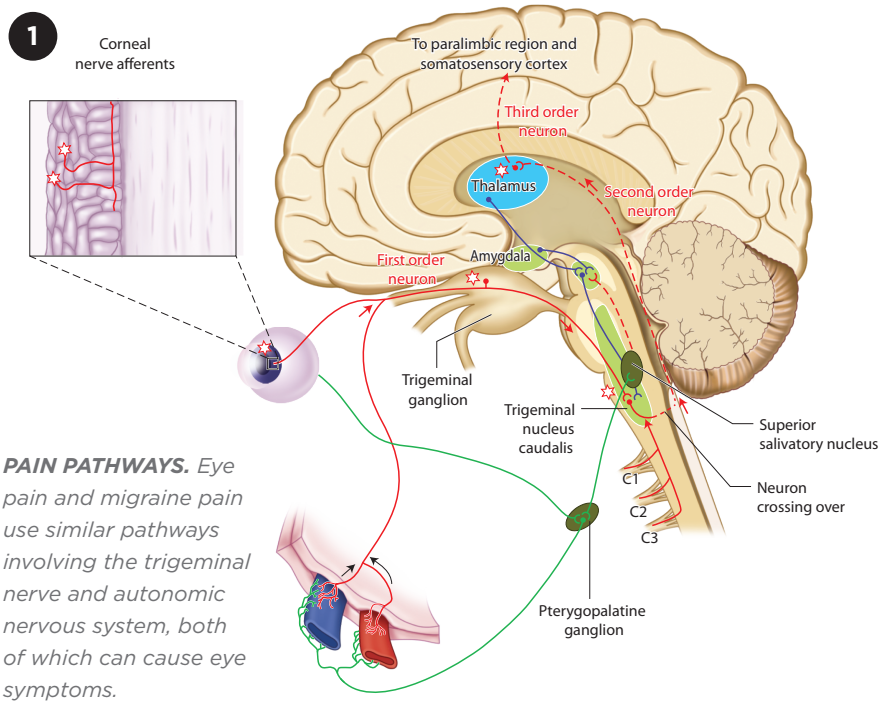
What Ophthalmologists Need to Know About Migraine

Although migraine is a neurologic illness, it is frequently accompanied by uncomfortable ophthalmic symptoms, which can cause significant reduction in visual quality of life. What's more, ocular surface diseases can exacerbate headaches in migraine patients, and migraines can also trigger intense symptoms of ocular surface disease. For these reasons, it's not surprising that ophthalmologists are often the first stop for patients who are experiencing migraine and associated symptoms.

By understanding the links between migraine and the eyes, ophthalmologists may be better able to support patients with education, treatment, and/or referral to specialists.



PAIN PATHWAYS. *Eye pain and migraine pain use similar pathways involving the trigeminal nerve and autonomic nervous system, both of which can cause eye symptoms.*

Visual Symptoms Connected to Migraine

Ocular manifestations of migraine can strike with or without accompanying head pain. Photophobia, visual aura, and eye pain are the most common and bothersome ocular symptoms.

Photophobia. Extreme light sensitivity affects up to 90% of migraine patients, said Kathleen Digre, MD, at Moran Eye Center, University of Utah in Salt Lake City. Although it can be a symptom of other eye conditions, including ocular surface diseases, chronic photophobia is a diagnostic criterion for migraine, she said.

Visual aura. About a quarter of migraine patients experience visual aura, which can include teichopsia, flashing lights, wavy lines or dots, blind spots, or loss of one or both sides of vision. These disturbances can precede or arrive with headache; they can even occur without a headache.

Although many ophthalmologists may refer to visual aura as "ocular migraine," in truth, there is no such thing, said Dr. Digre. "Ocular migraine appears nowhere in the International Classification of Headache Disorders." Patients—even those who are experienced migraineurs—frequently have trouble telling whether the aura affects one eye or both. Dr. Digre explained that this is because aura almost always originates in the brain, not the eyes. (She noted that retinal migraine is a rare migraine type that causes monocular visual loss and has been associated with central retinal artery vasospasm.)

Pain and ocular surface discomfort. Pain and pressure behind the eyes can be classic signs of migraine. But dryness, scratchiness, burning, irritation, and tearing can also be signals of migraine—and they can be associated with ocular surface diseases, including dry eye disease, blepharitis, and allergic conjunctivitis. When a comprehensive

BY REENA MUKAMAL, CONTRIBUTING WRITER, INTERVIEWING **KATHLEEN DIGRE, MD, ANAT GALOR, MD, MSPH,** AND **SEAN GRATTON, MD.**

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eye exam does not reveal signs of these disorders and when standard ocular surface disease treatments do not improve symptoms, it's important to look for other causes, such as migraine, said Anat Galor, MD, MSPH, at the Bascom Palmer Eye Institute in Miami. "Abnormal nerves underlie many diseases that we have traditionally thought about as ocular surface diseases. The answer is not always on the surface of the eye or visible at the slit lamp," she said.

