Incorporating Cyclosporine Ophthalmic into Your Treatment Regimen

Adding this advanced medication presents few issues for clinicians.

Unlike other medications, cyclosporine ophthalmic emulsion, 0.05% (Restasis) presents few challenges as you incorporate it into your practice. In fact, if your practice is similar to mine, you may already have had dry eye patients asking for this new therapy, perhaps after hearing about it in a dry eye support group.

Typically, these patients have gone from doctor to doctor in a fruitless search for relief. Now for the first time, we have a medication that can treat the cause of dry eye.

If you spend a little extra time with these frustrated patients to explain cyclosporine ophthalmic, how it works and what to expect, your dry eye patients will be extraordinarily grateful. In fact, my office has received letters thanking us for this new therapy.

Diagnosing dry eye

Incorporating cyclosporine ophthalmic into your treatment regimen starts with your diagnosis. Watch for a variety of symptoms. These can range from mild irritation to far more serious effects (see “Symptoms to Watch For”).

Besides a Schirmer test, make sure to do supersacral staining of the conjunctiva and cornea. Fluorescein, while helpful, doesn’t stain the early signs of dry eye, which involves loss of mucin that protects the ocular surface. Lissamine green and rose bengal facilitate a more accurate assessment. They aid the dry eye diagnosis by showing the classic conjunctival staining in the interpalpebral fissure. In severe cases, you’ll see frank corneal staining in the fissure.

Be sure to look for lid disease at the same time. Commonly, you’ll find meibomian gland dysfunction as well as dry eye. Decreased tear production is worsened if the tear film doesn’t have a lipid coating.

Educate patients

When incorporating cyclosporine ophthalmic into my treatment regimen, I make sure to spend time explaining dry eye and the treatments available to the patient. Remember some dry eye patients have had the disease all their lives. This warrants extra time for education.

I tell my patients that many treatment options are available and we’ll proceed in a stepwise fashion,
increasing the level of treatment based on their response. This can help prevent patients from seeking help elsewhere if they don’t get results from the first-line therapy offered.

In talking about cyclosporine ophthalmic, I tell patients that dry eye isn’t an involutional change that’s part of aging. Rather, it’s a disease where inflammatory cells have invaded the lacrimal gland. This damages the tear gland, causing a decrease in both quality and quantity of tear production.

**Step by step**

Here's the stepwise progression of treatment I currently use. We’ll likely develop more concrete algorithms as we learn more about the response to treatment.

First, I consider whether the dry eye is inflammatory. If the patient has a history of collagen vascular disease and mild dry eye, I’ll recommend transiently preserved artificial tears. If the dry eye doesn’t resolve, I’ll prescribe cyclosporine ophthalmic at the next visit.

If the patient has moderate dry eye and pre-existing systemic collagen vascular disease that’s dramatically predisposed to inflammatory damage to the lacrimal gland (Sjögren’s syndrome), I’ll start him on cyclosporine ophthalmic immediately. Generally, these are patients with rheumatoid arthritis, lupus or Hashimoto’s thyroiditis. Interestingly, patients without collagen vascular disease but with moderate dry eye have exactly the same T-cell infiltration of their lacrimal glands, which is why cyclosporine works equally well on these patients.

If the patient has collagen vascular disease and requests cyclosporine ophthalmic, I have no problem prescribing it on the first visit. Also, if a patient with dry eye and collagen vascular disease quickly worsens, I’ll prescribe cyclosporine ophthalmic immediately.

After prescribing cyclosporine ophthalmic, if the dry eye hasn’t resolved in 6 months, I’ll add

---

**Candidate Profile for Cyclosporine Ophthalmic**

<table>
<thead>
<tr>
<th>CANDIDATES</th>
<th>CANDIDATES</th>
<th>CANDIDATES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occasional Symptoms</td>
<td>*Frequent to Chronic Symptoms</td>
<td>Nonfunctioning Lacrimal Glands</td>
</tr>
<tr>
<td>Tears Used ≤ 3 Times Daily</td>
<td>*Frequent Tear Users</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tears Used &gt; 4 Times Daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td>*Functioning Lacrimal Glands</td>
<td></td>
</tr>
</tbody>
</table>

*Cyclosporine ophthalmic emulsion, 0.05% (Restasis) is indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca.

---

**PHOTO**

T/K

Rose Bengal Staining

Rose bengal staining shows characteristic triangular shaped interpalpebral pattern in patient with moderately severe keratoconjunctivitis sicca.

Be sure to look for lid disease. Meibomian gland dysfunction is a common companion to dry eye disease.
other more traditional therapies, such as ointments and punctal plugs.

