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Alternatives to Antibiotics GOAL: ELEVATING Antibiotic Resistance During the Post-COVID Period

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Abstract:

The COVID-19 outbreak offers an unmatched chance to take advantage of personalized medicine's benefits for the protection, detection, medication, monitoring, and administration of a fresh public health crisis. Antibiotics, which were formerly regarded as miracle cures and among the most difficult life-saving discoveries of the twentieth century, are now posing a hazard to society as a result of overuse and abuse. Antimicrobial resistance (AMR) is a widespread issue that is becoming worse, and the current COVID-19 pandemic might make things even worse. It has been shown that a significant portion of Covid-19 patients gets secondary microbiological infections. The medical industry is now facing difficulties because of this. As a result, several non-antibiotic techniques have been sought, and their processes have been examined, to slow the spread of AMR.

INTRODUCTION

The coronavirus disease 2019 (COVID-19) was classified as a pandemic by the World Health Organization in March 2020 (1). The majority of Coronavirus (COVID-19) individuals globally are most susceptible to secondary infections. Antimicrobial resistance (AMR) has increased as a result of the introduction of COVID-19 due to an increase in microbial pathogens as secondary infections (2,3). The World Health Organization has stated that by 2050, the number of human fatalities brought on by drug-resistant bacteria might increase from around 700,000 to 10 million (4). The biggest contributor to AMR has been the increasing use of antibiotics during covid outbreaks. However, high rates of incorrect antimicrobial prescription, improper use of biocides, and discontinuation of therapy for other disorders may be to blame for the establishment of antimicrobial resistance. Antibiotic use has increased, which has contributed to the creation and spread of antimicrobial resistance (AMR), a significant worldwide health issue. Antimicrobial stewardship programs include minimizing the use of antibiotics as one of their key suggestions for combating AMR (5). A concerning biological issue is the inability of some illnesses to be treated by currently available antibiotics (6,7). The need of integrating antimicrobial stewardship practices with the healthcare system's COVID-19 response has been emphasized by the World Health Organization. Researchers and doctors are scrambling to identify a medicine that may exert antiviral efficacy with minimal side effects and should be inexpensive in the wake of the COVID-19 epidemic (8). Since SARS-CoV-2 is a recently discovered virus, repurposed medications are the only effective treatments available outside vaccinations. Based on our prior experiences with these antiviral medications against extremely pathogenic RNA viruses including HIV, Ebola, influenza, etc., clinical studies are now being done.

In addition to antiviral medications, several clinical investigations have found that COVID-19 causes an increase in cytokine and chemokine production (9), and as a result, immuno-modulatory US FDA-approved medications may also be able to help reduce the abnormal inflammatory immune response. Overall, it is recommended that antiviral and anti-inflammatory medicine combination treatment may be able to mitigate the current COVID-19 pandemic (10).

Antibiotic Resistant Emergence Favouring Factors

•enhancing environmental use of bactericidal agents
•A halt to research into other infectious illnesses
•A halt to research into other pathogens
•Shortages of medications, particularly narrow spectrum antimicrobials, and personal protective equipment (e.g., hydroxychloroquine);
•Scarcity of medications, particularly limited spectrum antimicrobials, and personal protective (e.g., hydroxychloroquine);
•Overpopulation and overburden of medical systems (11).

Most antibiotic medications are used as prophylaxis to shield hospitalized patients from further bacterial infections. The widespread issue of antibiotic resistance is not the only one. Changes in the gut flora may be another unfavourable impact of antibiotic therapy in patients. Furthermore, individuals with COVID-19 may experience poorer outcomes as a result of gut microbiome abnormalities. It's interesting to note that COVID-19 patients with GI issues have been reported to have more respiratory discomfort than COVID-19 patients without GI symptoms (12).

Anti-Microbial Resistance (AMR)

using cleaning products and washing hands

While suffering from a covid-19 infection, using hand sanitizers and disinfectants commonly exposes the user to both pharmacological and non-pharmaceutical substances in various amounts (13). Phenol and hydrogen peroxides, which cause bacterial DNA damage, are included in the majority of commercial sanitizers (11–13).

Antimicrobial resistance gene transmission mechanisms

Inhibiting or restricting drug absorption, bypassing the pathway (compensatory tack) impeded by a drug, demeaning and inactivating a drug by modification/degradation enzymes, and pumping a drug out of the body by different types of active efflux pumps are the primary mechanism of resistance to antibiotics. Modifications in cellular membranes that reduce the permeability of the membrane and alteration in cell wall proteins are the prevalent antibiotic targets (14).

