Blepharitis Management: A Clinical Approach

John R. Favetta, MD

Blepharitis refers to a variety of eyelid conditions with multiple, often concomitant, etiologies. Characterized by eyelid inflammation, bacterial overgrowth or infection—or the risk of infection—is also frequently present in blepharitis. As definitions and sub-categories of blepharitis have changed over the years, clear-cut estimates of prevalence have been challenging to obtain; but blepharitis is very frequently seen in ophthalmology practices. Left untreated, the presence of blepharitis may affect the risk of infection following ocular surgery and can limit the success of contact lens wear. A detailed history and careful attention to the lids, lashes, and meibomian glands during the slit lamp examination will aid in blepharitis detection and diagnosis. At a minimum, treatment includes eyelid hygiene; and acute presentations may benefit from combined anti-inflammatory/antiinfective therapy. Combination agents can be particularly useful in the treatment of blepharitis.

Blepharitis is a catchall term encompassing the many, often overlapping, inflammatory and infectious conditions of the eyelids. Without a single, etiology-based definition, it has not been possible to gain a good idea of the prevalence of blepharitis. But the conditions that comprise blepharitis are among the most common encountered in a comprehensive ophthalmology practice. Indeed, nearly a third of the patients I see—from young adults to seniors—present with signs and/or symptoms of blepharitis.

It is often useful to distinguish types of blepharitis based on anatomical location. Thus, we have anterior blepharitis, which affects the area around the lashes and follicles, and posterior blepharitis, which affects the meibomian glands and proximate tissues. In either form, multiple causative factors and disease processes may be involved; and anterior and posterior blepharitis often coexist.

Comorbidities, including chalazion and hordeolum, conjunctivitis, keratopathy (from superficial punctate keratitis to peripheral ulceration), and dry eye disease may be present with blepharitis.2 Blepharitis affects a broad swath of our patients: we see it in younger patients, who may have associated seborrheic dermatitis or acne rosacea; we see it in contact lens wearers, and in candidates for refractive, cataract, or other ocular surgeries; and we see it in patients who come in simply because they are bothered by its symptoms. I consider it imperative to treat even mild blepharitis, as treatment can reduce the risk of infection and inflammation, and—of particular importance to me as a surgeon—help ensure success for surgical candidates.

PATHOGENESIS
Anterior blepharitis is often associated with excessive bacterial growth on the lid margins. The microbes involved are typically the same species that normally reside there, including Staphylococcus epidermidis and Staphylococcus aureus. While questions remain about the role(s) of bacteria in blepharitis, it appears that toxic exoenzymes produced by the colonizing species—particularly S. epidermidis—irritate the eyelids and ocular surface, causing the release of inflammatory mediators.1

In some cases, altered meibomian gland secretions may be an initiating factor, offering a supportive environment for bacterial proliferation.3 But bacteria can also cause blepharitis, often comprising blepharitis, which may be due to bacterial overgrowth or infection—or the risk of infection. Bacterial proliferation is often concomitant, etiologies. Characterized by eyelid inflammation, bacterial overgrowth or infection—or the risk of infection—is also frequently present in blepharitis. As definitions and sub-categories of blepharitis have changed over the years, clear-cut estimates of prevalence have been challenging to obtain; but blepharitis is very frequently seen in ophthalmology practices. Left untreated, the presence of blepharitis may affect the risk of infection following ocular surgery and can limit the success of contact lens wear. A detailed history and careful attention to the lids, lashes, and meibomian glands during the slit lamp examination will aid in blepharitis detection and diagnosis. At a minimum, treatment includes eyelid hygiene; and acute presentations may benefit from combined anti-inflammatory/antiinfective therapy. Combination agents can be particularly useful in the treatment of blepharitis.

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also alter ocular surface lipids. For example, lipolytic staphylococcal enzymes break down the wax and sterol esters in the tear film; and the release of irritating breakdown products, including free fatty acids, as well as the resulting tear film instability, contribute to inflammation of the lid margin and conjunctiva. A number of potential non-microbial factors (eg, age and hormonal changes, medication use) can contribute to the changes in meibum quality and the ductal keratinization that underlies posterior blepharitis. Obstructive meibomian gland dysfunction (MGD) may not be inflammatory in its early stages, but the tear film changes (instability and hyperosmolarity), ocular surface irritation, increased ductal pressure, and bacterial involvement all contribute to inflammation and frank posterior blepharitis.

