

A review of vaccination, a new strategy to prevent microbial infection

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Abstract

This document discusses the causes and problems of antibiotic resistance and the role of vaccines in fighting against antimicrobial resistance. It highlights the impact of vaccines in reducing the risk of infection due to antibiotic-resistant strains and their potential to prevent diseases by conferring immunity before infection with the pathogen. The document also emphasizes the need for tailored prevention and control strategies for each country and the combined efforts in antibiotics, new vaccine technologies, and monoclonal antibodies to tackle antimicrobial resistance. Additionally, it points out the challenges in predicting the impact of future vaccines and the limited published data on vaccines for pathogens other than influenza or pneumococci.

keywords: vaccine, microbial resistance, problems in new antibiotic production, impact of vaccine in AMR

Introduction

1.1. Main Causes of Antimicrobial Resistance

Antibiotic resistance is a significant global health concern that affects both human and animal populations. Similarly, the use of antibiotics in livestock production for growth promotion and disease prevention can contribute to the development of antibiotic resistance in animals and subsequent transmission to humans through the food chain. Irrational antibiotic (AB) usage poses a serious concern to third-world countries because of poor surveillance, lack of information, and patients' propensity for self-medication. Since degraded drugs contain less active principle, patients treated with antimicrobials often do not reach the optimal drug concentration, thus producing no effective results following their consumption.

1.2. Problems Militating New Antibiotics Development Antibiotics have transformed modern medicine.

Consequently, there is a dwindling number of companies and laboratories dedicated to delivering new antibiotics, resulting in which threatens our control of infections. Despite the ongoing need for new antimicrobial drugs, major pharmaceutical companies have abandoned this field.

Companies have been driven out of antibacterial research and development due to the increased cost of clinical trials, new regulatory uncertainties over approval requirements, and a low economic return. The ever-widening gap between the critical public health demand for new antibiotics and the declining potential for new antibacterial medication development has created a worrisome situation. The diminishing number of antibiotics approved for usage by the Food and Drug Administration (FDA) reflects the reluctance of pharmaceutical companies to engage in antibiotic development. Antibacterial drugs' low return on investment when compared with other therapeutics, the difficulty of identifying new compounds through traditional discovery methods, speculation that resistance will certainly develop for new antimicrobials, and regulatory requirements that necessitate large and complex clinical trials for antibiotic approval are all contributing to this decline. This indicates that rather than relying solely on the discovery of new antibacterial agents, efforts should be directed toward strategies or treatment alternatives to avoid the emergence or spread of resistance in microbes

1.3. The role of vaccines in the fight against AMR

Vaccines work by training the immune system to recognize and respond to a pathogen by mounting a rapid and effective immune defense, preventing the establishment of an infection/disease, or decreasing disease severity. Many vaccines have an added benefit and can protect unvaccinated individuals or subjects that cannot be vaccinated in a given population by a process called herd immunity, which greatly reduces disease in the overall population. Influenza vaccines for example do not only prevent influenza infections and disease but also decrease the likelihood of secondary bacterial infections, such as pneumonia and otitis media. The second mechanism by which viral vaccines can reduce AMR is by prevention of inappropriate antibiotic prescriptions for respiratory tract infections caused by viral pathogens. As discussed above, the

global disease burden and rising AMR rates in Gram-negative bacteria are very alarming so effective vaccines would be of great value. In addition, there is no limit to how many vaccines can be given to an individual as humans are exposed continuously to a myriad of infectious disease agents and the immune systems have been developed to deal with an almost infinite number of pathogens. Consequently, the morbidity and mortality caused by bacterial infections, as well as the healthcare-related costs, have been significantly reduced over the last few decades thanks to the availability of effective antibiotics. AMR is particularly alarming as it may cause persistent infections, as well as increased patient mortality and medical costs, and for this reason, is nowadays regarded as a serious global emergency.

2. Materials and methods

2. 1. Review methodology

The literature containing European data was systematically reviewed in a multi-step process was conducted. English language articles from 2018 to August 2023 were searched in Google Scholar and Pubmed databases. Search terms included vaccine, microbial resistance, problems in new antibiotic production, and perceptions and attitudes. Expert knowledge of the literature, snowball,

and Google searches was also used and was applied to extract the final set of articles for full review.

