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Immunomodulatory drugs in autoimmune disorder

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Abstract

When immunologic tolerance to autoreactive immune cells is compromised, the immune system targets self-molecules, leading to autoimmune disease. Predisposing variables related to genetics, infections, and/or environment have been found to be highly connected with several autoimmune illnesses. Immunomodulatory medications alter the immune system's response by either boosting or suppressing the generation of serum antibodies (immunostimulators). Prescription immunostimulators are used, among other things, to improve the immune system's defenses against tumors, infectious illnesses, primary or secondary immunodeficiency, and changes in antibody transfer. Immunosuppressive medications are used to treat autoimmune illnesses and to lessen the immune reaction against donated tissues.

Key words: Immunomodulatory drugs, Autoimmune disorder, Types of immunomodulatory drugs.

Introduction

Autoimmune disorder occurs when the body's immune system attacks and destroys healthy body tissue by mistake. A disease in which the body's immune system attacks healthy cells.[1]

Autoimmune disorder

Your immune system attacking and damaging your body's own tissues is the cause of autoimmune illnesses. Normally, the proteins known as antibodies that your immune system produces serve to shield you from dangerous substances including poisons, cancer cells, and viruses However, your immune system becomes unable to distinguish between invaders and healthy cells if you have an autoimmune condition.[2] A robust immune system protects the body against illness and infection. However, when the immune system isn't working properly, it starts attacking healthy tissues, cells, and organs. These attacks, which are also known as autoimmune diseases, can impact every area of the body, impairing physiological function and perhaps posing a threat to life. There are around 80 autoimmune illnesses that are known to science. Some are well-known, like rheumatoid arthritis, multiple sclerosis, lupus, and type 1 diabetes.[3]

1.Rheumatoid arthritis

What is rheumatoid arthritis (RA)?

RA, also referred to as rheumatoid arthritis, is an autoimmune disease that causes inflammation. It develops when your immune system mistakenly attacks healthy cells, causing excruciating swelling in the body's afflicted regions.The joints—often multiple joints at once—are the primary focus of RA. RA typically affects the wrists, knees, and hands. In RA-affected joints, inflammation of the joint lining damages the joint tissue. Deformity (misshapenness), unsteadiness (loss of balance), and chronic or persistent discomfort can all be brought on by this tissue injury. symptoms and signs associated with RA Referred to as flares, there are times when RA symptoms get worse and times when they get better. [4]

- Pain or aching in more than one joint
- Stiffness in more than one joint
- Tenderness and swelling in more than one joint
- The same symptoms on both sides of the body (such as in both hands or both knees)
- Weight loss
- Fever
- Fatigue or tiredness
- Weakness

causes RA

As part of an immune response that results in RA, the body's immune system attacks its own healthy cells. There are several factors that can increase an individual's risk of developing RA, even though the exact cause of the illness is unknown.[5]

risk factors for RA

To determine whether a person's risk of developing RA is influenced by genetic or environmental variables, researchers have examined a variety of these traits.

signs and symptoms of RA

There are periods when RA symptoms worsen, referred to as flares, and periods when they get better, referred to as remissions.

• Pain or aching in several joints
• Tightness.[6]

2.Lupus

As it affects various parts of the body, lupus is a chronic inflammatory autoimmune disease that can generate a wide range of clinical symptoms. Discoid, drug-induced, neonatal, and systemic lupus erythematosus (SLE), the variety that affects the majority of people, are the four main different kinds of lupus. Patients with lupus experience a loss of self-tolerance due to unusual immune responses and the generation of autoantibodies that lead to the formation of immunological complexes that can negatively impact healthy tissue.

Lupus symptoms and signs

- Muscle and joint pain.
- Fever. A fever higher than 100 degrees
- Rashes.
- Chest pain.
- Hair loss.
- Sun or light sensitivity.
- Kidney problems.
- Mouth sores.
- Prolonged or extreme fatigue
- Anemia.[7]

3.Multiple sclerosis

The central nervous system (CNS) is affected by lesions in multiple sclerosis (MS), a chronic inflammatory illness that can cause significant physical or cognitive impairment in addition to neurological problems.

Common symptoms include:

- Tingling in one or more limbs; usually, this sensation affects one side of the body at a time.
- Sensations for electric shock produced on by particular neck movements, especially bending the neck forward (Lhermitte sign)
- Lack of coordination
- unsteady gait or incapacity to walk
- partial or total blindness, generally in one eye at a time, frequently accompanied by discomfort while moving the eyes
- prolonged double vision
- blurry vision
- vertigo
- issues with bowel, bladder, and sexual function.[8]

Immunosuppression drugs

An immunosuppressant is a group of drugs that inhibit or reduce the intensity of the body's immune response.

