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Allergic Conjunctivitis

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Allergic conjunctivitis affects up to 40% of the general population [1–3] and is a common clinical problem for ophthalmic and allergic practices [4]. In one study of 5000 allergic children, 32% had ocular symptoms as the single manifestation of their allergies (Marrache, Brunet et al 1978). Although many cases are seasonal, a large number of patients have year-round symptoms.

The conjunctiva can be affected by allergies to airborne pollens, animal dander, and other environmental antigens. The conjunctiva, like the nasal mucosa, is an active immunologic tissue that undergoes lymphoid hyperplasia in response to a stimulant [5]. The conjunctiva represents a thin mucous membrane that extends from the limbus of the eye to the lid margin of the eyelid. The conjunctiva is divided into three portions: the bulbar conjunctiva, which covers the anterior portion of the sclera; the palpebral conjunctiva, which lines the inner surface of the eyelids; and the space bounded by the bulbar and palpebral conjunctiva, which is the fornix or the conjunctival sac. The conjunctiva is histologically divided into two layers: epithelial and substantia propria. The epithelial layer is composed of two to five cells of stratified columnar cells, whereas the substantia propria is composed of loose connective tissue.

As in other forms of allergic inflammation, the mast cell plays a key role. Mast cells are widely distributed, especially in connective tissue and mucosal surfaces. In the eye, they are classically found in the conjunctiva, choroid, ciliary body, iris, and optic nerve. Mast cells ($6000/mm^3$) and other inflammatory cells are normally found in the substantia propria, just below the

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epithelial junction [6]. Initial reports of conjunctival mast cell populations were based on the differential physiologic response to compound 48/80, which causes connective tissue mast cells (but not mucosal mast cells) to degranulate. In the rat animal model, the response to a single application of 48/80 suggested that the conjunctival mast cells primarily belong to the connective tissue type of mast cells (Barney, Briggs et al). Mononuclear cell populations of the normal human conjunctiva are primarily located in the epithelium and include Langerhans cells ($CD1^+$; 85 ± 16 cells/mm^2) and $CD3^+$ lymphocytes (189 ± 27 cells/mm^2), with a $CD4^+$:$CD8^+$ ratio of 0.75 [7]. The Langerhans cells are known to facilitate immune reactions in the skin by functioning as an antigen-presenting cell, but their function in the cornea has yet to be clarified [8]. Of interest, the Langerhans cells of the eye are recognized by the $CD1^+$ marker, not the $CD6^+$ thymocyte marker, which is commonly found on Langerhans cells of the skin or in histiocytes from patients who have histiocytosis X [9]. Normal ocular epithelium does not contain any mast cells, eosinophils, or basophils, although in ocular inflammatory disorders such as vernal and giant papillary conjunctivitis, such cells are seen, as evidenced by the conjunctival deposition of eosinophil major basic protein deposition [10]. Conjunctival epithelial cells, however, may also play an active role in allergic inflammation because they have been shown to express RANTES in large amounts when stimulated in vitro with tumor necrosis factor α or interferon-γ [11].

Histamine concentration in tears can reach values greater than 100 ng/mL compared with normal values of 5 to 15 ng/mL (Chibret 1985). Histamine can cause changes in the eye similar to changes in other parts of the human body, such as capillary dilatation, increased vascular permeability, and smooth muscle contraction. A histamine concentration of 240 nmol/L (10 μL of a 50-ng/mL histamine phosphate concentration) can cause conjunctival redness and increased vascular permeability in 50% of the subjects studied. Tear histamine levels in nonatopic control subjects were not found to be different from those in allergic patients during their symptom-free periods [12].

History

A detailed history may reveal recent exposure to individuals who have conjunctivitis or upper respiratory tract infection within the family, school, or workplace. Such a history may help confirm an adenovirus infection in an endemic area. Knowledge of the patient's sexual activities and any associated discharge may suggest chlamydial disease or *Neisseria* infection. Frequently, the patient does not mention the use of over-the-counter topical medications such as vasoconstrictors or artificial tears, cosmetics, or contact lens wear. Direct questioning often reveals the use of these products or other topical and systemic medications, which are capable of producing

inflammation that can mimic seasonal allergic conjunctivitis (SAC) or perennial allergic conjunctivitis (PAC). Knowledge of any systemic disease such as rheumatoid arthritis or other collagen vascular diseases raises the clinician's suspicion for keratoconjunctivitis sicca, although a patient referred for irritated eyes who has thyroid dysfunction suggests superior limbic keratoconjunctivitis.

