State of the art

Therapies offer relief to many patients

Treatments for ocular allergy have come a long way, but still have miles to go

By Paul J. Gomes, MS

Therapy for ocular allergy has shown significant progress in recent years. Topical antihistamine-mast cell stabilizers currently available provide rapid relief of the primary symptoms of allergy. The newest of these agents displays a duration of action that permits Q.D. dosing for most allergy sufferers. These drugs act directly by interfering with the action of histamine released by conjunctival mast cells following exposure to an allergen. They act indirectly by reducing the ability of allergens to stimulate histamine release.

The goal of any new therapy is to ‘calm’ the conjunctiva, allow the recruited cells time to dissipate and, at the same time, reduce the inflammatory features of this ‘late phase’ response.

Despite these improvements, many patients with chronic ocular allergies, particularly those with both seasonal and perennial allergies, do not fully respond to antihistamine therapy and so require anti-inflammatory agents, such as topical non-steroidals or corticosteroids. Therefore, a major focus of current and future anti-allergic drug development is to identify therapies to address this unmet need.

Chronic versus acute allergies

Chronic allergy differs from the more acute forms in that it is primarily mediated by cellular factors. It is dependent on the activity of immune cells, such as basophils and eosinophils, that have infiltrated the conjunctiva over the course of prolonged allergen exposure.

Increased prevalence of chronic atopic diseases, such as allergic conjunctivitis, in recent years also is believed to result from the “modern lifestyle” that includes exposure to exacerbating agents, such as air pollutants and volatile chemicals. Pollutants and allergens act to prime the immune response. At the same time, they promote a breakdown of the epithelial barriers that function as the first line of ocular defense. This combination accelerates the process of immune cell infiltration and ocular surface damage that is the hallmark of chronic allergy.

Chronic, breakthrough allergies

Patients who display poor or incomplete response to antihistamine therapy appear to fall into two groups: those with chronic allergies and those with breakthrough seasonal allergies. The first group comprises patients with both seasonal and perennial ocular allergies. For patients in this group, it is always allergy season. In the second group, patients exhibit robust responses to seasonal allergens. On days with particularly high pollen levels, they present with an allergic response that simply overwhelms the ability of any topical antihista mine to suppress.

Both patient types are subject to exacerbation of their allergies by environmental pollutants, such as auto exhaust and industrial haze. And, both show recruitment of immune cells to the conjunctiva.

With continued allergen exposure, these examples of chronic allergic conjunctivitis evolve into a pathologic condition dominated by ocular surface inflammation. The goal of any new therapy is to “calm” the conjunctiva, allow the recruited cells time to dissipate and reduce the inflammatory features of this “late-phase” response.

Currently, the best available treatments for chronic ocular allergy sufferers are topical steroids, such as prednisolone acetate or loteprednol etabonate. While effective, these drugs may only be used for brief periods because of adverse ocular effects, such as increases in intraocular pressure or risk of cataract.

Several recent clinical trials have evaluated the efficacy of other anti-inflammatories in a more severe form of ocular allergy: vernal keratoconjunctivitis. Similar compounds may also be candidates for therapy of chronic allergic conjunctivitis. As with seasonal allergic disease, the key to developing efficacious therapies is the availability of appropriate clinical models of the disease.

Applying the CAC model

In addressing the need for new treatments for chronic and breakthrough ocular allergy, our most recent efforts have focused on modifications to the well-established Conjunctival Allergen Challenge (CAC) model. Using a number of different paradigms of allergen exposure, we are able to create signs and symptoms that replicate those observed in chronic disease. In these and other studies, we employ a strategy of combining chronic allergen exposure, optimized inclusion criteria, and the established objective endpoints of the CAC to create a new model for chronic ocular allergy.

This approach is an ideal clinical path to assess the efficacy of either new chemical entities or re-purposed drugs as therapies for chronic ocular allergy. OP

References