
News in Review

COMMENTARY AND PERSPECTIVES

Dry Eye: A Harbinger of Sjögren Syndrome

Sjögren syndrome (SS) can be blinding and has many other serious implications, but dry eye is an early harbinger of the disease. These are the major findings of a retrospective review of 163

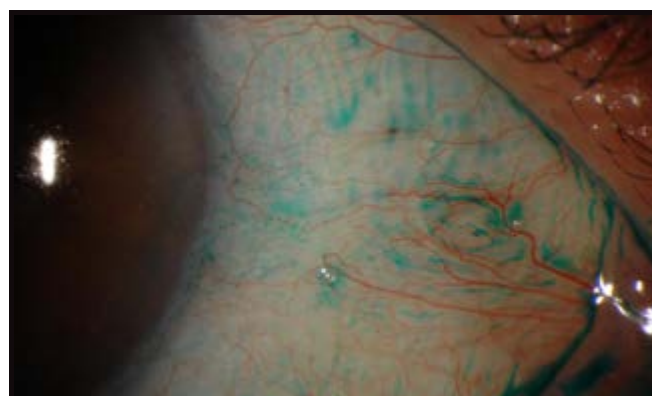
patients with primary SS—the first large, longitudinal case series of its kind.¹

An early clue. After discovering that 1 in 10 patients with clinically significant dry eye had underlying SS, researchers at Johns Hopkins—from both the Sjögren's Syndrome Center and the Ocular Surface Disease and Dry Eye Clinic—wanted to shed greater light on this multisystem autoimmune disease.

The researchers evaluated consecutive Sjögren's patients from January 2007 to May 2011 and found that nearly all had a history of dry eye, with a mean dura-

tion of 10.4 years before presentation. In addition, a quarter had one or more other ocular manifestations, such as sterile corneal necrosis, uveitis, or scleritis. Patients with vision-threatening complications (13 percent) were four times more likely to have serious systemic problems related to SS such as peripheral neuropathy, interstitial nephritis, or vasculitis.

Too often trivialized. Dry eye and dry mouth may be the hallmarks of SS, a disease characterized by lymphocytic infiltration of exocrine glands. However, the story clearly doesn't



MORE THAN DRY EYE? Slit-lamp appearance of significant lissamine green staining of the bulbar conjunctiva within the interpalpebral fissure. This should alert ophthalmologists to the possibility of an underlying autoimmune disease, most likely Sjögren syndrome.

end there, as evidenced by the study's findings—the syndrome can significantly affect a patient's mood, cognitive function, and levels of energy or pain. Lymphoma is one of its most serious complications.¹

"Unfortunately, none of this is well recognized," said lead author Esen K. Akpek, MD, director of the Ocular Surface Disease and Dry Eye Clinic at Wilmer Eye Institute in Baltimore. "In fact, many specialists, including ophthalmologists, tend to trivialize Sjögren's and its

accompanying dry eye," she said, adding that she, too, minimized its significance when first starting to see patients with SS.

Be on the lookout for Sjögren's. Given its diverse and nonspecific presentation, diagnosis of the syndrome can be delayed for many years.¹ Dry eye offers a critical clue, said Dr. Akpek, but ophthalmologists don't routinely screen for it, though its symptoms occur in as many as 20 million Americans. In addition, she said, the standard protocol

for dry eye testing used in the study—Schirmer testing, tear film break-up time, and ocular surface dye staining—is typically followed only by dry eye specialists.

It's even less common for ophthalmologists to be on the lookout for Sjögren's, said Dr. Akpek, perhaps because many aren't aware of the varied ocular manifestations of the disease, which include inflammation in any part of the eye, not just

the ocular surface. Over half of the patients with vision-threatening ocular findings in the study were undiagnosed with SS at the time of presentation.

The clinician's role.

When seeing patients with clinically significant dry eye—complaints of dry eye confirmed by appropriate testing—the physician should have a high index of suspicion for Sjögren's or another underlying autoimmune disease, said Dr.