Note that for a patient with inflammatory ocular disease who has dry eye, I’ll use cyclosporine ophthalmic instead of punctal plugs as first-line therapy. Inflammatory mediators reside in the tear film, meaning that plugs often will exacerbate the dry eye. Using plugs after cyclosporine ophthalmic makes sense because the drug improves both the quality and the quantity of the tear film.

I may place punctal plugs before cyclosporine ophthalmic for a patient who develops moderate dry eye after LASIK. This is because the dry eye in this case likely is related to neurotrophic issues rather than inflammatory disease.

Fewer tears

Cyclosporine ophthalmic lessens the need for artificial tears because patients start making endogenous tears. Also, patients get instant relief because cyclosporine ophthalmic has a vehicle that’s similar to the one used with Refresh Endura, an emulsion-based lubricant eye drop.

Note, though, that cyclosporine takes a month to have a clinical effect, and the effect doesn’t maximize for 6 months. Make sure to explain to your patient that he should use the medication for a minimum of 3 months, and preferably 6 months. Most patients will continue to need artificial tears but will use significantly fewer than before starting on cyclosporine. I always recommend a transiently preserved tear, such as Refresh for mild to moderate dry eye and a nonpreserved unit-dose tear for severe dry eye patients (see “Expectations for the First Months of Cyclosporine Therapy”).

Over the long term, a certain subclass of patients will be able to taper off cyclosporine ophthalmic. However, those with collagen vascular disease and dry eye will likely need cyclosporine ophthalmic indefinitely, perhaps taking the drug once or twice a week instead of twice a day.

Dealing with irritation

The FDA has warned not to use cyclosporine ophthalmic for patients with a hypersensitivity to the drug or for those with active ocular infection. One in seven patients will experience ocular burn-
Therapy for Moderate DryEye

One typical patient who’d benefit from cyclosporine ophthalmic emulsion, 0.05% (Restasis) is a 50-year-old woman without systemic disease whose dry eye symptoms have increased as she enters menopause. She may also be taking antibiotics or anti-allergy medications.

This patient might complain of ocular irritation and excessive blinking, especially when driving with the heat or air conditioning on. She may also have become contact lens intolerant for the first time in years.

After taking her history, looking for symptoms of dry eye, I’d examine the lids for signs of blepharitis and then examine the tear film looking for meniscus height and debris. Next, I’d add lissamine green looking for conjunctival and/or corneal staining.

This patient might have some superficial punctate keratitis ([DR. D: CORRECT?]) on the corneal surface, but significantly more interpaperal conjunctival staining. Finally, I’d perform a Schirmer test with anesthesia; results would likely be 3 mm to 8 mm after 5 minutes.

After discussing the cause of dry eye, I’d start this patient on a transiently preserved tear four times a day. If she didn’t improve symptomatically after a month, I’d reexamine her, looking specifically at conjunctival and corneal staining. If there was still no improvement, I’d discuss using cyclosporine, but I wouldn’t start it yet.

If conjunctival staining improved but symptoms continued, I’d increase the tears to 8 times a day and add a nonpreserved ointment at night and see her again in 1 month. If signs and symptoms persisted at her next visit, I’d start cyclosporine.

When starting this patient on cyclosporine, I’d explain that improvement would be gradual and chances were 1 in 7 she might experience ocular burning for a few weeks. I’d see this patient at 3 months and 6 months to monitor progress and adjust therapy as needed.

I generally ask patients to taper their transiently preserved tears as needed. If they continue to be symptomatic at 6 months, I’ll place temporary punctal plugs.

Patients who wear contact lenses can also use cyclosporine ophthalmic. I instruct them to wait 15 minutes after they instill the drop before they apply their lenses.

Finally, cyclosporine ophthalmic costs, on average, a little more than $100/month, which is more expensive than artificial tears. I explain to patients that this is an advanced medication and will likely improve symptoms better than artificial tears. Also, chances are that the patient’s drug plan will reimburse him for the medication.

For a patient with inflammatory disease who has dry eye, I’ll use cyclosporine ophthalmic instead of punctal plugs as first-line therapy.

Postmenopausal dry eye

Besides collagen vascular disease, women can experience postmenopausal dry eye as an inflammatory eye disease. These patients tend to worsen over time from lower levels of circulating androgens.

I treat these patients the same as those with collagen vascular disease, starting with artificial tears. If they don’t get relief and continue to have conjunctival or corneal staining, I prescribe cyclosporine ophthalmic. These patients do very well with cyclosporine ophthalmic.

Other considerations

Patients can use cyclosporine ophthalmic with transiently preserved artificial tears. However, I instruct them to wait an hour after instilling cyclosporine ophthalmic before instilling tears to avoid washing the drug out of the eye.

Dr. Donnenfeld practices at Ophthalmic Consultants of Long Island in Rockville Centre, N.Y.