Introduction: *Klebsiella* is a clinically relevant bacterial genus associated with multidrug resistance. Urease is a virulence factor and a potential target for inhibitor-based interventions (Shafik et al., 2023). Acetohydroxamic acid (AHA), a reversible urease inhibitor, has been used clinically to treat infections caused by urease-positive bacteria such as *Proteus mirabilis*.

Objective: To evaluate the binding of AHA to the immature (apoenzyme) and mature (holoenzyme) forms of urease from clinical isolates of *Klebsiella* spp.

Methods: Structural models were generated using AlphaFold3 (apo) and AlphaFill (holo), the latter incorporating Ni^{2+} cofactors in the active site.

Results: Docking simulations revealed binding affinities of −4.2 kcal/mol for the apo form and −4.4 kcal/mol for the holo form. In both forms, AHA interacted with overlapping residue sets, including His219 and Ala363. The apoenzyme formed hydrogen bonds with His134, His136, His219, His246, Asp360, and Ala363. In the holoenzyme, AHA maintained interactions with His219 and Ala363 and additionally formed bonds with Ala167 and both nickel ions, highlighting the structural role of metal coordination in the mature form. Despite these differences, most interacting residues were shared between apo and holo, indicating that AHA targets a structurally conserved binding region. To assess conservation among clinical isolates, multiple sequence alignment was performed on 438 urease sequences from *Klebsiella* clinical strains. All residues involved in AHA interactions were highly conserved, reinforcing their functional importance and supporting the broad applicability of AHA-based inhibition within this genus. The binding affinities of AHA to the active site were similar to those for the natural substrate urea (−4.0 kcal/mol) and to redocking values obtained with the crystallized structure (1FWE, −4.3 kcal/mol), whose inhibition of the holoenzyme has been experimentally validated *in vitro*.

Conclusion: These findings demonstrate that AHA can bind to both maturation states of urease, involving conserved catalytic residues, with holo-specific enhancement through metal coordination.

Keywords: *Klebsiella* spp., Acetohydroxamic acid, Molecular docking, Virulence attenuation, Urease.

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CARBAPENEM CONSUMPTION AND USE PROFILE IMPACTED BY A CARBAPENEM-SPARING STRATEGY

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Introduction: The increasing use of carbapenems has been associated with the emergence of multidrug-resistant microorganisms, particularly *Enterobacterales* producing carbapenemases. This highlights the urgency of implementing carbapenem-sparing strategies to preserve antimicrobial effectiveness.

Objective: To evaluate carbapenem consumption and usage profile in inpatient units following the progressive adoption of the carbapenem-sparing strategy implemented by the antimicrobial stewardship team in 2022.

Methods: A retrospective analysis was conducted in a pediatric hospital in southern Brazil (CAAE: 68382723.9.0000.5580), assessing meropenem consumption in non-critical clinical wards (15 total), which represent 71% of hospital beds. Consumption was measured using the indicator days of therapy (DOT/1,000 patient-days) between 2022 and 2025, with 2025 data extrapolated from January–June to the full year. Additionally, medical records of all patients receiving meropenem from January to June 2025 were reviewed to assess prescribing patterns.

Results: Regarding the 5-year historical series of DOT/1000 patient-days, the results were 562 (2021), 384 (2022), 428 (2023), 334 (2024), and 148 (2025). This demonstrates that the carbapenem-sparing actions, such as case monitoring and daily discussions by the antimicrobial stewardship team were effective, as there were significant reductions in therapy days of 30% (between 2021 and 2022), 22% (from 2023 to 2024), and 55% (estimated from 2024 to 2025). The exception was between 2022 and 2023, when an 11% increase in DOT was observed, which is considered an acceptable variation. Regarding the carbapenem use profile, data from 65 patients corresponded to 95 treatment courses, with a median age of 4.5 years. Empirical use accounted for 61% of cases, while 39% were guided. The ward with the highest indication for meropenem was Infectious Diseases (23% of patients). The mean treatment duration was 6 days, and the main infection sites were bloodstream (32%), urinary tract (21%), and pulmonary (19%).

Conclusion: This use profile indicates the presence of patients with some degree of clinical severity in the wards, but with an acceptable treatment duration. Furthermore, the progressive decrease in DOT over the years demonstrates the effectiveness of the carbapenem-sparing strategy.

Keywords: Meropenem, Carbapenems, Antimicrobial stewardship.

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CHALLENGES FOR SWITCHING INTRAVENOUS TO ORAL ANTIMICROBIALS: PHYSICIAN INERTIA AS A BARRIER IN A BRAZILIAN HOSPITAL

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