The offending allergens vary from one location to another, but the symptoms appear to be similar throughout the world. Often, symptoms are not severe enough to precipitate a visit to the allergist or the ophthalmologist. Among patients who seek help, some may not require treatment and others may simply be able to avoid the allergens responsible for their disease.

Symptoms usually consist of low-grade ocular and periocular itching (pruritus), tearing (epiphora), burning, stinging, photophobia, and watery discharge. Redness and itching seem to be the most consistent symptoms. Although symptoms persist throughout the allergy season, they are subject to exacerbations and remission, depending on the weather and the patient's activities. Symptoms are generally worse when the weather is warm and dry; cooler temperatures and rain tend to alleviate symptoms. Although itching is generally mild, occasionally it can be severe, and rarely patients may be incapacitated by their symptoms. Many of the symptoms of ocular allergy are nonspecific, such as tearing, irritation, stinging, burning, and photophobia.

The symptom of itching is strikingly characteristic of allergic conjunctivitis. It is often said that ocular itching implies allergy until proven otherwise. Furthermore, ocular itching is rare in other conditions, although it is not unknown. Patients who have blepharitis, dry eye, and other types of conjunctivitis may experience itching. It is worthwhile to pinpoint the location of itching. For example, patients who complain of ocular itching may be presumed to be describing conjunctival itching; however, some patients who have ocular itching describe symptoms related to the skin of their eyelids. Careful questioning can distinguish itching of the conjunctiva from itching of the eyelid skin. Although the former is usually associated with allergic rhinoconjunctivitis, which affects the conjunctiva, the latter may indicate contact allergy, which affects the skin and the conjunctiva. The discharge is usually watery and may be described as tearing. Sometimes there is a scan mucus component. The discharge may range from serous (watery) to mucopurulent and grossly purulent. A stringy or ropy discharge is characteristic of allergy. In severe forms of allergic conjunctivitis, such as vernal conjunctivitis, tenacious strands of mucus can be removed from the eye by the patient or the doctor. Environmental allergens are ubiquitous and nonselective, most commonly affecting both eyes at the same time. Conjunctival injection is commonly associated with discomfort, and when the patient complains of ocular pain, the physician must search for other causes.

In allergic patients, it is unusual to have conjunctival symptoms without nasal symptoms [13]. The nasal mucosa is expected to react in the same

fashion as the conjunctival mucosa; however, at times the physician encounters allergic patients whose symptoms appear to be ocular. These patients may indicate that they do not have systemic allergies because they have not experienced typical allergic rhinitis. It is not known why the conjunctiva should be the main target in certain patients who have allergies. There may be emotional or psychologic factors that make ocular symptoms more disturbing than nasal symptoms. Often, when patients deny nasal or respiratory symptoms, careful questioning can sometimes elicit such symptoms, even though they may be mild.

Examination

The eye should be carefully examined for evidence of eyelid involvement (ie, blepharitis, dermatitis, swelling, discoloration, ptosis, blepharospasm), conjunctival involvement (ie, chemosis), hyperemia, palpebral and bulbar papillae, cicatrization, and presence of increased or abnormal-appearing secretions. In addition, a funduscopic examination should be performed for uveitis associated with autoimmune disorders and chronic steroid use.

The bulbar conjunctiva is examined by looking directly at the eye and asking the patient to look up and then down while gently retracting the opposite lid (ie, looking down while holding up the upper eyelid). Examination of the palpebral (tarsal) conjunctiva is performed by asking the patient to look down, grasping the upper lid at its base with a cotton swab on the upper portion of the lid, and then pulling out and up. The patient should be looking down during the examination. To return the lid to its normal position, the patient should look up. The lower tarsal conjunctiva is examined by everting the lower eyelid while placing a finger near the lid margins and drawing downward. Conjunctivitis can be differentiated from inflammation involving the anterior portion of the eye by the involvement of the fornix and the palpebral conjunctiva. A velvety, beef-red conjunctiva suggests a bacterial cause. A ''milky'' appearance, the result of obscuration of blood vessels by conjunctival edema (Fig. 1), is characteristic of allergy. The combination of these two features gives the conjunctiva a pinkish or milky appearance. Because the conjunctival blood vessels are partially obscured, they are best evaluated with a slit-lamp microscope. Often, chemosis is so marked that it is obvious without magnification. If edema is severe, patients exhibit periorbital edema (Fig. 2), which is more prominent around the lower lids because of gravity. Ecchymosis, or the ''allergic shiner,'' has also been described in allergic patients and is thought to be the result of impaired venous return from the skin and subcutaneous tissues, although proof of this is lacking [14].

