TITLE: CEFTAZIDIM-AVIBACTAM ACTIVITY AGAINST CLINICAL ISOLATES OF MEROPENEM AND POLYMYXIN B-RESISTANT ENTEROBACTERALES IN A TERTIARY CARE HOSPITAL IN SOUTHERN BRAZIL

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ABSTRACT: The high rates of carbapenem-resistant Enterobacterales (CRE) infections are a public health problem. In a tertiary care hospital in Southern Brazil, CRE leads the rates of multidrug-resistant germs and meropenem is the most used antimicrobial. Ceftazidime/Avibactam (CzA) is a combination of a third-generation cephalosporin and a new beta-lactamases inhibitor approved by the FDA in 2015, acting against Ambler class A, C and D beta-lactamases-producing bacteria. Therefore, the detection of carbapenemase and the epidemiological profile of the institution are important for this therapeutic choice. The study aimed to evaluate the CzA activity and the agreement between the results of the phenotypic and genotypic detection of carbapenemases in carbapenem and polymyxin B resistant Enterobacterales (CREPR). Clinical isolates of CREPR from patients treated in a tertiary care hospital in Southern Brazil were collected from January to April 2022. The meropenem and CzA susceptibilities were determined by disk diffusion method and polymyxin B susceptibility by broth microdilution, both according BrCAST (EUCAST) 2022. The agreement of the phenotypic detections results by the inactivation of the carbapenem method and of immunochromatography NG TEST CARBA 5® (NG Biotech) were compared with the genotypic detection results for the KPC, OXA-48, VIM, IMP, NDM and GES resistance genes. A total of 71 CREPR were isolated and the susceptibility to CzA was determined in 64 samples. The CzA resistance rate was 32% (21/64). Among resistant isolates, 72% (15/21) were NDM producers, 10% (2/21) NDM and KPC co-producers, 10% (2/21) KPC producers and 6% (1/21) Oxa-48 producers according to genotypic results. CzA showed activity against 68% (43/64) of the tested isolates, of which 93% (40/43) were KPC producers, 2% (1/43) NDM and KPC co-producers, and 2% (1/43) were not carbapenemase producers. None of the CzA-sensitive isolates produced NDM. The agreement between the phenotypic and genotypic methods was observed in 91% (63/69) of the isolates. Of the isolates in which there was disagreement (9%, 6/69), 2 were attributed to a limitation of the phenotypic method of carbapenem inactivation, which did not detect co-producers of NDM and KPC. The evaluation of the activity of CzA and the detection of the type of carbapenemase involved in the resistance mechanism is importance, since we evidenced a high prevalence of isolates resistant to CzA.

Keywords: Ceftazidime/Avibactam resistance, carbapenem resistance, polymyxin B resistance, Enterobacterales, phenotypic and genotypic carbapenemase methods.

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