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Eye Care Newsletter

Omni Eye Specialists • Madison Street Surgery Center
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Neovascular Glaucoma

Neovascular glaucoma (NVG) is a potentially devastating result of serious underlying ocular and/or systemic diseases. Most cases of NVG are preceded by ischemic disease of the retina, and the subsequent release of diffusible angiogenic factors which promote new blood vessel growth. It is imperative to make the diagnosis early, and then initiate immediate and aggressive treatment. A delayed diagnosis or poor management can result in complete loss of vision, and possibly even loss of the globe itself.

The major histopathologic findings in the anterior segment consist of new blood vessels associated with a fibrous membrane. Diffusible angiogenic factors, such as vascular endothelial growth factor (VEGF), promote neovascularization (NV) of the iris and anterior chamber angle. Fine tufts of new vessels usually appear at the pupillary margin and then spread into and over the iris. Once in the anterior chamber angle, these vessels cross the scleral spur, spreading over and invading the trabecular meshwork. This fibrovascular membrane progressively obstructs the outflow pathway leading to secondary open-angle glaucoma. As the disease process continues, there is contraction of the membrane leading to ectropion uveae and peripheral anterior synechiae, and ultimately total synechial closure of the angle. At this stage, it is considered a form of secondary angle-closure glaucoma.

The three most common conditions responsible for NVG are diabetic retinopathy (DR), central retinal vein occlusion (CRVO) and carotid artery occlusive disease. Of these conditions, DR and CRVO produce nearly two-thirds of all cases of NVG. In cases of

DR, prevalence of NVG is significantly higher in proliferative DR than non-proliferative DR. The incidence of NVG in diabetic patients is further increased in patients who have undergone a lensectomy and/or vitrectomy. It is thought that a breach in the posterior capsule of the lens, due to a complicated cataract extraction or even from Nd:YAG capsulotomy, allows the introduction of angiogenic factors into the anterior segment.

NVG is seen more commonly in patients with ischemic CRVO than in non-ischemic CRVO. In general, the occurrence of iris neovascularization requires ischemia of at least half of the retina. Although many cases of NVG occur within three months of the CRVO, over 80% appear within the first six months, and glaucoma develops earliest in the eyes with the most extensive ischemia. However, since there is a one-third conversion rate from non-ischemic CRVO to ischemic CRVO, any patient with CRVO must be followed closely for the development of neovascularization. The most reliable predictor of NVG following CRVO is the presenting visual acuity, where over 30% of eyes with acuity less than 20/200 within one month of the occlusion developed anterior segment NV.

Carotid artery occlusive disease is the third most common cause of NVG, but is the most likely to be missed or misdiagnosed. It produces a paradoxically low intraocular pressure (IOP), despite the presence of anterior segment NV, and can diminish the amount of retinopathy on the side of the occlusion. It is imperative to recognize the significance of carotid artery obstruction since the result can not only be vision threatening, but also life threatening.

Gary Belen, M.D.

In early stages of NVG, patients may present with a normal or elevated IOP, and NV of the iris or angle may be seen. In advanced stages, patients will often complain of severe pain, headache, nausea and/or vomiting, photophobia, and decreased (sometimes counting fingers or hand motion) visual acuity. The examination will show conjunctival injection, corneal edema, possibly hyphema, and an elevated IOP (usually greater than 40mmHg). Extensive NV is seen both anteriorly and posteriorly.

The management of NVG is three-fold: 1) Reducing the VEGF production of ischemic tissue, 2) Reducing the IOP, and 3) Treating the underlying cause of the NV. The latter is usually accomplished in conjunction with the patient's primary care physician, and good communication is essential to improve patient outcomes.

Panretinal photocoagulation (PRP) is the treatment of choice for ischemic retinal disease, and has been shown to reduce and eliminate anterior segment NV. The exact mechanism of action for PRP is unknown, but it is possible that the laser simply decreases the total amount of retina available to produce angiogenic factors. Treatment usually includes about 1500 laser spots outside the vascular arcades. Close follow-up is essential to monitor the response and apply further treatment as necessary.

Anti-VEGF therapy can be used to block the angiogenic factors that promote NV. Treatment is given intravitreally, and less commonly intracamerally. The most common Anti-VEGF therapies are bevacizumab (Avastin) and ranibizumab (Lucentis). These can be given in conjunction with PRP, or as an alternate treatment when visibility of the posterior segment is limited.

