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Abstract

In Vitro Activity of Ceftazidime-Avibactam against Gram—Negative Bacteria Recovered from Blood and Fecal Samples of Patients after Hematopoietic Stem-Cell Transplantation †

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Patients receiving hematopoietic stem-cell transplantation (HSCT) are prone to develop invasive infections due to disease and transplantation-related immunosuppression. The main causative agents often originate from the digestive tract and are multidrug-resistant. Our aim was to investigate the in vitro activity of ceftazidime-avibactam (CZA) against extended spectrum beta-lactamase (ESBL)-producing and carbapenem-resistant (CR) Gram-negative bacteria recovered from blood and fecal samples of patients following HSCT, hospitalized in University Hospital "Saint Marina"—Varna, during 2019–2021.

A total of 48 isolates (*E. coli*, n = 20; *Enterobacter cloacae*, n = 9; *Klebsiella pneumoniae*, n = 6; *Serratia marcescens*, n = 1; *Acinetobacter baumannii*, n = 2; *Pseudomonas putida*, n = 4; *Pseudomonas aeruginosa*, n = 4; *Pseudomonas mendocina*, n = 1; *Pseudomonas composti*, n = 1) were studied. MALDI Biotyper Sirius (Bruker, Bremen, Germany) and the automated Phoenix system (BD, Franklin Lakes, NJ, USA) were used for species identification and susceptibility testing. Twenty-four isolates, included in this study, were resistant to third- and fourth-generation cephalosporins and, therefore, were identified as ESBL producers (*E. coli*, n = 12; *E. cloacae*, n = 7; *K. pneumoniae*, n = 4; *S. marcescens*, n = 1). A multiplex polymerase chain reaction was used for gene detection, associated with carbapenem resistance. In the studied group, eleven isolates (23%) were CR (*E. cloacae*, n = 1; *Pseudomonas* spp., n = 8; *A. baumannii*, n = 2). All 24 ESBL-producing isolates were CZA-susceptible. In the group of CR isolates, only 1 *P. aeruginosa* was susceptible to CZA, while 10 CR isolates were resistant. Genes associated with class B and class D carbapenemases were detected by PCR (bla_{VIM} and $bla_{OXA\text{-}like}$).

In conclusion, in our study, all ESBL producers were susceptible to CZA, while 91% of the CR isolates (all class B and class D carbapenemase producers) were resistant. CZA is a drug combination that is highly active against ESBL producers, but its spectrum of activity is limited against carbapenemase producers. Therefore, other novel antimicrobial agents are urgently needed.

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