programs using molecular techniques in providing insight into characteristics and global distribution of beta-lactamases among multi-drug resistant isolates. Tigecycline has maintained significant in vitro activity against these difficult to treat organisms.