Biological Therapy in Ophthalmology

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in

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Abstract

The application of the biological agents in certain aggressive types of ocular inflammation, such as *Behcet's* disease, represents a main topic in uveitis treatment. Adalimumab has shown a more comparable efficacy than infliximab in *Behcet's* disease, offering a better patient compliance due to the SQ administration. On the other hand, the limited number of trials available is limiting the use of adalimumab to those cases, which are not responding to the standard of care.

An important issue for the biological agents is represented by the pediatric use: the drugs seems to be better tolerated by children and did not show significant side effects during the treatment.

Ky words;

Biological Therapy in Ophthalmology

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Aim of the work

To review the uses of biological therapy in systemic diseases that Present by eye manifestations and isolated eye diseases.

We will also review the side effects of biological therapy.

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List of Abbreviations

5-FU	5-fluorouracil
AMD	Age related macular degeneration
ANA	Antinuclear Antibody
APCs	Antigen presenting cells
AS	Ankylosing spondylitis
BCC	Basal cell carcinoma
BD	Behcet' disease
CHAMPIONS	The controlled high risk avonex multiple sclerosis prevention study in ongoing neurologic surveillance
CHAMPS	The controlled high-risk subjects avonex multiple sclerosis prevention study
CL	Clearance
C_{MAX}	Maximum serum concentration
CME	Cystoid macular edema
CNV	Choroidal neovascularization
FDA	Food and drug administration
HLAB27	Human leukocytic antigen B27
HSV1	Herpes simplex virus 1
IBD	Inflammatory bowel disease

IGE	Immunoglobulin E
IL	Interleukins
INF	Interferon
JIA	Juvenile idiopathic arthritis
JRA	Juvenile rheumatoid arthritis
MIF	Migration inhibition factor
MS	Multiple sclerosis
RPE	Retinal pigment epithelium
SPA	Spondeloarthropathy
TB	Tuberculosis
TCR	T- cell receptor
TNF	Tumour Necrosis Factor
VKHS	Vogt Koyanagi Harada Syndrome

Introduction

Introduction

Biological therapy:

It is a type of treatment stimulates or restores the ability of the natural immune (defense) system to fight infection and disease.

Biological therapy is thus any form of treatment that uses the body's natural abilities that constitute the immune system to fight infection and disease.

***(*Rosenbaum JT, 2010)**

Types of Biological Therapy

There are two basic categories of biological therapy: immunotherapy and cytotoxic therapy.

Immunotherapy uses a variety of methods and drugs to manipulate the immune system. This creates a hostile environment for the existence or growth of cancer in the body.

Cytotoxic therapy involves changing the cancer cells' biology so that they become weak and die. ***(Moorthy, 2009).***

(1) Immunotherapy

Immunotherapy can be either active or passive. Active immunotherapy involves setting an immune response in the cancer patient to fight cancer cells. In passive immunotherapy, immune molecules are given to patients who do not produce them on their own. Both approaches can be specific or nonspecific

- **Specific Active Immunotherapy**: stimulate a specific immune response.

- **Nonspecific Active immunotherapy**: a general immune response, activating a wide range of Immune cells. The agents used in this method include interferons and interleukins (IL-2 and IL-12, for example)

-**Passive Immunotherapy**: adoptive immunotherapy that the patient adopts an immune response that has been developed in a test tube.

(2) Cytotoxic Therapy (Tumor Cell Modulation)

The second main category of biological therapy is sometimes called cytotoxic (cell-killing) therapy. This approach uses proteins called cytotoxins that are produced by the body's cells to attack the cancer either by destroying the cancer cells or by making it difficult for them to grow and reproduce. Another term for this approach is tumor cell modulation.

Tumor cell modulation changes the cancer cell's biology so that they become weak and die. Some of the agents used in this approach are called cytotoxins. Perhaps the best-known cytotoxin in this category is tumor necrosis factor (TNF), a toxin secreted by activated macrophages to selectively kill tumor cells, principally by interfering with their blood supply.

TNF is being used to treat conditions such as Crohn's disease and rheumatoid arthritis. Etanercept (Enbrel) and infliximab (Remicade) are examples of commercially available injectable TNF- blocking treatments.

Uses of biological therapy in ophthalmology:

Biological therapy used principally in cancer centers, organ transplantation, rheumatology therapy but they have not been licensed for treatment of ocular inflammatory conditions but clinical trials are currently in progress.

Uses in ophthalmology include:

- *Noninfectious inflammatory uveitis*. The main use of biological therapy.

-*Can be used in any autoimmune disorder* eg, peripheral ulcerative keratitis,

- Inflammatory macular edema

-*In pediatric age group* eg, treatment of juvenile idiopathic arthritis.

Uveitis by strict definition implies an inflammation of the uveal tract. However, the term is now used to describe many forms of intraocular inflammation involving not only the uveal tract but also the retina and its vessels ***(Jabs et al., 2005).***

The choice of treatment for noninfectious inflammatory uveitis depends on several factors. The diagnosis, the severity of the disease, the presence of concurrent systemic disease requiring immunosuppression, the duration of inflammation, the reversibility of visual loss and whether it is unilateral or bilateral are the main indicators. Other factors that need to be considered when choosing treatments are due to drug-related side effects and interactions, including the general health of the patient (e.g., the presence of diabetes, renal failure, liver dysfunction and hypertension), and patient compliance to medication and follow-up. There have been changes in the management of uveitis over the last few years, with immunomodulatory agents and new intraocular delivery systems ***(Fraser and Pavesio, 2008).***