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COMBATING THE ANTIMICROBIAL RESISTANCE BY PERSONALIZED MEDICINE: A MINI-REVIEW

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ABSTRACT

The emergence of drug-resistant microorganisms has resulted in the reduced effectiveness of traditional antimicrobial therapies. The World Health Organization (WHO) has recognized antimicrobial resistance (AMR) in bacterial infections as a significant global health crisis. If effective measures are not established by 2050, it is projected that annual deaths from diseases caused by drug-resistant bacteria could reach up to 10 million people. Antimicrobial resistance (AMR) arises due to the transfer of bacteria and genes among humans, animals, and the environment. While there are inherent barriers that impede the unrestricted movement of bacteria and genes, the acquisition of new resistance factors from various species is a common occurrence. This phenomenon undermines our capacity to effectively prevent and treat bacterial infections, posing significant challenges. The core of the problem lies in the evolution of pathogens, which enables bacteria to rapidly adapt to the selective pressures imposed by the use of antimicrobials in medical and agricultural settings. This adaptation encourages the spread of resistance genes or alleles within bacterial populations. To combat these challenges, there is a growing focus on the development of precision antimicrobial treatments that target the key virulence characteristics of individual infections. This approach aims to tailor treatment to specific infections, considering their unique characteristics. In this article, we explore the benefits, advancements, and challenges associated with the development of precision antimicrobial medicines. The goal is to enhance our ability to effectively combat drug-resistant bacteria and mitigate the impact of AMR on global health.

KEYWORDS: Antimicrobial resistance, Personalized medicine, MDR-TB, Tuberculosis, HER-2

INTRODUCTION

Antimicrobial resistance, also known as AMR, become a critical public health concern in the twenty-first century, presenting a significant challenge to effectively prevent and treat an expanding array of infections caused by different microorganisms. These pathogens have evolved to resist commonly used antibiotics, rendering them less effective. This concerning trend has developed over several decades, with bacteria responsible for both common and severe infections progressively developing resistance to newly introduced antibiotics. Urgent measures are imperative to prevent a looming worldwide healthcare crisis. Most bacterial infections caused by drug-susceptible organisms are treated with antibiotics, which are considered standard of care. Instead, the global proliferation of drug-resistant bacterial infections has severely reduced the number of medicines available to properly treat patients. Antimicrobial resistance poses a threat to individuals across all age groups, as well as to the healthcare, veterinary, and agriculture sectors. More than 70% of bacteria are resistant to all or parts of the existing antibiotics (1), necessitating the discovery of new forms of antibiotics "last-line" antimicrobial medicines to ensure best therapy, particularly in severe patients. World Health Organization (WHO) has devised a set of steps to combat the rising number of multidrug resistance (MDR) illnesses, including regulations on the marketing, administration, and dose of antibiotics (2). Treatment failures are formed because doses are evenly provided to the people without keeping in mind the progression of the infection or the clinical picture, which could result in sub-therapeutic or dangerous doses (3,4). Precision medicine promises that a better understanding of disease mechanisms can be a compass pointing to better treatments.

PERSONALIZED MEDICINE

Personalized medicine (PM) is an emerging and fascinating field within the medical and healthcare

industries. Providing personalized and effective therapeutic options based on an individual's genetic, epigenomic, and proteomic profile has the potential to revolutionize medical interventions (5). PM's impact extends beyond treatment and encompasses preventive measures as well. By employing molecular profiling techniques, such as genetic testing for drug resistance-related genes, healthcare professionals can have reliable evidence to guide treatment decisions for each patient. This advancement eliminates the need for trial and error prescribing methods, reducing potential negative side effects and improving patient outcomes (6,7). Today, when given medication is ineffective, the patient might choose to switch to another prescription called a medication switch. Patients who use this testing and failure approach experience poorer outcomes in terms of unfavorable drug effects, drug interactions, progression of disease, and dissatisfaction (8). In order to fulfill PM's vision for the twenty-first century, it is crucial to provide timely and effective therapy to patients while ensuring their satisfaction. A fundamental aspect of this vision is the delivery of "the appropriate medicine, in the right dosage, at the right time, to the right patient" (9). The availability of advanced diagnostic technologies plays a vital role in the success of precision medicine (PM) by facilitating the selection of optimal treatments, thereby improving patient outcomes. The FDA (Food and Drug Administration) emphasizes that PM aims to maximize benefits and minimize risks by precisely tailoring prevention and treatment strategies for individual patients. Rather than focusing on the development of new medications, PM also divides people into subpopulations based on their specific response to medication for a specific illness. For example, Herceptin has shown exceptional effectiveness in approximately twenty-thirty percent of cancer (breast) patients with higher HER2 protein expression. Thus, by identifying and categorizing patients appropriately, advanced molecular characterization of cancer (breast) patients at the genetic levels enables the best possible utilization of Herceptin (10)