The signs of allergic conjunctivitis may not be striking. One expects the allergic eye to show mild to moderate redness. Severe redness would suggest a different diagnosis. It seems, however, that swelling or chemosis is

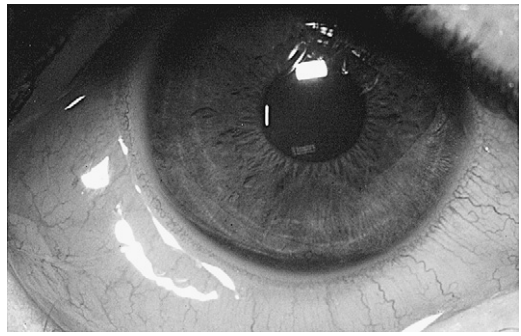

Fig. 1. Chemosis and injection of allergic conjunctivitis.

somewhat out of proportion to the amount of redness that is present. No doubt, some of the mediators released during allergic inflammation promote extravasation of serum out of the blood vessels and into the surrounding tissues. If chemosis is subtle, it can sometimes be detected at the medial aspect of the bulbar conjunctiva in the small fold of bulbar conjunctiva on the inner corner of the eye known as the plica semilunaris. This looser conjunctival tissue may appear more elevated and boggy than expected.

It is worthwhile to examine the superior limbus and the superior tarsal conjunctiva. In more severe allergies, these tissues are the site of Trantas' dots and giant papillae, respectively. They appear to be peculiar, anatomic targets for allergic inflammation and sometimes provide a subtle indication of the activity of ocular allergic disease. The direct (handheld) ophthalmoscope provides approximately 14× magnification. The physician may need to adjust the ophthalmoscope power setting to accommodate the patient's or the physician's refractive errors; the minus (red-numbered) lenses correct for nearsightedness, whereas the positive (green-numbered) lenses correct for farsighted errors. While using the lens, settings of +8 with the

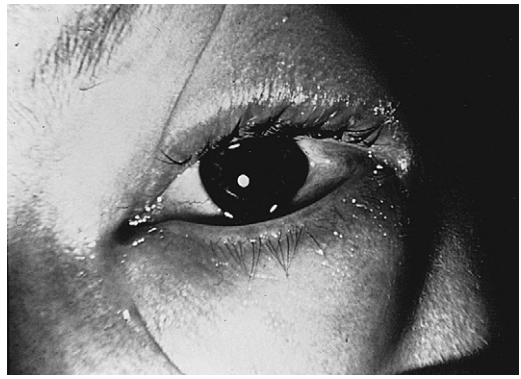

Fig. 2. Periorbital edema in acute ocular allergy.

ophthalmoscope held close to the patient's eye assist the physician in focusing on the anterior segment to reveal corneal opacities or changes in the iris or lens. Decreasing the power of the lens from +8 to −8 increases the depth of focus so that the examiner may move from the anterior segment progressively through the vitreous and reach the retina. The red-free (green) light filter is employed to sharply delineate small aneurysms and hemorrhages as black in patients who have autoimmune disorders (eg, systemic lupus erythematosus, vasculitis). Recently, attempts to measure the ocular allergic reaction objectively have been published [15]. The aim of objective measurements is greater accuracy and reproducibility, especially for clinical trials with antiallergic medications.

Seasonal and perennial allergic conjunctivitis

Because SAC and PAC are linked to allergic rhinitis (more commonly known as allergic rhinoconjunctivitis), they are the most prevalent forms of ocular allergy [6,16–18]. Of the two, SAC is more common. The importance of this condition is due more to its frequency than its severity [14].

