Current and Future Practices in Long-Term Antiinflammatory Therapy for Ocular Surface Diseases

TERRENCE P. O’BRIEN, MD  For patients who require prolonged antiinflammatory treatment for chronic conditions of the ocular surface, optimal management is rooted in a thorough understanding of available agents and tenets of chronic disease management, all the while keeping one eye on a promising pipeline of newer therapies.

Ocular surface disease (OSD) is the common end result for a range of pathogenic processes, including dry eye disease (DED), blepharitis, and ocular allergy. While patient predisposition, initiating triggers, and specific biomolecular pathways are somewhat distinct for each, they share a key pathogenic feature: inflammation.

Within the medical community, the collective awareness and acceptance of inflammation’s role in DED followed a trajectory similar to that of infection as a cause of peptic ulcer disease (PUD). For decades the medical community thought gastric acidity was the main culprit in PUD—until research revealed that Helicobacter pylori played a crucial role.1 As the etiologic paradigm shifted, management strategies expanded to include antibacterials in PUD treatment. Similarly, OSD due to DED was initially thought to result from desiccating stresses (still considered integral to its pathophysiology) without much thought toward downstream effects such as inflammation. Now, inflammation is recognized as a key player in the perpetuation of OSD; as such, antiinflammatory agents have become integral to treatment.2

Patients with mild transient flares of DED, blepharitis, or allergic conjunctivitis require only minimal intervention (eg, hypo-osmolar tear supplements, lid cleansing or compresses) to return to a state of ocular surface homeostasis. Many patients will require at least a brief course of antiinflammatory treatment in addition to artificial tears and adjunctive therapies, such as nutraceuticals, warm compresses, lid hygiene, and neurostimulation. And a significant minority of patients—those with repeated episodes, moderate-to-severe episodes, or sustained OSD inflammation (due to Sjogren’s syndrome, rheumatoid arthritis or other autoimmune conditions)—may require more intensive antiinflammatory treatment over the long term or even indefinitely. These are the patients we will focus on here.

See INSIDE for:
Managing Inflammation After Glaucoma Surgery by Valerie Trubnik, MD, FACS

FIGURE 1 Slit lamp biomicroscopic image of patient with meibomian gland dysfunction and evaporative dry eye demonstrating inspissation of meibomian glands with lid margin telangiectatic blood vessels. (Courtesy of Dr. O’Brien.)
Partnership with Patients

Partnering with patients—educating them about their condition, chronicity, progression, and possible treatment strategies while listening to their concerns—is an invaluable first step when long-term antiinflammatory therapy is needed. Communicating clearly about the aims and rationale for treatment, expectations, and associated risks can help patients feel more in command of their disease, and may improve compliance.

A powerful tool for communicating with patients and encouraging their commitment to long-term antiinflammatory therapy is high-resolution digital photography. Using a slit lamp biomicroscope camera, one can capture, for example, images of eyelids that reveal crusting, meibomian gland congestion, and inflamed blood vessels; or images of the ocular surface that show dryness and irregularities highlighted by vital stains. These images can be instantly shown to patients on the office computer screen (Figure 1).

Establish a Clear Baseline

Patients who may require long-term antiinflammatory therapy should have a comprehensive baseline assessment so that their response to therapy (or lack of response) can be identified and factored into future management decisions. As there is no one test for the diagnosis of DED, blepharitis, or ocular allergy, the choice of tests to perform should follow expert guidelines and clinical judgment.

STATEMENT OF NEED

The control of ocular inflammation is a critical aspect of medical and surgical ophthalmic practice. Despite their side effects, antiinflammatory drugs are used to treat a very wide range of conditions throughout the eye, from ocular surface disease and allergic conjunctivitis to posterior segment conditions. Use of antiinflammatory agents is also critical in ocular surgery, contributing greatly to patient comfort and positive outcomes.

The ocular antiinflammatory landscape is changing as research reveals more about the role of inflammation in a range of ocular conditions. New antiinflammatory agents enter the market.27 Twenty years ago, for example, the idea of using a topical corticosteroid to treat dry eye and/or allergic conjunctivitis was viewed with alarm; today, it is accepted practice.