Akpek. It's important to note that the vast majority of patients with SS are women—91 percent in the current study.

"A quick review of systems may then uncover other signs such as dry mouth, fatigue, joint pain, gastrointestinal problems, or shortness of breath," she said. Depending upon the systems affected, it's advisable to order a workup for conditions associated with dry eye, especially if there's

a family history of autoimmune disease. She added that, although still unproven, some biologic therapies show promise in managing SS, especially when the disease is diagnosed early.

—Annie Stuart

1 Akpek EK et al. *Ophthalmology*. Published online Aug. 29, 2014.

Dr. Akpek has received institutional research grants from Allergan and has consulted with Nicox.

Diabetes & the Eye

Fenofibrate Slows DR Progression

A study investigating medical interventions to reduce heart disease in persons with diabetes yielded important clinical recommendations for the eyes.¹ Specifically, the cholesterol-lowering drug fenofibrate appears to reduce the risk of progression of diabetic retinopathy (DR). The Action to Control Cardiovascular Risk in Diabetes (ACCORD) Eye Study also confirmed the importance of intensive glycemic control to reduce DR progression.

The Eye Study (n = 2,856) looked at a subset of patients in the primary ACCORD study (n = 10,251), which investigated treatments to affect cardiovascular disease (CVD) outcomes in patients with type 2 diabetes who had CVD or CVD risk factors. "The participants studied in ACCORD are

very typical type 2 diabetic patients," said Emily Y. Chew, MD, deputy director of the Division of Epidemiology and Clinical Research at NEI and head of the Eye Study group.

Earlier results confirmed. While glycemic control has long been a cornerstone in the management of diabetes, the findings on fenofibrate and dyslipidemia add something new to the armamentarium. Fenofibrate increases HDL cholesterol and reduces triglycerides, which can be markedly elevated in diabetes.

The four-year follow-up findings reaffirm what the Eye Study group reported in 2010: Controlling glycemia and dyslipidemia significantly slows the progression of DR, but controlling blood pressure to 120 mmHg showed no benefit in slowing DR progression.

Interestingly, all three interventions—lowering lipids, blood glucose, and blood pressure—failed to have an effect on CVD. In fact, the primary ACCORD study was stopped early because of increased mortality in those treated in the glycemic control group.

Fenofibrate findings. In the dyslipidemia arm of the study, patients received a statin (simvastatin) plus either placebo or fenofibrate. The fenofibrate effect was minimal among subjects without DR at baseline. In that group, progression occurred in 11.7 percent of the placebo group and 11.4 percent of the fenofibrate/statin group. But among patients with DR at baseline, only 3.1 percent of the fenofibrate/statin group progressed, compared with 14.6 percent of the placebo group. No major adverse effects were seen with this regimen, and the DR benefit was so robust that the researchers recommend considering fenofibrate for treatment of DR.

The beneficial effect of daily fenofibrate on DR progression was reported earlier by the Fenofibrate Interven-

tion and Event Lowering in Diabetes (FIELD) study.²

The ophthalmologist's role. Ophthalmologists will probably not be prescribing fenofibrate, said Dr. Chew, because its use requires follow-up for systemic side effects. But they should discuss with patients the importance of their lipid status on diabetic retinopathy and other systems.

"We have proven that lipid management is very important for the treatment of diabetic retinopathy. The serum lipids need to be in good control, and fenofibrate probably should be considered, especially for those unable to achieve good glycemic control," she said. "Fenofibrate has been around for years and is relatively inexpensive and appears to have a real effect on the progression of diabetic retinopathy."

—Miriam Karmel

1 Chew EY et al. *Ophthalmology*. Published online Aug. 26, 2014.

2 Keech AC et al. *Lancet*. 2007; 370(9600):1687-1697.

Dr. Chew reports no related financial interests.