Seasonal allergic conjunctivitis

SAC is the most common form of allergic conjunctivitis, representing more than half of all cases of allergic conjunctivitis [19,20]. The onset of symptoms is seasonally related to specific circulating aeroallergens. Grass pollens have been noted to be associated with increased ocular symptoms during the spring and, in some areas, during the fall (Indian summer). The ocular symptoms are frequently associated with nasal or pharyngeal complaints. Patients present with complaints of itchy eyes or a burning sensation with a watery discharge. A white exudate may form during the acute state, which becomes stringy in the chronic form. Rarely, SAC may also include corneal symptoms of photophobia and blurring of vision. The conjunctival surfaces are mildly injected with various levels of chemosis (conjunctival edema). Lid edema and papillary hypertrophy along the tarsal conjunctival surface may sometimes occur. Symptoms are usually bilateral, although the degree of involvement may not be symmetric. Affected individuals usually have a history of atopy. Allergic conjunctivitis, unlike several other ocular diseases, is seldom followed by permanent visual impairment.

Conjunctival cytology has revealed eosinophil infiltration in 25% of patients who have SAC. Elevated serum immunoglobulin (Ig)E levels have been noted in 78% of patients who have SAC, whereas tear fluid IgE is present in almost all (96%) tear fluid samples.

Perennial allergic conjunctivitis

PAC is considered to be a variant of SAC that persists throughout the year, although 79% of patients who have PAC experience a seasonal

exacerbation. Dust mites, animal dander, and feathers are the most common airborne allergens implicated in PAC, and PAC is more likely than SAC to be associated with perennial rhinitis. Patients who have PAC and SAC are similar in age and sex, and both patient groups have the same prevalence of associated symptoms of asthma or eczema. In the older literature, the prevalence appears to be much lower than SAC (3/5 per 10,000 population) [21], but recent epidemiologic studies have reflected this prevalence to be as high as 40%. PAC is similar to SAC in affected age range and length of history, although SAC is subjectively more severe. When patients who had PAC were compared with patients who had SAC, a history to exposure to house dust was more common (42% versus 0%), as was the association of perennial rhinitis (75% versus 12%).

SAC and PAC are typical mast cell–mediated hypersensitivity reactions affecting the eye, in which the allergens react with specific IgE antibodies bound to the surface of conjunctival mast cells. The activation of mast cells leads to the release of powerful vasoactive amines, which is responsible for the itching, vasodilatation, and edema encountered in allergic conjunctivitis.

Patients who have SAC and PAC have been noted to have aeroallergen sensitivity and elevated IgE in tears and in serum. Differences between PAC and SAC include the findings that 89% of patients who had PAC had specific serum IgE for house dust compared with only 43% of patients who had SAC. Similarly, 78% of patients who had PAC had tear-specific IgE for house dust, whereas no patients who had SAC had measurable IgE specific for house dust in tears [22]. Mediators released by the degranulation of mast cells include preformed mediators such as histamine and prostaglandins. Tear samplings have also been shown to contain elevated levels of eosinophil major basic protein. Eosinophils have been demonstrated in conjunctival scrapings from 25% to 84% of patients who have PAC and from 43% of patients who have SAC.

Procedures

Scraping the conjunctival surface to look for eosinophils is a helpful diagnostic test. The procedure is done by placing a drop of topical anesthetic such as tetracaine hydrochloride 0.5% in the lower conjunctival sac. The anesthetic takes effect within 10 seconds. Using a platinum spatula, the inner surface of the lower lid is gently scraped several times. The material is then spread on a microscope slide. The slide is stained with Hansel stain, Giemsa stain, or another common reagent. Slides are examined for the presence of eosinophils or eosinophil granules. Eosinophils are not ordinarily found in the conjunctival scrapings from nonallergic individuals. The presence of even one eosinophil or eosinophil granule is considerable evidence in favor of a diagnosis of allergic conjunctivitis [23]. The absence of eosinophils should not rule out a diagnosis of allergy. Eosinophils are often present in

the deeper layers of the conjunctiva and may be absent or undetectable in the upper layers. The frequency of eosinophils in the conjunctival scrapings from patients who have allergic conjunctivitis may vary from 20% to 80% [24] depending on the patient population, the chronicity of the allergic condition, and the persistence of the examiner [24]. Corneal infiltrates may occasionally be seen in severe allergic patients and tend to be nummular, subepithelial, and peripheral.