**DIAGNOSIS**

In blepharitis diagnosis, history is paramount. Questioning patients about their ocular symptoms throughout the day can be very revealing: when patients describe stickiness and burning upon waking, with improvement through the day and a worsening in the evening, I know to look closely for signs of posterior blepharitis on my examination.

Patients with anterior blepharitis report a gamut of symptoms. Some patients have red and swollen lids; others complain of irritation and burning. Contact lens wearers with anterior or posterior blepharitis may report discomfort and significantly reduced wearing time.

A close look at the lids forms a key part of the examination. Patients with anterior blepharitis often have reddened, swollen lids, telangiectasia, and debris or collarettes along the lashes. In addition, the tear meniscus may be foamy, a result of bacterial lipases causing breakdown of the meibomian lipids. In posterior blepharitis, we often see plugged, pouting meibomian glands that yield turbid, viscous meibum—or no meibum at all. Diagnostic gland expression is helpful in evaluating and grading a patient’s underlying MGD.

Again, because either anterior or posterior blepharitis can affect the ocular surface, corneal and conjunctival staining with lissamine green, rose Bengal, or fluorescein can help identify tissue changes indicative of blepharokeratoconjunctivitis or blepharokeratoconjunctivitis.

**TREATMENT**

Eyelid hygiene is a mainstay of my treatment regimen for virtually every stage and subtype of blepharitis. Cleaning the crust, keratinized tissue, and bacteria and bacterial byproducts off the lid margin removes some contributors to the condition. I recommend any of several commercially available lid cleansing pads for my patients, giving a brief demonstration of their use in the office.

For patients with posterior blepharitis, especially, I also add a hot compress and massage step to follow the cleansing scrub; an omega-3 fatty acid dietary supplement may also be part of the regimen. Lid hygiene may be performed once or twice a day; in cases where I add a topical pharmaceutical agent, I tell patients to instill their final dose of drug after performing their bedtime lid cleaning and warm compresses.

Because blepharitis is often chronic and recurring, I emphasize to patients that even after we bring their acute condition under control, continued eyelid hygiene and warm compresses will help them maintain a healthy ocular surface.

**PHARMACOLOGIC INTERVENTION**

Lid hygiene alone is often insufficient to bring the coexisting and mutually-reinforcing inflammatory and infectious aspects of blepharitis under control. Topical corticosteroids, powerful inhibitors of inflammation, can be extremely useful for treating the acutely inflamed lid margin and ocular surface. The risks associated with corticosteroid use—particularly increased intraocular pressure (IOP) and cataractogenesis—are important considerations when selecting an agent and determining the duration of therapy.

In many cases, the presence of bacterial overgrowth and the risk of superficial ocular infection also warrant the use of an antibiotic in treating blepharitis. A combination antibiotic/steroid agent is therefore well suited to address both the inflammatory and the potentially infectious components of this condition.

My agent of choice for treating blepharitis is ZYLET® (loteprednol etabonate and tobramycin ophthalmic suspension 0.5%/0.3%). The steroid component, loteprednol etabonate 0.5%, is one key reason I favor ZYLET® in the treatment of blepharitis. Loteprednol etabonate combines anti-inflammatory potency with an established safety profile. The loteprednol etabonate molecule contains an ester group in place of a ketone at the C-20 position. In the eye, the drug undergoes predictable hydrolysis into inactive metabolites, which is thought to contribute to its safety profile.

Tobramycin, the antibiotic in ZYLET®, is broadly effective against common ocular pathogens, including the staphylococci often implicated in blepharitis.
I typically prescribe ZYLET® QID for 10 to 14 days, depending on severity. To this I add eyelid hygiene and, where applicable, warm compresses and omega-3 supplements. I bring patients back within about 10 days to evaluate sign and symptom resolution and to check IOP. When I prescribe ZYLET® for blepharitis, I emphasize to patients that it is intended as short-term therapy only, and that long-term continuation of eyelid hygiene should help reduce the likelihood of recurrence.

CONCLUSION

Paying close attention to the lid margins can be beneficial for patients and practitioners. Neither a pristine surgical outcome nor successful contact lens wear is likely without a healthy ocular surface. Indeed, I have postponed surgeries for patients who present with significant blepharitis. To help get the acute inflammation and bacterial overgrowth of blepharitis under control, treatment with ZYLET® can be important.

