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Commentary

Advances in Monoclonal Antibody in the Development of Antibody-Based Therapies Drug-Resistant Bacterial Infections

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1. Description

Increasing numbers of hospital- and community-acquired diseases are being linked to antibiotic-resistant bacterial pathogens. Recent developments in the manufacture and engineering of Monoclonal Antibodies (mAbs) have rekindled interest in the creation of antibody-based therapeutics for the management of drug-resistant bacterial infections [1]. At least nine mAbs are now undergoing clinical studies, and the Food and Drug Administration (FDA) has approved three antibacterial mAb products. Antibacterial mAbs are frequently created to eradicate germs or to lessen bacterial pathogenic activity by neutralising bacterial toxins and virulence factors. Cross-resistance between small molecule antimicrobials and antibacterial mAbs is improbable since antibodies have different pharmacological pathways from conventional antimicrobials. Moreover, mAbs' characteristic lengthy biological half-lives may make dosing simple and provide prophylaxis against infection that is similar to that of a vaccine [2]. Yet, mAbs' high affinity and the host immune system's role in their pharmacological effects could result in complicated and nonlinear pharmacokinetic and pharmacodynamic processes. The pharmacokinetics and pharmacodynamics of the FDA-approved antibacterial mAbs and those undergoing clinical trials are summarised in this review. Furthermore mentioned are difficulties in the creation of antibacterial mAbs.

Immune Gamma Globulin (IgG) isotype makes up the majority of the clinical trial participants and all FDA-approved antibacterial mAbs. IgG, which makes up around 80% of the immunoglobulin in human serum, is the most common immunoglobulin isotype. The molecular weight of an intact IgG is around 150 kDa, and it has two antigen-binding domains as well as a highly conserved crystallizable region (Fc), which binds to immune cells' Fc gamma receptors (FcRs) and activates Fc-mediated effector activities [3]. In healthy human beings, IgG normally has linear pharmacokinetics, which means that the area under the drug concentration-time is directly proportional to the dose, with small distribution volumes comparatively slow clearance and lengthy half-lives (20–25 days). IgG is partially rescued from lysosomal degradation by the Brambell receptor (FcRn), which accounts for its prolonged biological persistence.

Therapeutic mAbs frequently exhibit nonlinear (i.e., AUC is not proportional to dose), depending on the total body load of the pharmacological target (i.e., the number of bacteria in the case of an antimicrobial (mAb), the accessibility of the targets, mAb-target affinity, and mAb doses, in contrast to the pharmacokinetics of pooled endogenous IgG. The main PK factors for antibacterial mAbs are outlined here, along with information on how mAbs are distributed in infected organs and factors influencing Target-Mediated Drug Disposition (TMDD) [4]. The Immune gamma Globulin (IgG) isotype makes up the majority of the clinical trial participants and all FDA-approved antibacterial mAbs. IgG, which makes up around 80% of the immunoglobulin in human serum, is the most common immunoglobulin isotype. The molecular weight of an intact IgG is around 150 kDa, and it has two antigen-binding domains as well as a highly conserved crystallizable region (Fc), which binds to immune cells' Fc gamma receptors (FcRs) and activates Fc-mediated effector activities [5].

The advantages of utilising antibody molecules to treat infectious disorders are their selectivity and adaptability. The creation of therapeutic antibody preparations would take far less time than the development of a vaccine, and the effects of antibodies can work in synergy with those of standard antimicrobial medicines. One such method is radioimmunotherapy, in which an antibody molecule is joined to a radionuclide. Radioimmunotherapy has the potential to be particularly effective in immunocompromised hosts because it does not require a healthy immune system. Radioimmunotherapy may be helpful to combat intracellular pathogens and persistent infections since it can kill diseased cells as a result of the "crossfire" effect. When considering antibody-based therapies, the high specificity of antibodies can also be a drawback because accurate identification of the microbial agent responsible for an infection is required, and it may be necessary to use a "cocktail" of various antibodies to treat infections caused by microorganisms that go through antigenic variation. Therapeutic antibody preparations may be most effective when used against infections where early diagnosis is achievable because their efficacy wanes with time. Also, the costs of antibody therapies can be higher than those of conventional antimicrobial therapies; nevertheless, the higher costs of the medication should be balanced out by the decreased rates of resistance brought on by antibody therapy

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