Conjunctival provocation tests (CPTs), which consist of instilling an offending pollen into the conjunctival sac, also produce the typical symptoms of hay fever conjunctivitis [25,26] and were the original method for evaluating allergic responses. Ocular challenge is used as a pharmacologic model for the evaluation of new antiallergic medications and immunotherapy [27]. The positivity of the challenge may be assessed by a sign and symptom scoring system that includes subjective and objective signs such as conjunctival erythema, chemosis, tearing, and pruritus. CPTs have also been shown to have a relatively good reproducibility in both eyes [25,28]. A CPT of ocular mast cells by way of opioid receptors has shown that 80% of normal patients reflect mast cell activation by detection of the release of histamine (7 versus 18 nm/L) and prostaglandin D_2 (0 versus 273 ng/L). The release of these mediators can be blocked by pretreating patients with cromolyn [29]. In assessing the potential usefulness of CPTs as a diagnostic tool, it was found that CPTs directly correlated to the radioallergosorbent test (RAST) in 71% (n = 130/183) of allergic patients. Of the 29% of uncorrelated cases, 23% (43/183) were positive by RAST but not by CPT, whereas 6% (10/183) were positive by CPT but not by RAST [30]. This finding suggests that there may be local sensitization of the target organ without evidence for systemic sensitization to the same antigen that clinically may reflect allergens causing ocular symptoms without any evidence of pulmonary or nasal allergic symptoms.

Late-phase reaction

A conjunctival late-phase reaction (LPR) has been described [31–34]. In the guinea pig model used by Leonardi and colleagues [35], the LPR manifested in several forms, including a classic biphasic response (33%), a multiphasic response (25%), and a single prolonged response (41%). The histologic evaluation of the conjunctiva revealed the typical influx of nonspecific cells of the inflammatory response, including neutrophils, basophils, and eosinophils. Tears collected from timed periods over the course of 6 hours after allergen challenge or CPT reflected the ability of mediators released during the LPR to reproduce the influx of cells commonly seen after ocular allergen testing (Bonini, Centofanti et al 1993); however, clinical symptoms were not reproduced in this single patient. Direct application of leukotriene B_4 has been found to increase the number of eosinophils and

neutrophils in rat conjunctiva [34]. Ocular challenge with platelet-activating factor also resulted in an inflammatory response (George, Smith et al 1990). The substantia propria was the primary site of the vascular changes that included endothelial cell swelling, capillary dilatation, and edema. In one study, 7 of 10 patients revealed a resurgence of ocular symptoms 6 hours after the initial challenge. Scrapings of the conjunctiva revealed an influx of eosinophils, neutrophils, and lymphocytes; however, the study did not evaluate the total time sequence for the arrival of the cells in the conjunctiva, and some researchers have questioned whether this may be part of the initial immediate hypersensitivity reaction. Ocular challenge with histamine revealed vascular permeability but not an inflammatory response, as measured by the epithelial expression of intracellular adhesion molecule (ICAM; CD54) [36]. In another study evaluating the efficacy of a new antihistamine, 14 of 22 patients (64%) developed signs and symptoms of an ocular LPR 2 to 9 hours after the ocular challenge dose [37]. In that study, the three most severe ocular LPRs occurred in patients who had previously been treated with a topical antihistamine, although the itching score of the LPR was less than the immediate reaction. Because the investigators were searching for an increased tolerance of allergen for an "immediate" reaction, this observation raises the possibility that the topical H_1 antagonist used in that study blocked the immediate ocular response but permitted the administration of a higher dose of allergen in the ocular conjunctival challenge. In another study, loratadine was thought to have a protective effect on the LPR induced in the CPT [38]. Various mediators have been detected in the tears of allergic patients and may help guide future drug development [39,40].

Treatment

Antihistamines

Antihistamines may be given systemically to relieve allergic symptoms. These drugs may only partially relieve ocular symptoms, and patients often complain of side effects such as drowsiness and dryness of the eyes, nose, and mouth. Antihistamines such as antazoline and pheniramine are available as eye drops and are usually combined with a topical vasoconstrictor such as naphazoline hydrochloride. These antihistamine-vasoconstrictor eye drops are now available over-the-counter and are useful in treating mild allergic conjunctivitis [41]. Most are used four times a day, and the side effects are minimal. They whiten the eyes by constricting the conjunctival blood vessels. They also relieve itching in most patients [23,42].

