Management of autoimmune bullous diseases: Pharmacology and therapeutics

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This article, published in the JAAD in 2004, discussed the pharmacological management of common autoimmune blistering diseases. It described individual drugs and subsequently presented the author's algorithms to use them.

Before initiating therapy, assessing extent and severity of disease and comorbidities is critical in determining which drug(s) and dosages to use. It is important to remember that these are potentially fatal diseases and that the most common cause of death is septicemia, not uncommonly from opportunistic infection due to prolonged immune suppression.

Corticosteroids remain the mainstay for treating pemphigus vulgaris. Tracking the total dose and regularly monitoring for side effects is good practice. In patients with pemphigus foliaceus, dapsone can be effective. Immunosuppressive agents (ISA) are usually necessary. When a recurrence occurs, another ISA is used. The use of cyclophosphamide has considerably decreased, primarily because of short- and long-term side effects. While mycophenolate mofetil is presently used frequently, methotrexate, with a once-a-week dosing schedule, is resurging as a beneficial agent.

A major advance occurred with the Consensus Statement on the Use of Intravenous Immunoglobulin (IVIg) to treat autoimmune mucocutaneous blistering diseases (AMBD) signed by 38 experts on blistering diseases from the United States, Canada, and Europe. It describes a specific protocol with a well-defined endpoint. This is the first biologic agent used in the treatment of AMBD for more than a decade. It has Medicare approval. It produces clinical control of disease, allows for discontinuation of corticosteroids and immunosuppressive agents, and produces long-term, sustained clinical remissions without any systemic therapy. In selected patients, dapsone with or without methotrexate enhances its efficacy. IVIg is safe. If patients are carefully screened and advised, adverse events can be reduced or prevented.

Recently, there has been an emerging interest in rituximab, as a B-cell–depletion therapy. Its effect is rapid and allows for reduction in dosages of corticosteroids and immunosuppressive agents. The majority of patients reported earlier were treated according to a protocol used in lymphoma. A significant number of patients have been treated by the protocol used to treat patients with rheumatoid arthritis (RA). Patients treated by both protocols received prednisone and ISA concurrently, and recurrences are common, requiring...
additional treatments. A major concern in both protocols is infection and mortality since B-cell levels are zero and many patients develop hypogammaglobulinemia. In 2011, a multinational conference of experts on RA has expressed several concerns regarding the 2006 FDA-approved rituximab protocol for RA.

A unique protocol for the use of rituximab, based on the biology of B cells, in combination with IVIg has been described and its effectiveness in producing long-term, sustained clinical remission in pemphigus and pemphigoid patients has been published.

The last few years have brought attention to the difficulties in treating mucous membrane pemphigoid (MMP) and consequences and sequelae of associated scarring. IVIg with or without rituximab has shown great promise in preventing total blindness and disease progression. The identification of subsets of MMP and their correlation with target antigens (integrin α6 and β4, laminin 332) have facilitated development of appropriate treatment strategies for each subset.

While limited EBA can be controlled by previously described therapies, widespread or severe disease, especially with mucosal involvement, successfully responds to IVIg. In such patients, corticosteroids and immunosuppressive agents produce only temporary relief but also produce unwarranted significant side effects that could be avoided. IVIg is the treatment of choice.

Emphasis on topical care is increasing. It results in reducing infections and enhancing re-epithelialization. Development of enzyme-linked immunosorbent assays for measurement of autoantibodies has aided management, but their accuracy in correlation with disease activity is not conclusive.

Therapies specific for each blistering disease will become possible only when the pathobiology of each disease is better understood and can be reversed. Such therapies may produce not short-lived but long-term, preferably lifetime sustained remissions (by restoring immune regulation) without need for any further systemic therapy. This goal will materialize as young dermatologists with research interests focus their careers on autoimmune blistering diseases.

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Wilma Bergfeld, MD, was the first woman to serve as AAD president. What year did she take office?

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