Journal Highlights

EXTRA
CONTENT AVAILABLE

NEW FINDINGS FROM *OPHTHALMOLOGY, AJO,* AND *JAMA OPHTHALMOLOGY*

Ophthalmology

Aflibercept for Myopic CNV

June *Ophthalmology*

In the first phase 3 study to evaluate intravitreal aflibercept in patients with myopic choroidal neovascularization (CNV), **Ikuno et al.** found that the drug was safe and effective.

A total of 122 patients with high myopia were enrolled in this double-masked, sham-controlled study (known by the acronym MYRROR) and randomized 3:1 to receive intravitreal injection of 2 mg of aflibercept or sham. In the aflibercept arm, patients (n = 91) received one injection at baseline and additional aflibercept as often as every four weeks based on disease activity through week 44. If active treatment was not needed, patients were given a sham injection to maintain the masking. In the sham arm, patients (n = 31) received injections every four weeks through week 20. At week 24, patients in this arm were given aflibercept—then, depending on disease activity, they received either aflibercept or sham injections every four weeks through the end of the study. Over the course of the trial, the patients in both groups received a median of three aflibercept injections.

The primary outcome measure was mean change in best-corrected visual acuity at week 24. At this point, patients in the aflibercept group had gained a mean of 12.1 letters, while those in the sham group had lost two letters. By week 48, patients in the aflibercept group had gained 13.5 letters, while those in the sham/aflibercept group had gained three letters.

Seven patients, all of whom were in the aflibercept group, experienced serious treatment-emergent adverse events. Four of the events were systemic and three were ophthalmic, with one patient experiencing a macular hole in the treated eye.

Refractive and Nonrefractive Visual Loss: Impact on Disability

June *Ophthalmology*

Does one type of visual loss have a greater impact on a person's functional ability than another? **Zebardast et al.** investigated this question and found that it does.

The researchers assessed participants in the first round of the Salisbury Eye Evaluation (SEE) study, a population-based study of older Americans that evaluated a broad range of vision-related abilities. For this cross-sectional study, the effects of uncorrected refractive error (URE) were compared with those of nonrefractive visual impairment (VI) on performance and disability measures.

Main outcome measures included the following: 1) objective measures of ability, notably timed performance of mobility (walking and climbing stairs) and near-vision tasks (such as inserting a key into a lock), 2) self-reported issues with driving, and 3) self-reported visual difficulties measured by the activities of daily vision scale.

Of the 2,469 individuals in the SEE study, 191 had decreased visual acuity as a result of VI, and 132 had decreased acuity from URE. Those with VI demonstrated poorer objective and subjective visual functioning in all metrics examined, while those with URE had difficulty with most but not all of the categories examined. Overall, the relative impact of VI on disability was considerably greater than that of URE, the researchers said.

The study had some limitations, the researchers acknowledged. For instance, they were unable to consistently identify the causes of nonrefractive vision loss and thus could not differentiate between specific eye diseases.

MMC in Excimer Laser Ablation Techniques

June *Ophthalmology*

In an *Ophthalmic Technology Assessment,* **Majmudar et al.** reviewed the published literature on the efficacy and safety of mitomycin-C (MMC)

when used as an adjunctive treatment in corneal excimer laser ablation procedures. They found good evidence of effectiveness for the intraoperative use of MMC but noted that several issues remain to be settled, including optimal dosage. They also presented several clinical pearls and highlighted opportunities for future research.

For this report, the authors selected 26 published articles that were considered to be of high or medium clinical importance. Of these, 10 studies were rated as level I evidence, five were rated as level II evidence, and the remaining 11 were rated as level III evidence.

The majority of articles reviewed support the role of MMC as an adjunctive treatment in surface ablation techniques, the authors said. When MMC is applied in the appropriate concentration and confined to the central cornea, it inhibits haze formation and improves visual acuity outcomes, particularly in highly myopic eyes.

While some studies found a reduction in endothelial cell density following MMC use—though no adverse outcomes were noted with as much as five years of follow-up—the clinical significance of this finding remains uncertain, the authors said. Other areas in need of additional research include optimal dosage and MMC's effectiveness when used in lower myopic and hyperopic ablations.

American Journal of Ophthalmology

Autorefraction-Based Preschool Vision Screening

June *AJO*

In this retrospective economic evaluation, **Lowry et al.** investigated referral criteria in preschool vision screening protocols. They sought to determine the criteria that produced the lowest cost per case detected. They found that commonly used referral criteria were more sensitive than is optimal for cost effectiveness, especially for myopia referrals.

