Results of a 12-month study of eyes with persistent diabetic macular edema (DME) after multiple anti-vascular endothelial growth factor (anti-VEGF) injections indicate that a dexamethasone implant combined with bevacizumab improves visual acuity and macular morphology significantly. The study, published in *Retina* in 2015, also found that visual acuity changes were not superior to those obtained by continued bevacizumab monotherapy.

Michael W. Stewart, M.D., chair of Ophthalmology at Mayo Clinic's campus in Jacksonville, Florida, and Raj K. Maturi, M.D., with the Midwest Eye Institute in Indianapolis, studied 40 eyes in 30 patients to determine whether a dexamethasone intravitreal implant 0.7 mg (dexamethasone drug delivery system, or dexamethasone DDS) combined with bevacizumab 1.25 mg provides greater benefit than bevacizumab monotherapy in eyes with diabetic macular edema with incomplete response to multiple anti-VEGF injections.

“We know that corticosteroids down-regulate VEGF synthesis, but unbound VEGF concentrations after corticosteroid treatment are still 100 times higher than those after anti-VEGF therapy,” says Dr. Stewart. “Therefore, combining corticosteroids with anti-VEGF drugs may produce the greatest possible suppression of vascular permeability. Adding triamcinolone to an anti-VEGF regimen fails to incrementally improve DME, but we aren’t aware of any trials that pair dexamethasone DDS with an anti-VEGF drug.”

**Eligibility, assignment and treatment**

Eligibility criteria included an age of 18 years or older, best-corrected visual acuity scores between 24 and 78 Early Treatment Diabetic Retinopathy Study letters (20/32 to 20/320 Snellen equivalent), and the presence of DME because of type 1 or 2 diabetes mellitus with a central subfield thickness of greater than 250 µm measured by time-domain optical coherence tomography.

Most of the enrolled eyes had previous treatment with multiple anti-VEGF injections. Fluorescein angiography was performed before enrollment to rule out significant foveal nonperfusion.

Subjects were randomly assigned to one of the two treatment groups in a 1:1 ratio. For patients in whom both eyes met the eligibility criteria, the right eye was randomized to a treatment group and the left eye was assigned to the other group.

The 21 eyes assigned to the combination group received bevacizumab 1.25 mg intravitreally at baseline followed by the dexamethasone implant at month one. Bevacizumab injections were repeated at months two, three, four, six, seven, eight, 10 and 11 when the central subfield thickness was greater than 250 µm and the Early Treatment Diabetic Retinopathy Study visual acuity score was less than 80 letters (20/25 Snellen equivalent). Dexamethasone implants were re-injected at months five and nine according to the same criteria.

The 19 eyes in the monotherapy group received bevacizumab 1.25 mg intravitreally at baseline and month one. Bevacizumab injections were repeated at months two, three, four, six, seven, eight, 10 and 11 when the central subfield thickness was greater than 250 µm and the Early Treatment Diabetic Retinopathy Study visual acuity score was less than 80 letters (20/25 Snellen equivalent). Dexamethasone implants were re-injected at months five and nine according to the same criteria.

The primary endpoints of the trial were an...
Intraoperative Torsional Forced Duction Test Assesses Obliques’ Tightness and Laxity

A research team in Ophthalmology at Mayo Clinic’s campus in Rochester, Minnesota, has developed a new method for quantifying intraoperative torsional forced ductions and validated the test by comparing patients with oblique muscle dysfunction and controls. The torsional forced duction test enables quantitative assessment of superior oblique (SO) and inferior oblique (IO) tightness and laxity, and is useful for intraoperative surgical planning.

“This simple method more precisely quantifies SO and IO tightness or laxity by measuring the number of degrees of allowable torsional movement,” says Jonathan M. Holmes, M.D. “The new test was validated by comparing the quantitative values obtained between patients with normal oblique muscles and controls, and now can be used to guide the surgeon in planning and performing oblique muscle surgery.” The study was published in Ophthalmology in September 2015.