Although corticosteroids and nonsteroidal antiinflammatory drugs (NSAIDs) have been the mainstays of the ocular anti-inflammatory armamentarium, a number of new agents with novel mechanisms of action (and new ocular drug delivery systems) have come to market or are being made ready for routine use (but nevertheless off-label) uses of corticosteroids and NSAIDs because important differences in efficacy, safety, and tolerability exist between these classes and among formulations within each class.

By putting the latest published evidence into the context of current clinical practice, Topics in Ocular Antiinflammatories equips ophthalmologists to maintain competencies and narrow gaps between their accepted and optimal inflammation management practices, across the range of clinical situations in which current and novel ocular antiinflammatories may be used.

REFERENCES


OFF-LABEL USE STATEMENT

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COMMERCIAL SUPPORTERS

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experience. In addition, performing a Schirmer’s test and an inflammatory biomarker (MMP-9) test such as InflammaDry® (RPS, Sarasota, FL) as well as tear osmolarity testing prior to initiating therapy is advisable to allow for monitoring of aqueous production and surface inflammation, respectively, at future visits (Figure 2).

Inflammatory biomarker testing is helpful because OSD signs and symptoms are commonly discordant; patients with moderate to severe signs may experience little or no discomfort, which can negatively impact adherence. I think of inflammatory biomarker testing as akin to hemoglobin A1c testing in diabetes: positive results indicate a lack of long-term control (of ocular surface inflammation or serum glucose, respectively). Negative results (or normal level in the case of hemoglobin A1c) on a follow-up visit indicate improved control and good response to therapy. The current MMP-9 test does not quantify inflammation (it yields a positive or negative result only) and only detects one of many inflammatory markers. Hopefully, in the future, more specific and sensitive quantitative biomarker tests for inflammation will be developed to facilitate diagnosis and monitoring of ocular surface inflammation.

**Treat Early and Aggressively**

In my experience, it is useful to have a low threshold for treating suspected or proven ocular surface inflammation; and initial treatment should be aggressive when presentation is moderate to severe. The goal is to interrupt the cycle of inflammation, allow normal proinflammatory/antiinflammatory balance to be restored, prevent episode recurrences, and forestall the development of any permanent damage to affected tissues, such as the meibomian glands, goblet cells, accessory lacrimal glands, or the ocular surface.

The current ocular surface antiinflammatory pharmaceutical armamentarium includes corticosteroids, nonsteroidal antiinflammatory drugs (NSAIDs), and small molecule immunomodulator agents (cyclosporine A and lifitegrast). As has been well described, corticosteroids are potent inhibitors of inflammation but carry significant risk for side effects—namely elevated intraocular pressure and secondary glaucoma, cataract formation, and increased risk for infection—when used long term. Corticosteroids with lower risk side effects include fluorometholone and loteprednol etabonate, the latter being a uniquely structured ester-containing corticosteroid that is rapidly hydrolyzed and inactivated on the ocular surface. A pulse of corticosteroid is a good way to initiate therapy for rapid reduction in inflammation, particularly since preferred agents for long-term use—cyclosporine A and lifitegrast—take a period of time to exert their full effect.

NSAIDs, which work by inhibiting prostaglandin synthesis through inhibition of cyclooxygenase enzymes 1 and 2, offer some advantages in controlling inflammation without some of the side effects of the more broadly acting corticosteroids, which work further upstream on phospholipase A2 and other membrane-bound enzymes and receptors. However, NSAIDs should be used cautiously in patients with significant OSD because of potential drying and anesthetic effects along with a past association with corneal melting. A main role for NSAIDs is treatment of postsurgical pain and inflammation and prevention of cystoid macular edema. NSAIDs may also be used as second- or third-line agents in the management of ocular allergy.