Why Immunomodulatory Drugs Are Made: - Immunomodulatory drugs are made to alter or control immune system activity.

1. Immunosuppression: A number of medications work to reduce or inhibit the immune system. This is especially crucial in circumstances involving organ transplants or autoimmune illnesses, where the immune system is hyperactive. These medications work by suppressing the immune system, which helps stop the body's own tissues from being attacked by the immune system (in autoimmune illnesses) or from rejecting an organ transplant.

2. Immunostimulation: The immune response is boosted or stimulated by other medications. This is frequently applicable to cancer treatments or specific diseases when a more potent immune response is required to fight the illness.[9]

Minimization of Tissue Damage and Inflammation:

As a component of immunomodulatory therapy, immunosuppressive medications help to lower tissue damage and inflammation. Inflammation plays a major role in the course of diseases such as autoimmune disorders. When the body's immune system unintentionally targets its own tissues, inflammation results, which can hurt, swell, and harm joints and organs. Immunosuppressive medications assist in lowering tissue damage and discomfort by suppressing this inflammatory response.[10]

- Immunosuppression is essential in organ transplantation to stop the recipient's immune system from rejecting the donated organ. These medications aid in preserving the transplanted organ's viability and functionality by reducing the immune response.

In summary, immunosuppression, as achieved by the use of immunomodulatory drugs, serves to modulate the immune response. This modulation is particularly important in conditions where an overactive immune system can lead to inflammation, tissue damage and other harmful effects on the body. Reducing inflammation and tissue damage is a key therapeutic goal in the management of various autoimmune diseases and in the prevention of rejection after organ transplantation.[11]

Type of immunomodulatory drugs

a.Corticosteroids:

1. Mechanism:

- Corticosteroids such as prednisone, dexamethasone and hydrocortisone are synthetic drugs that mimic the effect of corticosteroid hormones naturally produced by the adrenal glands.

- They bind to glucocorticoid receptors in the cytoplasm of target cells, which leads to the formation of a receptor-ligand complex.

- This complex translocates to the nucleus, where it modulates gene transcription, suppresses the expression of pro-inflammatory genes and enhances the transcription of anti-inflammatory genes.

- The overall effect is a strong anti-inflammatory and immunosuppressive response.

2. Clinical indications:

- Corticosteroids are used for a wide range of medical conditions, including inflammatory and autoimmune disorders.

- Common indications include rheumatoid arthritis, asthma, allergic reactions, dermatological conditions (eczema, psoriasis) and autoimmune diseases (lupus, inflammatory bowel disease).

3. Administration:

- Corticosteroids can be administered orally, topically, intravenously or by injection, depending on the specific medical condition and severity.

4. Side effects:

- Long-term use or use of high doses of corticosteroids can lead to various side effects.

- Short-term side effects may include insomnia, mood changes, increased appetite and fluid retention.

- Long-term use may result in more serious side effects such as osteoporosis, diabetes, adrenal suppression and increased susceptibility to infections.

5. Considerations:

- Corticosteroids are often prescribed in a tapering regimen to minimize withdrawal effects and adrenal suppression when treatment is discontinued.

- The risk-benefit ratio is carefully considered and the lowest effective dose is prescribed to minimize side effects.[12]

b.Non-Steroidal Anti-Inflammatory Drugs (NSAIDs):

The innate immune system's activity and the growth and evolution of the inflammatory process are closely related. Vasodilation and increased blood flow are two of inflammation's primary early symptoms. This causes erythema and raises the temperature in the area impacted by the inflammation. Tissue edema and swelling are caused by inflammatory cells infiltrating the tissue from the blood flow due to increased vascular permeability. Bradykinins and prostaglandins are examples of inflammatory mediators that heighten pain sensitivity and

induce hyperalgesia (63). The capacity of neutrophils to chemotaxis, which is activated by a gradient of chemokines generated by the injured tissue, makes cleaning up the infected area possible (64) (Figure 3). An infected organism is forced to produce a fever and "flu-like" symptoms such as hot flashes, sweats, chills, rigors, headache, and exhaustion.[13]

1. Mechanism:

- NSAIDs work by inhibiting the activity of cyclooxygenase (COX) enzymes, especially COX-1 and COX-2.

- COX enzymes are involved in the conversion of arachidonic acid into prostaglandins, which are mediators of inflammation, pain and fever.

- Inhibition of COX enzymes by NSAIDs leads to a reduction in prostaglandin synthesis, resulting in a reduction in inflammation, pain and fever.[14]

2. Clinical indications:

- NSAIDs are commonly used for symptomatic relief of pain and inflammation associated with a variety of conditions, including musculoskeletal disorders, arthritis, and menstrual cramps.

- They have anti-inflammatory, analgesic and antipyretic properties.

