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SCIENCE: FROM
THEORETICAL
FOUNDATIONS TO
PRACTICAL IMPACT

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CARDIOMEGALY IN CHILDREN: MODERN APPROACHES TO DIFFERENTIATION OF STRUCTURAL AND FUNCTIONAL CHANGES (LITERATURE REVIEW)

Abstract. This review summarizes modern approaches to evaluating cardiomegaly in children, focusing on clinical, laboratory, and instrumental criteria distinguishing organic heart disease from functional alterations. Integration of echocardiography, radiological findings, and laboratory data improves diagnostic accuracy and enables early detection of severe pathology.

Keywords: cardiomegaly, children, echocardiography, cardiomyopathy, heart failure, differential diagnosis.

PROSPECTS FOR THE USE OF HYBRID ANTIBACTERIAL AGENTS

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Annotation: This study reveals a therapeutic potential of hybrid antibiotics, specifically in the environments where many multidrug-resistant pathogens are prevalent.

Key words: bacterial resistance, antibiotic, hybrid antibiotic, antibiotic combinations, antibiotic conjugates, drug design.

Introduction and relevance. The rapid spread of multidrug-resistant strains and the diminishing utility of standard monotherapy requires new molecular structures and treatment protocols to slow the progression of bacterial resistance. For Ukraine, this

issue is of particular importance given the urgency of addressing antimicrobial resistance, the need for rational antibiotic use, and the need to implement modern antibacterial treatment strategies in clinical practice. Hybrid antibacterial agents (HAAs) are synthetic compounds composed of two or more pharmacophores, that is, antibiotics from different classes or an antibiotic and an adjuvant, linked by a stable or biodegradable linker into a single integral molecule.

Aim of the study. To assess the ability of HAAs to overcome bacterial resistance mechanisms, to evaluate their advantages over combination therapy, to identify current strategies for HAA design, and to determine the most promising directions for their implementation in clinical practice.

Materials and Methods. An analysis of contemporary scientific literature and clinical studies on the development and use of hybrid molecules was conducted.

Results and discussion. Current strategies involve combining two pharmacophores via linkers that either enable simultaneous action on distinct targets or block resistance mechanisms. One of the main advantages of HAAs over combination therapy is the potential for simultaneous entry and activity of both active fragments within the bacterial cell at a coordinated concentration ratio, which may theoretically reduce the risk of resistance developing to a single agent. Hybridisation may enable the effective dose to be reduced and minimise adverse effects. Among the new antibacterial molecules, contezolid (MRX-I), a novel oxazolidinone, deserves particular attention; in studies using resistant strains and linezolid as a comparator, it demonstrated superior or comparable efficacy [1]. A lower risk of adverse effects was also observed in a phase I clinical study of the next iteration of the molecule, contezolid acefosamil (MRX-4) [2]. Related resistance-overcoming strategies include siderophore-based antibiotic conjugates, particularly cefiderocol, which is a conjugate of a cephalosporin and a catechol-type siderophore that mimics an iron transport molecule. Thus, the drug actively penetrates the membranes of Gram-negative pathogens via active iron transport systems, thereby enhancing delivery of the antibacterial agent. A systematic review and meta-analysis demonstrated high therapeutic activity in infections caused by multidrug-resistant bacteria, with a trend toward improved clinical outcomes [3]. Another promising experimental approach is combining antibiotics with natural adjuvants, particularly flavonoids. For example, quercetin may act as an efflux pump inhibitor and a modulator of biofilm formation. Studies in *Pseudomonas aeruginosa* have shown enhanced antibiotic activity and partial restoration of susceptibility in resistant strains. The use of flavonoids reduced the minimum inhibitory concentration (MIC) of the antibiotic; however, these findings remain predominantly experimental at present [4]. The meropenem/vaborbactam combination is not a hybrid molecule but rather a fixed combination of an antibiotic and a β -lactamase inhibitor; it also represents an effective strategy for overcoming bacterial resistance. It has demonstrated high efficacy against carbapenem-resistant Enterobacteriaceae compared with certain alternative treatment regimens [5]. However, the use of HAAs is associated with challenges in complex molecular chemical architecture and in developing stable linkers. Promising linker types include

ester, carbamate, and β -lactam linkers. Such variants may ensure the release of active components directly within the bacterial cell under the action of its own enzymes (β -lactamases, esterases). This allows avoiding steric hindrance during target interaction and reducing the MIC compared with stable conjugates. [6]

Conclusions. Hybrid antibacterial agents demonstrate potentially greater efficacy than monotherapy due to their ability to act simultaneously on several targets or to use alternative transport pathways. The simultaneous delivery of active pharmacophores into the bacterial cell may minimise the risk of resistance developing to a single component, which is one of the main advantages of HAAs over traditional combination therapy with separate drugs. Structural modifications and the use of natural adjuvants, such as flavonoids, make it possible to consider the potential to reduce the frequency of adverse effects. Certain novel antibacterial constructs and related strategies, particularly cefiderocol and contezolid, show promising results in treating infections caused by multidrug-resistant pathogens. For Ukraine, the development and study of such approaches are important for containing antimicrobial resistance and optimising antibacterial therapy.

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