Topical ophthalmic immunomodulatory agents cyclosporine A and lifitegrast have more targeted mechanisms of action and are therefore good candidates for long-term use. Cyclosporine A is a fungal derived peptide that inhibits T cell activation and consequently reduces production of pro-inflammatory cytokines (selectively inhibits IL-1). In the normal situation, T-cell receptor activation leads to the influx of calcium (Ca++) into the cytoplasm. Intracellular calcium binds the cytosolic protein calmodulin, which in turn binds and activates calcineurin. This calmodulin/calcineurin complex then dephosphorylates the nuclear factor of activated T cells (NFATc), a transcription factor which translocates into the nucleus and increases the activity of genes coding for IL-2 and other inflammatory cytokines. CsA exerts its action after it enters the cytoplasm of T cells and binds to cyclophilin. The CsA/cyclophilin complex affects T-cell activity by blocking the action of calcineurin and preventing NFATc dephosphorylation. The subsequent reduction in IL-2 levels also reduces the function of effector T cells. Cyclosporin A 0.05% topical suspension (Restasis®; Allergan, Irvine, CA), available for the treatment of DED since 2002, has been shown to reduce inflammation and increase tear production. However, cyclosporine A suspension contains a non-reducing oligosaccharide solubilizing agent as vehicle, which can contribute ocular surface irritation and limit long-term use in some patients. Administering a corticosteroid concomitantly during the initial treatment stage of cyclosporine A therapy can improve tolerability and “jump-start” the antiinflammatory effect until cyclosporine A has time to reach maximal effect and improve tolerability.

Lifitegrast ophthalmic solution 5% (Xiidra®; Shire, Lexington, MA), a lymphocyte function-associated antigen 1 (LFA-1) antagonist, is a newer antiinflammatory immunomodulatory agent approved for the treatment of signs and symptoms of DED and represents a possible alternative to cyclosporine A. Lifitegrast reduces inflammation by blocking a central
mechanism in DED-associated pathogenesis and T cell activation/infiltration into ocular surface tissues. In clinical trials, lifitegrast’s onset of action was as early as 14 days. The most common treatment-related side effects in clinical trials were dysgeusia (unpleasant taste) and instillation site irritation.

Monitor Over the Long Term

Once inflammation is under control, the antiinflammatory regimen should be maintained at the lowest effective dose using the most patient-friendly dosing possible. Patients should be periodically evaluated for response to therapy—perhaps including Schirmer’s test for aqueous production, tear breakup time (TBUT), MMP-9 for inflammation, tear osmolarity testing, and other relevant baseline metrics—side effects, and changes in tolerability to medications. While both lifitegrast and cyclosporine A are generally associated with good long-term tolerability, patients may develop temporary redness, burning upon instillation, and blurring of vision over time.

FUTURE INNOVATIONS

The advances furthest along the development pipeline seem to herald a shift in thinking away from a me-too mindset—that is, making minor changes within an established class to effect a comparable or slightly improved version. Noteworthy technologies with the potential to one day become part of our treatment paradigm include electrostatically charged particles, drug-eluting punctal plugs, mucus-penetrating nanoparticles, and transscleral iontophoresis.

Cyclosporine A Cationic Emulsion

Cationic oil-in-water emulsions are novel formulations that extend the ocular surface residence time of ophthalmic medications. Cationic emulsions contain positively charged (cationic) nanosized droplets that adhere electrostatically to negatively charged ocular surface glycosyl amino glycans, increasing ocular retention and absorption of the active ingredient. Lipids in the emulsion stabilize both the drug and, simultaneously, the tear film.

Cationic emulsions may also have inherent antiinflammatory properties. In an animal model of DED-induced keratitis, a cationic emulsion vehicle reduced corneal staining at least as effectively as the potent glucocorticoid comparator methylprednisolone, indication that these emulsions have ocular surface healing properties independent of the active ingredient.

Recently, a preservative-free cationic emulsion formulation of cyclosporine A called Ikervis® CsA 0.1% CE (Santen, France) has become available in parts of Europe and Asia (and pending approval in Canada) for treatment of severe keratitis in adults with DED unresponsive to artificial tears. The phase 3 SANSIKA trial showed that after 6 months, 0.1% cyclosporine A CE was associated with greater improvement in most efficacy assessments compared with vehicle, including corneal staining (observable by month 3) and inflammatory marker human leukocyte antigen DR, in patients with severe DED (N = 246). The main adverse event reported with cyclosporine A CE was instillation site pain (29.2% vs. 8.9% with vehicle alone), which was mostly mild. Similarly, SICCANOVE, a subsequent phase 3 trial among patients with moderate or severe DED (N = 481) treated for 6 months with 0.1% CsA CE vs. vehicle demonstrated high long-term tolerability and adherence as well as statistically superior efficacy in reducing corneal staining and ocular symptoms.