John R. Favetta, MD, practices in North Arlington, NJ.

Please see Important Risk Information on page 1 and the full prescribing information for ZYLET® on this page and the next.

REFERENCES

8. Zylet (loteprednol etabonate and tobramycin ophthalmic suspension 0.5%/0.3%) prescribing information. Tampa, FL: Bausch & Lomb; Inc, 2013.

BAUSCH + LOMB

Zylet.
Loteprednol etabonate 0.5% and tobramycin 0.3% ophthalmic suspension

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Zylet (loteprednol etabonate and tobramycin ophthalmic suspension) safely and effectively. See full prescribing information for Zylet (loteprednol etabonate and tobramycin ophthalmic suspension, 0.5%/0.3% ophthalmic suspension).

Loteprednol etabonate and tobramycin ophthalmic suspension 0.5%/0.3%.

Initial U.S. Approval: 2004

INDICATIONS AND USAGE

Zylet is a topical anti-infective and steroid combination for steroid-responsive inflammatory ocular conditions for which a corticosteroid is indicated and where superficial bacterial ocular infection or a risk of bacterial ocular infection exists. (1)

- DOSAGE FORMS AND STRENGTHS

Apply one or two drops of Zylet into the conjunctival sac of the affected eye every four to six hours. (2.1)

- CONTRAINDICATIONS

- Use of ocular steroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex). (5.5)
- Fungal infections-Fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid application. Fungal invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. (5.6)

ADVERSE REACTIONS

Most common adverse reactions reported in patients were injection and superficial punctate keratitis, increased intraocular pressure, burning and stinging upon instillation. (6)

- INTRAOCULAR PRESSURE (IOP) INCREASE

In a 42 day safety study comparing Zylet to placebo, ocular adverse reactions included injection (approximately 20%) and superficial punctate keratitis. (3) Adverse reactions have occurred with steroid/anti-infective combination drugs which can be attributed to the steroid component, (6)

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5.3 Delayed Healing
The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation. In those diseases causing thickening of the cornea or sclera, penetrating keratoplasties have been known to occur with the use of topical steroids. The initial prescription and renewal of the medication order should be made by a physician only after examination of the patient with the aid of magnification such as a slit lamp biomicroscopy and, where appropriate, fluorescein staining.

5.4 Bacterial Infections
Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute uveitis, control of the eye signs may mask infection or enhance existing infection. If signs and symptoms fail to improve after 2 days, the patient should be re-evaluated.

5.5 Viral Infections
Employment of a corticosteroid medication in the treatment of patients with a history of herpes simplex requires great caution. Use of ocular steroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex).

5.6 Fungal Infections
Fungal infections of the cornea are prone to develop with long-term local steroid application. Fungal invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal cultures should be taken when appropriate.

5.7 Amniocencephaly/Spina Bifida
Sensitivity to topically applied aminoglycosides may occur in some patients. If hypersensitivity develops with this product, discontinue use and institute appropriate therapy.

4. ADVERSE REACTIONS
Adverse reactions have occurred with steroid/anti-infective combination drugs which can be attributed to the steroid component, the anti-infective component, or the combination.

Zylet
In a 42 day safety study comparing Zylet to placebo, ocular adverse reactions included injection (approximately 20%) and superficial punctate keratopathy (approximately 15%). Increased intraocular pressure was reported in 10% (Zylet) and 4% (placebo) of subjects. Nine percent (9%) of Zylet subjects reported burning and stinging upon instillation.

Ocular reactions reported with an incidence less than 4% include vision disorders, discharge, itching, lacrimation disorder, photophobia, conjunctival discharge, conjunctival papillae, eyelid disorders, and other unspecified eye disorders.

The incidence of non-ocular reactions reported in approximately 14% of subjects were headache; all other non-ocular reactions had an incidence of less than 5%.

5.1 Pregnancy
Reactions associated with ophthalmic steroids include elevated intraocular pressure, which may be associated with intropnic optic nerve damage, visual acuity and field defects, posterior subcapsular cataract formation, delayed wound healing and secondary ocular infections from pathogen(s) of the cornea or sclera. In a controlled clinical study of Zylet 0.5% and Lotemax 0.5%, the incidence of significant elevation of intraocular pressure (≥2 mm Hg) was 2% (10/501) among patients receiving loteprednol etabonate, 7% (17/238) among patients receiving prednisolone acetate 1%, 6% (12/212) among patients receiving dexamethasone 0.1%, and 6% (14/231) among patients receiving corticosteroids (Terry Vision).