Links Between the Eyes and the Brain

Trigeminal system. The primary mechanism that links eye pain and migraine pain is the trigeminal system (Fig. 1). The trigeminal nerve innervates the eye, and it has a foundational role in pathophysiology of migraine, said Sean Gratton, MD, at the University of Missouri–Kansas City. Dr. Digre added that migraine patients are believed to have a problem with sensory integration, in which "the brain itself is more sensitive to light, sound, odors, pain, touch, and other stimuli. Something may trigger the migraine, and this activates the trigeminal system, which innervates not just the dura and blood vessels in the head causing head pain but also the eye and cornea, which can cause eye pain. That is why the eye can be integral in the migraine mechanism."

Autonomic nervous system. The trigeminal pathway is also integrally related to the autonomic nervous system (ANS), which can also contribute to migraine, according to Drs. Digre and Gratton. "This is why some migraineurs have droopy eyelid, red eyes, tearing, pupillary changes, and other symptoms regulated by the ANS," Dr. Digre said.

When Ocular Surface Disease Is Related to Migraine

Symptoms of ocular surface disease are more common among individuals with migraine than among those who don't get migraines, according to Dr. Galor. She noted that both individuals with migraine and those with symptoms of ocular surface disease often report exacerbation of symptoms with exposure to light. Studies have shown increased corneal sensitivity both in patients with migraine and in those with symptoms of dryness, she said. "Patients with dry eye symptoms are continuously stimulating their trigeminal system," said Dr. Digre. This can increase the frequency of migraine in those who are susceptible to the condition. Additionally, "individuals with migraine are, in general, hypersensitive to all kinds of stimuli, so they may be more likely to experience ocular surface symptoms as severe," said Dr. Gratton. It can be a vicious cycle, in which one condition continually aggravates the other, he said. The ocular surface disease can stimulate the trigeminal afferents (also known as peripheral sensitization) so much that the nuclei in the brain stem (central sensitization) actually start signaling pain when the underlying initial stimulus is gone, said Dr. Digre.

Ocular surface disease root causes should be identified and treated comprehensively, Dr. Gratton said.

Assess neurologic contributors. To help determine whether ocular surface pain and ocular surface disease symptoms exist independently or are related to migraine, Dr. Digre suggests asking patients the following: 1) does the pain interfere with life, 2) is there light sensitivity, and 3) is there nausea or vomiting accompanied by eye pain? If patients answer yes to two of these three questions, migraine or other neurologic contributors should be investigated. "Other tell-tale signs include light sensitivity at examination, prominent venous pulsations, and reduced pain with superficial temporal artery compression or superficial supraorbital artery compression," said Dr. Digre. When nerve contribution is suspected, Dr. Galor puts a drop of proparacaine into each eye and checks for a decrease in pain. Persistence of pain following anesthesia suggests central sensitization or other nonocular surface-related contributors.[1]

Migraine Management

While ophthalmologists may not be equipped to diagnose or prescribe exhaustively for migraine, they can uncover neuropathic connections to eye symptoms, educate patients, and create established referral pathways with providers who offer comprehensive migraine treatment, said Dr. Gratton. He emphasizes a three-part approach to management: "abortive treatments that are taken when a headache starts; preventive therapy to decrease the frequency, intensity, and duration of migraine; and lifestyle changes aimed to reduce migraine triggers."

Dr. Galor said, "When I see an individual with eye pain whom I believe has neuropathic mechanisms and shares features with migraine [e.g., photophobia], I use strategies that I borrow from neurologists along with tools I have in my ophthalmology office. I also lean on connections built with neurology and pain specialists in my community."

Pain and Symptom Relief

For acute migraine, Drs. Digre and Gratton recommend several treatments, including timolol eye drops (see "Can Glaucoma Drops Help Migraine?" online with this article at aao.org/eyenet).

Treat the pain. For acute pain relief, Drs. Digre and Gratton start with over-the-counter medicines including acetaminophen/paracetamol and ibuprofen.

Triptans are an often-prescribed family of treatments; "they are tried and true with a long track record of safety," Dr. Gratton said. They can, however, cause blood vessels to constrict and are not recommended for people with heart conditions. Lasmiditan (Reyvow) is an alternative for patients who may be at risk of stroke or heart attack, according to Dr. Gratton.

Gepants are a newer class of medicines that work by blocking the receptor for calcitonin gene-related peptide (CGRP), a pain signal–carrying protein released during migraine. These treatments, which include rimegepant (Nurtec ODT) and ubrogepant (Ubrelvy) are more expensive and may not be covered by insurance as a first-line treatment, cautioned Dr. Digre.