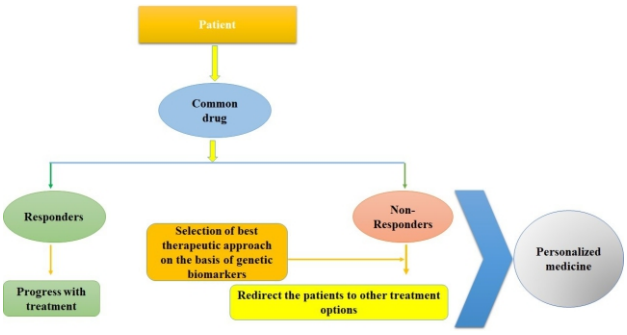

Fig. 1. General Overview of Personalized Medicine.

PERSONALIZED MEDICINE IN ANTIMICROBIAL RESISTANCE

The commercialization of genetic medicine has propelled the emergence of pharmacogenetics, now known as Personalized Medicine. This novel concept has revolutionized the field and presents lucrative opportunities for pharmaceutical companies. Not only does it involve the development of molecularly targeted drugs, but it also focuses on optimizing the usage and repurposing of existing pharmaceuticals and combination therapies.

The adoption of Personalized Medicine has brought about a paradigm shift in diagnosis and treatment approaches, leading to greater patient involvement during and after therapy. For instance, in the context of antimicrobial resistance (AMR), active surveillance allows patients to choose between immediate curative treatment with its potential problems and discomfort, or waiting until there is evidence of disease progression (11). This patient-centric aspect of Personalized Medicine takes into account individual circumstances in determining the most suitable treatment method, considering the patient as a whole person rather than just a medical case.

Personalized medicine holds great promise for delivering targeted therapy and improving medication choice while also lowering side effects, boosting patient compliance, and shifting the focus of medicine from curative to preventive measures. It also has the capacity to enhance cost-effectiveness and in still patient confidence through the post-marketing approval of innovative therapeutic strategies, thereby transforming the perception of medicine within the healthcare system (5). Given the complexity of an individual's cost-benefit connection with an antibiotic prescription, there is a solid argument for moving toward a more individualized strategy. The more individualized approach of oncologists has changed cancer treatment, as we can see. At-risk patients are identified through genetic screening, allowing for surveillance or preventative treatment. To maximize efficacy and reduce toxicity, the tumor subtype and patient characteristics define the therapeutic medication monitoring method. The evolutionary responses of pathogens to antimicrobial drugs used in vivo are multifaceted, influenced by intricate interactions with the host, local environment, and resident microbiome. In this context, Precision Medicine plays a crucial role. It is imperative to accurately characterize bacterial infections by identifying the specific pathogen taxa, the location(s) of infection, phenotypic and genotypic profiles of drug resistance, as well as the unique characteristics of the individual host and their microbiome. This

comprehensive understanding enables the improvement and prolongation of treatments, addressing the immediate need for more effective and durable solutions.

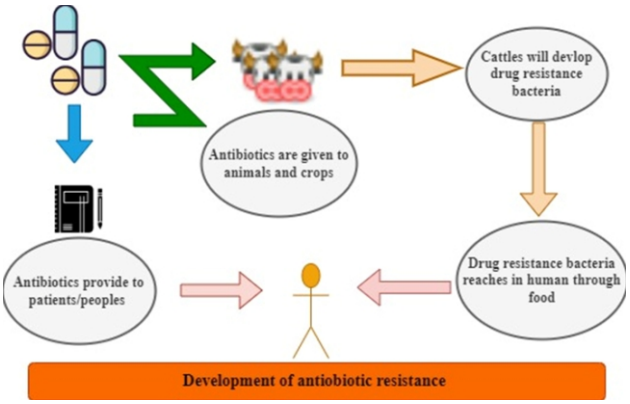

Fig. 2. Development of Antimicrobial Resistance.

