Researchers find low risk of COVID-19 transmission in tears
Study did not detect virus in tears of infected patients

By Lynda Charters

DAY AFTER DAY, new information is added to the current knowledge about the severe acute respiratory syndrome COVID-19 virus and how it works. While it currently is clear that the virus is transmitted in droplets spread through coughing and sneezing by infected patients, a new study found that the virus does not persistently in younger patient populations.

The National University Hospital Department of Ophthalmology, Singapore, offers an example of infection control strategies at the National University Hospital Singapore. Armed with this knowledge, ophthalmologists may be able to balance the infectious disease risks with continuing care for ophthalmology patients during this period, prompting this perspective of infection control strategies at the National University Hospital Singapore.

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Researchers found no evidence of the virus in the tears of 64 patients who were not infected with COVID-19. The study was published in the Journal of Ophthalmology.

In this study, the investigators collected 64 tear samples from patients who had been tested for the virus in Singapore between February 26 and March 13, 2020. The patients had no symptoms of COVID-19; they were being tested as part of routine care for the virus. The investigators found no evidence of the virus in any of the samples.

The researchers said their findings suggest that the virus is not transmitted through tears. They noted that this finding is consistent with other research showing that the virus is not transmitted through saliva. However, they said more research is needed to confirm these findings.

The researchers said their findings are important because they suggest that ophthalmologists and other health care providers can continue to perform eye procedures without fear of transmitting the virus through tears.

Reference:
1. Data on file, Aerie Pharmaceuticals, Inc.

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Researchers find low risk of COVID-19 transmission in tears

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DAY AFTER DAY, new information is added to the current knowledge about the severe acute respiratory syndrome COVID-19 virus and how it works. While it currently is clear that the virus is transmitted in droplets spread through coughing and sneezing by infected patients, a new study found that the virus does not seem to be present in the tears of those patients.

“Transmission through infected ocular tissue or fluid has been controversial. It is hypothesized that the nasolacrimal system can act as a conduit for viruses to travel from the upper respiratory tract to the eye,” said researchers. “Hence, ocular tissue and fluid may represent a potential source of the virus,” the investigators said.

Before appearances in Europe, North America, South America, and Africa, Singapore experienced local transmission in multiple clusters across the country.

The National University Hospital Department of Ophthalmology, a high-volume ophthalmology center in Singapore, offers an example of infection control measures implemented in the setting of COVID-19 infections that may be of value as other ophthalmology clinics begin to experience and plan for potential increases of COVID-19 risks.

Armed with this knowledge, ophthalmologists may be able to balance the infectious disease risks with continuing care for ophthalmology patients during this period, prompting this perspective of infection control strategies at the National University Hospital Department of Ophthalmology, Singapore.

Lead author Ivan Seah Yu Jun, MBBS, and colleagues from the National University Hospital and several other institutions in Singapore set out to determine in a prospective study if the virus is transmitted in tears by assessing for its presence using quantitative reverse transcription polymerase chain reaction (RT-PCR).

In this study, the investigators collected 64 tear samples from 17 patients with the virus at different time points following the onset of the initial symptoms (range, days three to 20). The samples were collected from both eyes of the patients using Schirmer's test strips over the course of the study with 12, 28, and 24 samples, having been obtained during the first, second, and third weeks of the initial symptoms, respectively, and then analyzed by RT-PCR. All patients had tested positive for the infection by

Continues on page 12: MGD

Recently, the American Society of Cataract and Refractive Surgery (ASCRS) published an algorithm for the preoperative diagnosis and treatment of OSD, including dry eye. This algorithm suggests screening for OSD using non-invasive techniques prior to any refractive surgery. If visually significant OSD is detected, delaying surgery until after the patient’s OSD is resolved is recommended.

Addressing OSD (including dry eye) is important from both a patient and a clinician perspective.

By improving ocular surface health, symptomatic patients (and those who did not realize they were symptomatic in the first place) may notice less burning and/or irritation. Patients that suffer from symptoms or show signs of dry eye may benefit from treatment, including refractive and cataract surgical patients (patients receiving either a monofocal or an advanced technology intraocular lens [AT-IOL]).

Continues on page 26: COVID-19

Device Technology

Addressing MGD with thermal pulsation system

Targeting disease may refine cataract surgery preoperative measurements

By Ivan Mac, MD, MBA;
Special to Ophthalmology Times®

Affecting more than 30 million Americans, dry eye disease is a chronic condition that, in addition to being highly prevalent in the elderly, is being diagnosed more consistently in younger patient populations.

Multiple factors contribute to the increasing prevalence of dry eye, including increased screen time and dietary factors (e.g., low consumption of omega-3). Up to 86% of patients with dry eye show signs of the complex, multifactorial disorder known as meibomian gland dysfunction (MGD).

In obstructive MGD patients, the meibomian glands located in the upper and lower eyelids are blocked. Reduced meibum secretion may result in changes to the composition of the tear film, leading to quicker tear evaporation, eye irritation, inflammation, and ocular surface disease (OSD).

Continues on page 12: MGD

Issue Highlights

Imaging
Widefield retinal imaging in pediatric ophthalmology practice

Gene Therapy
Endophthalmitis detection by whole genome sequencing and qPCR

Surgery
New minimally invasive surgery for bleb leaks developed

Therapeutics
Investigational topical corticosteroid demonstrates efficacy for dry eye

Continues on page 12: MGD
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The most commonly reported adverse reactions at ≥2% are eye irritation, posterior capsule opacification, increased intraocular pressure, and anterior chamber inflammation.

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Device Technology

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Use of a thermal lid pulsation device can prove to be an important component of routine treatment practice.

10 FEMTOSECOND LASER-ASSISTED RLE OFFERING BETTER OUTCOMES
Pairing the refractive lens exchange with presbyopia-correcting IOL offers patient satisfaction.

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COVID-19 TEAR TRANSMISSION
A research team has found that there is a low risk of viral shedding in the tears of patients with COVID-19.

+ COVID-19 ONLINE COVERAGE
A roundup of COVID-19 coverage, including videos, available now online. PAGE 24

ON THE COVER
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21 BLEB LEAKS TREATED WITH MINIMALLY INVASIVE CONJUNCTIVAL SURGERY
An surgeon offers a simple, safe procedure for treating bleb leaks by injecting lidocaine.
We are all getting acclimated to a new kind of normal

Mike Hennessy Sr., Chairman and founder of Ophthalmology Times® parent company, MJH Life Sciences

THE NATION CONTINUES to deal with the COVID-19 pandemic, and we continue to provide information you need to know in print and online.

The Ophthalmology Times® team continues to be the voice of reliable coverage of the coronavirus, detailing the facts without any hype. For the latest ophthalmology-related information, you can follow us on social media. You also can find coverage online at OphthalmologyTimes.com/Coronavirus.

In this issue, we offer a roundup of some video content we offer online. Check out Page 24 for this information.

On the cover of this issue, our clinical diagnosis content includes research that shows there is little risk of viral shedding in the tears of patients with COVID-19. The National University Hospital Department of Ophthalmology, a high-volume ophthalmology center in Singapore, offers an example of infection control measures implemented in the setting of COVID-19 infections that may be of value as other ophthalmology clinics begin to experience and plan for potential increases of COVID-19 risks.

Device technology shares our front page in this issue, with Ivan Mac, MD, MBA, examining the use of a thermal lid pulsation device as an important component of routine practice for the treatment of meibomian gland dysfunction. Inside, R. Luke Rebenitsch, MD, discusses femtosecond laser-assisted refractive lens exchange with presbyopia-correction intraocular lenses, which he says achieves excellent refractive and visual outcomes.

Gene Therapy coverage with Cecilia Lee, MD, MS, details how worse outcomes after development of endophthalmitis postoperatively are associated with the presence of bacteria and higher bacterial loads of pathogens other than Staphylococcus epidermidis as detected by whole-genome sequencing and quantitative polymerase chain reaction.

In our surgery core, Neel R. Desai, MD, discusses how preoperative treatment of ocular surface disease is an asset that many cataract surgeons tend to undervalue. He maintains that treating OSD prior to surgery is an important goal in itself, not a speed bump on the road to surgery. We also talk to Neeru Gupta, MD, PhD, MBA, who explains how bleb leaks can be treated with minimally invasive surgery.

We also offer some interesting information in our therapeutics section, as Elizabeth Yeu, MD, details an investigational corticosteroid that demonstrates efficacy for dry eye. She explains that results of a two-week phase III study demonstrate efficacy of loteprednol etabonate ophthalmic suspension 0.25% found the investigational treatment was well-tolerated and had a favorable safety profile. We also talk to Jose Gomes, MD, PhD, who explains how crosslinking may be adjunctive treatment for infectious keratitis. He points out that several factors are prompting researchers to consider new approaches to treat corneal disease.

We also offer a special section that looks at the challenges of examining visual fields in children. According to Mitchell Strominger, MD, this work can be challenging, and OCT may be a good place to start. He explains that physicians should be aware that some children compensate for their visual field defects, with, for example, head turns related to visual field loss that are not related to strabismus.

What’s Trending
See what the ophthalmic community is reading on OphthalmologyTimes.com

1 Pearls for handling glaucoma cases amid COVID-19 pandemic
OphthalmologyTimes.com/Coronavirus/GlaucomaCasePearls

2 Astigmatism: A ‘clear-as-mud’ concept to patients
OphthalmologyTimes.com/Astigmatism/ClearAsMud

3 AAO: New recommendations to EyeMDs for urgent, nonurgent care amid COVID-19
OphthalmologyTimes.com/AAOEyeMDRecommendations
**INDICATION**

DEXTENZA is a corticosteroid indicated for the treatment of ocular inflammation and pain following ophthalmic surgery.

**IMPORTANT SAFETY INFORMATION**

**CONTRAINDICATIONS**

DEXTENZA is contraindicated in patients with active corneal, conjunctival or canalicular infections, including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella; mycobacterial infections; fungal diseases of the eye, and dacryocystitis.

**WARNINGS AND PRECAUTIONS**

Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. Steroids should be used with caution in the presence of glaucoma. Intraocular pressure should be monitored during treatment.

Corticosteroids may suppress the host response and thus increase the hazard for secondary ocular infections. In acute purulent conditions, steroids may mask infection and enhance existing infection.

Use of ocular steroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex).

Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal culture should be taken when appropriate.

Use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation.

**ADVERSE REACTIONS**

The most common ocular adverse reactions that occurred in patients treated with DEXTENZA were: anterior chamber inflammation including iritis and iridocyclitis (10%); intraocular pressure increased (6%); visual acuity reduced (2%); cystoid macular edema (1%); corneal edema (1%); eye pain (1%) and conjunctival hyperemia (1%).