3. result

Vaccines exert their primary effect by reducing or eliminating the risk of infection due to antibiotic-resistant strains. Vaccines can also have a secondary effect on ABR by obviating antibiotic use by reducing the rates of febrile illness and the likelihood of secondary infections following the prevented episode. Disease prevention through vaccination began at least 200 years ago in Europe with Edward Jenner and the development of the smallpox vaccine in 1798 (The Immunisation Advisory Centre, 2017). A century after Jenner's breakthrough and following Pasteur's first vaccinations against chicken cholera, anthrax, and rabies, vaccine development continued to develop and flourish. While resistance is a predictable outcome of antibiotic use, resistance to vaccines is an extremely rare event. One possibility is that vaccines typically restrict the ability of the pathogen to establish a foothold in the host, by conferring immunity before infection with the pathogen. By focusing on prevention rather than treatment, vaccines can prevent diseases developing just after exposure to the pathogen, thus reducing the chance that some bacteria mutate and become resistant, and also reducing the chance that these resistant genes are spread to other bacteria. In addition, veterinary vaccines not only improve animal health but can also have a positive impact on human infections for certain diseases by reducing the use of antimicrobials in food-producing animals, and thus control the development of antibiotic resistance in pathogens, such as *Campylobacter*, *Salmonella*, *Escherichia coli*, and *Staphylococcus aureus*, that can infect humans. Wherever thorough studies have been performed, *Haemophilus influenzae* type b (Hib) is an important cause of childhood meningitis and a major cause of bacterial pneumonia in children. Although little population-based incidence data are available from most of Asia and the Newly Independent States, Hib is estimated to cause at least 3 million cases of serious disease and hundreds of thousands of deaths annually, worldwide. These vaccines are now used as part of routine childhood vaccination programs in more than 20 countries including Canada, the United States of America, Australia, and New Zealand, and many countries in Western Europe, and have proven to be highly efficacious and virtually free from serious side effects. Also, excellent results of trials or national introduction in Chile, Uruguay, and the Gambia show that Hib conjugate vaccines are effective in developing country settings. Recent results of efficacy trials of a heptavalent pneumococcal conjugate vaccine bring hope that protein conjugate vaccines will have a similar impact on pneumococcal disease. A recent systematic review examining the effects of conjugate Hib vaccine in preventing Hib disease or death in children <5 years, when compared with placebo/control, included four trials in a meta-analysis. The relative risk for invasive Hib disease following vaccination was 0.2 (95% CI 0.07, 0.54) compared with no vaccination, but there was statistically significant unexplained variation between the effects in the four trials ($p = 0.002$). Within 4 years after the introduction of the pneumococcal conjugate vaccine in children younger than 2 years in South Africa, reductions of greater than 80% were recorded in incidence of invasive pneumococcal disease caused by penicillin, ceftriaxone, and multidrug non-susceptible serotypes. Valneva has completed a phase II trial with a vaccine (VLA84) containing a fusion protein of truncated forms of TcdA and TcdB41. about *Staphylococcus aureus*, StaphVAX, a conjugate vaccine, developed by Nabi Biopharmaceuticals, targeting capsular polysaccharides type 5 (CP5) and CP8 failed to show efficacy in terms of reduction of *S. aureus* bacteremia in individuals with end-stage renal disease who received haemodialysis⁴⁷. V710, a vaccine targeting

the iron-scavenging protein IsdB, developed by Merck, was tested in patients undergoing cardiothoracic surgery in a phase IIb and phase III study to evaluate the efficacy of the vaccine in reducing the proportion of patients with postoperative *S. aureus* bacteremia and/or deep sternal wound infections. About, *Neisseria gonorrhoeae* No vaccine against *Neisseria gonorrhoeae* is currently available, and vaccine development has proven complicated in the past few decades for the following main reasons: *N. gonorrhoeae* surface proteins are subject to antigenic diversity and phase variation; knowledge of the type of immune responses that are needed to protect individuals is lacking as is information on reliable correlates of protection; and preclinical models to study the pathogenesis and measure the effectiveness of new antigens are limited.

4. Conclusion

Novel approaches are being explored for the development of vaccines against antimicrobial-resistant pathogens: OMV-based vaccines are at the preclinical stage for many pathogens, and innovative synthetic and bioconjugation strategies are replacing more traditional conjugation approaches and are more advanced in terms of clinical development (for example, for *Shigella* species or ExPEC). In 2015, the burden of resistant infections in EEA countries was measured in terms of cases, deaths, and DALYs. This information helps public health decision-makers prioritize interventions for infectious diseases. The contribution of antibiotic-resistant bacteria varies greatly between countries. Tailored prevention and control strategies are needed for each country. Combined efforts in antibiotics, new vaccine technologies, and monoclonal antibodies are needed to tackle antimicrobial resistance. Vaccines have great potential in reducing AMR, but predicting the impact of future vaccines is challenging. Cost-effectiveness analyses for future vaccines often do not consider their impact on AMR. Limited published data is available on vaccines for pathogens other than influenza or pneumococci. Current analyses can only give a partial picture of the potential impact of vaccination on reducing antimicrobial use.