3. Classification:

- NSAIDs can be divided into non-selective NSAIDs, which inhibit both COX-1 and COX-2, and selective COX-2 inhibitors, which primarily target COX-2.

4. Common examples:

- Non-selective NSAIDs: Ibuprofen, naproxen, diclofenac.

- Selective COX-2 inhibitors: celecoxib.

5. Side effects:

- NSAIDs are associated with potential side effects, especially with long-term use or high doses.

- Gastrointestinal effects, including ulceration and gastrointestinal bleeding, are notable side effects.

- Other side effects may include kidney damage, fluid retention and cardiovascular risks.

6. Considerations:

- NSAIDs should be used with caution in individuals with a history of gastrointestinal disorders, renal impairment, or cardiovascular disease.

- The choice of NSAID and dosage is often adapted to the patient's specific condition and medical history.[15]

c. Disease-modifying antirheumatic drugs (DMARDs):

1. Mechanism:

- DMARDs are a class of drugs that modify the immune response to slow the progression of autoimmune diseases, especially rheumatoid arthritis.

- They target different components of the immune system to reduce inflammation and prevent joint damage.[16]

2. Clinical indications:

- DMARDs are primarily used in the treatment of rheumatoid arthritis (RA) and other autoimmune diseases, including psoriatic arthritis and ankylosing spondylitis.

- Their goal is to control symptoms, improve joint function and inhibit disease progression.

3. Types of DMARDs:

- Conventional synthetic DMARDs (csDMARDs): methotrexate, hydroxychloroquine, sulfasalazine.

- Biological DMARDs (bDMARDs): Tumor necrosis factor (TNF) inhibitors (e.g. infliximab, adalimumab), interleukin inhibitors (e.g. tocilizumab) and others.

- Targeted synthetic DMARDs (tsDMARDs): Janus kinase (JAK) inhibitors (eg tofacitinib).

4. Administration:

- Conventional synthetic DMARDs are often taken orally.

- Biologic DMARDs are usually given by injection or intravenous infusion.

- Targeted synthetic DMARDs are usually taken orally.

5. Side effects:

- Adverse effects vary depending on the particular DMARD, but may include gastrointestinal symptoms, hepatotoxicity, myelosuppression, and increased risk of infections.

- Biologic DMARDs in particular may be associated with an increased risk of immunogenicity and infusion reactions.[17]

6. Monitoring:

- Regular monitoring of blood count, liver function and other relevant parameters is often necessary during DMARD treatment.

- Careful monitoring helps manage potential side effects and ensures treatment effectiveness.

1. Mechanism:

- JAK inhibitors are a class of drugs that target Janus kinases, a family of enzymes critical to the signaling of various cytokines and growth factors involved in the immune response.

- By inhibiting JAK, these drugs interfere with the signaling pathways of cytokines such as interleukins and interferons, modulating the immune response and reducing inflammation.

2. Clinical indications:

- JAK inhibitors are primarily used in the treatment of autoimmune diseases, especially those involving dysregulated immune responses.

- Common indications include rheumatoid arthritis, psoriatic arthritis and inflammatory bowel diseases such as ulcerative colitis and Crohn's disease.

3. Common examples:

- Tofacitinib, baricitinib, upadacitinib are examples of JAK inhibitors used in various autoimmune conditions.

4. Side effects:

- Common side effects include an increased risk of infections, gastrointestinal symptoms and changes in liver function.

- Long-term safety, especially with regard to the risk of serious infections, is subject to ongoing research and monitoring.[18]

5. Considerations:

- JAK inhibitors are often considered in patients who have not responded to or are intolerant to other disease-modifying antirheumatic drugs (DMARDs).

- Careful monitoring is required due to potential adverse effects and dosage adjustments or discontinuation may be necessary based on individual patient response.[19]

d. Monoclonal Antibodies:

1. Mechanism:

- Monoclonal antibodies (mAbs) are laboratory-made molecules designed to mimic the immune system's ability to fight harmful pathogens.

- They are created by cloning identical immune cells, resulting in antibodies that specifically target a particular antigen.

- Monoclonal antibodies can exert their effects through a variety of mechanisms, including:

- Blocking specific cell receptors.

-Marking cells for destruction by the immune system . - Delivery of cytotoxic substances directly to cancer cells.

2. Clinical indications:

- Monoclonal antibodies have various clinical applications, including therapeutic and diagnostic purposes.

- As part of therapeutics, they are used to treat various conditions such as autoimmune diseases, cancer and infectious diseases.[20]

3. Production:

- Monoclonal antibodies are typically produced using hybridoma technology or recombinant DNA technology.

- Hybridoma technology involves fusing a specific type of immune cell (B cell) with a myeloma cell to create a hybrid cell that continuously produces identical antibodies.

