TITLE: EVALUATION in vitro OF ANTIBIOTIC THERAPY AGAINST CLINICAL ISOLATES OF Klebsiella pneumoniae CARRIERS OF blaNDM, blaKPC, aac(6)-Ib and aph(3)-VI GENE AND POLYMYXIN-B-RESISTANT


ABSTRACT:
Multidrug-resistant Klebsiella pneumoniae and carriers of β-lactam antibiotics resistance genes, such as blaNDM and blaKPC, cause healthcare-associated infections worldwide, and are highly relevant due to therapeutic limitations. In the search for effective treatment options, the use of combination therapy based mainly on the use of polymyxins in combination with aminoglycosides or carbapenems has been indicated by the Agência Nacional de Vigilância Sanitária (Anvisa) in Brazil. Therefore, the aim of this study was to evaluate in vitro the polymyxin-B (PB) activity combined with meropenem (MEM), amikacin (AMK) and gentamicin (GEN) in two clinical isolates of K. pneumoniae carriers of blaNDM, blaKPC, aac(6)-Ib and aph(3)-VI genes from patients at a hospital in Recife-PE, Brazil. The combinations of antimicrobial (PB/MEM, PB/GEN and PB/AMK) were tested in two clinical isolates by the checkerboard. The variation of antimicrobial concentrations was determined from the Minimum Inhibitory Concentration (MIC) in all assays. MIC was defined as the lowest concentration of combinations, in which no visible growth was observed and the Fractional Inhibitory Concentration (FIC) was determined. The FIC values ≤ 0.5, 0.5 - 4 and ≥ 4 were considered synergistic, indifferent and antagonistic, respectively. Two isolates showed resistance to gentamicin, meropenem and polymyxin-B, and sensitivity to amikacin. Synergisms of PB/MEM, PB/GEN and PB/AMK were observed in both clinical isolates by the checkerboard. The combination of polymyxin-B with amikacin was more efficient. Accordingly, the use of these combinations may contribute to the therapy of patients with infections caused by multidrug-resistant K. pneumoniae, particularly carriers of blaNDM and blaKPC genes.

Keywords: NDM, checkerboard, synergism, Klebsiella pneumoniae

Development Agency: Programa de Pesquisa para o SUS (PPSUS) – Ministério da Saúde – Fundação de Amparo à Ciência e Tecnologia do Estado de Pernambuco (FACEPE).