Therapies without antibiotics to target AMR

To solve the AMR issue, suitable antimicrobial alternatives must be taken into consideration. Probiotics, phages, and phytomedicines are a few non-antibiotic methods for treating and preventing different illnesses (15).

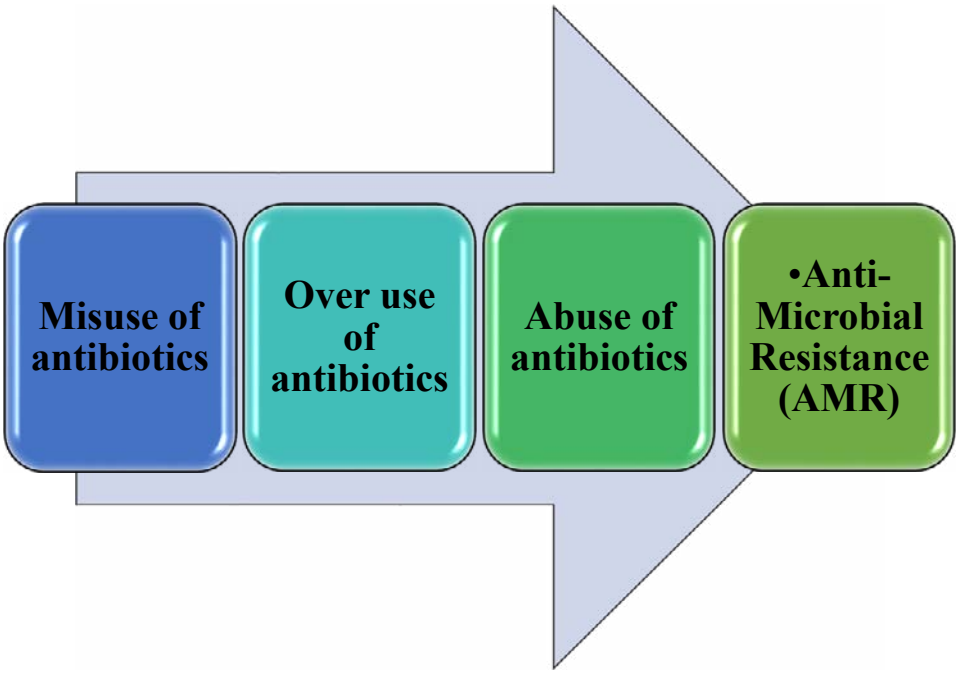

Fig1. Development of Antibiotic Resistance.

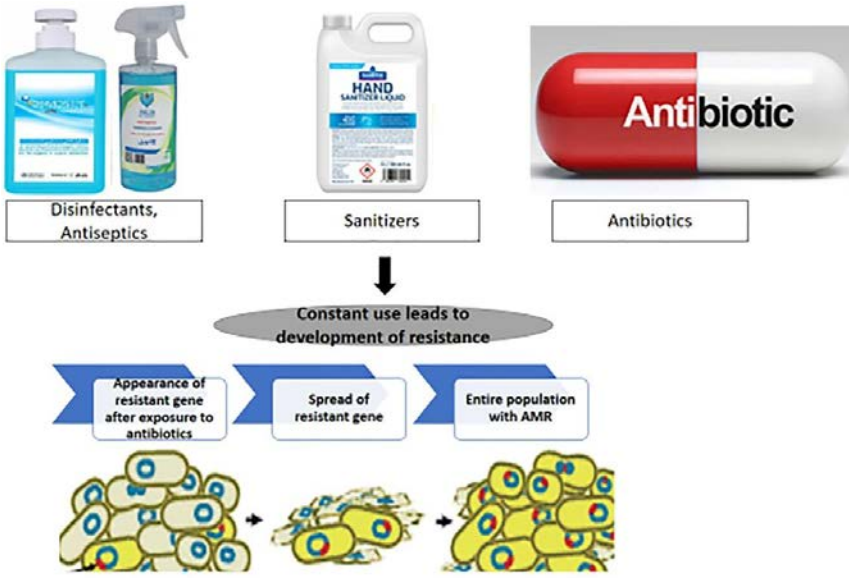

Fig2. Antimicrobial resistance gene transmission mechanisms.

