BIOLOGICAL THERAPIES IN THE TREATMENT OF AUTOIMMUNE DISEASES: A NARRATIVE REVIEW OF THE LITERATURE

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ABSTRACT

Objective: To analyze biological therapies in the treatment of autoimmune diseases. Autoimmune diseases (ADs) are dysfunctions that occur when the individual's immune system does not have the ability to differentiate what is proper from what is not proper to the body. Among the most prevalent and studied autoimmune diseases are rheumatoid arthritis, systemic lupus erythematosus, and multiple sclerosis. Each of these diseases has unique characteristics, although they share the common foundation of a dysregulated immune response (Wang; Wang; Gershwin, 2015; Fallahi et al., 2016). Final thoughts: It is noteworthy that ongoing research and development of new biologic therapies should be prioritized, aiming to further enhance the treatment and management of these debilitating conditions. The medical and scientific community must remain vigilant about the safety and efficacy of these therapies, promoting robust evidence-based clinical practice.

Keywords: Biological therapies, Autoimmune, Immune system.

INTRODUCTION

Autoimmune diseases (ADs) are dysfunctions that occur when the individual's immune system does not have the ability to differentiate what is proper from what is not proper to the body. This is known as self-tolerance, which can be maintained by the action of B and T cells through central or peripheral mechanisms. These types of diseases can be organ-specific or systemic, caused by intrinsic or extrinsic factors. Intrinsic immunity is characterized by factors of the individual himself that may have as causes, the polymorphisms found in the histocompatibility molecules, the cells that are part of innate immunity and those of acquired immunity, as well as some hormonal factors. Extrinsic causes, on the other hand, are related to issues of involvement with the environment, through bacterial and viral infections, contact with physical and chemical agents, as well as drugs and pesticides (SOUZA et al., 2010).

B lymphocytes play a critical role in the pathogenesis of several autoimmune diseases due to their ability to produce cytokines, present antigens, interact with T cells, and transform into antibody-producing plasma cells.3-5 The loss of immunotolerance of these cells contributes to the pathogenesis of autoimmune diseases, especially those mediated by immune complexes.

In the last three decades, there has been a significant increase in the incidence and prevalence of AD (LOHI et al., 2007). Because of this, it was important to discover an effective therapy through several studies to improve the conditions of patients diagnosed with some type of autoimmune disease (BACH, 2002). There are a variety of existing ADs, some examples that can be cited such as Multiple Sclerosis, Type 1 Diabetes, Crohn's Disease, Systemic Lupus Erythematosus, Primary Biliary Cirrhosis, Myasthenia Gravis, Autoimmune Thyroiditis, Autoimmune Hepatitis, Rheumatoid Arthritis, Bullous Pemphigus and Celiac Disease, among others (LERNER; MATTHIAS, 2015).

The treatment of autoimmune diseases has evolved in recent decades, especially with the advent of biological therapies, which use proteins derived from living organisms to modulate the immune system, have shown promising results in terms of efficacy and safety. However, despite the advances, many challenges still exist, including variability in patient response, high costs, and potential adverse effects. Thus, a critical and up-to-date review of emerging biological therapies is important to understand their impact on the management of these diseases.

LITERATURE REVIEW

Autoimmune diseases are complex conditions in which the immune system, which normally protects the body against infection and other diseases, mistakenly attacks the body's own healthy tissues. Among the most prevalent and studied autoimmune diseases are rheumatoid arthritis, systemic lupus erythematosus, and multiple sclerosis. Each of these diseases has unique characteristics, although they share the common foundation of a dysregulated immune response (Wang; Wang; Gershwin, 2015; Fallahi et al., 2016)

These ADs present themselves in various forms that affect about 8 to 10% of the population of the West, showing themselves as a concern for society. Current therapies for AD are mainly based on systemic immunosuppression, which are characterized by the interruption of disease progression, in most cases and an improvement in symptoms, but end up causing some long-term side effects, have higher costs and the need for daily administration. Although these treatments have brought many benefits, the cure of these diseases remains achieved. Due to these negative points, new therapies to treat autoimmunity have been emerging, such as Hematopoietic Stem Cell Transplantation (HSC). Therapy that has been growing as a promising form, especially for patients resistant to more aggressive treatments (TOBIAS et al., 2019).

In addition to CTH to treat autoimmunities, immunotherapies have emerged as a form of biological therapies that can change the individual's immune system, to allow tolerance to be reestablished (AMORIM et al., 2017). Among the main immunotherapies used for the treatment of ADs, monoclonal antibodies were the first to be used. This type of therapy aims to selectively "attack" the immune cells responsible for the exacerbation of the disease (RANADE; HOLLINGER, 2005).

Still, within the context of immunotherapies, cell therapy has gained strength in recent years. T-cell therapy is something that attracts many researchers, as it allows the treatment to be more targeted when compared to other conventional therapies, and it is not so specific that it only brings immunosuppression. Monoclonal antibodies have a more specific interaction with their target antigen, allowing for a more selective result, with toxic side effects. Although some more selective immunosuppressants have less toxicity and side effects, they do not allow the permanent restoration of the balance of the immune system. This objective was shown to be possible with the emergence of CAAR-T cell therapy (Chimeric Autoantibody Receptor T Cells) (THEMELI; RIVIÈRE; SADELAIN, 2015).

The treatment of AD with CAAR-T therapy has achieved important goals. In pemphigus vulgaris disease, human T cells have been modified to express only one chimeric autoantibody receptor (CAAR), seeking selectivity towards autoimmune B cell

receptors. The objective of this is to induce the apoptosis of autoreactive B cells, and consequently decrease the production of autoantibodies, without the side effects of conventional therapies and other immunotherapies (COLLIOU et al., 2013).

Interleukin-1 (IL-1) inhibitors, such as anakinra, are also effective biologic therapies. IL-1 is another pro-inflammatory cytokine that participates in joint destruction by promoting cartilage degradation and bone resorption. Anakinra, an IL-1 receptor antagonist, prevents IL-1 from binding to its receptor, thereby decreasing inflammation and joint damage. Although not as widely used as TNF or IL-6 inhibitors, anakinra represents a therapeutic option, especially for patients who do not respond to other biologic therapies (Nikfaret al., 2018).

Rituximab, a monoclonal antibody that targets B cells, offers another effective approach to treating rheumatoid arthritis. B cells play an important role in the pathogenesis of rheumatoid arthritis through the production of autoantibodies and the presentation of antigens. Rituximab, by depleting CD20+ B cells, reduces autoimmune activity and inflammation, providing clinical benefits for patients with rheumatoid arthritis refractory to other treatments (Cohen; Keystone, 2015).

The effectiveness of biologic therapies is largely attributed to their ability to target specific targets in the immune response, reducing inflammation more precisely than conventional therapies. However, the safety of these treatments is also an important consideration. Clinical studies and post-marketing data indicate that while biologic therapies are generally well tolerated, they may be associated with increased risks of infections, infusion reactions, and, in some cases, malignancies. Continuous monitoring and evaluation of adverse events are essential to mitigate these risks and ensure patient safety.

FINAL CONSIDERATIONS

It is noteworthy that continuous research and development of new biological therapies should be prioritized, aiming to further improve the treatment and management of these debilitating conditions. The medical and scientific community must remain vigilant about the safety and efficacy of these therapies, promoting robust evidence-based clinical practice. Expanding knowledge about the immunological mechanisms underlying these diseases and continued therapeutic innovation will provide better clinical outcomes and a substantial improvement in patients' quality of life.

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