The most common non-ocular adverse reaction that occurred in patients treated with DEXTENZA was headache (1%).

*Please see brief summary of full Prescribing Information on adjacent page.*
HHS using ‘discretion’ in HIPAA probes
No penalties for some infractions during pandemic

By Chris Mazzolini

THE U.S. HEALTH and Human Services Department (HHS) announced that it was exercising “discretion” in pursuing HIPAA privacy violations during the COVID-19 pandemic.

“The Office for Civil Rights (OCR) at the U.S. Department of Health and Human Services (HHS) announced, effective immediately, that it will exercise its enforcement discretion and will not impose penalties for violations of certain provisions of the HIPAA Privacy Rule against healthcare providers or their business associates for the good faith uses and disclosures of protected health information (PHI) by business associates for public health and health oversight activities during the COVID-19 nationwide public health emergency,” reads a news release.

The revised rules were issued to support federal public health authorities and health oversight agencies, like the Centers for Disease Control and Prevention (CDC) and Centers for Medicare and Medicaid Services (CMS), state and local health departments, and state emergency operations centers who need access to COVID-19 related data, including protected health information (PHI). The HIPAA Privacy Rule already permits covered entities to provide this data, and this announcement now permits business associates to also share this data without risk of a HIPAA penalty.

“The CDC, CMS, and state and local health departments need quick access to COVID-19 related health data to fight this pandemic,” said Roger Severino, OCR Director, in the news release. “Granting HIPAA business associates greater freedom to cooperate and exchange information with public health and oversight agencies can help flatten the curve and potentially save lives.”

COVID-19 also is altering how patients approach healthcare, and the impact of these changes could last long after the pandemic is over, according to a survey of 500 healthcare consumers in the United States by healthcare consultancy Sage Growth Partners and Black Book Market Research.

Concerns about the safety of healthcare settings is driving more interest in telemedicine, such as virtual visits and remote health monitoring. In fact, 59% of survey respondents said they are more likely to use telehealth services now than in the past, and 36% would switch their physician in order to have access to virtual care.

The Centers for Medical and Medicaid Services (CMS) recently announced in a press release it released a number of new policies to help physicians and hospitals during the pandemic. These actions include Medicare coverage for telephonic services, significant additions to the list of covered telehealth services, such as emergency visits, greater clarity on the use of remote patient monitoring for acute conditions like the virus and allowing Ambulatory Surgery Centers to contract with local healthcare systems to provide hospital services.

CMS sets and enforces essential quality and safety standards for the nation’s healthcare system, and is the nation’s largest health insurer serving more than 140 million Americans through Medicare, Medicaid, the Children’s Health Insurance Program, and Federal Exchanges.

Providers also can bill for telehealth visits at the same rate as in-person visits. Telehealth visits include emergency department visits, initial nursing facility and discharge visits, home visits, and therapy services, which must be provided by a clinician that is allowed to provide telehealth. New as well as established patients now may stay at home and have a telehealth visit with their provider.

In addition, CMS is allowing physicians to supervise their clinical staff using virtual technologies when appropriate, instead of requiring in-person presence.
Ophthalmology Times

Ophthalmology Times is a physician-driven media brand that presents cutting-edge advancements and analysis from around the world in surgery, clinical diagnosis, therapeutics, device technology, imaging, and gene therapy to elevate the delivery of progressive eye health from patient to physician.

Ophthalmology Times’ vision is to be the leading content resource for ophthalmologists.

Through its multifaceted content channels, Ophthalmology Times will assist physicians with the tools and knowledge necessary to provide advanced quality patient care in the global world of medicine.
Echoes of history
COVID-19 pandemic stirs memories, tests our mettle

A LOYAL Ophthalmology Times® reader shared with me a recent illuminating editorial on the history of physicians’ responses to plagues and the duties of us doctors in the current coronavirus epidemic. The author, a cardiologist, notes that multiple medical societies assert that physicians have no right to deny care to patients in order to protect themselves or their family members:

The AMA, in 1847, issued a Code of Medical Ethics stating that “When pestilence prevails” its members have a duty “to face the danger, and to continue their labors for the alleviation of suffering, even at the jeopardy of their own lives.” This remains the AMA’s stand today.

The American College of Physicians asserts that “the ethical imperative for physicians to provide care” overrides “the risk to the treating physician, even during epidemics.”

In a fascinating bit of history, the author then describes cases when physicians fell far short of idealistic standard:

When the Antonine Plague struck Europe from 165 to 180 A.D., about one-third of the population died and many of the Roman legions that ensured peace and stability were rendered inoperative. Terror-stricken physicians, including the famous Galen, fled cities such as Rome for the safer countryside.

In 1382, Venice, Italy passed a law forbidding doctors from leaving the city.

In 1793, many distinguished Philadelphia physicians fled the city in the face of a yellow fever epidemic. Closer to our own time, he describes “health workers” abandoning patients during an Ebola epidemic in the Democratic Republic of Congo in 1995, and points out that a SARS outbreak in Toronto in 2003 saw “many health care workers refusing to show up at their jobs.” So much for policy statements by medical associations!

When I think about this issue, I recall my father’s experience. Medical schools in the United States were shortened to three years during World War II in order to speed the arrival of doctors to war zones where they were desperately needed to care for soldiers and injured civilians.

After a quick one-year fellowship in surgery, my father was sent to California and placed on a hospital ship where he would perform trauma surgery on the U.S. soldiers who would be invading the Japanese home islands. His older brother, an orthopedic surgeon, was already in the Philippines. Because of the fierce defense that was anticipated, the expectation was for 250,000 U.S. casualties in this phase of the war.

Because the hospital ships would need to be fairly close to the action, they would be attacked by Japanese Naval vessels and aircraft. My father and his family thought there was a reasonable chance he would not survive, and the nurse who he had asked to marry him declined because she did not want to marry a military doctor a week before he shipped off to war and never see him again. “Ask me again when you come home” she told him.

He was scared, but never considered trying to avoid the assignment he had been given. He knew his skills would be needed by the young soldiers who were his countrymen.

As it turned out, my father’s ship was leaving San Francisco harbor when news was received that an atomic bomb had been dropped on Hiroshima. By the time the ship arrived, the war had ended. He stayed in Japan for two years, running a hospital and performing surgery on both American and Japanese soldiers as well as Japanese civilians. After his two years were over, he returned to New Jersey and civilian life, and the pretty nurse who had waited for him said “yes” this time around (fortunately, for my sisters and me).

A lengthy career as an ophthalmologist has ill-prepared me to help care for patients with respiratory disease or to have any useful knowledge of ventilators. But if my colleagues in medicine or the emergency room think I can be helpful, I will try my best. My family history leaves me no choice.

REFERENCE
- Sandeep Jauhar, M.D. In a Pandemic, Do Doctors Still Have a Duty to Treat? New York Times, April 2, 2020
Xiidra® (lifitegrast ophthalmic solution) 5% is indicated for the treatment of signs and symptoms of dry eye disease (DED).

**Important Safety Information**

Xiidra is contraindicated in patients with known hypersensitivity to lifitegrast or to any of the other ingredients.

In clinical trials, the most common adverse reactions reported in 5-25% of patients were instillation site irritation, dysgeusia and reduced visual acuity. Other adverse reactions reported in 1% to 5% of the patients were blurred vision, conjunctival hyperemia, eye irritation, headache, increased lacrimation, eye discharge, eye discomfort, eye pruritus and sinusitis.

To avoid the potential for eye injury or contamination of the solution, patients should not touch the tip of the single-use container to their eye or to any surface.

Contact lenses should be removed prior to the administration of Xiidra and may be reinserted 15 minutes following administration.

Safety and efficacy in pediatric patients below the age of 17 years have not been established.

**References:**


There’s no FDA-approved therapeutic equivalent. Check out patient resources, insurance coverage, and more at Xiidra-ECP.com
Surgical intervention for childhood glaucoma

XIIDRA® (lifitegrast ophthalmic solution), for topical ophthalmic use
Initial U.S. Approval: 2016

BRIEF SUMMARY: Please see package insert for full prescribing information.

1 INDICATIONS AND USAGE
Xiidra® (lifitegrast ophthalmic solution) 5% is indicated for the treat-
ment of the signs and symptoms of dry eye disease (DED).

4 CONTRAINDICATIONS
Xiidra is contraindicated in patients with known hypersensitivity to
lifitegrast or to any of the other ingredients in the formulation [see Adverse Reactions (6.2)].

6 ADVERSE REACTIONS
The following serious adverse reactions are described elsewhere in the labeling:

- Hypersensitivity [see Contraindications (4)]

6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in clinical trials of a drug cannot be
directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In five clinical studies of DED conducted with lifitegrast ophthalmic
solution, 1401 patients received at least one dose of lifitegrast
(1287 of which received lifitegrast 5%). The majority of patients
(84%) had ≤ 3 months of treatment exposure. One hundred-seventy
patients were exposed to lifitegrast for approximately 12 months. The
majority of the treated patients were female (77%). The most common
adverse reactions reported in 5%-25% of patients were instillation-
site irritation, dryness, and decreased visual acuity.

Other adverse reactions reported in ≥ 1% patients were blurred
vision, conjunctival hyperemia, eye irritation, increased lacrimation,
eye discharge, eye discomfort, eye pruritus, and sinusitis.

6.2 Postmarketing Experience
The following adverse reactions have been identified during post-
approval use of Xiidra. Because these reactions are reported volun-
tarily from a population of uncertain size, it is not always possible to
reliably estimate their frequency or establish a causal relationship
to drug exposure.

Rare cases of hypersensitivity, including anaphylactic reaction, bron-
chospasm, respiratory distress, pharyngeal edema, swollen tongue,
and urticaria have been reported. Eye swelling and rash have been
reported [see Contraindications (4)].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary
There are no available data on Xiidra use in pregnant women to inform
any drug-associated risks. Intravenous (IV) administration of lifitegrast
to pregnant rats, from pre-mating through gestation Day 17, did not
produce teratogenicity at clinically relevant systemic exposures.

Intravenous administration of lifitegrast to pregnant rabbits during
organogenesis produced an increased incidence of omphalocoele at
the lowest dose tested, 3 mg/kg/day (400-fold the human plasma
exposure at the RHOD, based on the area under the curve [AUC] level). Since human sys-
temic exposure to lifitegrast following ocular administration of Xiidra
at the RHOD is low, the applicability of animal findings to the risk of
Xiidra use in humans during pregnancy is unclear [see Clinical Phar-
macology (12.3) in the full prescribing information].

