Evaluating the Effectiveness of New Generation Antibiotics against Resistant Bacteria

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- Recent developments and approvals
- Alternate sources of antimicrobials
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Introduction

Antibiotics are drugs which prevent the growth of or destroy pathogenic bacteria, usually by intervening with crucial steps of metabolic pathways, and are given to patients for the treatment of an infectious disease caused by bacteria. Most antibiotics have highly target specific mechanisms of action and interfere with one particular cellular function.

Selection of antibiotic resistances and the spread of antibiotic-resistant pathogens are a dynamic process and cause a serious health problem. The search for new agents that are active on MRSA strains and that do not select easily for resistant strains becomes increasingly important. Alternatives to environmentally critical disinfectants and existing antibiotics are antimicrobial polymers. Hence the development of new generation antibiotics is a high unmet medical need. Antimicrobial resistance (AMR) poses a significant global health threat, rendering many traditional antibiotics ineffective against various bacterial infections.

Emerging classes of antibiotics

Infections in the ICU are often caused by Gram-negative bacteria. When these microorganisms are resistant to third-generation cephalosporines (due to extended-spectrum (ESBL) or AmpC beta-lactamases) or to carbapenems (for example carbapenem producing Enterobacterial (CPE)), the treatment options become limited.[1]

There are several bacteria called superbugs that are resistant to multiple antibiotics which can be life threatening specially for critically ill and hospitalized patients.[2]

Recent developments and approvals

An update on eight “new” antibiotics against multidrug-resistant gram-negative bacteria is that in the last six years, fortunately, there have been new antibiotics approved by the U.S. Food and Drug Administration (FDA) with predominant activities against Gram-negative bacteria, aimed to review these antibiotics: plazomicin, eravacycline, temocillin, cefiderocol, ceftazidime/avibactam, ceftolozane/tazobactam, meropenem/vaborbactam, and imipenem/relebactam. Temocillin is an antibiotic that was only approved in Belgium and the UK several decades ago, reviewed the in vitro activities of these new antibiotics, especially against ESBL and CPE microorganisms. At present, all of these new antibiotics are approved by the U.S. Food and Drug Administration for cUTI (except

eravacycline). Infections caused by multidrug-resistant (MDR) bacteria are a major public health threat.[3] It was aimed to assess the data supporting US Food and Drug Administration (FDA) approval of new agents aimed to treat MDR bacterial infections and the data provided by postmarketing studies. So identified all drugs with in vitro activity against MDR bacteria was recently approved.

The treatment of infections caused by the pathogens Neisseria gonorrhoeae, including multidrug-resistant isolates, and Clostridium difficile) have been approved during the same period. It concludes with the advantages that can result from the use of these compounds, also mentioning other approaches, still poorly developed, for combating antibiotic resistance: Nanoparticles delivery systems for antibiotics.[4]

Alternate sources of antimicrobials

No doubt that antibiotics are a miracle drugs. They stand against various infectious diseases for decades and saved millions of lives. However, the recent failure of antibiotics due to the dramatic emergence of multidrug resistant pathogens and the rapid spread of the new infections, urge the health organizations and pharmaceutical industries all over the world to change their strategy. There are considerable alternative sources of natural antimicrobials from plants with different mode of actions, some of them are employed in traditional medicine for centuries and was found to have competitive effects compared to some commercial antibiotics. For example: Iboxamycin is orally bioavailable, safe and effective in treating both Gram-positive and Gram-negative bacterial infections in mice.[5]

Role of artificial intelligence in antibiotic discoveries:

Artificial intelligence (AI) has emerged as a powerful tool in the discovery of new antibiotics. For instance, researchers at MIT utilized AI to identify a novel antibiotic, Halicin, which is effective against a broad spectrum of pathogens, including drug-resistant strains. AI models can analyze vast chemical libraries and predict molecular structures with potential antibacterial properties, accelerating the drug discovery process and offering new avenues to combat AMR. The emergence of new antibiotic classes and the integration of AI in drug discovery represent significant strides in combating antibiotic resistance. However, the transition from discovery to clinical application requires extensive testing to ensure safety and efficacy.

Conclusion

New-generation antibiotics offer promising solutions against resistant bacterial strains. Ongoing research, interdisciplinary collaboration, and responsible antibiotic stewardship are crucial to mitigate the global impact of antibiotic resistance. The approval of new drugs with potential clinical activity against MDR bacteria is supported by trials evaluating infections caused by non-MDR organisms, using noninferiority design and excluding the patients most likely to require these agents. Subsequent postmarketing efficacy data against these organisms are scarce. Healthcare professionals and regulators should demand more robust data to support clinical decision making.

References

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