Reduction of intraocular pressure is usually initiated with medical therapy. Aqueous suppressants can be given topically or systemically, and are often accompanied by anti-inflammatory and cycloplegic agents for inflammation and pain control. Osmotic agents may provide acute, but transient lowering of IOP by reducing vitreous volume. Topical glycerin may help to clear corneal edema, facilitating accurate diagnosis and delivery of PRP.

Unfortunately, the elevated IOP in many cases of NVG are refractory to pharmacological treatment and go on to need surgical intervention. Glaucoma drainage implants are preferred over trabeculectomy since they are less prone to post-operative scarring, however the use of anti-metabolites such as Mitomycin-C have improved the success rates of trabeculectomy in cases of NVG. In cases with limited visual potential, cyclodestructive procedures can be considered to destroy the ciliary body to reduce aqueous production. Alcohol injection or enucleation offer alternative options for pain control in eyes unlikely to derive any potential benefit from laser or surgical intervention.

Allergic Conjunctivitis Overview **Ketty Lee, O.D.**

Springtime in Colorado is well on its way and along with that typically comes seasonal allergies. We are already seeing several allergic conjunctivitis cases present in our clinics. With new medications available on the market, an overall update on allergic conjunctivitis treatment may be helpful.

Etiology:

- Type I hypersensitivity reaction to specific airborne allergens. Conjunctival mast cells degranulation releases histamine and proinflammatory mediators into the tear film and tissues. This causes dilation of conjunctival vessels leading to red eyes, overall edema of tissues, and significant itch.
- Seasonal Allergic Conjunctivitis – related to hay fever. This is caused by seasonal allergens such as tree pollen, weeds, grasses, and fungal spores
- Perennial Allergic Conjunctivitis: This is typically caused by allergens that surround us more commonly such as dust mites, mold, or animal dander. The symptoms are typically throughout the year. This is typically less severe than the seasonal type.

Main Symptoms:

- Itching of eyes
- Red eyes
- Watery eyes
- Mild to Moderate lid edema
- Chemosis, hyperemia, and possible diffuse papillary reaction of the bulbar and tarsal conjunctiva

Allergic Cascade:

The allergic reaction is typically triggered by antigens which cross link with Immunoglobulin E antibody (IgE) on the mast cells, resulting in mast cell degranulation. This in turn releases histamine and proinflammatory mediators such as prostaglandins, tryptase and heparin. The histamine binds with H1 receptors on nerves and causes the severe itch sensation. It also binds to the H1 receptor sites on the blood vessels causing chemosis, edema, and chemosis.

Since there are over 50 million mast cells in the human conjunctiva, the mast cell is crucial to the ocular allergic response. As allergies cause the mast cell degranulation and the release of histamines and other proinflammatory mediators, it makes sense that the most effective medications will address both problems and therefore are able to quickly address, relieve, and prevent the symptoms. On the market there are several options in medications, typically in the categories of antihistamines, mast cell stabilizers, and dual action combination antihistamine/mast cell stabilizers. There are also anti-inflammatory agents, such as low dose steroids to treat more chronic and severe cases.

Antihistamine Options:

- Vasocon-A (antazoline and naphazoline) - OTC
- Visine-A (pheniramine maleate and naphazoline) - OTC

- Opcon-A (pheniramine maleate and naphazoline) - OTC
- Naphcon-A (pheniramine maleate and naphazoline) - OTC

Most are in combination with naphazoline, a vasoconstrictor. The antihistamine stops the itch and the vasoconstrictor decreases conjunctival redness.

The limitations of these medications are that they have a short duration of action and are indicated for QID dosage. Chronic use of these medications can also lead to rebound vasodilation and chronic red eyes.

Prescription Antihistamine Option:

- Emadine (emedastine) tends to have fewer side effects but still does not provide full day coverage and requires QID dosage

Mast Cell Stabilizers Options:

- Opticrom (cromolyn sodium) – QID dosage
- Alamast (pemirolast potassium – QID dosage
- Alocril (nedocromil sodium) – BID dosage
- Alomide (lodoxomide tromethamine) – QID dosage

These medications interfere with calcium intake following allergen-IgE binding, which prevent degranulation. Mast cell stabilizers are effective prophylactically, but they are quite ineffective in relieving existing signs and symptoms of ocular allergies. Advanced QID dosing is also required (except for Alocril) prior to the allergy season for maximum efficacy, and the exact timing can often be missed.

