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Opinion Article

Immunosuppressant Drugs: Mechanism, Use and Adverse Effects

Rupert Federer*
Department of Pharmacy, University of Mississippi, MS 38677, Mississippi, United States

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Correspondence:
Rupert Federer
Department of Pharmacy, University of
Mississippi, MS 38677, Mississippi, United States
Email: rupert.fed1@gmail.com

DESCRIPTION

Immune system of the body protects the body against harmful foreign molecules/tissue and also prevents the body against various infections. However, this protection can result in rejection of the transplanted tissue. This is happened as transplanted organ work as a foreign organ of the body, so body own immune system oppose this organ, which results into the rejection of the transplanted organ. So to prevent rejection of transplanted tissue/organ, it is requiring suppressing immune system of the body. In transplant patients, various immunosuppressant drugs are prescribed to suppress immune system and so prevent the rejection.

Few commonly used immunosuppressant drugs are described as below:

Induction antibody

Preparations:

Muromonab-CD3 (OKT3) Muromonab-CD3 is a murine monoclonal antibody and is synthesized by hybridoma technology.

Use:

Muromonab-CD3 is used for treatment of corticosteroid-resistant acute allograft rejection in cardiac and hepatic transplant patients, for acute rejection of renal allograft, and to deplete T cells from donor bone marrow prior to transplantation.

Mechanism of action:

OKT3 produce its immunosuppressant drug effect by binding the T-cell receptor-associated CD3 glycoprotein, leading to initial activation and cytokine release, followed by blockade of function and T-cell depletion.

Adverse effects:

It produces anaphylactic reactions, infections, high fever, cerebral edema, seizures, aseptic meningitis, encephalopathy, and headache. Because of more adverse effects of OKT3 and development of more tolerable rabbit anti-thymocyte globulin and IL-2 receptor antagonists, OKT3 is rarely used for transplant patients.

Anti-thymocyte Globulin (ATG)

Based on derived source, ATG is divided into two types; one is derived from horses (ATGAM) and second is rabbits (thymoglobulin) derived.

Use:

In combination with other immunosuppressive agents, ATG is used to prevent early allograft rejection at the time of transplantation. ATG is also used to treat corticosteroid-resistant acute rejection and severe rejection episodes. Intraoperative administration of ATG was associated with a lower incidence of Delayed Graft Function (DGF) and shorter hospital stay.

Mechanism of action:

They produce their immunosuppressant effect by binding to various cell surface markers, leads to complement dependent lysis of lymphocytes.

Adverse effects:

Chills, skin rashes, fever, thrombocytopenia, leucopenia, and infections due to CMV or other viruses will be produced after the usage of ATG. Several studies conducted to compare thyroglobulin with ATGAM shows that thymoglobulin was associated with better graft survival and more effective in preventing rejection, than ATGAM.

IL-2-receptor antagonists IL-2 receptor

Antibodies are Daclizumab and Basiliximab. Basiliximab is consists of 75% human protein and 25% murine, and hence it is designated as "chimerized". While Daclizumab is consist of 90% human protein, and hence it is designated as "humanized."

Use:

IL-2-receptor antagonists are used as a prophylaxis in low-to-moderate risk renal transplantation recipients in combination with CyA and corticosteroids to prevent acute rejection after transplant.

Mechanism of action:

Daclizumab and Basiliximab are anti-CD25 antibodies. They bind to α chain of the IL-2 receptor on activated T cells and interfere with the proliferation of T cells. Basiliximab is about 10-fold more potent than daclizumab. Blockade of this receptor foils the ability of any antigenic stimulus to activate the T-cell response system.

Adverse effects:

Both daclizumab and basiliximab are well tolerated. Commonly observed adverse event with this class of drug is related to GI tract.