Data
Animal Data
Lifitegrast administered daily by IV injection to rats, from pre-mating
through gestation Day 17, caused an increase in mean pre-implantation
loss and an increased incidence of several minor skeletal anomalies
at 30 mg/kg/day, representing five, 400-fold the human plasma expo-
sure at the RHOD of Xiidra, based on AUC. No teratogenicity was
observed in the rat at 10 mg/kg/day (460-fold the human plasma
exposure at the RHOD, based on AUC). In the rabbit, an increased
incidence of omphalocoele was observed at the lowest dose tested,
3 mg/kg/day (400-fold the human plasma exposure at the RHOD,
based on AUC), when administered by IV injection daily from gesta-
tion Days 7 through 19. A fetal no observed adverse effect level
(MDAEL) was not identified in the rabbit.

8.2 Lactation

Risk Summary
There are no data on the presence of lifitegrast in human milk, the
effects on the breastfed infant, or the effects on milk production.

However, systemic exposure to lifitegrast from ocular administration
is low [see Clinical Pharmacology (12.3) in the full prescribing infor-
mation]. The developmental and health benefits of breastfeeding
should be considered, along with the mother’s clinical need for Xiidra
and any potential adverse effects on the breastfed child from Xiidra.

8.4 Pediatric Use

Safety and efficacy in pediatric patients below the age of 17 years
have not been established.

8.5 Geriatric Use

No overall differences in safety or effectiveness have been observed
between elderly and younger adult patients.

Manufactured for:
Novartis Pharmaceuticals Corporation
One Health Plaza
East Hanover, NJ 07936
T2019-110

Study details safety, effectiveness with use of MIGS device

By Cheryl Guttman Krader;
Reviewed by Alana L. Grajewski, MD

Surgical intervention for childhood glaucoma

Single-incision ab interno trab-
euclecetomy with the Trab360
(SightSciences) provided safe
and effective treatment for childhood glaucomas, accord-
ing to the findings of a retro-
spective multicenter study.

sized outcomes from 46 eyes of 41 pa-
ients who ranged in age from one to 325
months (median 12 months) when they
underwent the minimally invasive glau-
coma surgery (MIGS).

After a median follow-up of 14.5 months,
median IOP was reduced from 30 mm Hg
(range 18 to 49 mm Hg) preoperatively to
18 mm Hg (range 5 to 40 mm Hg). Fur-
thermore, the surgery was associated with
a decrease in medication burden. Median
number of medications fell from 2.5 (range
0 to 5) preoperatively to 1 (0 to 4).

Success, defined as postoperative IOP ≤
24 mm Hg with or without medications,
no additional surgery needed to control
IOP, and absence of devastating or severe
complications was achieved in two-thirds
of eyes. With eyes categorized by diagnos-
sis, subgroup analyses showed the high-
est success rate was achieved in eyes with
primary congenital glaucoma (PCG), which
was also the most common diagnosis in
the series (45.5%). Of 21 eyes with PCG,
81% met the criteria for success. Exclud-
ing three eyes with PCG that had under-
gone prior glaucoma surgery, the success
rate was 83.3%.
Cycldialysis occurred in two eyes (4.3%). One required surgical treatment and the other resolved spontaneously.

There were no other significant complications, according to the study.

EARLY RESEARCH
The study authors pointed out that theirs is the first study to critically evaluate outcomes of the Trab360 procedure to treat childhood glaucomas. They observed that the success rates reported correspond well with those published previously for childhood glaucoma angle surgery.

The study authors pointed out that theirs is the first study to critically evaluate outcomes of the Trab360 procedure to treat childhood glaucomas.

Noting that the MIGS device used in the surgeries has been replaced by its manufacturer with new technology (OMNI Surgical System), the authors also suggested that the findings of the study could be generalized to any “sufficiently similar technique” of single-incision ab interno trabeculotomy.

However, they also noted that there is a learning curve for safe use of the Trab360 device and that the procedures were performed by surgeons with significant experience performing angle surgery in children.

MORE DETAILS
The children were operated on by one of four surgeons practicing at four different academic centers. Children needed to have sufficient corneal clarity to undergo the ab interno procedure. To be included in the retrospective analysis, they were required to have at least three months of postoperative follow-up.

A variety of childhood glaucoma types were represented in the series. According to the study, subgrouping of the cases by diagnosis was based on the World Glaucoma Association’s Childhood Glaucoma Classification System.

Aside from PCG, other diagnoses were glaucoma associated with a nonacquired systemic disease or syndrome (17%), juvenile open-angle glaucoma (13%), glaucoma following cataract surgery (11%), glaucoma associated with an acquired condition (8.5%), and glaucoma associated with a nonacquired ocular anomaly (4%).

Researchers pointed out that success was achieved in 83% of eyes with juvenile open-angle glaucoma, 60% of those with glaucoma following cataract surgery, 50% of those with glaucoma associated with a nonacquired systemic disease or syndrome, and 50% of those with glaucoma associated with an acquired condition.

Neither of the two eyes with glaucoma associated with a nonacquired ocular anomaly achieved success.

Acknowledging that the numbers of eyes in each subgroup is small, the authors suggested that the MIGS procedure could be considered reasonable for treatment of eyes with uveitic glaucoma or glaucoma after cataract surgery prior to resorting to a glaucoma drainage device, trabeculectomy, or a cyclodestructive procedure.

The most common reason for failure was the need for additional surgery, either for IOP control or to address complications. Of the 15 failures, 12 occurred within the first three months after surgery.

SAFETY CONSIDERATIONS
The authors acknowledged that the research was subject to the limitations inherent in a retrospective analysis. They also observed the need for cost analyses, but suggested that the cost associated with the device itself could be offset by its benefits relative to a 360-degree ab externo procedure for reducing operating time and duration of general anesthesia exposure in children.

CONCLUSIONS
The authors acknowledged that the research was subject to the limitations inherent in a retrospective analysis. They also observed the need for cost analyses, but suggested that the cost associated with the device itself could be offset by its benefits relative to a 360-degree ab externo procedure for reducing operating time and duration of general anesthesia exposure in children.

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None of the study authors had any financial conflict of interest to report.

in case you missed it

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Bleb leaks treated with minimally invasive conjunctival surgery PAGE 21

PACK-CXL researchers clearing hurdles of topical drugs PAGE 29

next issue...

> Innovative Procedures in Cornea and Presbyopia

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MGD

(Continued from page 1)

It is estimated that up to 34% of patients at a routine eye care practice may have dry eye.

Experience at Metrolina Eye Associates suggests that up to 80% of patients at a cataract/refractive practice can show objective signs or symptoms of dry eye, and in many instances, these symptoms may have been undetected for some time. Therefore, my practice of aggressively treating dry eye was born of necessity.

Clinicians today have an array of tools at their disposal to optimize pre-operative measurements for both refractive and cataract procedures, including biometry, optical coherence tomography, intraoperative aberrometry, and premium phacoemulsification platforms (Centurion Vision System, Alcon).

Despite these technological advancements, the value of any tests conducted pre-operatively depends on having a healthy ocular surface, especially because dry eye causes fluctuating vision. With the recent, and uptake of AT-IOIs, accurate refractive readings going into cataract surgery are critical to minimize the risk of implanting the wrong lens, avoid under- or over-correcting astigmatism, and maximizing vision potential.

MANAGING MGD

In treating dry eye, the underlying disease mechanism must be considered; the eyelids are often identified as a cause of dry eye, with many patients having MGD. The current approach to addressing MGD at Metrolina Eye Associates involves thermal lid pulsation with a thermal pulsation system (iLUX, Alcon).

The Alcon system is cleared by the FDA with clinically demonstrated results in reducing the signs and symptoms of MGD.

The hallmarks of the system include its portability, rapid treatment for patients, and significant improvements in MGD symptoms. Typically, after an initial iLUX treatment, patients will experience objective improvements in Meibomian Gland Score, tear break-up time, and ocular surface disease index.

Taking the time to address MGD, in general routine eye care as well as prior to refractive or cataract surgery, may help refine cataract surgery pre-operative measurements and improve ocular health.

Patients who are satisfied with their pre-operative care are likely to bring repeat business and refer their family and friends. If a patient exhibits signs of MGD, it is important to take the time to explain the disease to them (including its chronic, progressive, and irreversible nature), outline their treatment options, and highlight that the thermal pulsation system addresses the root cause of MGD (i.e., clears blocked meibomian glands) and supports a holistic approach to reducing the signs and symptoms associated with MGD. Even though this conversation only requires two minutes of time, it garners trust from patients and helps to set reasonable expectations.

At Metrolina Eye Associates, the majority of patients who have been treated with the thermal pulsation system have experienced a reduction in the signs and symptoms of MGD.

The thermal pulsation system was first implemented at Metrolina Eye Associates’ clinics approximately 1.5 years ago. Since that time, each clinic has been outfitted with one system and these devices have been used to treat thousands of patients with MGD.

When adopting the thermal pulsation system as part of standard MGD management practice, only minor hurdles were encountered, including ensuring the device was always charged and that enough sterile tips were consistently on-hand. Treatments last less than 10 minutes.

There is a spectrum of eye care professionals whose patients may exhibit the signs and symptoms of MGD and could benefit from treatment with the thermal pulsation system. I urge other eye care professionals to take the time and initiative to identify MGD and consider adopting the use of a thermal lid pulsation device as an important component of routine practice. Addressing MGD is important not only to reduce the signs and symptoms of MGD, but also to optimize cataract surgery pre-operative measurements, patient comfort, and overall ocular health.

IMPORTANT PRODUCT INFORMATION

Indication: The iLUX® Device is indicated for the application of localized heat and pressure therapy in adult patients with chronic disease of the eyelids, including Meibomian Gland Dysfunction (MGD), also known as evaporative dry eye.

Contraindications:

Do NOT use the iLUX Device in patients with the following conditions: Patients whose pupils have been pharmacologically dilated; patients who have undergone ocular surgery within prior 12 months; patients with ocular injury or trauma, chemical burns, or limbal stem cell deficiency (within prior 3 months); patients with active ocular herpes zoster or simplex of eye or eyelid or a history of these within prior 3 months; patients with cicatricial lid margin disease; patients with active ocular infection, active ocular inflammation or history of chronic, recurrent ocular inflammation within prior 3 months; patients with an ocular surface abnormality that may compromise corneal integrity; patients with lid surface abnormalities that affect lid function in either eye, patients with aphakia; or patients with permanent makeup or tattoos on their eyelids.