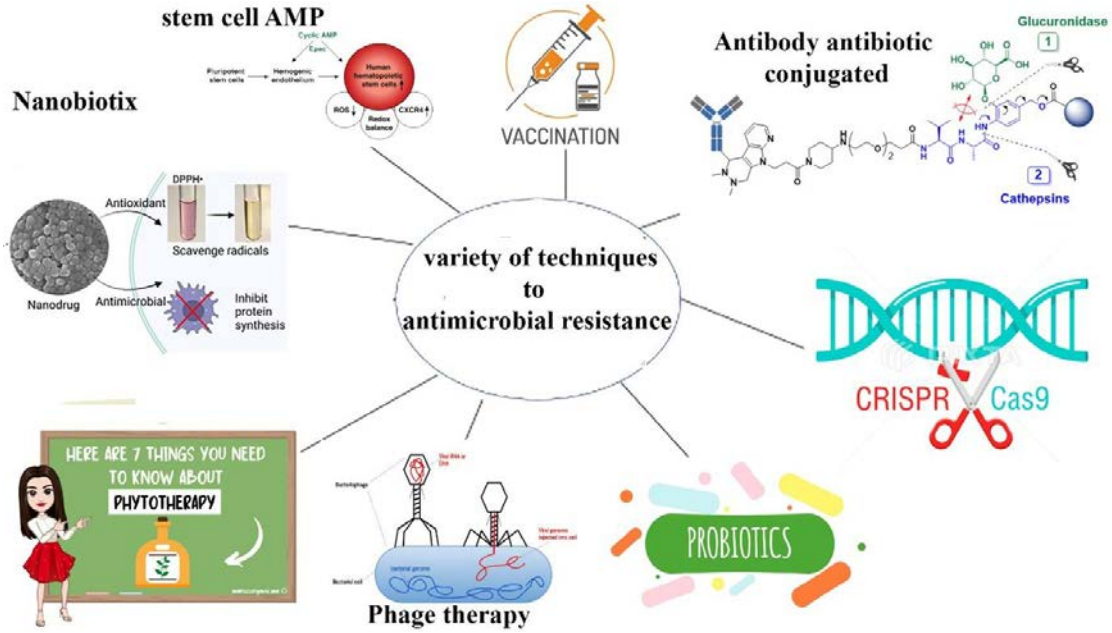

Fig3. Multiple strategies are used to address antimicrobial resistance.

The probiotic and prebiotic

Probiotics have been used as an alternative therapy for several intestinal illnesses, including gastroenteritis and diarrhea brought on by antibiotics. By granting immunity to infection or getting rid of infectious agents, probiotics have a positive impact on the digestive and other systems. As probiotics, several bacterial and yeast species have been employed (16).

Prebiotics are non-absorbable polysaccharides (like inulin and fructo-oligosaccharides) that promote the variety of the human gut microbiota and demonstrate health advantages in the host. According to studies, giving prebiotics to individuals who suffer diarrhea brought on by antibiotics has worked well (17).

Antimicrobial agents based on Bacteriophages

Bacteriophage treatment involves lysing bacterial pathogens with phages. Bacteriophage treatment has gained increased attention as antibiotic resistance has become a significant issue in contemporary medicine (18).

Phytomedicines

Bioactive substances that are obtained from plants

are known as phytomedicines. To treat diverse illnesses, several phytocompounds are utilized as lead molecules. Approximately 25% of all prescription pharmaceuticals used in the USA contain one or more bioactive chemicals derived from vascular plants. It is estimated that more than two-thirds of the world's population now depends on plant-derived medicines (19). According to estimates, plant ingredients make up or have served as models for 50% of current Western pharmaceuticals (20). Many of the commercially successful medications used in contemporary medicine were first used in undeveloped forms in conventional or folk medicine, or for other uses that showed potential biological activity. Additionally, researcher (21) found that extracts from 15 widely used Indian medicinal herbs were effective against enteric bacteria that produce ESBLs and are multidrug resistant. 45 Iranian medicinal herbs were shown to have an action against many drug-resistant human diseases, according to researches (22). Additionally, beta-lactamase generating methicillin-resistant Staphylococcus aureus was observed to be affected by several bioactive plant extracts (23). Several studies have been conducted to support the claims made for alternative treatments.

Faecal microbiota transplantation (FMT)

FMT involves transferring a healthy person's feces to a patient to repair the patient's damaged gut flora. According to research, this FMT can cure infections brought on by vancomycin-resistant enterococci or multidrug-resistant K. pneumonia, two examples of drug-resistant microorganisms (24).

Stem Cell-Derived Antimicrobial Peptides

Mesenchymal stem cells (MSCs) have undergone substantial research to provide a safe and effective therapeutic solution for several chronic disorders. MSCs have remarkable potential for enhancing immunomodulation, tissue repair, and inflammation management (25). According to a recent investigation, human MSCs behave as antimicrobial peptides (AMPs) that kill bacteria in a variety of ways, including preventing the formation of bacterial cell walls (26).

