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THE ACETOHYDROXAMIC ACID INHIBITOR INTERACTS WITH CRITICAL RESIDUES IN THE ACTIVE SITE OF UREASE FROM CLINICAL *ACINETOBACTER* SPP. ISOLATES

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Introduction: Acetohydroxamic acid (AHA) is a reversible urease inhibitor already used clinically in the treatment of urinary tract infections caused by urease-positive bacteria. Urease is a nickel-dependent enzyme that hydrolyzes urea into carbon dioxide and ammonia. In addition to providing carbon and energy for bacteria, the produced ammonia raises the pH and allows survival inside macrophage phagolysosomes or in acidic environments such as the stomach [1]. Although well studied in *Helicobacter pylori* and *Proteus mirabilis*, its role in *Acinetobacter* spp. remains poorly explored. In addition to gastric and urinary tract infections, AHA could also be associated with antibiotic therapy to attenuate virulence in other sites, especially in multidrug-resistant *A. baumannii* strains, if it is capable of inhibiting their urease.

Objective: To evaluate the binding of AHA to the urease of clinical *Acinetobacter* isolates using docking simulations in immature (apoenzyme) and mature (holoenzyme) forms.

Methods: The apo form of urease was modeled with AlphaFold3, and nickel ions were positioned at the active site of the holo form using AlphaFill. Molecular docking was performed with AutoDock Vina. The interactions between AHA and the protein were analyzed in PyMOL, and conservation of active site residues was assessed through multiple sequence alignment with MAFFT.

Results: AHA showed similar affinities for both forms (−4.3 kcal/mol for apo, −3.9 kcal/mol for holo). However, the holoenzyme presented a more canonical binding mode, with AHA coordinating both Ni^{2+} cofactors and interacting with the main catalytic residues His218, Asp359, and Ala362. These residues correspond to those observed in the crystallographic structure of *Klebsiella aerogenes* urease bound to AHA (PDB ID: 1FWE). In the apo form, AHA interacted with conserved residues Gly276 and Thr297, suggesting possible inhibition even before enzyme maturation. Multiple sequence alignment of urease from 233 clinical *Acinetobacter* spp. isolates revealed high conservation rates in all residues involved in AHA binding, supporting the functional relevance of the observed interactions.

Conclusion: Our findings support the use of AHA to inhibit urease activity in clinical *Acinetobacter* spp. isolates from different clinical sites, and further clinical studies are still needed.

Keywords: *Acinetobacter* spp., Urease, Acetohydroxamic acid, Docking, Virulence attenuation.

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THE WEIGHT OF INTUITION: COGNITIVE BIASES AND SUBOPTIMAL ANTIMICROBIAL PRESCRIPTION IN INTENSIVE CARE

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Introduction/Objective: Antimicrobial prescription is a complex decision often influenced by cognitive biases that may contribute to inappropriate use and increased bacterial resistance. In the intensive care environment, where decisions are rapid and high-impact, understanding these factors is essential. The objective of this study was to assess the prevalence of cognitive biases among physicians working in intensive care units and analyze their influence on decisional accuracy in standardized clinical scenarios.

Methods: An observational, cross-sectional study was conducted with 150 physicians from different specialties working in intensive care units. Data were collected via an anonymous online form using a non-validated instrument developed by the authors based on cognitive biases established in the literature. The questionnaire contained statements on a five-point Likert scale to assess nine cognitive biases and accuracy in two standardized clinical cases. A descriptive analysis of the data was performed.

Results: The results revealed a paradox between high subjective confidence and low objective performance. Descriptive analysis of bias prevalence ("strongly agree" or "partially agree" responses) showed that the most frequent were the IKEA effect (84.7%), hyperbolic discounting (78.7%), optimism bias (76.0%), and impact bias (71.3%). Other relevant biases included diagnostic momentum (64.0%) and availability bias (54.0%). To a lesser degree, commission bias (32.7%) and negativity bias (28.0%) were observed. Notably, anchoring bias showed the lowest agreement (16.7%). Additionally, 34.0% admitted following the dogma of completing therapies in multiples of seven days. In contrast to the high prevalence of confidence-related biases, the accuracy in choosing the antimicrobial in clinical cases was only 7.3% (11/150) in the first and 19.3% (29/150) in the second.

Conclusion: The high prevalence of confidence-related biases (IKEA, optimism) in contrast to low objective decisional accuracy is the central finding of this study. This suggests that antibiotic therapy is strongly influenced by subjective factors, demanding strategies that transcend conventional education. Future studies should focus on prospectively and multicentrically evaluating the impact of interventions designed to mitigate the most prevalent biases on clinical and microbiological outcomes.

Keywords: Antibiotics, Cognitive biases, Stewardship, Rational use, Behavior.

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