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A Review Study on Biological Therapy and Dentistry

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ABSTRACT

Background: The treatment of autoimmune, allergy, infectious, and many other disorders has recently undergone a radical change thanks to a new class of medications. This novel class of medications consists of three groups—cytokines, monoclonal antibodies, and fusion proteins—that may only target particular damaged cells. These medications could cause infections, hypersensitivity, hematologic problems, malignancy, hepatotoxicity, and neurologic issues as side effects. The mechanism of action and adverse effects of these medications, however, are not well understood due to a lack of data or extensive trials. Patients undergoing biological therapy might require particular care in dental procedures. The classification, method of action, side effects, and dental considerations for patients undergoing biological therapy are all reviewed in this essay.

1. INTRODUCTION

Biologics are a novel class of therapeutic drugs that have been introduced to the medical community and are useful in the treatment of diseases including cancer and autoimmune diseases. Recombinant DNA technology is used to create this type of medicines, which use living organisms or a synthetic version of them. 1Biologic products are those that are "any virus, therapeutic serum, toxin, antitoxin, or comparable product applicable to the prevention, treatment, or cure of sickness or injuries of man," according to the Food and Drug Administration (FDA). [2] Another example of biological therapy is the use of genetic therapy or biological prosthetic valves. [3] Consequently, in addition to the novel biologics, biological medications also comprise vaccines, blood and blood-derived preparations, antitoxins, growth hormones, human insulin, gene therapy, and recombined therapeutic proteins and allergens.

Monoclonal antibodies have been proven to have notable effects in the treatment of cancer. Targets in the tumour stroma (consisting of blood vessels, fibroblasts, or inflammatory cells), targets in the tumour vasculature, or cell surface proteins of solid tumours or circulating cancer cells are only a few possible targets for these medicines.Monoclonal antibodies have been proven to be more effective at targeting hematologic neoplasms such lymphomas because they can quickly enter the tumour cells. [5]

Biological drugs' classification

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Cytokines and signalling proteins

A wide class of soluble proteins, peptides, or glycoproteins known as cytokines aids cell signalling. Immunomodulators called cytokines control how the body reacts to infections and inflammation. Cytokines include interferons a and b and interleukin 2 (IL-2). [5] The name of soluble cytokine receptors ends with the prefix cept (e.g., etanercept and abatacept). [1]

The signalling proteins can integrate several simultaneous signals from nearby or distant cells to create an action, or they can process information from their local surroundings (outside the cells). Chemicals that operate locally or move to distant areas of action, such as hormones or neurotransmitters, or mechanical stimuli, such sensory cells in the skin, can produce the signals.

To start physiologic changes, signalling chemicals attach to receptor proteins produced on the cells. Receptors might be nuclear or cytoplasmic. In these circumstances, receptors attach to carrier molecules to help them transit through the cell membrane (such as estrogen). [6]

A monoclonal antibody

In order to cure a disease, antibodies, which are highly specialised naturally occurring molecules, bind to pathogenic cells or antigens. Monoclonal antibodies (also known as moAbs or mAbs) are specific molecular species that have one target antigen that they are active against. They are artificial molecules that are identical with the same affinity and bind to the same target or epitope as their unique parent immune cell. In order to improve immunological recognition, monoclonal antibodies are designed to bind certain cells or a portion of a particular cell. [7]

The spleen of a mouse exposed to the target antigen of interest is typically used to produce monoclonal antibodies. The resulting mAbs function by interacting with their particular molecular targets to deliver signal arrests that cause the targeted tumour cells to apoptose, modulate the receptor, or obstruct ligand binding. [14]

In cancer therapy, mAbs bind to antigens that are particular to the disease and either change the cancer cells' signalling pathways or cover up bound surface antigens. In addition, radioisotopes, cytokines, and other substances can be delivered via monoclonal antibodies (sometimes known as "naked antibodies") to directly kill tumour cells. "Payloads" refer to the agents carried by mAbs. [5] Brentuximab vedotin, a chemolabeled monoclonal antibody used to treat Hodgkin lymphoma, or britumomab tiuxetan, a radiolabeled monoclonal antibody used to treat non-Hodgkin lymphoma, are two examples of these conjugations. Conjugated antibodies may be more potent than monoclonal antibodies (mAbs) on their own and may also cause more negative effects. [7]

Some mAbs, including basiliximab, daclizumab, and muromonab-CD3, are used as supplemental immunosuppressive medications in organ transplant recipients. MuromonabCD3 prevents T cells from functioning. Daclizumab (Zenapax) and basiliximab (Simulect), which are IL-2 receptor antagonists, prevent T-cell activation and proliferation. [15]

Fusion proteins

Transmembrane proteins that are joined to another molecule make up fusion proteins, often known as soluble cytokine receptors or ligands. Typically, the Fc region of human IgG acts as the linker. It is possible to alter the linked Fc part of the fusion receptor to make it operate or not. To prevent adverse effects, fusion receptors competitively inhibit a ligand's binding to

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a given receptor. By employing fusion procedures, a therapeutic cytokine's biological characteristics can be enhanced or changed. For instance, research has shown that fusing to Fc or albumin can extend half-life, fusion to bacterial toxins can boost cytotoxicity, and fusion to cytokine agonists can increase activity. [6]

The objective of this paper is to evaluate the adverse effects of the biologic agents reported in the literature and provide a suggestion for dentists to take into account when treating patients who use these drugs. The terms biological, medications, autoimmune disorders, cancer, side effects, dental care, and dental advice were searched for in PubMed/NCBI. There was no set time constraint, and we used data that was pertinent to the goal. Position papers on the treatment of autoimmune disorders were also reviewed. We used clinical case reports even with minor cases due to the dearth of research publications on this topic in the literature.