Warnings/Precautions:

Federal law restricts this device to sale by or on the order of a licensed healthcare practitioner.

The Disposable may not fit all eyes, such as eyes with small palpebral surfaces. Use of the iLUX device is NOT recommended in patients with the following conditions: moderate to severe allergic, vernal or giant papillary conjunctivitis; severe eyelid inflammation; systemic disease conditions that cause dry eye; in patients who are taking medications known to cause dryness; or patients with punctal plugs.

Potential Adverse Reactions:

Potential adverse effects may include eyelid/eye pain requiring discontinuation of the treatment procedure, eyelid irritation or inflammation, temporary redness of the skin, ocular surface irritation or inflammation (e.g., corneal abrasion, conjunctival edema or conjunctival injection (hyperemia)), and ocular symptoms (e.g., burning, stinging, tearing, itching, discharge, redness, foreign body sensation, visual disturbance, sensitivity to light).

Attention: Please refer to the User Manual for a complete list of contraindications, instructions for use, warnings and precautions for the iLUX® Device.

BY IVAN MAC, MD, MBA

Dr. Mac is a consultant and/or speaker for Alcon, Allergan, Kala Therapeutics, Newday, Sun Pharmaceuticals; and an investor with Ellex, Tear Film Innovations/TearClear/Equi- one, CorneaGen/NeoSight (Investor), and Visionary Opthalmic Group.
Ultra-widefield imaging adding depth to pediatric ophthalmology

Physicians finding technology has a major role to play in managing ROP

By Lynda Charters; Reviewed by Anthony T. Moore, BM Bch, FRCOphth

Ultra-widefield imaging has added a whole new dimension to fundus imaging in children, with up to 200 degrees of the retina now visible compared with standard fundus photography that provides 30 to 50 degrees of visibility.

Two ultra-widefield imaging systems, the RetCam (Clarity Medical Systems) providing 120 to 130 degrees of view and the Optos (Optos Inc.) 200 degrees, according to Anthony T. Moore, BM Bch, FR-COphth, professor of ophthalmology at the University of California San Francisco School of Medicine, San Francisco.

“These systems also are capable of fluorescein angiography [FA],” he said.

The RetCam, a contact lens-based system, requires pupillary dilatation and clear media and although the imaging can be performed in awake preterm infants or neonates older children need to be sedated. The RetCam system is useful in the operating room to document fundus images at examination under anesthesia.

“The RetCam images are available in real time but the resolution is low,” Dr. Moore noted. “The system has video capability and is particularly useful for FA in the operating room.”

The Optos is a confocal dual-laser system, can be used in awake patients of any age.

“This system is ideal for use in a clinic setting. In a pediatric ophthalmology practice, it can be used in young infants using a ‘flying baby’ technique with or without using a speculum,” he said. “A disadvantage however is the lack of real-time imaging. It has a useful fundus autofluorescence mode and FA and indocyanine green angiography capabilities.”

EFFECTS ON PRACTICE

The RetCam system, Dr. Moore pointed out, has revolutionized the care of patients with retinopathy of prematurity (ROP) and retinoblastoma. Many institutions are currently using telemedicine for ROP screening in remote areas.

It is also useful for in patient consultations for children with suspected nonaccidental injury and in other situations, such as viral retinitis, where there needs to careful documentation of the retinal findings. Dr. Moore noted that the system is less valuable for use with older children and adults unless they are sedated.

He described the case of a 14-month-old boy who presented with leukocoria in the right eye. The left fundus appearance was normal. During an examination in the OR a diagnosis of Coat’s disease was made and FA was performed using the RetCam in video mode, which allowed the full extent of the retinovascular abnormalities to be identified and treated.

Repeat imaging seven months following laser treatment indicated a good response to treatment with no further vascular leakage: retinal detachment had been prevented.

The Optos widefield system can be used in the clinic in patients with or without pupil dilatation it can be used in awake infants with or without a speculum. The FA and FAF capabilities are also helpful. However, Dr. Moore noted the importance of having a highly skilled technician when using this instrument.

In the case of an infant born prematurely at 25 weeks gestation and now 39.5 weeks, using a speculum, the ROP could be seen to be regressing. The retina was visible out to the peripheral ridge of neovascularization.

“This approach is more comfortable for the infant than when the physician uses the indirect ophthalmoscope and scleral depression,” Dr. Moore noted. Another beneficial use of this technology was demonstrated in the case of a 5-month-old infant. The mother was a carrier of the RS1 gene and the male infant was at 50% risk of being affected. The technician imaged the fundus without using a speculum using her fingers to hold the lids apart. The retinal findings were abnormal, with a silvery reflex toward the periphery. Use of the zoom function showed in this case the typical foveal schisis seen in this disorder.

The Optos FAF mode is also useful for identifying abnormalities of the retinal pigment epithelium and retina. Dr. Moore also noted the case of bear track retinopathy in a 7-year-old boy; the pathology was very well highlighted in FAF mode.

“The fluorescein capability of this instrument is extremely useful,” he said.

In the case of a 15-year-old girl who presented with a sudden onset of floaters in the right eye. Indirect ophthalmoscopy showed an abnormality in the extreme periphery, which would have been difficult to image with a normal camera; however, widefield FA clearly showed a small area of nonperfusion in the left eye and peripheral non perfusion and neovascularization in the right eye. These findings resulted in a diagnosis of familial exudative vitreoretinopathy treated with laser in the right eye. The technology can be used to monitor disease progression.

Dr. Moore cited the non-mydriatic mode of the Optos instrument as extremely useful in a pediatric population. “It is useful in children who are drop-phobic, as an alternative to annual dilated fundus examination in patients with stable strabismus and normal vision, and as a fundus examination for use in parents to identify suspected inherited eye diseases.

An illustrative example is that of a 10-year-old boy with blurred vision referred for an inpatient consult who had undergone a failed stem cell transplant. He was drop phobic and he and his father refused instillation of drops fundus exam through an undilated pupil but Optos imaging showed bilateral disc swelling and a macular star. The boy was diagnosed with idiopathic intracranial hypertension and was followed with regular OPTOs imaging without the use of eye drops.

CONCLUSION

“Widefield fundus imaging has a major role to play in managing ROP, retinoblastoma, and retinovascular disease in young infants and the technology has improved documentation in medicolegal cases,” Dr. Moore concluded. “Optos imaging can be performed without pupil dilatation and helps improve the efficiency of the strabismus clinic and is helpful in children who are drop-phobic.”

Dr. Moore has no financial interest in any aspect of this report.
VISION TO LIVE

SCIENCE IS JUST THE BEGINNING OF OUR INNOVATION.

LET'S PARTNER IN DOING MORE TO GIVE PEOPLE THE
SCIENCE IS JUST THE BEGINNING OF OUR INNOVATION. LET’S PARTNER IN DOING MORE TO GIVE PEOPLE THE VISION TO LIVE
THE CHALLENGES OF EXAMINING VISUAL FIELDS IN CHILDREN

Technologies may ease diagnostic burden

By Lynda Charters; Reviewed by Andrew G. Lee, MD

The biggest challenge in visual field testing is recognizing when a child may have a visual field defect. A number of symptoms may be clues, including difficulty finding words, difficulty reading as evidenced by missing words or hemifield slip, difficulty during tests as the result of skipping letters, not reading an entire line, or only seeing one number of the Ichihara test when there actually are two.

Mitchell Strominger, MD, pointed out that physicians should be aware that some children compensate for their visual field defects, with, for example, head turns related to visual field loss that are not related to strabismus.

“They may have head turning or head thrusting toward the nonseeing field or use touch to help navigate around,” said Dr. Strominger, professor of ophthalmology and pediatrics, Renown Medical Center, University of Nevada Reno School of Medicine, Reno.

Some children can have associated motor or sensory deficits, for example, children with cerebral palsy may have a hemiparesis on the side of the visual field deficit.

Children with a known central nervous system abnormality that includes perinatal stroke, encephalomalacia, periventricular leukomalacia, craniofaryngioma, pituitary adenoma, or optic pathway glioma, or a known systemic or genetic abnormality, such as neurofibromatosis, should undergo visual field testing, Dr. Strominger pointed out.

Other indications for visual field testing are the presence of retinal abnormalities and anterior visual pathway congenital disorders.

OPTIONS IN VISUAL FIELD TESTING

Many options are available that can be used to evaluate the visual fields, each with limitations. Visual field testing generally is done binocularly and monocularly. However, Dr. Strominger noted, if a patient has a bitemporal defect, testing should be done monocularly because the defect may not be apparent when binocularly is done.

Confrontation visual field testing, in which the child is shown toys and the clinician monitors the responses, is the most basic procedure that has not changed markedly over the decades.

Using the saccadic technique, a confrontation test, the clinician moves objects in front of young children in order to observe the saccades; in older children, counting fingers or the red object test can be used.

Arc perimetry is an old time-tested technique during which babies can be tested with the use of a flashing light to test the child’s response to the light.

Goldmann perimetry is another testing method in which a light moves from the periphery to the center of a hemisphere. The child signals when he or she detects the light by tapping on a buzzer; this method works best with cooperative patients.

The Humphrey visual field analyzer, the latest technology, is another option, but its use is extremely difficult in small children, Dr. Strominger noted.

CONTRIBUTION OF OCT

OCT can provide valuable information about the nerve fiber layer. He advises doctors to also measure the ganglion cell layer.

“The ganglion cell layer provides a lot of information that might not be available if only the nerve fiber layer is assessed,” he said.

Specifically, in a patient with café au lait spots and glioma, the visual field deteriorate was progressing. OCT performed in this patient showed that the glioma was progressing along with a decrease in the nerve fiber layer over time.
Monitoring ganglion cell loss is informative. In a child with a suspect visual field, in whom assessing the nerve fiber layer may not provide a great deal of information, the ganglion cell layer may shed some light on the retinal status.

Dr. Strominger described a patient with binasal ganglion cell loss secondary to a suprasellar lesion, who was diagnosed with bitemporal hemianopsia.

In another case, in which a change in vision in the right eye was found, the bilateral vision was 20/20. The right eye appeared to have a subtle change in the visual field. Analysis of the nerve fiber layer on OCT showed a good structural appearance; however, a small ganglion cell loss was apparent in the left eye.

“This defect is seen more and more often in patients with demyelinating disease,” Dr. Strominger said. “The visual acuity can be completely normal, the color vision may be good, but there is a decrease in the ganglion cells.”

In a case of left homonymous hemianopsia, OCT showed a corresponding loss of ganglion cells with a lesion in the occipital lobe.

