development of strategies for new compounds acting on devices and surfaces remains limited.

Methods: The study was conducted with clinical isolates from a hospital in southern Brazil. The ability to form microbial biofilms was determined as proposed by Halicki et al. (2019). Subsequently, in polystyrene plates, 10^6 CFU/mL of each isolate was exposed to three concentrations of EDTA (12, 0.6, and 0.3 mM). After incubation for 24 hours at 37°C, the inhibitory capacity of biofilm formation was evaluated using 0.4% crystal violet as an indicator.

Results: Half of the isolates (5/10) were classified as moderate biofilm formers. Regarding the biofilm inhibition potential of EDTA, which has a high capacity for metal ion chelation, it was observed that the mean inhibition was 90.8% at a concentration of 12 mM, 82.2% at 0.6 mM, and 22% at 0.3 mM.

Conclusion: The ability of the chelating agent EDTA to interact with cations that maintain the structural stability of the bacterial outer membrane may make it more susceptible to the entry of antimicrobial agents and to cell lysis, thereby inhibiting the initial stages of biofilm formation. In this context, EDTA demonstrates potential to inhibit this important virulence mechanism of *A. baumannii*, highlighting the relevance of further studies exploring its mechanism of action and potential as a biocidal agent.

Keywords: Biocide, Chelating agents, Virulence, Infection.

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3

THE IMPORTANCE OF THE CLINICAL PHARMACIST IN MANAGING THE SAFE USE OF CEFTAZIDIME/AVIBACTAM AND THE IMPACT OF THE SMART-CAZ/AVI ALGORITHM

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Background: The treatment of infections caused by gram-negative bacteria has been associated with reports of resistance through different mechanisms of action. Therefore, CAZ/AVI should be reserved for multidrug-resistant infections, and rational use is essential to ensure safe antibiotic therapy and minimize adverse events. In this context, the clinical pharmacist plays a key role in the stewardship of CAZ/AVI, with a strategic role in promoting safety in prescribing and administration.

Aim: The aim of this study was to evaluate pharmaceutical interventions related to the use of CAZ/AVI and the impact of implementing a time-out tool on the frequency and acceptability of interventions.

Methods: Descriptive, quantitative, retrospective study conducted between January 2022 and December 2024 in a private hospital in Rio de Janeiro. Pharmaceutical interventions related to electronic prescription errors of CAZ/AVI were analyzed. These errors were classified as decision or writing errors, and further subdivided according to the PRAT tool. In August 2023, the SMART-CAZ/AVI algorithm was implemented to standardize prescription analysis, using the time-out as a monitoring tool (CAAE: 77108523.5.0000.5533).

Results: A total of 56 pharmaceutical interventions were performed, with 98.2% classified as decision errors and 1.8% as writing errors. Among decision errors, 74.5% were overdoses according to creatinine clearance (ClCr), 14.5% were underdoses according to ClCr, 9.1% were due to treatment duration requiring suspension, and 1.8% were due to inappropriate scheduling. In writing errors, 100% involved inappropriate units of measurement. Of the interventions performed, 70.2% were accepted by the medical team. After implementation of the SMART-CAZ/AVI tool, there was a 103.03% increase in the number of interventions and a 12.31% increase in the acceptance rate.

Conclusion: The role of the clinical pharmacist was essential for ensuring the safe use of CAZ/AVI, particularly in dose adjustment according to renal function. The SMART-CAZ/AVI tool contributed to increased detection of prescription errors and acceptance of interventions, highlighting the positive impact of standardization and systematization of pharmaceutical care, optimizing the stewardship of rational CAZ/AVI use, and promoting safe antibiotic therapy for patients.

Keywords: Ceftazidime/Avibactam, Antimicrobial stewardship, Clinical pharmacy service, Rational drug use.

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4

N-ACETYLCYSTEINE EXHIBITS POTENTIAL TO INHIBIT THE ACTIVE SITE OF UREASE FROM CLINICAL ISOLATES OF *KLEBSIELLA* SPP.

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Introduction: Urease is a nickel-dependent enzyme linked to the pathogenesis of several bacterial species[1], including carbapenemase-producing *Klebsiella*, which are often associated with hospital infections and multidrug resistance to antimicrobials. N-acetylcysteine (NAC), a clinically approved compound with mucolytic properties, has also shown *in vitro* inhibitory activity against *Klebsiella pneumoniae* urease[2] and other bacteria[3].

Objective: This study evaluated the binding of NAC to the immature (apoenzyme) and mature (holoenzyme) forms of urease from clinical isolates of *Klebsiella* spp.

Methods: Sequences were aligned, and structural models were generated with AlphaFold3 (apoenzyme) and AlphaFill (holoenzyme), with insertion of Ni^{2+} ions. Docking was performed with AutoDock Vina, and interactions were evaluated using the Protein–Ligand Interaction Profiler (PLIP). The obtained affinities were compared with those of urea as the reference natural substrate.