Combination Mast Cell Stabilizers and Antihistamine Options:

- Patanol (olopatadine HCL 0.1%) BID dosing
- Pataday (olopatadine HCL 0.2%) QD dosing
- Zaditor (ketotifen fumarate) BID dosing – now OTC
- Optivar (azelastine HCl) BID dosing
- Elestat (epinastine) – BID dosing
- Bepreve (bepotastine besilate) – BID dosing

These combination medications are typically the most effective in addressing symptoms quickly and preventing new symptoms. With BID dosing, they have been effective in increasing patient compliance versus either mast cell stabilizers or antihistamine medications alone. Pataday's QD dosage has made usage even simpler, especially for contact lens wearers. Zaditor is certainly a welcome addition to the OTC market since most OTC drops only provide 3-4 hours of relieve of symptoms as compared to Zaditor's up to 12 hour relief from significant itch.

Most of us believe that targeting multiple sites of the ocular allergic response pathway is important for effective treatment. So, these medications that provide both mast cell stabilization and antihistamine action are currently still the longest lasting, best tolerated, and most effective ocular allergy treatments.

Flaps in Lasik were traditionally made with a high speed blade, contained in a device called a microkeratome. Bladed keratomes have a good safety record, but complications can occur. Because flap creation is responsible for the majority of LASIK complications and safety issues, it is the source of most patients' fear of the procedure. Addressing this problem, the Femtosecond (Intralase) laser was approved by the FDA in 2001. After a slow period of adoption, Intralase is gaining significant market share. There have now been 3 million flaps created with FS, almost half of all flaps now created.

The Femtosecond laser is an ultrahigh frequency (pulse duration 10^{-15} seconds) laser with very low energy per pulse. Each pulse of the laser creates a bubble of air inside the cornea at a specific depth. By aligning thousands of these bubbles, we can create a dissection of the cornea along a given plane creating a safer flap. The first studies using a Femtosecond laser for Lasik were done in Hungary in 1998 with a 2Khz laser that took 5 minutes to make a flap. Each generation of Intralase has produced advantages over it's predecessor. The current iteration has a hertz rate of 150, reducing flap creation time to about 10 seconds.

Advantages of Femtosecond over Bladed keratomes

- Greater safety, with virtually no chance of a buttonhole
- Increased flap stability
- The ability to create thinner and more customizable flaps. By making the flap thinner, some patients who were considered poor Lasik candidates can now be successfully treated.
- Clinical studies show more patients achieve vision that is 20/20 or better when their LASIK procedure is performed with the IntraLase Method. And patients report better quality of vision overall, particularly in terms their ability to see well in low light such as at dusk or at night.

Advantages of the New 5th Generation iFS over other Femtosecond Lasers

- A beveled side cut angle that slows stronger flaps because of it's inverted edge, essentially creating a tongue and groove configuration which essentially "locks" back into position (150 vs. 60 degrees).
- A higher rep rate that can produce a flap in under 10 seconds reducing pt anxiety.
- Increased patient comfort and decreased inflammation because of lower energy needed to make the flap.
- Decreased Postop light sensitivity
- Smoother flap bed proven with EM.

iFS is the final frontier of Femtosecond laser technology used in the iLASIK procedure: NASA approved the LASIK procedure for its astronauts following review of extensive military clinical data, which showed the use of two lasers (Femtosecond & wavefront-guided) provides superior safety and vision as compared to earlier forms of the procedure. A study of 200 Naval airmen by Steve Schallhorn, M.D., showed that eyes treated with the Femtosecond laser had better acuity and better contrast sensitivity than those treated with a blade. The downside was that the laser treated patients had higher Postop light sensitivity (this problem has been solved with the newer generations of the Femtosecond).

Another application of the Femtosecond is corneal transplants. Donor and recipient buttons have historically been cut with scissors and a blade. The inherent inaccuracy of this technique made wound leaks possible and created the potential for very high Postop astigmatism. The Femtosecond, which precisely create any incision configuration, allows the donor and recipient corneas to fit together like the pieces of a puzzle. This significantly improves the quality and safety of the surgery.

The iFS costs over 6X what the bladed keratome costs, and adds a few hundred dollars to the cost of the procedure. After doing tens of thousands of bladed procedures during my first 10 years of Lasik, I believe that the added predictability, safety and stability of the flap makes the extra cost a good value



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www.omniye.com – www.spivack.com

Omni Eye Specialists
55 Madison St, Suite 355
Denver, CO 80206
303-377-2020
www.omniye.com

Spivack Vision Center
6881 S. Yosemite St
Centennial, CO 80112
303-733-2020
www.spivack.com

Madison Street Surgery Center
55 Madison St, Suite 200
Denver, CO 80206
303-388-0599
www.madisonstreetsurgerycenter.com