“Patients are being identified with retrograde axonal degeneration that can be identified by evaluating the ganglion cell layer,” he said. “In cases in which a visual field examination cannot be performed and in which ganglion cell loss is found, physicians should be concerned about a posterior defect.”

In a similar case, the patient had a superior quadrantic defect; the nerve fiber layer was normal on examination but the ganglion cell layer was defective and corresponded to that defect. The patient was diagnosed with post-lateral geniculate disease.

In commenting on the importance of OCT, Dr. Strominger noted that the nerve fiber layer thickness should be affected in anterior visual pathway disorders except in some cases with demyelinating disease in which the ganglion cell layer only may be affected.

“Some ganglion cell loss can be seen in retrograde axonal degeneration. OCT can be easier to perform in children and the findings can correspond to visual field defects,” Dr. Strominger explained.

TECHNOLOGIES ON THE HORIZON

Saccadic vector optokinetic perimetry uses fixation targets and an eye tracking device to monitor real-time eye movement responses to visual field stimuli. The system includes separate patient and examiner displays, the eye tracker, and a height-adjustable table.

A head-mounted eye tracking perimeter (Virtual-Eye, BioFormatix Inc.) device capable of vector analysis is under development.

While many options are available to assess the visual fields in young patients, Dr. Strominger generally starts with OCT because of the wealth of information that the technology provides. Performing Humphrey visual field testing can be useful in cooperative patients. Some newer technologies in the pipeline may soon add to the ophthalmologist’s armamentarium in this challenging patient population.

MITCHELL STROMINGER, MD

Dr. Strominger has no financial relationships related to this report.
Worse outcomes after development of endophthalmitis postoperatively are associated with the presence of bacteria and higher bacterial loads of pathogens other than *Staphylococcus epidermidis* as detected by whole-genome sequencing (WGS) and quantitative polymerase chain reaction (qPCR).

The incidence rate of endophthalmitis that develops after intravitreal injections is low, but more and more injections are being administered annually in the US and the rate of endophthalmitis is climbing. However, the current gold standard, cultures, seems less than adequate, in that the Endophthalmitis Vitrectomy Study *(Arch Ophthalmol. 1995;113:1479-96)* found that only 69.3% of cases were culture-positive, leaving the rest with no etiologic diagnosis.

In addition, the culture-positive rates may be even lower in endophthalmitis that develops following intravitreal injections, in that among 23 cases of endophthalmitis analyzed following 27,736 injections, 16 cases were found to be culture-negative *(Arch Ophthalmology. 2011;118:2028-34)*.

According to Cecilia Lee, MD, MS, and colleagues, “the prognosis of endophthalmitis appears at least partially dependent on the causative organism, the high rate of culture-negative cases suggests a need for a more sensitive modality for pathogen detection.”

In light of this, Dr. Lee and colleagues conducted a prospective cohort study in which MidAtlantic Retina, the Retina Service of Wills Eye Hospital, Philadelphia, and the University of Washington, Seattle, participated. Consecutive patients were enrolled who had a clinical diagnosis of endophthalmitis after any intraocular procedure or surgery within 6 weeks of presentation. The day that they were recruited into the study, all patients underwent either intraocular fluid biopsy or pars plana vitrectomy. qPCR for specific pathogens and WGS were performed, the investigators recounted.

**STUDY FINDINGS**

Fifty patients (52% men; mean age, 72 years) were enrolled in the study. Following qPCR and WGS, 24 cases were culture-positive and the remainder culture-negative. WGS identified the cultured organism in 76% of the culture-positive cases and identified potential pathogens in 33% of the culture-negative cases,” said Dr. Lee, who is from the Department of Ophthalmology, University of Washington, Seattle. They published their findings on behalf of the Endophthalmitis Study Group in the *American Journal of Ophthalmology*. (2020; doi: https://doi.org/10.1016/j.ajo.2020.03.008.)

The most frequently cultured organisms were *S. epidermidis* followed by other *Staphylococcus* and *Streptococcus* species.

Regarding bacterial load, the median load was 3.32 (mean, 53.50; range, 0.028-480) in the culture-positive cases. In the WGS-positive but culture-negative cases, the median bacterial load was 1.44 (mean, 2.04; range, 0.35-6.19).

The visual outcomes in cases with *S. epidermidis* endophthalmitis did not differ from the visual outcomes in cases that were pathogen-negative; however, the patients who tested positive for organisms other than *S. epidermidis* had worse visual outcomes.

The investigators found that in cases that had higher baseline bacterial DNA loads of pathogens other than *S. epidermidis* that were detected by WGS had worse visual acuity levels at months 1 and 3. Interestingly, the bacterial loads of *S. epidermidis* did not seem to affect the outcomes, the investigators reported.

qPCR identified Torque teno virus in 49% of cases and Merkel cell polyomavirus in 19% of cases. When Torque teno virus was present, there was a higher rate of secondary pars plana vitrectomy and retinal detachment.

The authors concluded that the culture/molecular pathogen testing status (for bacteria and virus) as well as the baseline visual acuity has prognostic significance for clinical outcomes including the visual acuity and secondary vitrectomy in endophthalmitis.

“Molecular studies provide more extensive and sensitive characterization of pathogens and have the potential to allow for improved treat paradigms,” they wrote. “Further development of rapid, point-of-service molecular diagnostics and subsequent prospective randomized controlled clinical trials will allow for testing of new paradigms for risk stratification and individualized treatment for endophthalmitis.”

**TAKE-HOME**

- Quantitative polymerase chain reaction and whole genome sequencing contribute to pathogen identification in endophthalmitis.

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By Lynda Charters

**CECILIA LEE, MD, MS**

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Dr. Lee has no financial interest in the subject of this report.
IN THE RACE AGAINST GLAUCOMA, DURABILITY WINS

Glaucoma demands outcomes that endure. Results from the largest MIGS pivotal trial to date have shown that the Hydrus® Microstent delivers the greatest improvement compared to cataract surgery alone for IOP reduction and medication elimination at 24 months.1-4,*

And now, at 3 years the Hydrus Microstent is the only MIGS device with results from a pivotal trial showing a statistically significant reduction in risk of invasive secondary glaucoma surgeries.†

When durability matters, choose the MIGS option that endures—Hydrus Microstent.

Delivering a new confidence.
OSD: Hard facts and a protocol for cataract patients

Optimizing ocular surface elevates patient satisfaction, word-of-mouth referrals

By Neel R. Desai, MD

Operative treatment of ocular surface disease (OSD) is an asset that many cataract surgeons tend to undervalue. I often talk to peers who treat OSD as a nuisance problem that gets in the way of them proceeding with the ultimate goal of cataract surgery, but for those of us who are outcome-driven and see that those outcomes help build the reputation and good will that we need to grow our practices, treating OSD prior to surgery is an important goal in itself, not a speed bump on the road to surgery.

If you think treating OSD before surgery is a burden, consider these numbers:

- In Trattler’s landmark PHACO study, up to 76.8% of patients presenting for cataract surgery had some form of OSD. At least 50% of them had severe enough OSD central to the visual axis that could negatively affect surgical outcomes if it were left untreated.

- In my own practice, I treated patients with epibulbar basement membrane dystrophy affecting pre-operative biometry with traditional dry eye therapies, superficial keratectomy, and placement of a cryopreserved amniotic membrane biologically active bandage (Prokera, Bio-Tissue) for 5 days. After following this protocol, average Ks changed by at least 1D in 50% of patients and up to 2D in 19%. BCVA improved 1-2 lines. If we hadn’t treated the problem before surgery, inaccurate IOL powers would have led to refractive surprises after surgery.

As these studies help illustrate, by treating OSD, our practices accumulate better outcomes and happier patients, reduce costly postoperative chair time and enhancements, and get reimbursed for OSD treatment. It’s a win for patients, physicians, and our businesses.

‘As these studies help illustrate, by treating OSD, our practices accumulate better outcomes and happier patients.’

- Neel R. Desai, MD

Mild OSD: The vast majority of my cataract patients with OSD have the mild form. A below-normal TRUT and clinical signs might indicate mild blepharitis, MGD or SPK. The traditional course of therapy (artificial tears, hot compresses, lid cleansers and nutriceuticals) is usually enough to optimize the ocular surface.

If the patient’s OSD involves MGD, rosacea or evaporative dry eye, I may use intense pulsed light (IPL) therapy (M22 Optima IPL, Lumenis) to reduce lid and eye area telangiectasia and break the vicious cycle of inflammation. I try to get in as many IPL treatments as I can before the cataract surgery (spaced 2 weeks apart), but I generally don’t hold up cataract surgery for the IPL series. If I am concerned about biometric accuracy due to OSD, I use a cryopreserved amniotic membrane biologically active bandage to normalize the surface rapidly for cataract planning.
Bleb leaks treated with minimally invasive conjunctival surgery

Ophthalmologist shares simple approach that proves simple, efficacious

By Lynda Charters; Reviewed by Neeru Gupta, MD, PhD, MBA

BLEB LEAKS ARE a complication of trabeculectomy that occur despite improved success rates with local application of mitomycin C. Neeru Gupta, MD, PhD, MBA, shared her useful and simple approach for dealing with bleb leaks.

Dr. Gupta is the chief of Glaucoma and professor and Dorothy Pitts Chair, Departments of Ophthalmology and Vision Sciences and director, glaucoma research at the Keenan Research Centre for Biomedical Science, Li Ka Shing Knowledge Institute of St. Michael’s Hospital, Unity Health Toronto, University of Toronto.

Bleb leaks can occur after trabeculectomy with mitomycin C in the conjunctival epithelial surface. The affected area can be seen under high-power microscopy to have a minute microscopic break in the epithelial that is sufficient to cause a bleb leak.

“The bleb leak has dogged ophthalmologists for some time. Our biggest fear is the ticking time bomb of potential infection,” Dr. Gupta said. “The break allows pathogens to enter the eye, which can lead to endophthalmitis and loss of the eye.”

In addition to this risk, serious structural abnormalities can accompany leaking fluid and hypotony. Corneal striae, shallow anterior chambers, fluid build-up through the choroidals, and hypotony maculopathy also can develop, she pointed out, that can result in loss of vision.

MANAGING BLEB LEAKS

In the presence of a small bleb leak, Dr. Gupta prefers a conservative approach that includes an antibiotic to prevent infection and reduction of any topical steroids.

Continues on page 22: Bleb surgery

(FIGURE 1) Minimally invasive conjunctival surgery (MICS) technique to repair a leaking bleb in a 64-year-old woman, 11.3 years following right eye combined trabeculectomy and cataract surgery.