Offer FL-41 lenses. Patients who struggle with photophobia can benefit from FL-41 lenses. These rose-tinted glasses developed in the 1980s can help alleviate light sensitivity by blocking out wavelengths of light known to

exacerbate migraine and photophobia. "The FL-41 lens is my favorite device, and it is backed by research," said Dr. Digre. Dr. Galor agrees that FL-41 lenses are a go-to tool for any patient with photophobia.

"They can be especially helpful for people who have chronic photophobia that persists in between migraines," said Dr. Gratton.

Prevention

"If the patient is taking abortive drugs more than twice a week, I suggest finding a preventive treatment," said Dr. Gratton.

Traditional medications. When it comes to reducing migraine recurrence, traditional prophylactic medications are the starting point for many patients. These drug families were originally designed to treat other conditions and later discovered to also prevent or reduce the frequency of migraines. Antiepileptic drugs (e.g., topiramate), beta blockers (e.g., propranolol), and antidepressants (e.g., amitriptyline) may be prescribed as a first step because they are generally covered by most insurance, said Dr Digre. "The process of finding the right preventive medication can involve a lot of trial and error, and some side effects are likely to be generated with all of these drugs," said Dr. Gratton.

CGRP monoclonal antibodies. Designed to prevent and alleviate migraine, CGRP monoclonal antibodies work by blocking release of the neurotransmitter CGRP or neutralizing it in order to prevent headaches.[2] The drug is delivered through injection (self-administered) or infusion (at the doctor's office) monthly or quarterly. "There are now four FDA-approved options—eptinezumab (Vyepti), erenumab (Aimovig), fremanezumab (Ajovy), and galcanezumab (Emgality)—and they are extremely well-tolerated and effective," said Dr. Gratton. "These drugs are game-changers for patients with migraine, and they have few side effects. But they are very expensive [approximately $600 per month] and not covered by many insurance payers as a first line of treatment," said Dr. Digre, adding that some payers require prior authorization. Dr. Galor is less enthusiastic about these medicines. "In my experience, they are solidly mediocre when it comes to addressing eye pain with neuropathic contributors," she said.

Onabotulinim toxin. Onabotulinim toxin is an FDA-approved preventive treatment for chronic migraine. By inhibiting the release of acetylcholine—another neurotransmitter involved in the trigeminal pain pathway—injections every 12 weeks can reduce the frequency of headaches.[2] Botox is one of several preparations. "Onabotulinim toxin is already being used in many ophthalmology offices for various oculoplastic issues, including blepharospasm and hemifacial spasm," said Dr. Galor. Dr. Gratton said, "It's a good option for people who have very frequent migraine. It's especially good for patients who take many other medicines because it's noninteractive." He added that several small studies have shown that onabotulinim toxin also has the potential to help with dry eye symptoms and photophobia. The cost of this treatment is comparable to that of CGRP monoclonal antibodies, and insurance coverage varies and often requires prior authorization.

Neuromodulation devices. These devices use electrical currents or magnets to adjust or change activity of the nerve pathways involved in a migraine.[3] They can be applied acutely to stop headaches that are already underway, and they are increasingly being used for prevention, according to Dr. Gratton. Neuromodulation, which offers a drug-free alternative for patients who have tolerability issues with pharmacological medications, carries no systemic side effects, he said. Treatments can be self-administered daily at home.

There are currently four FDA-approved devices on the market targeting different nerves: Cefaly Dual Enhanced (Cephaly), gammaCore (electroCore), Nerivio (Theranica), and SpringTMS (eNeura). One device—Cefaly—is available for purchase without a prescription. "Nerve modulation can take two to three months before you get a preventative effect. Patients have to buy in and stick with the treatment," said Dr. Galor. "These noninvasive devices make sense for patients who take a lot of medications, but they can cost hundreds of dollars, and not all of them offer a money-back guarantee," said Dr. Gratton.

Lifestyle Changes

Manage triggers. Dr. Digre emphasized the importance of asking patients about migraine risk factors, including family history, stress, depression, and sleep apnea, and talking about obesity[4] when necessary. "Education about lifestyle management is free and easy and can make a world of difference to patients," she said. Dr. Gratton informs patients that both the frequency and the intensity of migraine is influenced by factors that the patient has some control over. "Stress is a big influencer. Others include poor sleep, poor hydration, inconsistent nutrition/skipping meals, and not exercising," he said. He also tells patients that overuse of acute medications can lead to medication-overuse headache. Both Dr. Digre and Dr. Gratton often recommend supplementing with magnesium oxide and riboflavin (vitamin B2), which they say have minimal risks and have been found effective as preventive strategies.

1 Baksh B. et al. *Eye Brain*. 2021;13:41-57.
2 Siddiqui M. et al. *Cureus*. 2021;13(1):e13002.
3 Ailani J. et al. *Headache*. 2021;61(7):1021-1039.
4 Martami F. et al. *Headache*. Published online July 19, 2022.

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