Sustained-release Dexamethasone

Ocular Therapeutix (Bedford, MA) is investigating a single-use, bioabsorbable, sustained release dexamethasone-loaded intracanalicular depot (punctal plug) which dispenses a tapering dose of dexamethasone onto the ocular surface over the course of up to 30 days after placement. Dextenza™ (dexamethasone insert, 0.4 mg for intracanalicular use), which is currently undergoing FDA review for the treatment of pain following cataract surgery, demonstrated favorable results in phase 3 trials—including reduced pain, anterior chamber flare and cell counts, and need for rescue medication compared with vehicular control. The plug was reported to be well tolerated and, importantly, not associated with significant elevations in intraocular pressure compared with placebo.

The sustained-release dexamethasone-containing punctal plug is also in phase 3 trials for the treatment of chronic allergic conjunctivitis and phase 2 for the treatment of DED. Should research be successful, potential benefits of this product in the treatment of DED (compared to repeated drop use) might include reduced administration burden on the patient, more consistent medication levels on the ocular surface, and reduced medication-related toxicity.

Loteprednol Etabonate Mucus-penetrating Particle

Drug delivery via nanoparticles is hindered by the obstructive properties of the ocular mucin layer, a problem that may be surmounted by a new drug delivery platform, mucus-penetrating particles (MPPs). Drug-loaded MPPs are designed to penetrate the mucin layer, prolong residence time on the ocular surface, and enhance drug delivery to ocular tissues. In animals, loteprednol etabonate 0.4% MMP demonstrated ocular tissue penetration superior to loteprednol etabonate 0.5% gel.

Phase 3 trials investigating loteprednol etabonate 1.0% MPP for treatment of postoperative pain have been completed by researchers at Kala Pharmaceuticals (Waltham, MA).

Top-line results indicate that coprimary endpoints (measures of pain and inflammation reductions) and all secondary endpoints were met in at least one of the trials. Two phase 3 trials investigating loteprednol etabonate 0.25% MPP in the treatment of DED are ongoing.

Ocular Iontophoresis

The Eyegate II® Delivery System (Eyegate Pharmaceuticals, Waltham, MA) is an iontophoresis device designed for transscleral delivery of charged molecules; it is being tested for delivery of a proprietary formulation of dexamethasone phosphate 40 mg/mL EGP-437. Iontophoresis works by applying a
Managing Inflammation After Glaucoma Surgery

**VALEMAR TRUBNIK, MD, FACS** Excessive postoperative inflammation can threaten the success of surgical treatment of glaucoma. Various modes of treatment are appropriate for different patients but may pose different risks in terms of inflammation or complications. Topical corticosteroids and nonsteroidal antiinflammatory drugs are effective in controlling inflammation, but the choice of medication should take into account the risks of adverse reactions.

Despite the emergence of new technologies and implantable devices, conventional trabeculectomy and tube placement remain the most commonly performed methods of lowering intraocular pressure (IOP) in patients with advanced glaucoma. This is attributed to the significant IOP reductions—approximately 50%—observed with such techniques. However, these techniques also pose a relatively high risk—>35%—of postsurgical complications.

**CURRENT TRENDS IN MIGS**

The newer techniques of minimally invasive glaucoma surgery (MIGS), often combined with cataract removal, target either aqueous production or drainage via the trabecular meshwork, suprachoroidal space, or subconjunctival space.