(A) The eye was rotated downward to expose the superior avascular bleb and posterior bulbar conjunctiva. (B and C) Subconjunctival anesthetic was injected behind the bleb and ballooned conjunctival tissue to the outer edge of the bleb. (D) Raised conjunctival tissue was gently grasped and stretched over the thin bleb toward the limbus. (E) A suture (10-nylon) was used to anchor the leading folded edge to limbal tissue with (F) a surgical knot. (G and H) Adjacent mobile conjunctiva was similarly brought anteriorly and sutured in place. (I) Conjunctival tissue brought over to cover the leaking bleb was held in place at the limbus with 4 surgical knots.

(Images courtesy of Neeru Gupta, MD, PhD, MBA)
bleb

(Continued from page 21)

Patients experience better outcomes not only thanks to more accurate biometry, but also because they have expanded access to high-technology lenses and procedures.

OSD

(Continued from page 20)

surgery. For patients with moderate keratitis (PEK or SPK), I consider placing a cryopreserved amniotic membrane biologically active bandage for 3–5 days without a superficial keratectomy in the more severe eye, and then treating the second eye.

Severe OSD: Patients with severe OSD may have moderate to severe staining inside the 6 mm visual axis zone, significant topographical irregularities, pronounced inconsistency between modalities of biometry, an RMS value greater than 4, Salzmann nodular degeneration, or recurrent erosion syndrome.

I follow the same treatments as mild and moderate OSD, while adding other appropriate therapies. For example, I may combine treatments, following thermal pulsation therapy with IPL. For some patients, I combine superficial keratectomy with a cryopreserved amniotic membrane biologically active bandage. Not only is the intensity of treatment higher for severe OSD, but it also requires more time for therapies to produce optimal results. Hence, it is important to impress upon patients the value-added benefit of this optimization process in terms of better, more accurate outcomes and greater breadth of choice in lens implant opportunities.

Outcomes, Post-Op Care

Postoperative care for OSD begins before surgery, when we teach patients that the problem is chronic and requires long-term treatment. My patients have a long-term plan before surgery, which usually involves continuing traditional at-home therapies and prescription medications. If they have had thermal pulsation therapy and/or IPL, they will return for follow-up sessions, which usually taper to once per year. Patients understand that we have optimized their ocular surface, delivered the surgical outcomes they desired, and now we need to keep their ocular surface healthy and clear.

In our practice, we have seen that optimizing the ocular surface elevates patient satisfaction and word-of-mouth referrals. It also boosts our rates of refractive cataract surgery. Before treating OSD, we would offer refractive surgery to about 50% of cataract patients, but after treatment, that number rises to about 90%. Patients get better outcomes not only thanks to more accurate biometry, but also because they have expanded access to high-technology lenses and procedures. When our patients have better vision and our practice is growing, we cannot look at treating OSD as a nuisance—it’s most definitely an opportunity.

Pharmacologic therapy is the foundation of treatment for OSD. For some patients, I combine superficial keratectomy with a cryopreserved amniotic membrane biologically active bandage for 3–5 days. For some patients, I combine treatments, following thermal pulsation therapy with IPL. For some patients, I combine superficial keratectomy with a cryopreserved amniotic membrane biologically active bandage. Not only is the intensity of treatment higher for severe OSD, but it also requires more time for therapies to produce optimal results. Hence, it is important to impress upon patients the value-added benefit of this optimization process in terms of better, more accurate outcomes and greater breadth of choice in lens implant opportunities.

References


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Dr. Gupta has no financial disclosures related to this report.

Take-home

Injecting lidocaine and stretching adjacent conjunctiva over it to tie and anchor into sclera offers a simple and safe procedure for treating bleb leaks, a complication of trabeculectomy.
INTRODUCING THE LATEST INNOVATION IN GLAUCOMA MANAGEMENT:
The first and only FDA-approved, biodegradable, intracameral implant indicated to reduce IOP in patients with open angle glaucoma or ocular hypertension via a sustained-release drug delivery system.¹²

INDICATIONS AND USAGE
DURYSTA™ (bimatoprost implant) is indicated for the reduction of intraocular pressure (IOP) in patients with open angle glaucoma (OAG) or ocular hypertension (OHT).

IMPORTANT SAFETY INFORMATION
Contraindications
DURYSTA™ is contraindicated in patients with: active or suspected ocular or periocular infections; corneal endothelial cell dystrophy (e.g., Fuchs’ Dystrophy); prior corneal transplantation or endothelial cell transplants (e.g., Descemet’s Stripping Automated Endothelial Keratoplasty [DSAEK]); absent or ruptured posterior lens capsule, due to the risk of implant migration into the posterior segment; hypersensitivity to bimatoprost or to any other components of the product.

Warnings and Precautions
The presence of DURYSTA™ implants has been associated with corneal adverse reactions and increased risk of corneal endothelial cell loss. Administration of DURYSTA™ should be limited to a single implant per eye without re-treatment. Caution should be used when prescribing DURYSTA™ in patients with limited corneal endothelial cell reserve.

DURYSTA™ should be used with caution in patients with narrow iridocorneal angles (Shaffer grade < 3) or anatomical obstruction (e.g., scarring) that may prohibit settling in the inferior angle.

Macular edema, including cystoid macular edema, has been reported during treatment with ophthalmic bimatoprost, including DURYSTA™ intracameral implant. DURYSTA™ should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

Prostaglandin analogs, including DURYSTA™, have been reported to cause intraocular inflammation. DURYSTA™ should be used with caution in patients with active intraocular inflammation (e.g., uveitis) because the inflammation may be exacerbated.

Ophthalmic bimatoprost, including DURYSTA™ intracameral implant, has been reported to cause changes to pigmented tissues, such as increased pigmentation of the iris. Pigmentation of the iris is likely to be permanent. Patients who receive treatment should be informed of the possibility of increased pigmentation. While treatment with DURYSTA™ can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly.

Intraocular surgical procedures and injections have been associated with endophthalmitis. Proper aseptic technique must always be used with administering DURYSTA™, and patients should be monitored following the administration.

Adverse Reactions
In controlled studies, the most common ocular adverse reaction reported by 27% of patients was conjunctival hyperemia. Other common adverse reactions reported in 5%-10% of patients were foreign body sensation, eye pain, photophobia, conjunctival hemorrhage, dry eye, eye irritation, intraocular pressure increased, corneal endothelial cell loss, vision blurred, iritis, and headache.

Please see Brief Summary of full Prescribing Information on the following page.

References: 1. Allergan receives FDA approval for DURYSTA™ (bimatoprost implant) the first and only intracameral biodegradable sustained-release implant to lower intraocular pressure in open-angle glaucoma or ocular hypertension patients (press release). Dublin: PR Newswire; March 5, 2020.

IOP = intraocular pressure.
The presence of DURYSTA™ implants has been associated with corneal adverse reactions and increased risk of corneal endothelial cell loss. Administration of DURYSTA™ should be limited to a single implant per eye without retreatment. Caution should be used when prescribing DURYSTA™ in patients with limited corneal endothelial cell reserve.

Indocorneal Angle: Following administration with DURYSTA™, the intracameral implant is intended to settle within the inferior angle. DURYSTA™ should be used with caution in patients with narrow indocorneal angles (Shaffer grade < 3) or anatomical obstruction (e.g., scarring) that may prohibit settling in the inferior angle.

Macular Edema: Macular edema, including cystoid macular edema, has been reported during treatment with bimatoprost implant, including DURYSTA™ intracameral implant. DURYSTA™ should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

Intraocular Inflammation: Prostaglandin analogs, including DURYSTA™, have been reported to cause intraocular inflammation. DURYSTA™ should be used with caution in patients with active intraocular inflammation (e.g., uveitis) because the inflammation may be exacerbated.

Pigmentation: Ophthalmic bimatoprost, including DURYSTA™ intracameral implant, has been reported to cause changes to pigmented tissues, such as increased pigmentation of the iris. Pigmentation of the iris is likely to be permanent. Patients who receive treatment should be informed of the possibility of increased pigmentation. The pigmentation change is due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes. While treatment with DURYSTA™ can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly.

Endophthalmitis: Intracocular surgical procedures and injections have been associated with endophthalmitis. Proper aseptic technique must always be used with administering DURYSTA®, and patients should be monitored following the administration.

Adverse Reactions

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The most common ocular adverse reaction observed in two randomized, active-controlled clinical trials with DURYSTA™ in patients with OAG or OHT was conjunctival hyperemia, which was reported in 27% of patients. Other common ocular adverse reactions reported in 5-10% of patients were foreign body sensation, eye pain, photophobia, conjunctival hemorrhage, dry eye, eye irritation, intraocular pressure increase, corneal endothelial cell loss, vision blurring, and iritis. Ocular adverse reactions occurring in 1-5% of patients were anterior chamber cell, lacrimation increased, corneal edema, aqueous humor leakage, iris adhesions, ocular discomfort, corneal touch, iris hyperpigmentation, anterior chamber flare, anterior chamber inflammation, and macular edema. The following additional adverse drug reactions occurred in less than 1% of patients: hypotension, iridocyclitis, uveitis, corneal opacity, product administered at inappropriate site, corneal decompensation, cystoid macular edema, and drug hypersensitivity.

The most common nonocular adverse reaction was headache, which was observed in 5% of patients.

Use in Specific Populations

Pregnancy: There are no adequate and well-controlled studies of DURYSTA™ administration in pregnant women to inform a drug associated risk. Oral administration of bimatoprost to pregnant rats and mice throughout organogenesis did not produce adverse maternal or fetal effects at clinically relevant exposures. Oral administration of bimatoprost to rats from the start of organogenesis to the end of lactation did not produce adverse maternal, fetal or neonatal effects at clinically relevant exposures.

In embryofetal developmental studies in pregnant mice and rats, abortion was observed at oral doses of bimatoprost which achieved at least 1770 times the maximum human bimatoprost exposure following a single administration of DURYSTA™ (based on plasma Cmax, levels: blood-to-plasma partition ratio of 0.858).

In a prenatal/postnatal development study, oral administration of bimatoprost to pregnant rats from gestation day 7 through lactation resulted in reduced gestation length, increased late resorptions, fetal deaths, and postnatal pup mortality, and reduced pup body weight at 0.3 mg/kg/day (estimated 470-times the human systemic exposure to bimatoprost from DURYSTA™; based on plasma Cmax, and a blood-to-plasma partition ratio of 0.858). No adverse effects were observed in rat offspring at 0.1 mg/kg/day (estimated 350-times the human systemic exposure to bimatoprost from DURYSTA™; based on plasma Cmax, levels: blood-to-plasma partition ratio of 0.858).