Cosmetic Cautions

Eye Whitening May Be Hazardous to Eye Health

Eye whitening is touted as a cosmetic procedure that transforms tired, red, “dirty-looking” eyes into bright, healthy-looking specimens. But ophthalmologists who have treated its consequences warn of potentially severe complications.

How does the procedure work? To eliminate conjunctival hyperemia or pigmentation, the eye-whitening procedure involves extensive resection of bulbar conjunctiva with intraoperative and postoperative mitomycin C (MMC) therapy. It has been compared to pterygium excision, but in pterygium surgery, only abnormal conjunctiva is removed. In eye whitening, an extensive amount of normal conjunctiva

is resected, and grafts are generally not used to cover the area, said Sophie X. Deng, MD, PhD, associate professor of ophthalmology at the Jules Stein Eye Institute, University of California, Los Angeles. “Loss of such a large amount of normal tissue on the eye surface likely leads to instability and recurrent ulceration,” she said. In addition, the use of MMC may impair wound healing on bare sclera.

The procedure, popularized in South Korea, has gained a foothold in the United States. Several proprietary methods exist, which vary in technical details.

Range of complications. Some of the possible consequences were reported by



SEVERE COMPLICATIONS. Scleral melt beneath a calcific plaque in a patient who had eye whitening.

doctors at three institutions who treated nine patients (17 eyes) who’d undergone eye whitening at the hands of one surgeon.¹ All study eyes developed persistent conjunctival erosions and scleral thinning. Nine of those eyes progressed to scleral ulceration, and one developed endophthalmitis. Other complications included calcific degeneration of the sclera, secondary limbal stem cell deficiency, and infectious scleritis.

Although the current study did not assess the complication rate, other authors have reported compli-

cation rates between 56 and 92 percent.¹

A long-running case.

In one case, treatment of endophthalmitis secondary to scleral melt included two rounds of intravitreal antibiotics followed by an amniotic patch graft and a scleral patch graft plus 60 sessions of hyperbaric oxygen. Subsequently, the patient developed recurrent scleral thinning and inflammatory uveitis. Four years later, she was on daily doses of oral cyclosporine, mycophenolate mofetil, and prednisone.

The authors urge aggressive treatment of the ocular surface in patients with early symptoms. “This eye-whitening procedure can lead to sight-threatening complications,” Dr. Deng said. “We believe that the risks outweigh the benefit.”

—Miriam Karmel

1 Vo RC et al. *Am J Ophthalmol*. Published online July 26, 2014.

Dr. Deng reports no related financial interests.

Cataract & AIDS

Role of Accelerated Aging

Highly active antiretroviral therapy (HAART) has reduced the incidence of opportunistic infections among individuals with AIDS. In those who respond to HAART, AIDS has become a chronic disease with an expectation of long-term survival. However, signs of accelerated aging may accompany longer survival.

Higher incidence, ear-

lier onset. To explore this hypothesis, investigators studied the risk of cataract in 1,606 participants (3,212 eyes) who had AIDS—but no opportunistic ocular infections.¹

Among 2,812 eyes that were initially free of cataract and were followed longitudinally for a median of 4.6 years, the cataract incidence was 0.37 percent per eye-year. Both the age-adjusted

risk of cataract and the age-specific incidence of cataract surgery were higher than in a comparable survey of the general population.

Implications of “accelerated aging.” “Cataract may be a marker of dysfunctional aging, and so there was interest in whether patients with AIDS would have accelerated cataract formation,” said lead author John H. Kempen, MD, PhD, professor of ophthalmology and epidemiology at the Perelman School of Medicine, University of Pennsylvania.

“Our study lacked a contemporaneous comparison

group followed under the same protocol. Nonetheless, in perhaps the best feasible study of the matter, the age-adjusted risk of cataract and cataract surgery appears to be higher for patients with AIDS free of ocular opportunistic infections. As the population living with AIDS grows, the burden of cataract in this group probably will grow substantially.”

—Marianne Doran

1 Kempen JH et al. *Ophthalmology*. Published online Aug. 8, 2014.

Dr. Kempen reports no related financial interests.