Blood Filtration Variations

In some illnesses, controlling the cytokine storm is crucial to avoiding organ damage. Devices are used in hemofiltration or renal replacement therapies to bind to and remove circulating bacterial products, inflammatory mediators, and cytokines (27) as well as some pathogens. Mannose-binding lectins and bound heparin are two of the frequently used tools (28). It is believed that even in cases of multidrug resistance, the host immune system will be able to combat the remaining pathogens if a significant reduction in the pathogenic bacterial load is achieved by this hemo-filter (29).

Quorum sensing blockers

The two crucial characteristics of microbial pathogens boosting their survival chances in harsh conditions are the ability to form biofilms and quorum sensing. Numerous organic and synthetic compounds have been demonstrated to inhibit quorum sensing (30).

Role of CRISPR-Cas against AMR

In microbial species, CRISPR-cas is a particular adaptive immunological characteristic that offers defence against invasive bacteriophages (18, 31).

Significance of Nano-antibiotics to combat AMR

It is possible to use nanoparticles to deliver antimicrobial agents or for them to already contain such agents. Due to their improved antimicrobial and anticancer activity and low toxicity, metal and metal oxide-based nanomaterials and drugs are viewed as attractive therapeutic options for use in biological sciences in the future (32). Through a variety of mechanisms, including bacterial wall disruption, biofilm suppression, immune response activation in the host, production of reactive oxygen species, and damage to important DNA and protein molecules of the resistant bacteria, nanoparticles can be used as carriers for the delivery of drug candidates and also have antimicrobial effects (33).

Change in the microbial community

The entire number of microbes present in a person's body is called their microbiota, and their microbiome contains all of their genomes. More than 160 bacterial species, primarily Bacteroidetes and Genera, have been linked to the regulation of physiological processes in a healthy adult gut. Many disorders, including diabetes, cardiovascular disease, asthma, autism, inflammatory bowel disease (IBD), antibiotic-associated diarrhea, and cancer, have been linked to the dysbiosis of this ecosystem. diseases, asthma, autism, inflammatory bowel disease (IBD), antibiotics-associated diarrhoea and cancer (34).

Personalized medicine and the treatment of the corona virus

The coronavirus cannot currently be treated with a particular antiviral medication. The only medications that have only a marginal impact on the coronavirus are recombinant IFN interferons and ribavirin. This is especially true for the brand-new coronavirus COVID-19. Because of this virus's mutation, which affects a crucial enzyme as a receptor, therapy is more challenging (35). Numerous anti-coronavirus medications have been created in response to the coronavirus epidemics caused by SARS and MERS,

but none of them have yet completed clinical trials. These medications target coronavirus enzymes such as proteases, polymerases, and MTases, as well as entrance proteins. They have encountered failure (36). The major therapy up till now has been suggested to use antibodies and plasma from recovered patients. Given the intense epidemic character of COVID-19 and its low fatality rate, this plasma and antibody collection from recovered patients may be the sole treatment option available right now for people with the disease. As coronaviruses are not curable or preventable, the best strategy to handle a serious coronavirus infection is to restrict the source of infection, receive an early diagnosis, supportive therapies, and prompt information distribution, rather than spreading fear. The outbreak must be controlled with panic (37). This virus can be prevented from spreading via preventative measures including good personal cleanliness, using an appropriate N95 mask, ventilating enclosed spaces properly, and avoiding needless transportation in congested areas (38). Currently, outpatient diagnostic and treatment services and inpatient services can be used to classify therapeutic services. When personalized medicine was implemented in Covid19, activities were created to specify how genomes, evolutionary biology, metabolomics, and viral genomes interacted to create events like infection, serious infections, therapeutic response, and sensitivity to immunization (39). In order to manage specimens in the strategy to personalized medicine in COVID-19, a joint directive from the Secretary General for Research, Development, and Innovations in Health and the Executive Directorate of the Andalusian Health Service was implemented on January 2020. Additionally, medical practitioners will have electronic biochemistry request accessibility to the whole genomic research of the SARS-CoV-2 virus (MPA) (40).

CONCLUSIONS

The development of alternative medicines is advised to lessen reliance on chemical medications because antibiotic resistance might prove fatal. Antibiotic effectiveness is decreasing as a result of the rise of drug resistance. Therefore, it is crucial to find new approaches and therapies to address the issue and cut down on the usage of antibiotics. The epidemic has forced us into a new situation that encourages collaboration and relationships between states and research institutes. Professionals have also arisen to treat this complicated illness, and technology has been introduced to ensure home health care. Understanding the interplay between the virus and the host might be improved with the use of sequence analysis, bioinformatics, and medical professionals focusing on tailored treatment. Physicians ought to have access to these technologies and be able to use them in their regular decision-making processes. Big data, AI systems, and the growing need for customized treatment are enabling the development of algorithms based on individual factors (genomic), the host, and the guest (pathogen and patient subject).

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