**CONCLUSION**

Patients requiring long-term antiinflammatory treatment of the ocular surface require a more intensive workup, more aggressive treatment, and careful follow-up. Topical cyclosporine A and lifitegrast are excellent choices for long-term antiinflammatory treatment, when needed. Concomitant administration of a corticosteroid taper (preferably one with a strong safety profile) may bring rapid relief until a long-term agent has time to achieve potency. The development of novel formulations and drug delivery techniques will hopefully lessen current difficulties associated with long-term antiinflammatory use, such as low bioavailability, daily dosing schedules, and a potential for side effects.

**O’BRIEN REFERENCES** begin on page 9

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**CORE CONCEPTS**

✦ Different types of surgery target specific approaches to lowering IOP.
✦ Conventional surgery and MIGS are appropriate for different patients and vary in their inflammation risk.
✦ Assessing the patient’s potential for inflammation is critical to the success of surgery.
✦ Controlling inflammation is vital to minimize risk of complications and failure.
✦ Choosing the right steroid and NSAIDs helps to balance inflammation control and the risk of adverse reactions.

The lower risk profile of MIGS compared to conventional trabeculectomy or tube placement makes it attractive for cases of mild to moderate glaucoma that are not adequately controlled by topical medication or trabeculoplasty. Cytophotocoagulation (CPC) reduces aqueous production by laser coagulation of ciliary bodies. Transcleral CPC is usually indicated for severe glaucoma with limited visual potential, and where medication and conventional surgery have failed, showing IOP reductions of up to 45%. Endocyclophotocoagulation (ECP), while often indicated in similar cases, can also be used to safely treat mild-to-moderate glaucoma showing modest IOP reductions of 10% to 14.5%. Micropulse transcleral diode CPC (MP-TCP), utilizing the IRIDEX Cyclo G6™ laser system, is a milder approach that may be appropriate for
patients who have greater visual potential due to the lower risk of complications, although clinical experience suggests it may be less effective in reducing IOP.

Targeting trabecular outflow either by partial disintegration of the juxtacanalicular meshwork (eg, Trabectome®) or insertion of stents that bypass the trabecular meshwork (eg, iStent-inject®, Hydrus®) is appropriate for mild to moderate open-angle glaucoma. Trabectome® and iStent-inject® are capable of delivering approximately 40% IOP reductions, while the Hydrus®, which is not yet FDA approved, shows IOP reductions of 26%. Implants targeting suprachoroidal drainage can be used in addition to other approaches. CyPass® can provide approximately 35% IOP reduction, and the iStent-Supra® (not yet FDA approved) confers a greater than 20% reduction in IOP. The subconjunctival space offers a third, non-physiological route for increased aqueous drainage and is a target site for MIGS that potentially reduces IOP further than those utilizing trabecular outflow or the suprachoroidal space. IOP reductions of more than 40% have been achieved with the XEN®45 Gel Stent®, and reductions of more than 50% have been achieved with InnFocus MicroShunt® (not yet FDA approved).

FDA APPROVAL STATUS OF MIGS DEVICES
- Trabectome® (NeoMedix Corporation): FDA approved
- IRIDEX Cyclo G6™ (IRIDEX Corporation): FDA approved
- iStent-inject® (Glaukos): FDA approved
- CyPass® (Alcon): FDA approved
- XEN®45 Gel Stent (Allergan): FDA approved
- iStent-Supra® (Glaukos): Not yet FDA approved
- Hydrus™ (Ivantis): not yet FDA approved
- InnFocus MicroShunt® (Santen): not yet FDA approved

Laser trabeculoplasty can be considered an alternative or adjunct to topical medication. Argon laser trabeculoplasty (ALT) and selective laser trabeculoplasty (SLT) provide similar IOP reductions to topical medication and are time-efficient procedures associated with a low risk of complications. The more recently developed micropulse laser trabeculoplasty (MLT) is less destructive than ALT and, like SLT, does not cause scarring of the trabecular meshwork. MLT appears to deliver similar IOP reductions to SLT and ALT.

HAZARDS OF POSTOP INFLAMMATION

Excessive postoperative inflammation from glaucoma surgery is a significant concern due to its potential to either raise or lower IOP and impact visual acuity. Associated inflammatory cytokine production, which induces cell migration and proliferation, tissue remodeling, and subsequent scarring around the filtration site (Figure 1), can lead to poor filtration, changes in IOP, and ultimately failure of the surgery. Conversely, significant inflammation can lead to loss of ciliary body activity and reduced production of aqueous fluid, resulting in hypotony. Iritis (anterior uveitis) is the most common type of inflammation encountered after surgery, but posterior uveitis and cystoid macular edema are also possible.