For the development of DURYSTA™, the safety and tolerability of bimatoprost in human pregnancy have not been established.

Lactation: There is no information regarding the presence of bimatoprost in human milk, the effects on the breastfed infants, or the effects on milk production. In animal studies, topical bimatoprost has been shown to be excreted in breast milk. Because many drugs are excreted in human milk, caution should be exercised when DURYSTA™ is administered to a nursing woman.

The developmental and health benefits of breastfeeding should be considered, along with the mother’s clinical need for DURYSTA™ and any potential adverse effects on the breastfed child from DURYSTA™.

Pediatric Use: Safety and effectiveness of DURYSTA™ in pediatric patients have not been established.

Geriatric Use: No overall differences in safety or effectiveness have been observed between elderly and other adult patients.

Nonclinical Toxicology

Carcinogenesis, Mutagenesis, Impairment of Fertility

Bimatoprost was not carcinogenic in either mice or rats when administered by oral gavage at doses up to 2 mg/kg/day and 1 mg/kg/day respectively for 104 weeks (approximately 1000 and 1700 times, respectively, the maximum human exposure [based on plasma Cmax, levels: blood-to-plasma partition ratio of 0.858]).

Bimatoprost was not mutagenic or clastogenic in the Ames test, in the mouse lymphoma test, or in the in vitro mouse micronucleus tests. Bimatoprost did not impair fertility in male or female rats up to doses of 0.6 mg/kg/day (1770-times the maximum human exposure, based on plasma Cmax, levels: blood-to-plasma partition ratio of 0.858).

PATIENT COUNSELING INFORMATION

Treatment-related Effects: Advise patients about the potential risk for complications including, but not limited to, the development of corneal adverse events, intraocular inflammation or endophthalmitis.

Potential for Pigmentation: Advise patients about the potential for increased brown pigmentation of the iris, which may be permanent.

When to Seek Physician Advice: Advise patients that if the eye becomes red, sensitive to light, painful, or develops a change in vision, they should seek immediate care from an ophthalmologist.

Rx only

SPECIAL COVID-19 Coverage

COVID-19: Impact of pandemic on Switzerland’s ophthalmic space

Robert Pinelli, MD, CEO, and founder of the Switzerland Eye Research Institute, shares how operations at the facility have adapted to the growing coronavirus pandemic spreading across the globe.

OphthalmologyTimes.com/Coronavirus/ PinelliSwitzerlandimpact

Putting safety measures into practice

As the COVID-19 pandemic continues to alter life in every corner of the country, ophthalmologists have been forced to evaluate the needs of their patients, shift schedules and change the way they manage their practices.

OphthalmologyTimes.com/Coronavirus/ PatientsAmidPandemic

Dealing with patients amid pandemic

As the COVID-19 pandemic continues to alter life in every corner of the country, ophthalmologists have been forced to evaluate the needs of their patients, shift schedules and change the way they manage their practices.

OphthalmologyTimes.com/Coronavirus/ PatientsAmidPandemic
Simplicity key to diagnosing, treating vitreoretinal lymphoma

Treatment with intraocular injection of methotrexate achieves positive response

By Lynda Charters; Reviewed by Jacob J. Pe’er, MD

Primary vitreoretinal lymphoma (VRL), the most common and most aggressive intraocular lymphoma, is readily diagnosed by determining the interleukin (IL)-10:IL-6 ratio in the vitreous. Treatment with intraocular injections of methotrexate achieved a 100% response rate of the VRL, with rare recurrences, Jacob Pe’er, MD, said.

Primary VRL is mostly a high-grade B-cell lymphoma. The other less aggressive forms are primary choroidal lymphoma, typically a low-grade B-cell lymphoma; primary iridal lymphoma, a rare form characterized by either B cells or T cells; and secondary uveal lymphoma, he explained.

Primary VRL, first identified in 1951, generally is associated with primary central nervous system lymphoma (PCNSL), which usually is a high-grade B-cell lymphoma that remains confined to the CNS.

“Intraocular involvement occurs in about one quarter of those with PCNSL; however, in about 85% of VRL, PCNSL is present,” said Dr. Pe’er, past head, Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem. In addition, a diagnosis of VRL can become evident before, at the time of, or years after CNS lymphoma develops.

Diagnosing VRL

The disease is characterized by the presence of clumps or sheets of vitreal cells and in about a third of the patients also by yellow-white subretinal infiltrates seen during clinical examinations. Dr. Pe’er pointed out that these cells often can be misdiagnosed as nonresponsive uveitis.

Optical coherence tomography is helpful in diagnosing this pathology by visualizing subretinal pigment epithelial infiltrates.

Laboratory evaluation is by far the most decisive method of diagnosis, based on the analysis of specimens obtained during vitrectomy.

“Cytology is the gold standard, but it often is insufficient to confirm primary intraocular lymphoma. In addition, the specimen must be tested very rapidly because of the cellular fragility,” he advised.

Gene rearrangement is another hallmark of the disease as exhibited by polymerase chain reaction (PCR) in which B-cell lymphoma shows immunglobulin heavy-chain rearrangement (IgH) and T-cell receptor gene arrangement for T-cell lymphoma, he explained.

Cytokine analysis performed using an enzyme-linked immunosorbent assay (ELISA) can detect IL-10 and IL-6 in the vitreous; the IL-10 level is higher in lymphoma. “The objective is to determine the ratio between IL-10 and IL-6,” Dr. Pe’er said.

They recently compared the three methods to determine the efficacy in diagnosing VRL in 146 patients (54.1% women; mean age 62 years) in whom the disease was suspected. Using the three methods, 74 patients were diagnosed with VRL.

Cytology provided data from 130 patients; 53 were diagnosed with malignant cells and the others with inflammatory diseases. PCR provided results from 90 patients and showed IgH gene rearrangement in 33.3%. Cytokines provided data from 112 patients. An IL-10:IL-6 ratio exceeding 1 was seen in 49 patients; the positive patients had a mean value of 74.7 ± 131.3 and the negative values ranged from 0.003 to 0.9, Dr. Pe’er recounted.

The cytokine ratio was the most sensitive of the tests with the best positive predictive value (PPV) and negative predictive value (NPV) (sensitivity 88.6%; specificity, 81.8%; PPV, 79.5%; NPV, 90.0%). PCR was the least helpful of the tests. Other studies have confirmed these results in large numbers of patients.

“We recommend that the IL-10:IL-6 ratio should be included in the diagnostic process of VRL,” he advised.

Treatments for VRL

A variety of treatments are available, i.e., in the past enucleation for advanced cases, radiation therapy, systemic and intraocular chemotherapy, biologic therapy, and investigational immunotherapies are possible options for these patients.

Dr. Pe’er and colleagues have achieved the best results with intraocular chemotherapy. He reported that among their 79 patients (130 eyes) with VRL, most cases (64%) were affected bilaterally; the vast majority had B-cell lymphoma. Interestingly, only 38.2% of cases with VRL had retinal involvement.

The three-phase chemotherapy treatment protocol used by Dr. Pe’er and colleagues was intravitreal injection of 400 µg/0.1 ml of methotrexate via the pars plana through a 30-gauge needle. During the induction phase, patients received twice-weekly injections (n=8) for 1 month; the consolidation phase included a once-weekly injection (n=8) for 2 months; and the maintenance phase included a once-month injection for 9 months (n=9). The overall mean follow-up was 55.7 months for patients with and without CNS involvement.

“All 130 eyes of 79 patients achieved complete remission of VRL after a mean of five injections..."
LYMPHOMA

(Continued from page 25)

(range, 1-16) of methotrexate,” Dr. Pe’er said. “There was no difference between the patients with monocular and binocular disease. Only two patients developed locally recurrent VRL, and they responded again to the same treatment protocol.”

COVID-19

(Continued from page 1)

RT-PCR analysis of nasopharyngeal swabs.

The patients were assessed for ocular symptoms that included red eye, tearing, blurred vision, discharge, and color desaturation, the investigators reported, which are the ocular symptoms manifested by other coronaviruses that infect humans and animals. Patients also were assessed for other symptoms of COVID-19 that included fever, cough, shortness of breath, rhinorrhea, and sore throat. No patients presented with ocular symptoms. During the hospital stay, one patient developed conjunctival injection and chemosis; 14 patients presented with upper respiratory symptoms that included cough, rhinorrhea, and sore throat.

FINDINGS

“All patients tested negative for COVID-19 on viral isolation and RT-PCR,” Dr. Jun reported. The findings were reported in Ophthalmology (https://doi.org/10.1016/j.ophtha.2020.03.026).

The authors reported that they are unaware of any other study that compared viral shedding in tears with the results of nasopharyngeal swab results during the course of COVID-19 infection, although a previous study reported positive results, but the virus could not be successfully isolated (J Med Virol. 2020; 2020 Feb 26. doi: 10.1002/jmv.25725. [Epub ahead of print]).

Dr. Jun pointed out that in the study under discussion there was no evidence of COVID-19 shedding in tears through the course of the disease and the viral load in the nasal and throat swabs are elevated for about two weeks from the onset of the viral symptoms (N Engl J Med. 2020; 2020; 382:1177-1179; DOI: 10.1056/NEJMc2001737). The time points at which the tears were sampled in the current study covered the 2 weeks of active infection, and all tear samples tested negative even when the nasopharyngeal specimens continued to test positive.

“Patients with symptoms of upper respiratory tract infections did not demonstrate any viral shedding in tears, suggesting that the hypothesis of the lacrimal duct as a viral conduit may not be true,” the investigators commented.

They also pointed out that only one patient developed ocular symptoms and there was no evidence of virus in the tear samples, thus “suggesting that transmission through tears regardless of the phase of infection is likely to be low.”

However, the investigators issued the caveat, i.e., that “COVID-19 has been known to infect cells via ACE2 receptors” and they noted that further studies are needed to prove the presence of ACE2 receptors on corneal and conjunctival cells. In addition, more studies are warranted to determine the association between serum viral load and viral shedding in tears.

As more information about COVID-19 emerges, these measures likely will continue to undergo revision to try to ensure eye care services can be provided safely. Meanwhile, these measures may serve as a starting point for those beginning to consider this new threat for ophthalmology practices, especially in areas where the number of cases may climb rapidly in the near future.

TAKE-HOME

➢ According to a research team, there is a low risk of viral shedding in the tears of patients with COVID-19.