- Recombinant DNA technology enables the production of antibodies by inserting the genetic code of the antibody into a host organism such as bacteria or yeast.

4. Examples and clinical applications:

- Rituximab: Used to treat certain types of lymphoma and rheumatoid arthritis.

- Trastuzumab: Used in HER2-positive breast cancer.

- Infliximab: Used to treat autoimmune diseases such as rheumatoid arthritis and inflammatory bowel disease.

5. Side effects:

- Adverse effects of monoclonal antibodies vary depending on the specific antibody and its target.

- Common side effects may include infusion reactions, allergic reactions and increased risk of infections.

6. Considerations:

- Monoclonal antibodies are often administered intravenously and may require monitoring for adverse effects during the infusion.

- This is a rapidly evolving field and ongoing research aims to develop new antibodies with improved specificity and therapeutic efficacy.[21][22]

e. Risks of immunosuppression:

A. Increased risk of infections:

- Immunosuppression involves suppressing the activity of the immune system, which can significantly increase the risk of infections.

- The immune system plays a key role in the body's defense against bacteria, viruses, fungi and other pathogens. When suppressed, the body's ability to create an effective immune response to invading microorganisms is impaired.

- Opportunistic infections that are usually controlled by a healthy immune system may become more severe in individuals receiving immunosuppressive therapy.[23]

B. The Importance of Careful Monitoring:

- Due to the increased risk of infections, careful monitoring is necessary in individuals undergoing immunosuppressive treatment.

- Regular medical check-ups, laboratory tests and monitoring for signs of infection are essential for quick detection and resolution of problems.

- Monitoring may include blood tests to assess white blood cell count, immune function and markers of infection. Imaging studies may also be used to evaluate for latent infections or other complications.

- Careful monitoring allows health care providers to adjust the dosage of immunosuppressive drugs, balance the risk of infection with the need for immunosuppression, and intervene quickly in case of complications.[24]

f.Personalized Treatment:

A. Tailoring Treatment to the Autoimmune Disorder:

- Personalized treatment in the context of autoimmune disorders involves tailoring therapeutic approaches based on the specific characteristics and mechanisms of the individual's condition.

- Autoimmune disorders vary greatly in terms of the organs affected, the intensity of the immune response, and the underlying molecular and cellular processes.

- Tailoring treatment means selecting drugs, such as immunomodulatory drugs, that specifically target pathways involved in a particular autoimmune disorder. For example, drug choices for rheumatoid arthritis may differ from drugs for systemic lupus erythematosus.[25]

B.Complementary Approaches:

1. Lifestyle factors:

- Lifestyle factors play a key role in the treatment of autoimmune disorders as complementary approaches.

- This involves a range of behaviors and options, including sleep hygiene, smoking cessation and minimizing exposure to environmental toxins.

- Healthy lifestyle habits can positively affect immune function and overall well-being, potentially reducing the frequency and severity of autoimmune flare-ups.[26]

2. Diet, Exercise, and Stress Management:

- Diet: Certain dietary habits, such as a Mediterranean or anti-inflammatory diet, have been linked to reduced inflammation and better outcomes in autoimmune disorders. These diets typically emphasize fruits, vegetables, whole grains, and healthy fats while limiting processed foods and added sugars.

- Exercise: Regular physical activity is beneficial for overall health and can help manage autoimmune conditions. Exercise helps maintain joint flexibility, muscle strength and cardiovascular fitness. However, the intensity and type of exercise should be adapted to individual possibilities and the state of the disease.

- Coping with stress: Chronic stress can worsen autoimmune disorders by triggering inflammatory responses. Stress management techniques such as mindfulness, meditation, yoga and relaxation exercises can help reduce stress levels and positively impact the immune system. Complementary approaches, including attention to lifestyle factors, diet, exercise, and stress management, can provide valuable support in managing autoimmune disorders. While these strategies do not replace medical treatment, they contribute to overall well-being and can help individuals better cope with the challenges of autoimmune conditions. It is important that individuals work with health care providers to integrate complementary approaches into their overall treatment plan.[27]

Conclusion:

A comprehensive approach combining medications such as corticosteroids with lifestyle modifications is essential in the management of autoimmune disorders. Immunomodulatory drugs play a key role, emphasizing the need for personalized treatment plans. Complementary strategies such as dietary changes and stress management not only contribute to overall well-being but also complement medical treatments.

Vigilant monitoring, especially during immunosuppression, is essential to address risks such as increased susceptibility to infections. Personalized treatment, taking into account factors such as age and disease severity, ensures that interventions are tailored to individual needs. Healthcare professionals play a critical role and collaborative communication is key to informed decision-making and optimal outcomes. Navigating autoimmune disorders requires integrating medical precision with adaptable lifestyle modifications, recognizing the uniqueness of each patient for a more compassionate approach to management.

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