The likelihood of postoperative inflammation and scarring is greater with conventional surgeries than with MIGS. Clinical experience suggests differences in risk of inflammation among MIGS; for example, ECP can induce more inflammation than the iStent® and Trabectome®. While SLT induces transient inflammation, the energy levels used correlate with both the degree of IOP reduction and inflammatory response.

RISK FACTORS FOR POSTOP INFLAMMATION

When considering surgical approaches for treating glaucoma, it is important to assess the patient’s propensity for inflammation. For example, clinical experience suggests that patients with preexisting uveitis, cystoid macular edema, or diabetic macula edema are at a higher risk of developing postsurgical inflammation; thus ECP may not be the best choice in such situations. Similarly, immunocompromising conditions, such as rheumatoid arthritis and lupus, are associated with an increased risk of uveitis and postoperative fibrosis. In such cases, scarring can occur quickly even when preoperative symptoms are minimal and the condition is only detectable through blood analysis. Controlling systemic inflammation before surgery often leads to better outcomes by reducing the risk of postsurgical complications.

African descent is also a risk factor for failure of glaucoma surgery: African-American patients have a tendency to develop inflammation and scar more rapidly than Caucasians. The use of glaucoma drainage implants is likely to be a more suitable approach than a trabeculectomy for these patient populations.

Assessing the condition of the ocular surface is important to assess the patient’s inflammatory potential. For patients who have been on topical glaucoma medication for many years, there is a benefit in switching them to low-dose steroids and oral glaucoma medication such as Diamox® for two weeks prior to surgery.

ASSESSING POSTOP INFLAMMATION

Early identification of the signs and symptoms of postoperative inflammation is critical to the success of glaucoma surgery. At the postsurgical visit, patients should be queried regarding any symptomatic ocular pain, discomfort, itching,
visual fluctuations, and/or visual decline. Further, assessments of IOP, visual acuity, appearance of the corneal surface, and flare in the anterior chamber are important, as are investigations into any signs of conjunctival or periorbital infection and even macular inflammation. For a procedure that creates a bleb—such as a trabeculectomy, tube shunt or XEN® implant—the thickness and degree of vascularity of the bleb should also be examined.

Infection is potentially one of the most serious complications following filtration surgery and must be excluded as a cause of inflammation. Infections can occur days or even years after surgery.26 Symptoms and concerns reported by the patient are important in identifying postsurgical complications: the sudden onset of pain, redness, or blurred vision could indicate blebitis, which may progress to endophthalmitis (Figure 2).27 In such instances, a microbiological work-up should be performed quickly and the infection treated aggressively. Often the infection is treated immediately without waiting for the results and the antibiotic choice can be tailored accordingly after the results of the cultures come back.26

CORTICOSTEROIDS AND NSAIDS

Post-surgical inflammation can be managed with topical corticosteroids supplemented with nonsteroidal anti-inflammatory drugs (NSAIDs) to guard against subsequent complications.24 The choice of corticosteroid requires careful consideration and is influenced by the type of procedure, the length of time the patient is likely to require medication, and the likelihood of an adverse response. Certainly, corticosteroids can result in raised IOP, possibly via impaired trabecular outflow due to reduced degradation or increased deposition of extracellular matrix.29

For patients who have undergone trabeculectomy, tube placement, or XEN® implant procedures, prednisolone acetate administered 4 times per day for 4 weeks and then tapered for 4 weeks, supplemented with NSAIDS for 4 to 6 weeks is effective. The more potent diluprednate may be more effective in patients with uveitis when administered twice daily, although care should be taken as it can occasionally induce large spikes in IOP that are difficult to treat.30 Following MIGS, a lower dose corticosteroid such as loteprednol starting at four drops per day and tapered over 4 weeks can be used. If patients have scarring or a very vascularized bleb, corticosteroids may be continued for longer. Conversely, if there are signs of a steroid response, steroids should be tapered faster. Vigilance is required in postsurgical care of glaucoma patients to monitor for inflammation and IOP spikes.