In a study of healthy volunteers, the plasma levels of loteprednol etabonate were comparable in the Zylet treatment group compared to Lotemax.

5.5 Viral Infections
The development of secondary infection has occurred after use of combinations containing steroids and antimicrobials. Fungal infections of the cornea are particularly prone to develop coincidently with long-term local steroid application. Fungal invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal cultures should be taken when appropriate.

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Zylet:

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5.6 Fungal Infections

Employment of a corticosteroid medication in the treatment of patients with a history of herpes simplex requires great caution. Use of ocular steroid therapy is not recommended for treatment of herpes simplex keratitis. (5.5) Fungal infections: Fungal infections of the cornea are particularly prone to develop concurrently with long-term topical steroid application. Fungal invasion must be considered in any persistent corneal ulceration where a stromal scar has been identified. (5.5)

ADVERSE REACTIONS:

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FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

See 17 for PATIENT COUNSELING INFORMATION

Rev: 08/2013

2.2 Prescription Guideline

Care should be taken not to discontinue therapy prematurely.

DOSAGE AND ADMINISTRATION

inoculum for ZYLET (loteprednol etabonate and tobramycin ophthalmic suspension) safely and effectively. See full prescribing information for ZYLET (loteprednol etabonate and tobramycin ophthalmic suspension) suspension, 0.5%/0.3%).

4.1 Nonbacterial Etiology

The use of a combination drug with an anti-infective component is indicated where the risk of superficial ocular infection is high or where chronic anterior uveitis and corneal injury from chemical, radiation or thermal burns, or penetration of foreign bodies.

Prolonged use of corticosteroids may result in glucagon with damage to the optic nerve, defects in visual acuity and fields of vision. If this product is used for more than 5 days, IOP should be monitored. (1.1)

• Delayed healing–The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation. In those diseases causing swelling of the cornea or iris, prolonged use of immunosuppressive drugs is contraindicated in most viral diseases of the cornea and conjunctiva including ocular herpes simplex keratitis (zosteriform lesions), keratoconjunctivitis, vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal diseases of ocular structures. (4.3)

- CONTRAINDICATIONS TO STEROID USE: Zylet, as with other steroid anti-infective ophthalmic combination drugs, is contraindicated in certain infectious conjunctivitis where there is no risk of cross-contamination. In chronic anterior uveitis and corneal injury from chemical, thermal burns, or penetration of foreign bodies.

• Severe glaucoma
• Hypersensitivity to any of the components
• Known or suspected fungal infection
• Active eye infection

DOSAGE AND ADMINISTRATION

1. Recommended Dosage

one to two drops of Zylet into the conjunctival sac of the affected eye every four to six hours. During the initial 24 to 48 hours, the dosage may be increased, to every one to two hours. Frequency should be decreased gradually as warranted by improvement in clinical signs. Care should be taken not to discontinue therapy prematurely.

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Corticosteroids inhibit the inflammatory response to a variety of inciting agents and probably delay or slow healing. They inhibit the edema, vasoconstriction, vascular permeability, leukocyte adherence, and local inflammatory reaction associated with inflammation. There is no generally accepted explanation for the mechanism of action of ocular corticosteroids. However, corticosteroids act mainly by decreasing leukocyte adherence, decreasing the vascular permeability, and decreasing the chemotactic response to chemotaxic factors. The effectiveness of corticosteroids in reducing inflammation is related to the dose and duration of therapy and the degree of inflammation present. A topical corticosteroid is more effective in reducing acute inflammatory reactions than in reducing chronic inflammatory reactions.

**12 CLINICAL PHARMACOLOGY**

Loteprednol etabonate is structurally similar to other corticosteroids. However, the number 20 position ketone group is absent. As a result, loteprednol etabonate is not as hydrophobic as other corticosteroids and therefore is not depot formulations used in the treatment of non-infectious anterior uveitis.

Loteprednol etabonate and tobramycin ophthalmic suspension is a sterile, multi-dose topical anti-inflammation corticosteroid and anti-infective combination for ophthalmic use. Each loteprednol etabonate and tobramycin ophthalmic suspension contains loteprednol etabonate and tobramycin.

Chemical name: chloride of loteprednol and chloride of tobramycin.

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