in small and rural hospitals, compromises patient safety and contributes to the spread of resistant bacteria. These findings highlight the urgent need for targeted interventions and public policies to strengthen health infrastructure.

Conclusion: The study reveals significant challenges in implementing ASPs, particularly in hospitals outside major urban centers. Overcoming these barriers is crucial to strengthening the healthcare system as a whole, especially in the current global context of a "One Health" approach.

Keywords: Antimicrobial Stewardship, Antimicrobials, Resistance, Stewardship, Brazil.

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FIVE HOURS FOR THE DETECTION OF ANTIBACTERIAL SYNERGISM AGAINST *KLEBSIELLA PNEUMONIAE* CO-PRODUCING KPC AND NDM: PROPOSAL OF A RAPID METHOD

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Introduction/Objective: Infections caused by *Klebsiella pneumoniae* producing KPC and NDM simultaneously (Kp-KPC +NDM) are associated with high mortality due to the extreme difficulty of treatment. Combinations of antibacterial agents can be synergistic, indifferent, or antagonistic; therefore, the rapid detection of synergism is extremely important. This study proposes an easy and rapid methodology for detecting antibacterial synergism against Kp-KPC+NDM isolates.

Methods: Meropenem (MEM), polymyxin B (PMB), fosfomycin (FOS), and tigecycline (TGC) were used, either alone or in combination. Molecularly distinct isolates, identified by ERIC-PCR and co-producing KPC and NDM, were included. The disk elution method using resazurin was compared with the standard checkerboard method. For the disk elution method, commercial antimicrobial disks were added to Mueller-Hinton broth, reaching therapeutic peak and trough concentrations (according to BrCAST). After overnight elution, the therapeutic concentrations of each antibacterial, alone or in combination, were tested. After 4 hours of incubation at 37°C, 22 μL of resazurin were added, followed by 1 additional hour of incubation for reading. In parallel, the checkerboard method was performed. The new method was tested only for isolates with MICs higher than the therapeutic trough concentration (TC) of the drugs.

Results: Five Kp-KPC+NDM isolates with distinct molecular characteristics were selected. Synergism by the disk elution method could be evaluated in all isolates for the MEM+FOS combination, showing 80% concordance with the checkerboard method, and for FOS+TGC, showing 40% concordance. Since the interpretation parameters for Kp-KPC+NDM are complex, the lower concordance may be related to the difficulty of standardizing these agents. For the combinations PMB+MEM, PMB+FOS, PMB+TGC, and MEM+TGC, only one isolate could be evaluated for each combination due to MICs lower than the TC of PMB, all showing 100% concordance with the checkerboard method.

Conclusion: The disk elution test proved to be effective for detecting synergism among antibacterial combinations that are usually employed for treating infections caused by Kp-KPC+NDM, providing results in only five hours. This method offers faster and clinically applicable results, especially when tested at therapeutic concentrations, and may contribute to successful treatment of severe infections caused by this important pathogen.

Keywords: *Klebsiella pneumoniae*, Carbapenem resistance, Pharmacological synergism, Rapid methods.

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IN VITRO COMBINATION OF SIX ANTIBACTERIAL ASSOCIATIONS AGAINST ENTEROBACTERALES ISOLATES PRODUCING KPC OR NDM WITH INTRINSIC OR ACQUIRED RESISTANCE TO POLYMYXIN B

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Introduction/Objectives: Therapeutic alternatives for infections caused by Gram-negative bacilli of the order *Enterobacterales* producing KPC or NDM (E-KPC/NDM) and resistant to polymyxins are virtually nonexistent; therefore, combining antibacterial agents emerges as a promising strategy. This study aimed to evaluate the *in vitro* activity of six antimicrobial combinations against E-KPC/NDM isolates with intrinsic or acquired resistance to polymyxins (PM-RI and PM-RA).

Methods: Three E-KPC/NDM isolates intrinsically resistant to polymyxins were tested: *Proteus vulgaris*, *Providencia stuartii*, and *Morganella morganii*, all NDM producers; and three isolates with acquired resistance: two *Klebsiella pneumoniae* (one producing KPC and the other NDM) and one *Escherichia*