DRUG-RESISTANT TUBERCULOSIS AND PATHOGEN-BASED PRECISION MEDICINE

The public health challenge posed by drug-resistant strains within the Mycobacterium tuberculosis complex (MTBC) is escalating. Ominously high rates of multidrug-resistant tuberculosis (MDR-TB) has documented in cases of previously treated TB. The World Health Organization reports alarming figures, such as 72% in Belarus and 65% in the Russian Federation. However, there is a silver lining in the form of advanced next-generation sequencing techniques has revolutionized tuberculosis (TB) research. This ground breaking advancement allows for a comprehensive, cost-effective, and timely understanding of the genetic makeup of MTBC pathogens. By leveraging WGS, researchers can obtain in-depth insights into the genetic composition of these pathogens, shedding light on drug resistance mechanisms, transmission patterns, and epidemiological factors. This information is essential for developing effective policies to combat the blowout of drug-resistant TB. The incorporation of advanced sequencing techniques has significantly accelerated our ability to identify drug-resistant strains, enabling early detection and prompt implementation of appropriate treatment regimens. Moreover, WGS offers a valuable tool for monitoring the dynamics of TB outbreaks and evaluating the efficacy of interventions. The integration of WGS into TB research has the potential to inform precision medicine approaches, facilitating the identification of optimal drug combinations tailored to individual patients based on their specific genetic profiles. This personalized treatment approach holds promise for enhancing therapeutic outcomes and mitigating the development of further drug resistance. In conclusion, the utilization of advanced next-generation sequencing techniques, particularly whole-genome sequencing, in tuberculosis research has opened up new avenues for combating drug-resistant strains within the MTBC. Through a comprehensive understanding of genetic composition, we can develop targeted interventions, improve treatment outcomes, and ultimately overcome the challenges posed by drug-resistant tuberculosis.

This advancement holds great promise for advancing the ongoing battle against TB. Moreover, it is widely recognized that the human genome exhibits distinct patterns that contribute to an individual's susceptibility to various diseases, and these patterns can vary among different populations (13). In recent years, there has been a revolution in biomedical research as well as the utilization of modern biological techniques. This has had the effect of simplifying the task of capturing the net genetic variations present in the population, which has made it possible to do so more quickly than ever before. As a result, understanding of the connections between human genes and various diseases has started to advance, and personalized medicine, or therapy based on a person's genetic make-up, is now being used to treat a range of conditions. Chemotherapy is the sole approved treatment for tuberculosis under the current guidelines. The response to treatment for tuberculosis (TB) varies among individuals, indicating the presence of genetic heterogeneity that influences the effectiveness of drug metabolism. Not every person achieves complete cure after completing the prescribed treatment regimen. Furthermore, the efficacy of TB treatment can be influenced by variations in the strain of the infecting mycobacterium, particularly in terms of its sensitivity to drugs. For instance, an infection with drug-resistant M. tuberculosis, categorized as multiple-drug resistant (MDR) or extremely drug-resistant (XDR), can impact the effectiveness of the treatment (14). The success of TB therapy is determined by both these factors the individual's ability to metabolize drugs effectively and the presence of drug-resistant mycobacterium. These elements significantly contribute to the overall success of TB elimination programs. Significant progress has been made in identifying human genes that influence susceptibility to mycobacterial diseases, and these genes have a substantial impact on mitigating these characteristics. Human genetic factors play a critical role in the context of tuberculosis (TB). For instance, specific genetic mutations in the gene that codes for chemokine ligand-2, which is necessary for the

recruitment of monocytes and T-cells, can increase the risk of contracting tuberculosis (15). A diminished response to TB treatment has also been linked to a specific polymorphism in the human tumour necrosis factor gene (16). Khan et al. have proposed that genotype-based dosage determination in the NAT2-INH system for TB treatment is a straightforward approach, highlighting the potential of precision medicine in TB management (17). In light of the rising concern surrounding M. tuberculosis strains that are resistant to isoniazid and rifampicin, individualised treatment approaches may present a promising method for preventing MDR-TB (18).