The test

The new torsional forced duction test is performed in the anesthetized patient using a commercially available Mendez ring, 0.3-mm forceps and a skin-marking pen.

At the start of surgery, while the patient is under deep general anesthesia, the surgeon marks the 12 and 6 o’clock positions at the limbus. Then the globe is maximally excyclorotated without retroposition until the first resistance is felt. Then the surgeon reads the angle of rotation (in degrees) on a Mendez ring and a photograph can be taken. The procedure is repeated for incyclorotation.

The study

The team studied 33 eyes with oblique dysfunction — nine with presumed congenital superior oblique palsy (SOP), 13 with acquired SOP, seven with Brown syndrome and four with inverted Brown syndrome — and 31 controls. They also studied six eyes after SO disinsertion and two eyes after inferior oblique disinsertion.

Patients with a history of strabismus surgery, ocular trauma, or any restriction of the horizontal or vertical rectus muscles, based on standard intraoperative forced duction tests, were excluded, except for cases of suspected inverted Brown syndrome.

The team also evaluated 31 patients as controls (ages 8–77 years). One eye was randomly selected from each control patient (n = 31 eyes) for analysis. The control subjects:

• Had no restriction of any horizontal or vertical rectus muscles
• Had negative Guyton’s exaggerated forced duction tests for SO or IO tightness or laxity
• Were scheduled to undergo horizontal muscle surgery to correct purely horizontal strabismus

Researchers also measured maximal excyclorotation after complete SO disinsertion, before

In the 10 patients (20 eyes) who received treatment in each eye, improvements in central subfield thickness at 12 months were significantly greater for the eyes receiving combination as opposed to monotherapy, a difference that far exceeded that seen in patients who had only one eye enrolled.

“This fellow-eye comparison provides the strongest evidence for the superior ability of combination therapy with anti-VEGF and dexamethasone-with-bevacizumab therapy to resolve DME thereby warranting further investigation,” says Dr. Stewart.

For more information

Intense Pulsed Light for Treatment of Dry Eye Disease

In a retrospective study of patients with refractory dry eye who had exhausted conventional treatment and elected to receive intense pulsed light and meibomian gland expression (IPL/MGX), 58 percent of patients’ symptoms improved from as much as 25 to more than 50 percent after treatment. Study results were published in *Cornea* in 2016.

Joanne F. Shen, M.D., Ophthalmology chair and director of the dry eye clinic at Mayo Clinic’s campus in Phoenix/Scottsdale, Arizona, and a research team studied 35 patients treated with IPL/MGX. The team reviewed demographics, ocular histories, Standard Patient Evaluation of Eye Dryness 2 (SPEED2) symptom survey scores, slit-lamp examinations and meibomian gland evaluations at baseline and at each visit before IPL/MGX treatments. All patients had a minimum of six months of follow-up after the first treatment and typically received one to four treatments spaced four to six weeks apart.

After four IPL/MGX treatments, a paired sample t-test showed a significant ($P < 0.0001$) decrease in SPEED2:

- 8 patients (23 percent) had a ≥ 50 percent decrease in SPEED2 scores
- 23 patients (66 percent) had a 1 to 49 percent decrease in SPEED2
- 1 patient (3 percent) had no change in SPEED2

In research published in *Pediatric Ophthalmology: Current Thought and a Practical Guide* in 2009 and *Journal of the American Association for Pediatric Ophthalmology and Strabismus* in 2013, who studied maximal excyclorotation and maximal incyclorotation under general anesthesia, but did not describe how they quantified the degree of rotation. The new test quantifies the amount of torsion using a Mendez ring and seemed to be less variable in control subjects.

“This new test is particularly useful in the diagnosis of congenital SOP, Brown syndrome and inverted Brown syndrome, and may guide intraoperative surgical planning in these conditions or when these conditions are suspected,” says Dr. Holmes. “It is also also useful in confirming complete or incomplete intraoperative disinsertion of the SO tendon or IO muscle, and may help prevent unwanted surgical undercorrection when disinsertion or recession of the obliques is indicated.”