NSAIDs that can be applied once per day are also options. Clinical experience suggests that branded NSAIDs are easier to administer and less likely to cause irritation, keratopathy, visual acuity decline, and corneal surface issues than generic ketorolac. The transient inflammation induced by SLT does not usually require treatment with NSAIDs or steroids, and studies demonstrate similar outcomes irrespective of whether patients are treated for inflammation.31,32

Oral steroids are rarely necessary. If a patient presents with hypotony, ciliary body shutdown, and closely apposed choroidal effusions (kissing choroids), oral steroids could be considered. Patients that are being treated for preexisting uveitis may have already been prescribed oral NSAIDS. Pre- or postoperative cyclosporine can improve the corneal surface and reduce pain after trabeculectomy34 and may be especially critical for patients with a long history of topical glaucoma medication use. Human amniotic membrane, which is commonly used to promote healing of ocular surface disorders,35 may improve outcomes for patients with preoperative dry eye.

PATIENT COMPLIANCE

Patient compliance and cost of medications are major issues in the management of postoperative inflammation. New drug delivery methods have the potential to reduce the patients’ need for postsurgical medication. For example, transzonal injections of antibiotics and steroids during cataract and combined cataract-MIGS surgery have been shown to improve the overall patient experience.36 Dextenza™, a punctal plug inserted into the tear duct for long-term dexamethasone delivery, is currently undergoing clinical evaluation in the US.37 Nonetheless, these new developments will not remove the need for careful monitoring of postsurgical complications including inflammation and steroid-induced IOP spikes.

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REFERENCES

TRUBNIK REFERENCES continue on page 9
1. Which of the following is NOT a rationale for sharing digital photographs of inflamed periocular and ocular tissues with patients in the office?
   A. To enhance commitment to treatment
   B. To help them better understand their symptoms and condition
   C. To supply images for their Instagram page
   D. To establish a loose basis for tracking improvement

2. Excessive inflammation can lead to:
   A. Scarring, poor filtration, higher IOP
   B. Loss of ciliary body activity, reduced aqueous production, hypotony
   C. Scarring, poor filtration, age-related macular degeneration
   D. All of the above

3. Which of the following conditions has NOT been associated with increased risk for OSD?
   A. Ocular allergy
   B. Dry eye disease
   C. Blepharitis
   D. All may be associated with OSD

4. In addition to artificial tears and adjunctive therapies, what course of antiinflammatory treatment will many patients require?
   A. Nutraceuticals
   B. Warm compresses
   C. Neurostimulation
   D. All of the above

5. What are the risk factors for developing postsurgical inflammation?
   A. Rheumatoid arthritis
   B. African descent
   C. Pre-existing macular edema
   D. All of the above

6. Which of the current pipeline therapies or technologies is NOT currently in development for the treatment of DED?
   A. Cationic emulsion of cyclosporine A
   B. Mucus-penetrating particle formulation of loteprednol etabonate
   C. Oral formulation of lifitegrast
   D. Sustained-release dexamethasone-eluting punctal plug

7. The most common and effective approach to controlling IOP in advanced glaucoma is:
   A. Trabectome and iSTENT
   B. Trabeculectomy
   C. Tube placement
   D. B and C

8. A possible adverse reaction to corticosteroid use is:
   A. Reduced aqueous outflow and raised IOP
   B. Increased aqueous production and raised IOP
   C. Increased aqueous outflow and hypotony
   D. Reduced aqueous outflow and hypotony

9. Blebitis would be suspected in cases of:
   A. Blurred vision
   B. Eye pain
   C. Redness
   D. A, B and C

10. Topical first line therapy for long-term (months to years) antiinflammatory treatment for chronic or severe OSD may include:
    A. Cyclosporine A
    B. Lifitegrast
    C. A mild corticosteroid
    D. A or B
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To obtain CME credit for this activity, go to http://cme.ufl.edu/ed/self-study/toai/

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