CONCLUSION

Personalized medicine has the potential to play a key role in combatting antimicrobial resistance (AMR). Personalized medicine, through the customization of treatments according to individual patients' genetic profiles, lifestyle factors, and microbiome composition, has the potential to enhance the utilization of antimicrobial drugs, diminish the risk of resistance development, and ultimately enhance patient outcomes. Overall, personalized medicine holds great promise in combating antimicrobial resistance. By tailoring treatments to individual patients, we can optimize the use of antimicrobials, reduce the selective pressure driving resistance, and improve patient outcomes. However, the successful implementation of personalized medicine requires collaboration among healthcare providers, researchers, policymakers, and patients to ensure its widespread adoption and the development of effective strategies to address AMR on a global scale.

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REFERENCES

1. O'Neill J. Review on antimicrobial resistance. Antimicrobial resistance: tackling a crisis for the health and wealth of nations. 2014 Dec 11;2014(4).
2. Garzón V, Bustos RH, G. Pinacho D. Personalized medicine for antibiotics: the role of nanobiosensors in therapeutic drug monitoring. Journal of Personalized Medicine. 2020 Sep 25;10(4):147.
3. Chang HH, Cohen T, Grad YH, et. al. Origin and proliferation of multiple-drug resistance in bacterial pathogens. Microbiology and Molecular Biology Reviews. 2015 Mar;79(1):101-16.
4. Touw DJ, Neef C, Thomson AH, et. al.. Cost-effectiveness of therapeutic drug monitoring: a systematic review. Therapeutic drug monitoring. 2005 Feb 1;27(1):10-7.
5. Mathur S, Sutton J. Personalized medicine could transform healthcare. Biomedical reports. 2017 Jul 1;7(1):3-5.
6. Vogenberg FR, Barash CI, Pursel M. Personalized medicine: part 1: evolution and development into theranostics. Pharmacy and Therapeutics. 2010 Oct;35(10):560.
7. Vogenberg FR, Barash CI, Pursel M. Personalized medicine: part 2: ethical, legal, and regulatory issues. Pharmacy and therapeutics. 2010 Nov;35(11):624.
8. Jakka S, Rossbach M. An economic perspective on personalized medicine. The HUGO Journal. 2013 Dec;7(1):1-6.
9. Sadee W, Dai Z. Pharmacogenetics/genomics and personalized medicine. Human molecular genetics. 2005 Oct 15;14(suppl_2):R207-14.
10. Vu T, Claret FX. Trastuzumab: updated mechanisms of action and resistance in breast cancer. Frontiers in oncology. 2012 Jun 18;2:62.
11. Romero-Otero J, García-Gómez B, Duarte-Ojeda JM, et. al. Active surveillance for prostate cancer. International Journal of Urology. 2016 Mar;23(3):211-8.
12. Huyen MN, Cobelens FG, Buu TN, et. al. Epidemiology of isoniazid resistance mutations and their effect on tuberculosis treatment outcomes. Antimicrobial agents and chemotherapy. 2013 Aug;57(8):3620-7.
13. Prohaska A, Racimo F, Schork AJ, et. al. Human disease variation in the light of population genomics. Cell. 2019 Mar 21;177(1):115-31.
14. Joshi JM. Tuberculosis chemotherapy in the 21st century: Back to the basics. Lung India. 2011 Jul 1;28(3):193-200.
15. Feng WX, Flores-Villanueva PO, Mokrousov I, Wet. al. CCL2-2518 (A/G) polymorphisms and tuberculosis susceptibility: a meta-analysis. The International journal of tuberculosis and lung disease. 2012 Feb 1;16(2):150-6.
16. García-Elorriaga G, Carrillo-Montes G, Mendoza-Aguilar M, et. al. Polymorphisms in tumor necrosis factor and lymphotoxin A in tuberculosis without and with response to treatment. Inflammation. 2010 Aug;33:267-75.
17. Khan N, Das A. Can the personalized medicine approach contribute in controlling tuberculosis in

general and India in particular?. Precision Clinical Medicine. 2020 Sep;3(3):240-3.

18. Seung KJ, Keshavjee S, Rich ML. Multidrug-resistant tuberculosis and extensively drug-resistant tuberculosis. Cold Spring Harbor perspectives in medicine. 2015 Sep 1;5(9):a017863.

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