Immunotherapies in Dermatologic Disorders

Robyn S. Fallen, BHSc[a], Collin R. Terpstra, MD[b], Hermenio C. Lima, MD, PhD[c,*]

KEYWORDS

• Biologics • Immunotherapy • Immunostimulants
• Immunosuppressants • Skin diseases

Key Points

- The skin is an immunologic organ and many dermatoses are characterized by inflammatory responses triggered by infections and environmental antigens or autoantigens.
- Immunotherapy in dermatologic disorders involves the use of immunomodulators, such as immunosuppressants or immunostimulants, to re-establish skin homeostasis.
- Biologics used for immunotherapy are not a homogeneous group. They are allergenic extracts, blood or blood components, cytokines, fusion proteins, monoclonal antibodies, and vaccines.
- Improved understanding of the mechanisms of skin disease will assist clinicians in counseling patients on available immunomodulators and in selecting appropriate therapy.

INTRODUCTION

In no other part of the body are inflammatory reactions more apparent than in the skin.[1] Human integument is an immunologic organ that has antigens for lymphocytes and produces many types of cytokines and inflammatory mediators.[2] Complex relationships between cells and inflammatory mediators in the skin have been unveiled. Many dermatoses are defined by immune responses developed after contact with infectious or environmental antigens.[3] Some may result from the triggering of antibodies and lymphocytes reactive to autoantigens of the epidermis or dermis.[4] Health disorders of this tissue may be caused by either an exacerbation or reduction of the immune response.

Many therapies exist to treat dermatoses. The treatment of disease arising from immune dysregulation is considered a form of immunotherapy.[5] Therapies that try

[a] Michael G. DeGroote School of Medicine, Waterloo Regional Campus, McMaster University, 10-B Victoria Street South, Kitchener, Ontario N2G 1C5, Canada
[b] Division of Allergy, Department of Medicine, Michael G. DeGroote School of Medicine, McMaster University, HSC Rm 3W11, 1280 Main Street West, Hamilton, ON L8S 4K1, Canada
[c] Division of Dermatology, Department of Medicine, Michael G. DeGroote School of Medicine, McMaster University, 10-B Victoria Street S-Office #3017, Kitchener, Ontario N2G 1C5, Canada
* Corresponding author.
E-mail address: hlima@mcmaster.ca

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to modify the immune response to re-establish the skin homeostasis are also defined as immunotherapy. Immunotherapy involves the use of immunomodulators. By redirecting the orientation of the immune response, immunomodulators may have potential use as immunostimulants or immunosuppressants.

Definitions of immunotherapy are diverse and therefore immunotherapy can include many types of immunomodulators. Until recently, chemicals from diverse sources used to manipulate the immune system were known as immunosuppressants. These immunotherapeutic agents are now better considered immunomodulators and are used to reduce exaggerated activity of the immune system. Several publications on this group of drugs have shown the important role of these therapies as essential pharmacotherapy agents and as a type of immunotherapy in dermatology. This type of immunotherapy is not included in this review.

The modification of the antigen-specific IgE immune response profile by the repeated administration of an antigen to patients with a specific allergy is a type of immunotherapy.[6] There are examples of its application in dermatology, mainly for atopic dermatitis (AD).[7,8] The other group of immunomodulators is the biologics. Biologics are complex preparations of organic substances obtained from animals or modified organisms isolated by biotechnological methods or assays. Biologics are blood products, vaccines, protein extracts, recombinant protein, and monoclonal antibodies. These products usually must be injected or infused into the body to be effective. Its pharmacologic action depends on interactions with biochemical or immunologic processes in the body. With recent developments in the understanding of the pathophysiology of the immune system, new immunomodulatory therapies using cytokines and monoclonal antibodies have been developed. These novel agents are especially useful in the treatment of diseases caused by immune system dysregulation or the lack of immune response.[9]

From the basic science standpoint, immunomodulators are used to characterize immunologic events in a variety of biological processes. Studies have already led to important discoveries about the pathophysiology of skin diseases. From a clinical standpoint, there is no doubt about the important role of these therapies as essential components in the pharmacotherapy of clinicians in any field of medicine. Immunomodulators have high potential utility in the daily dermatologic clinic. The objective of this article is to discuss the immunomodulators most used by dermatologists.

In this review we sought to conduct a literature search on immunotherapies used to treat skin disease and summarize the most relevant data obtained. All studies, including reviews, clinical trials, editorials, letters, meta-analyses, practical guides, randomized clinical trials, and controlled clinical trials published up to January 2012 were included. There was no restriction on the language of the studies.

Articles and summaries were analyzed to identify relevant studies. Potentially relevant texts were obtained for evaluation. The authors decided on the publications that satisfied the inclusion criteria and methodological quality parameters and performed this appraisal without conflict of interest.

IMMUNOTHERAPIES USED IN DERMATOLOGY

Many immunomodulators are used to treat skin diseases. The following sections present procedures of immunomodulation used in dermatology.

Biologic Agents Used in Immunotherapies

Biologics have been in use for more than 100 years as vaccines.[10] However, they received renewed attention when they started to be used for the treatment of