

coli producing KPC. Combinations were performed using the checkerboard method with the following antibacterials: polymyxin B (PMB), meropenem (MEM), fosfomicin (FOS), and tigecycline (TGC).

Results: The minimum inhibitory concentrations (MICs) for PMB among isolates varied between 8 and 1024 $\mu\text{g/mL}$. The PMB+TGC combination was the most effective, showing synergism in 66% (4/6) of isolates, three PM-RA and one PM-RI. PMB+FOS showed synergistic activity in 50% (3/6) of isolates, two PM-RI and one PM-RA. MEM+FOS showed synergism in 50% (3/6) of isolates, two KPC producers and one NDM producer. For MEM+TGC, synergism was obtained in 33% (2/6) of isolates, both NDM producers. FOS+TGC showed synergism in 33% (2/6) of isolates, one KPC and one NDM producer. There was no difference in synergism between isolates with intrinsic or acquired resistance to PMB. Despite being one of the most widely used combinations, MEM+PMB showed synergism in only one isolate (PM-RA, KPC producer). No antagonism was observed in any combination, and even when synergism was absent, there was a decrease in the MIC, allowing the recovery of antibacterial activity.

Conclusion: The results show that the association between antibacterials can be an alternative for effective treatment against E-KPC/NDM isolates resistant to PMB, highlighting the PMB+TGC combination. Interestingly, the MEM+PMB combination, although widely used, showed limited synergism, suggesting the importance of considering other therapeutic options to optimize the treatment of infections caused by multidrug-resistant bacteria.

Keywords: Pharmacological synergism, Multidrug-resistant *Enterobacterales*, Carbapenems, Polymyxin B.

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COMPARISON BETWEEN BROTH MICRODILUTION AND AN INNOVATIVE DISK DIFFUSION METHOD SUPPLEMENTED WITH AZTREONAM SOLUTION FOR DETECTING SYNERGISM WITH CEFTAZIDIME/AVIBACTAM IN ENTEROBACTERALES PRODUCING NDM OR NDM AND KPC

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Introduction/Objectives: Since the aztreonam/avibactam combination has not yet been approved for use in Brazil, the treatment of infections caused by *Enterobacterales* producing New Delhi metallo-beta-lactamase (NDM), either alone or in co-production with the serine-carbapenemase *Klebsiella pneumoniae* carbapenemase (KPC), is empirically performed using ceftazidime/avibactam (CZA) combined with aztreonam (ATM). The objective of this study was to compare the performance of an innovative method (IM) with the gold standard method for the *in vitro* detection of synergism between ATM and CZA in *Enterobacterales* producing NDM or NDM and KPC.

Methods: Sixty *Enterobacterales* isolates producing NDM or NDM and KPC were selected from a bacterial isolate bank with reduced susceptibility to meropenem. Half were NDM producers only, and the other half were coproducers of NDM and KPC. The type of carbapenemase was determined by high-resolution melting PCR (HRM-qPCR) and/or NG-Test[®] Carba 5 (NG Biotech[®], France). For isolates producing NDM as the only carbapenemase, a phenotypic test for Extended-Spectrum Beta-Lactamase (ESBL) was performed, which was positive in 17 isolates. Synergism between CZA and ATM was detected by broth microdilution (gold standard), defined as a reduction of at least two concentrations compared to each agent tested alone. The IM consists of inoculating a solid culture medium with the bacterial suspension, followed by placing a CZA disk and adding 10 μL of ATM solution onto it. A synergistic effect is observed when the inhibition zone increases by more than 5 mm compared with each disk tested alone.

Results: Synergism between CZA and ATM was detected by both methods in all coproducing NDM and KPC isolates and in NDM producers that also produced ESBL (78%). Among the isolates producing only NDM, seven showed synergism, four did not, and two could not be evaluated due to limitations of the gold standard method. The IM detected synergism in only one isolate producing NDM alone; the others could not be evaluated due to technical limitations.

Conclusion: The IM showed 100% concordance with the gold standard method, demonstrating its feasibility for incorporation into routine laboratory practice, offering lower cost and easier execution.

Keywords: Ceftazidime-avibactam, Aztreonam, Synergism.

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STRUCTURAL INSIGHT INTO THE BINDING OF ACETOHYDROXAMIC ACID TO CONSERVED RESIDUES OF APO AND HOLO UREASE IN CLINICAL ISOLATES OF KLEBSIELLA SPP.

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