Mast cell stabilizers

Mast cell stabilizers have been a useful addition to the other drugs available for treating allergic conjunctivitis. Several studies have confirmed their

therapeutic value in allergic conjunctivitis [43,44]. Often, patients notice improvement within 24 to 48 hours. Mast cell stabilizers are most useful for relief of mild and moderate symptoms of allergic conjunctivitis. More severe cases may require the addition of topical corticosteroids. Unlike corticosteroids, mast cell stabilizers have minimal ocular side effects. An acute chemotic reaction to cromolyn was reported in two patients [45–47], but as in the treatment of asthma, cromolyn side effects are rare. An extra benefit of mast cell stabilizers is the relief of nasal symptoms caused by the drainage of tear fluid into the nasal passages. Nedocromil sodium is available in the United States and in Europe.

Lodoxamide tromethamine 0.1% (Alomide)

Lodoxamide tromethamine 0.1% (Alomide) is a mast cell stabilizer that prevents the release of histamine and leukotrienes [48]. Lodoxamide inhibits mediator release from mast cells, presumably by inhibiting calcium influx, thereby indirectly inhibiting increased vascular permeability. It is 2500 times more potent than cromolyn in inhibiting mediator release from mast cells; however, it appears to be roughly equivalent to cromolyn in controlling the symptoms of allergic conjunctivitis, vernal conjunctivitis, and giant papillary conjunctivitis. It is preserved in benzalkonium chloride.

Ketorolac tromethamine (Acular)

This nonsteroidal anti-inflammatory drug (NSAID) is preserved in benzalkonium chloride. It has been shown to relieve itching associated with allergic conjunctivitis. It also reduces levels of prostaglandin (PG)E_2 in tears. There may be some burning on instillation. It is unexpected that an NSAID would relieve itching, but research by Woodward and colleagues [49] suggested that some of the prostaglandins, particularly PGE_2 and PGI_2, may be pruritogenic.

Olopatadine (Patanol, Pataday)

Olopatadine inhibits mast cell degranulation and antagonizes histamine receptors to manage the itching, redness, chemosis, tearing, and lid swelling of the ocular allergic reaction [50,51]. Its mast cell stabilizing ability has been demonstrated in vitro (using human conjunctival mast cells) and in vivo (human clinical experience). A new formulation has recently been approved for once-a-day administration [52].

Ketotifen (Zaditor)

This benzocycloheptathiopen derivative is approved for the temporary prevention of itching due to allergic conjunctivitis (Avunduk, Tekelioglu et al 2005). It is a selective, noncompetitive blocker of the H_1 histamine

receptor. It inhibits inflammatory mediator release from mast cells, basophils, and eosinophils. It inhibits chemotaxis and degranulation of eosinophils, type 1 hypersensitivity reactions, and leukotriene activity. It is also an inhibitor of platelet-activating factors. In animal studies, it decreases vascular permeability and extravasation of Evan's blue dye in rat and guinea pig models of anaphylaxis. In human clinical trials using conjunctival allergen challenge, it reduces itching significantly and has a more modest effect on the reduction of conjunctival injection associated with allergy.

Nedocromil (Alocril)

This disodium salt of pyranoquinolone dicarboxylic acid is approved for treatment of itching associated with allergic conjunctivitis. It inhibits histamine, LTC4, and tumor necrosis factor α. It decreases chemotaxis of neutrophils and eosinophils and renders them unresponsive to mediators. It blocks the expression of cell surface adhesion molecules involved in eosinophil chemotaxis and decreases vascular permeability induced by inflammation. It reduces itching and, to a lesser extent, redness associated with allergic conjunctivitis. It has an onset of action 2 minutes after dosing and a duration of about 8 hours.

Pemirolast (Alamast)

Pemirolast is a mast cell stabilizer with antihistamine properties [53]. It is approved for the prevention of itching associated with allergic conjunctivitis. In SAC studies, it decreased itching and, to a lesser extent, redness, throughout the allergy season. It also decreased itching after conjunctival allergen challenge.

Azelastine (Optivar)

This phthalazinone derivative has been approved for the prevention or treatment of itching due to allergic conjunctivitis [54]. It inhibits histamine release from allergen-stimulated mast cells and suppresses inflammation. It decreases expression of ICAM-1, reduces eosinophil chemotaxis, and inhibits platelet-activating factor. It interferes with calcium influx in mast cells and inhibits the H_1 histamine receptor. It reduces itching, and, to a lesser extent, redness in SAC, in PAC, and after conjunctival allergen challenge.