Comparative advantages

The new torsional forced duction test offers several advantages over current test procedures:

- The new test complements the qualitative exaggerated forced duction test described by David L. Guyton, M.D., published in *Ophthalmology* in 1981, because the new test is quantitative, yielding a value in degrees and performed in a more physiologic field of rotation.
- The new test extends the qualitative test described by Burton J. Kushner, M.D., published in *Archives of Ophthalmology* in 2007, because the new test provides a value in degrees and allows values in one eye to be compared with control values and compared with values in the fellow eye. The new test also allows quantitative monitoring of stepwise effects during the surgical procedure.
- The new test procedures expand on the test described by Irene H. Ludwig, M.D., and others in research published in *Pediatric Ophthalmology: Current Thought and a Practical Guide* in 2009 and *Journal of the American Association for Pediatric Ophthalmology and Strabismus* in 2013, who studied maximal excyclorotation and maximal incyclorotation under general anesthesia, but did not describe how they quantified the degree of rotation. The new test quantifies the amount of torsion using a Mendez ring and seemed to be less variable in control subjects.

For more information


Education Opportunities

Practical Clinical Case-Oriented Neuro-Ophthalmology 2016
Dec. 8-10, 2016, in Las Vegas

This course reviews papilledema, pseudopapilledema, diplopia, nystagmus and neuroradiology, plus practical approaches to patient evaluation and management of common neuro-ophthalmologic conditions such as optic neuritis, neuroretinitis, neuromyelitis optica, ischemic optic neuropathy, Horner syndrome, downbeat nystagmus and myasthenia gravis.

For more information or to register, visit https://ce.mayo.edu/ophthalmology, call 800-323-2688 (toll-free) or email cme@mayo.edu.

3 patients (9 percent) had an increase in SPEED2

“The combination of IPL and MGX can significantly improve dry eye symptoms — in this retrospective analysis, in 89 percent of patients — and meibomian gland function, which in this study improved in 77 percent of patients in at least one eye,” says Dr. Shen. “The study confirms that IPL treatment for meibomian gland dysfunction can improve dry eye symptoms and is a reasonable option for patients who have not shown improvement with other therapies.”

IPL/MGX procedure
At the first treatment, each patient underwent Fitzpatrick skin typing, and the IPL machine was set to appropriate settings — 1D, 2D or 4A. At each treatment, the eyelids were bilaterally closed and sealed shut with disposable eye shields. After generous application of ultrasonic gel to the treated skin, patients received approximately 30 pulses (with slight overlapping applications) from the right preauricular area, across the cheeks and nose to the left preauricular area, treating up to the inferior boundary of the eye shields.

Each treatment was followed by MGX with a cotton tip applicator and digital pressure to empty meibum from bilateral upper and lower eyelids. Patients used preservative-free ketorolac drops twice a day for two days after IPL treatment. Slit-lamp examination was performed before each treatment.

“Patients underwent four monthly examinations and IPL/MGX treatments or until symptoms were resolved to their satisfaction, treatments became intolerable or they were unable to continue the treatment protocol,” says Dr. Shen.

After the first IPL/MGX treatment, early-responder patients experienced five to seven days of symptomatic improvement followed by regression until the next treatment. After the second treatment, patients experienced one to two weeks of improvement. Slow responders did not see improvements until after the second or third treatment. After the fourth treatment, most patients had at least three months of sustained improvement.

“Interestingly, 63 percent of this IPL/MGX-responsive group previously failed to respond to LipiFlow thermal pulsation,” says Dr. Shen. “However, these therapies are not a permanent fix. Once regression occurs, we recommend a single IPL/MGX treatment that varies between patients. In our patient population, a few patients are in remission, but most will require repeat single treatments every three to six months.”

Use of topical and systemic medications usually can be discontinued after IPL/MGX, but the dry eye clinic team prescribes omega-3 fatty acids at 1,200 mg daily for patients after treatment. “My philosophy has shifted over the past five years, from handing out the multiple tear substitutes available to now, instead, focusing on restoring the ocular surface and tear film,” says Dr. Shen.

For more information