Results: Docking simulations showed strong binding for both forms: -4.8 kcal/mol for the apoenzyme and -5.2 kcal/mol for the holoenzyme. In both states, NAC interacted with a conserved set of residues. Shared interactions included hydrogen bonds with His219 and Asp360, and salt bridges with His134, His136, His219, and His272. In the apoenzyme, a specific hydrogen bond with His246 was observed, whereas in the holoenzyme, NAC formed additional hydrogen bonds with Ala363 and metal coordination with Ni^{2+} ions, absent in the apo form. Despite these subtle differences, the interaction core was highly conserved. Multiple sequence alignment of 438 urease sequences from *Klebsiella* clinical isolates confirmed that all interacting residues are highly conserved across the genus, indicating functional and structural robustness of the NAC binding interface.

Conclusion: These results indicate that NAC has the potential to interact with conserved urease residues, although full inhibition may depend on enzymatic maturation and the presence of metal ions. This binding potential supports the repositioning of NAC as an anti-virulence compound against infections caused by multidrug-resistant *Klebsiella* spp.

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ANALYSIS OF *IN VITRO* ACTIVITY OF CEFTAZIDIME-AVIBACTAM AGAINST CLINICAL ISOLATES OF *PSEUDOMONAS AERUGINOSA* COLLECTED FROM BRAZILIAN CENTERS FOR THE ATLAS SURVEILLANCE PROGRAM, 2018-2023

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Introduction: *Pseudomonas aeruginosa* is a pathogen that causes severe infections that are difficult to treat, as this bacterium can express multiple resistance mechanisms, in addition to its intrinsically limited susceptibility to many antibiotics. In this study, the *in vitro* activity of ceftazidime-avibactam was evaluated against clinical isolates of *P. aeruginosa*, both carbapenemase-producing and non-producing, collected as part of the global ATLAS surveillance program.

Methods: A total of 1239 non-duplicate *P. aeruginosa* isolates were evaluated, collected from different infection sites in hospitals across Brazil between 2018 and 2023. Susceptibility testing was performed using broth microdilution. The antimicrobial susceptibility profile was analyzed according to the breakpoints established by BrCAST (2025). The search for carbapenemase-encoding genes was performed by PCR followed by sequencing. Results Ceftazidime-avibactam (90.0% susceptible; MIC50/90, 2.0/8.0 mg/L) and colistin (99.8% susceptible; MIC50/90, 1.0/1.0 mg/L) were the antibiotics with the best *in vitro* activity. Approximately 70% of isolates tested for imipenem, cefepime, ceftazidime, and piperacillin-tazobactam were classified as susceptible with increased exposure, according to BrCAST criteria (range 68.7% to 74.5%). Susceptibility to ceftolozane-tazobactam was 84.3% (MIC50/90, 1.0/32.0 mg/L), but this antibiotic was evaluated in only 949/1239 isolates. Resistance gene screening was performed on 153 isolates, of which 17 (11%) were blaKPC-2 producers (4 also coproduced blaGES-1). The beta-lactamases found in 22 (18%) of the 123 ceftazidime-avibactam resistant *P. aeruginosa* isolates were: NDM-1 (n = 5), KPC-2 (n = 5), VIM-2 (n = 5), SPM-1 (n = 1), SPM-1+GES-1 (n = 1), IMP-16 (n = 1), IMP-56 (n = 1), KPC-2+GES-1 (n = 1), NDM-1+VEB-9 (n = 1), and NDM-1+VEB-14 (n = 1).

Conclusion: The results demonstrated that both ceftazidime-avibactam and ceftolozane-tazobactam maintain excellent *in vitro* activity (> 80%) against clinical isolates of *P. aeruginosa*. Although the presence of carbapenemases was relatively low among the isolates studied, ceftazidime-avibactam was 5 times more potent (MIC90) compared to ceftolozane-tazobactam, which may be partly explained by the presence of these beta-lactamases identified in the evaluated isolates.

Keywords: Bacterial resistance, Metallo-β-lactamases, Carbapenemases, KPC, Gram-negatives.

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ANALYSIS OF PHARMACEUTICAL INTERVENTIONS IN ANTIMICROBIALS AFTER IMPLEMENTATION OF A CLINICAL PHARMACIST SPECIALIZED IN THE ANTIMICROBIAL STEWARDSHIP PROGRAM

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Introduction: Inappropriate use of antimicrobials is a global challenge and contributes to increased microbial resistance and clinical complications. Effective management of these drugs is essential to optimize treatment and preserve the efficacy of antimicrobials. Antimicrobial Stewardship Programs (ASP) aim to ensure the appropriate use of antimicrobials (ATM) and achieve better clinical and microbiological outcomes, and several studies demonstrate the essential role of the clinical pharmacist in this context. Our objective was to evaluate pharmaceutical interventions in antimicrobials after the implementation of a clinical pharmacist dedicated to the ASP and specialized in infectious diseases.

Methods: A retrospective and quantitative analysis of pharmaceutical interventions in antimicrobials was conducted in the years 2023, 2024, and the first quarter of 2025. Data were collected monthly, recording the reasons for interventions, total number and monthly average of interventions, and the adherence rate of medical teams.