Considerations of biologics

Various side effects can be brought on by various biologic medicines. Rash, itching, discomfort, redness, and swelling at the injection or infusion site are typical side effects. Flu-like symptoms, hematologic disorders, infections, malignancies, hepatotoxicity, and neurologic diseases are less frequent but potentially dangerous adverse effects. 3Susceptibility to infection is arguably the most significant side effect of biologics. It has been shown that opportunistic illnesses like tuberculosis, hepatitis, and fungal infections are becoming more common. [13]

Molecules like tumour necrosis factor (TNF), which are necessary for typical inflammatory responses, are inhibited by biologics. Patients may have changes in immune system composition and function, making them more susceptible to infection. [12] Inhibiting TNF-a, a cytokine that promotes inflammation, may increase the risk of immunosuppression. During therapy with TNF inhibitors, intact humoral, innate, and cell-mediated immune responses have been observed in the literature. [12] According to animal research, TNF-a suppression might prevent wounds from healing properly. It is unclear whether the interference speeds up19 or slows down [2, 3] the healing process.

After foot and ankle surgery, postoperative infection and wound healing were compared in patients using etanercept or infliximab to controls (patients not taking these medications). Patients who got a TNF-a blocker had stronger healing responses, and complications related to infection and recovery were nearly the same in both groups. [13] Etanercept, adalimumab, and infliximab have all been associated with injection/infusion site reactions. [14, 15] After adjusting for age, gender, and surgical procedures, Marchal et al. observed no statistically significant differences in problems between the patient and control groups in their postoperative analysis of Crohn disease patients who had used infliximab preoperatively. [16] Additionally, early postoperative problems were nearly identical in a retrospective study of 270 Crohn disease patients who had taken infliximab and/or immunomodulating drugs prior to abdominal surgery. Despite the positive findings, all of the researchers advised care and close monitoring for potential infections. [1]

One important negative effect of biologics is lower respiratory infections, including tuberculosis. TNF inhibitors present the greatest risk among biologics. Immediately following the start of the biologic therapy is typically when tuberculosis develops, which is the reactivation of a dormant infection. Abatacept treatment for COPD patients led to 24 patients experiencing more severe lower respiratory infections compared to the placebo group. [3]

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Leukopenia and thrombocytopenia have been linked to the usage of anti-eTNF-a medications (etanercept and infliximab), according to reports. [14-16] There are cases of bone marrow infections in patients using TNF-a antagonists, hypoplasia.30,31According to Rajakulendran et al. (2006), 14.3% of the 133 patients who were on anti-TNF medications had neutropenia.The neutropenic patients only had one infection. It is unclear how TNF-a inhibitors and pancytopenia are related in aetiology and causality. Because TNF-a exerts its effects by controlling proinflammatory cytokines (IL-1, IL-6, and IL-8) that are important for stem cell differentiation, it is believed that inhibiting TNF-a will suppress stem cell differentiation and lead to bone marrow hypoplasia, including neutropenia and thrombocytopenia. [13] TNF-a inhibitor use has been linked to cases of postoperative infection and sluggish wound healing, according to a few studies. [4, 3] Additionally, the environmental trigger for autoantibodies recognising citrullinated self-peptides may be the bacterial pathogens that cause periodontal disease, particularly Porphyromonas gingivalis. [15] This bacterium, a typical periodontal disease pathogen, has a special enzyme called peptidyl arginine deaminase that changes citrulline's arginine residues. In roughly 80% of people with rheumatoid arthritis, antibodies against citrullinated proteins are present. [14]

Dental opinions

One of the most significant negative consequences of biologic therapy is infection. The usual adverse effects include bacterial and viral upper respiratory infections, as well as tuberculosis. Before beginning a biologic medication, all patients have TB testing done. Chest radiography, a PPD skin test, and review of the patient's medical history are all considered screening tests for TB. Repeat TB skin testing should be requested if there is a history of TB exposure while using a biologic treatment. [9] After doing dental work, dentists should keep an eye on their patients for opportunistic infections as well as mycobacterial infection symptoms and signs.

According to the British Association of Dermatologists' guidelines for biologic interventions for psoriasis, TNF antagonist therapies should be stopped 4 to 5 times the half-lives of the individual medications (2 weeks for etanercept, 6-8 weeks for adalimumab, and 4-6 weeks for infliximab) prior to surgery. If postoperative wound healing is satisfactory and there are no signs of infection, biologic therapy can be resumed. [13]

Patients receiving biologic medicines are advised to receive the following dental care:

If bleeding occurs during a dental procedure, get a complete blood count (CBC) and platelet count.

- Neutropenia: Antibiotic prophylaxis may be required if the absolute neutrophil count is less than 1000 cells/mm3.
- The necessity for platelet transfusion to a level over 50,000/mm3 is indicated by a platelet count of less than 50,000/mm3.

If the patient has liver disease, assess the PT, PTT, and INR.

- Dental procedures are regarded as safe when the INR is between 2 and 3.5. To assess the patient's condition, a doctor consultation is required.

Prior to dental surgical treatments (such as numerous extractions, periodontal surgery, or dental implants), patients should speak with their primary care physician about the possibility of stopping biologic drugs for 4 to 5 times the drug's half-life. When the wound has sufficiently healed, biologic medications are resumed. Depending on the medicine, different agents may or may not be recommended for suspension.

2. CONCLUSION

In the treatment of cancer and autoimmune diseases, biologic medicines are employed more and more frequently. Clinicians must comprehend these medications and broaden their understanding of these side effects. The results of a review of the literature led to these conclusions. In order to guarantee that patients receiving biologic drugs experience the best results from dental care, a clinical retrospective research is recommended.

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