RUPESH AGRAWAL, MD
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Dr. Agrawal has no financial interests related to the content in this report. The authors reported that they had no conflicts of interest associated with the subject of this report.
Only the OMNI® Surgical System allows you to target the three points of resistance in the conventional outflow pathway - trabecular meshwork, Schlemm’s canal and distal collector channels - with one sophisticated, implant-free device.

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loteprednol etabonate (LE) ophthalmic suspension 0.25% (Eysuvis, Kala Pharmaceuticals) met its primary and key secondary endpoints in a third phase III clinical trial investigating the corticosteroid in a novel formulation as a treatment for dry eye disease (DED).

The LE 0.25% suspension is formulated with a proprietary mucus-penetrating particle drug delivery technology (AMPPLIFY) that improves bioavailability of the active ingredient at the target site.

Topline results from the phase III study known as STRIDE III showed statistical superiority of LE 0.25% suspension (formerly known as KP-121) compared with vehicle for improving signs and symptoms of DED. In addition, the investigational corticosteroid was well-tolerated and had a favorable safety profile.

Elizabeth Yeu, MD, an investigator in the LE 0.25% studies, is assistant professor of ophthalmology, Eastern Virginia Medical School, Norfolk, VA, and a partner, Virginia Eye Consultants, Norfolk, VA.

“The results from STRIDE III showing benefit of LE 0.25% suspension for improving both signs and symptoms of DED are quite positive and replicate what was seen in STRIDE I and II,” Dr. Yeu said. “Collectively, these studies enrolled almost 3000 patients, making STRIDE the largest DED clinical trial program to date, and the results indicate that LE 0.25% suspension is a rapid-acting, safe, and effective anti-inflammatory therapy.”

Dr. Yeu added that if approved, LE 0.25% suspension will be an important therapeutic addition for the temporary relief of the signs and symptoms of DED.

**Investigational topical corticosteroid demonstrates efficacy for dry eye**

Symptomatic benefit may be seen early in more severely affected patients

*By Cheryl Guttman Krader; Reviewed by Elizabeth Yeu, MD*
“It is estimated that more than 17 million people in the US suffer from DED and 80% to 90% of those individuals experience flares for which a steroid can be appropriate treatment,” she said. “While eye care providers have used topical steroids to quiesce acute DED flares, we are always cautious about the potential for IOP elevations. It is noteworthy that no patients treated with LE 0.25% suspension in STRIDE III had an IOP increase >5 mmHg leading to IOP >21 mmHg.”

STRIDE III was a multicenter, double-masked study that randomly selected 901 patients 1:1 to treatment four times a day for two weeks with LE 0.25% or vehicle.

Patients were eligible for study enrollment if they had a documented clinical diagnosis of DED in both eyes and were only randomized to treatment if they still met the study’s eligibility criteria after a two-week run-in period during which they used the investigational product’s vehicle four times a day.

Using a 0 to 100 mm visual analog rating scale, patients were instructed to record Ocular Discomfort Severity (ODS) daily in a diary. Patients returned for follow-up visits on days eight and 15 after randomization for evaluations that included conjunctival hyperemia, corneal staining, and safety.

The primary endpoint looked at change in ODS score at day 15 in the overall intent-to-treat (ITT) population and in the subgroup of ITT patients with more severe baseline discomfort (ODS ≥ 68 mm).

STRIDE III achieved both of its independent primary endpoints, demonstrating a statistically significant difference in the LE 0.25% group compared to vehicle in the overall ITT population (p = .0002) and the subgroup (n = 602) with more severe baseline ocular discomfort (p = .0007).

In analyses of secondary endpoints, LE 0.25% suspension demonstrated statistical superiority for improving conjunctival hyperemia at day 15 (p < .0001), ODS at day 8 (P = .0282), and total corneal staining at day 15 (p = .0042).

Instillation site pain was the most common adverse event in both the LE 0.25% suspension and vehicle groups (2.9% and 1.5%, respectively). No patients in either group experienced an IOP increase >5 mmHg that resulted in an IOP ≥21 mmHg nor did any patient have an IOP increase >10 mmHg.

Results of a two-week phase III study demonstrated efficacy of loteprednol etabonate ophthalmic suspension 0.25% found the investigational treatment was well-tolerated and had a favorable safety profile.

PRIOR PHASE II RESULTS

In STRIDE I, LE 0.25% suspension achieved the sign and symptom endpoints and demonstrated rapid and sustained improvement in the ODS score. In STRIDE II, LE 0.25% suspension achieved its sign endpoint and showed a significant benefit for reducing corneal staining and for improving the ODS score at day eight.

Kala Pharmaceuticals is working on finalizing resubmission of the NDA for LE 0.25% suspension as a treatment for the temporary relief of the signs and symptoms of DED utilizing a two-week course of therapy.

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ANTIMICROBIAL RESISTANCE, EPITHELIAL toxicity resulting from frequently instilled fortified and toxic drugs, and lack of compliance with drug regimens are all problems associated with topical therapies. These three factors cry out for a new approach to treating corneal diseases, and collagen crosslinking (CXL) may be a new strategy, according to Jose Gomes, MD, PhD, professor of ophthalmology, Cornea and External Disease Service, Paulista Medical School/Federal University of Sao Paulo, Brazil.

Photochemical CXL works by increasing the stiffness of the corneal tissue. Besides, CXL has the added benefit of a disinfectant effect that is achieved by combining ultraviolet A (UVA) plus riboflavin, he said.

Photo-activated chromophore for keratitis (PACK) CXL may be considered the next therapeutic step in cases of confirmed infectious keratitis in which antimicrobial resistance rears its head. The technology has been used to treat non-infectious keratitis for years, and in 2016 started to be used to treat mild cases of infectious keratitis, Dr. Gomes pointed out.

**INDICATIONS, LIMITATIONS**

In vitro and in vivo studies and clinical case series have reported the beneficial effects of PACK-CXL for infectious keratitis.

Dr. Gomes cited a pre-clinical study of the in vitro effect of riboflavin/UVA for treating bacterial and fungal isolates that reported that some gram-positive and gram-negative bacteria but not fungi are susceptible to CXL (Martins et al. *Invest Ophthalmol Vis Sci.* 2008;49:3402-8). However, previous treatment with amphotericin B allowed riboflavin/UVA effectiveness against *Candida*, *Fusarium*, and *Aspergillus* (Sauer et al. *Invest Ophthalmol Vis Sci.* 2010;51:3950-3953).


In clinical studies, case series have reported that CXL helps in managing advanced microbial keratitis refractory to topical medical therapy (Shetty et al. *Br J Ophthalmol.* 2014;98:1033-5). A combination of medical therapy and CXL or CXL alone can be efficacious, Dr. Gomes said. He also described a case of Pseudomonas keratitis treated with PACK-CXL at the Paulista Medical School, Sao Paulo. The case resolved well by day 18 after treatment with CXL. CXL also was shown to reduce the time to resolution of suppurative fungal corneal ulcers, as reported recently (Basaiawmoit et al. *Cornea.* 2018;37:1376-8).

“We in Brazil also found that some cases of fusarium keratitis responded well to CXL, especially when the fungal infection was more superficial in the corneal tissue,” Dr. Gomes said.

**STUDY OF INFECTIOUS KERATITIS**

Another study of 40 cases with infectious keratitis showed that PACK-CXL was effective when the depth of the infection was shallow, and the success rate was higher for bacterial infections compared with fungal infections.

An important finding was that riboflavin/UVA should not be applied in eyes with a previous herpes simplex infection. (Price et al. *J Refract Surg.* 2012;28:706-13).

*Acanthamoeba* may be the pathogenic exception to the response to CXL. The in vitro results did not show a good response to *Acanthamoeba* trophozoites or cysts.

This finding also was true for the in vivo model of infection. However, in the clinical setting, a few reported cases had contradictory results. In 2011, Khan et al. (*Ophthalmology.* 2011;118:324-331) described the resolution of three cases of acanthamoeba infection following CXL.

In a multicenter, prospective, comparative study including eyes with infectious keratitis and corneal melting treated with PACK-CXL and antimicrobial therapy (21 eyes) or only antimicrobial therapy (19 eyes), Said et al. (*Ophthalmology.* 2014;121:1377-82) found a complication rate of 21% in the control group, whereas there was no incidence of corneal perforation or recurrence of the infection in the PACK-CXL group.

These results indicate that PACK-CXL may be an effective adjuvant therapy in the management of se-

(FIGURE 1) Collagen corneal CXL. (Photo courtesy of Jose Gomes, MD, PhD)
vere infectious keratitis associated with corneal melting.

A few meta-analyses are evaluating the efficacy of PACK-CXL. One of them included 12 reports with a total of 104 eyes treated with CXL showed the same results as found previously and corroborated the results with bacterial infections and acanthamoeba cases more so than with fungal keratitis (Papaioannou et al. Cornea. 2016;35:62-71).

NEW PERSPECTIVES

The period of 2018 to 2019 saw the introduction of accelerated CXL. As seen previously, cases of bacterial keratitis fared well. A new device (C-Eye Technology, EMAGine) that can be mounted onto the slit lamp is available and facilitates more focused treatment.

Rose Bengal plus 518-nanometer green light (Rose Bengal photodynamic antimicrobial therapy) is another new wrinkle in CXL. With this technology, fungal and bacterial keratitis both responded well to CXL and more so than riboflavin (Amescua et al. Cornea. 2017;36:1141-1144).

Dr. Gomes reported that researchers at the Paulista Medical School are conducting in vitro studies using PACK-CXL with 0.1% rose Bengal under green light-emitting diode irradiation and found complete growth inhibition of Staphylococcus, Pseudomonas, and Mycobacterium. When the technology was applied to clinical cases, the researchers achieved better results with fungal keratitis than the results previously achieved with riboflavin.

Dr. Gomes concluded that these studies have shown that CXL can be considered an adjunct treatment for infectious keratitis, especially in cases that have been refractory to conventional therapy.

“CXL is effective for both bacterial and some cases of more superficial fungal and acanthamoeba keratitis,” he said. “Fast CXL and new photoactivated chromophores such as rose Bengal can improve the results by making the procedure faster and safer.”

Dr. Gomes is a consultant to Alcon, Allergan, Bausch + Lomb, Mundipharma, and Ofta Vision Health.

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Pack CLX in a case of Pseudomonas keratitis with corneal melting. (Photo courtesy of Jose Gomes, MD, PhD)

Flowchart for indication of PACK-CXL. (Chart courtesy of Jose Gomes, MD, PhD)
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For More Information Contact: Deb Salava, Sanford Physician Recruitment at (605) 328-6993 or (866) 312-3907 or email: debra.salava@sanfordhealth.org
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