Epinastine (Elestat)

Epinastine is a topically active, direct H_1 receptor antagonist and has affinity for the H_2, α_1, α_2, and 5-HT_2 receptors [55]. It also inhibits histamine release from mast cells. Epinastine has a duration of action of at least 8 hours and it is administered twice a day. It is indicated for the prevention of itching associated with allergic conjunctivitis. It can be used safely in patients older than 3 years.

Corticosteroids (Vexol, Lotemax)

Corticosteroids may be extremely effective in relieving symptoms of allergic rhinitis, but because the disease is a chronic, recurrent, benign condition, these drugs should be used only in extreme situations, commonly as a "burst" treatment for no more than 1 to 2 weeks. Topical steroids are associated with glaucoma, cataract formation, and infections of the cornea and conjunctiva [56]. Any prolonged use (ie, longer than 2 weeks) should therefore be used with the greatest caution, and the patient should preferably be monitored by an ophthalmologist. Under no circumstances should patients be allowed to use corticosteroid eye drops without medical supervision or be given prescriptions for unlimited refills.

Fluorometholone 0.1% eye drops are often selected as a useful treatment of external ocular inflammation. This steroid is highly effective in allergic conjunctivitis. It appears that fluorometholone penetrates the cornea well but is inactivated quickly in the anterior chamber. Thus, the complications of fluorometholone are rare. It may be that fluorometholone is inactivated before it has an opportunity to combine with trabecular meshwork or lens receptors. Thus, the incidence of glaucoma and cataract formation is expected to be lower than with prednisolone or dexamethasone.

Two "modified" steroids have recently been investigated for their efficacy in allergic conjunctivitis. Rimexolone (Vexol) (Lehmann, Assil et al 1995) is a derivative of prednisolone that is quickly inactivated in the anterior chamber. During a 4-week treatment period in patients who had uveitis, rimexolone caused an increase in intraocular pressure of 10 mm or more in 5% of patients, whereas prednisolone acetate 1% caused elevation in nearly 14% of patients. In a 6-week steroid-responder study, prednisolone 1% and dexamethasone 0.1% caused mean pressures to rise to 30 mmHg after 3 weeks. Rimexolone and fluorometholone caused mean pressures to rise to only 22 mmHg at 3 weeks and 24 mmHg at 6 weeks. Rimexolone has recently been approved for treatment of postcataract inflammation and for iritis.

Another modified corticosteroid that shows great promise is loteprednol etabonate (Lotemax) (Friedlaender 1995). Lotemax also seems to be highly effective in allergic conjunctivitis and is only rarely associated with a significant rise in intraocular pressure. A low-dose loteprednol etabonate (Alrex) has been approved for the relief of allergic conjunctivitis. Alrex is a useful treatment when mast cell stabilizers have been inadequate.

Other antiallergic drugs are being investigated and show promising results in the treatment of allergic conjunctivitis, including emedastine (Sharif, Xu et al 1995), a selective blocker of the H_1 histamine receptor. Cyclosporine, a fungal antimetabolite that can be used as an anti-inflammatory drug [57,58], inhibits interleukin-2 activation of lymphocytes. It is used systemically to prevent rejection of various solid-tissue transplants. It has been used as an eye drop in a variety of conditions including dry eye vernal conjunctivitis and in high-risk corneal transplants patients. Cyclosporine

appears to interfere with antigen processing and presentation of antigen to the uncommitted T lymphocytes.

Immunotherapy has been successful in treating allergic conjunctivitis and may alter the progression of other atopic conditions [59].

Summary

Allergic conjunctivitis is common, especially during the allergy season. Ocular symptoms are usually accompanied by nasal symptoms, and there may be other allergic events in the patient's history that support the diagnosis of ocular allergy. Diagnostic tests can be helpful, especially conjunctival scrapings, to look for eosinophils. Consultation with the allergist to perform skin tests or in vitro tests may be useful and confirmatory in the diagnosis of ocular allergy. Symptoms may be mild, and many patients do not require treatment. If treatment is necessary, several antiallergic drugs are available. The selection of an antiallergic drug is based on the patient's need and a determination of which drug is well tolerated and most effective. Various antiallergic drugs are available for the eye. Antihistamines, mast cell stabilizers, and NSAIDs are safe and reasonably effective. Corticosteroids are an order of magnitude more potent than noncorticosteroids; however, they have attendant side effects that are best monitored by the ophthalmologist. The development of modified corticosteroids has been a boon to the treatment of ocular allergy because these drugs may reduce potential side effects without sacrificing potency.

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