Preschoolers in San Francisco and Oakland received preschool-based Retinomax autorefraction screening with a standard referral protocol and as-needed comprehensive eye examinations in 2012-2013. Positive predictive values and referral criteria that minimized cost per case detected were derived from the San Francisco data. This model of referral criteria was then retrospectively tested in Oakland for cost-effectiveness, with sensitivity analysis, against two other commonly used referral criteria. Cases were defined according to the American Association for Pediatric Ophthalmology and Strabismus (AAPOS) criteria for amblyopia risk factors.

In San Francisco, 3,974 children were screened, 631 referred, and 412 examined. Forty-eight percent of referrals (301 children) met more than one of the referral criteria. Positive predictive values ranged from 7 percent for myopia to 56 percent for astigmatism. In Oakland, 2,359 children were screened, and 269 were examined. When the referral model derived from San Francisco was applied to the study population in Oakland, the cost per case detected was $258. This cost was lower than that of either the original referral criteria or the criteria based on the Vision in Preschoolers study, which were $424 and $371, respectively, per additional case detected.

The authors concluded that more stringent referral criteria may reduce the cost per case detected in vision screening and allow more at-risk children to be detected with the same financial resources.

Bleb-Related Infections After Trabeculectomy

June *AJO*

Kim et al. reported the incidence of late-onset bleb-related infections and identified risk factors for bleb-related infections after trabeculectomy for the treatment of glaucoma.

In this retrospective case series, bleb-related infections were defined as blebitis, endophthalmitis, or blebitis with endophthalmitis. A total of 1,959 eyes of 1,423 patients who underwent trabeculectomy and were followed for one year or longer were included. During a mean follow-up period of 5.4 years, 24 eyes were diagnosed with bleb-related infections, of which 15 eyes had blebitis, and nine had endophthalmitis. Among the 15 eyes with blebitis, two eyes developed endophthalmitis while under treatment. The Kaplan-Meier estimated incidence of bleb-related infections was 2 percent at 10 years.

A Cox multivariate analysis showed the significant risk factors for a bleb-related infection to be diagnosis of pigmentary glaucoma or juvenile glaucoma, history of bleb leak, intraocular pressure sustained below the target pressure, chronic blepharitis, and the presence of punctal plugs. Surgical bleb revision demonstrated a protective effect against bleb-related infections when risk factors were present.

The authors warned that clinicians should be constantly vigilant for, and patients made aware of, the possibility of bleb-related infections long after trabeculectomy, especially in the presence of identified risk factors.

Intermediate-Stage AMD in Patients With AIDS

June *AJO*

Jabs et al., from the Studies of Ocular Complications of AIDS Research Group, used a cross-sectional study of their patients with AIDS to evaluate the prevalence of intermediate-stage age-related macular degeneration (AMD). They found that the prevalence of intermediate-stage AMD was significantly greater in participants with AIDS than among people who were not infected with HIV.

Intermediate-stage AMD was determined from enrollment retinal photographs by graders at a centralized reading center, using the Age-Related Eye Disease Study grading system. Graders were masked as to clinical data. Of 1,825 participants with AIDS and no ocular opportunistic infections, 9.9 percent had intermediate-stage AMD. Risk factors included age, with the risk increasing every decade; the prevalence of AMD ranged from 4 percent among participants 30 to 39 years old to 24

percent for participants aged 60 years or older. Other risk factors included the HIV risk groups of injection drug use or heterosexual contact. Compared with the HIV-uninfected population in the Beaver Dam Offspring Study, there was an approximately fourfold increased age-adjusted prevalence of intermediate-stage AMD.

This increased prevalence is consistent with findings on higher rates of other age-related diseases in antiretroviral-treated, immune-restored HIV-infected persons compared with non–HIV-infected persons.

JAMA Ophthalmology

Telemedicine for Diabetic Retinopathy

May *JAMA Ophthalmology*

Mansberger et al. compared the long-term effectiveness of telemedicine and traditional eye examinations in providing screening examinations for diabetic retinopathy.

From Aug. 1, 2006, through Sept. 31, 2009, 567 participants with diabetes were randomized and followed for up to five years (last patient follow-up date was Aug. 6, 2012) as part of a multicenter randomized clinical trial with an intent-to-treat analysis. Participants were assigned to one of two groups: telemedicine (n = 296), in which images were taken with a nonmydriatic camera in a primary care medical clinic and reviewed off site; or traditional surveillance with an eye care professional (n = 271). Two years after enrollment, telemedicine was offered to all participants.

The main outcomes were percentage of participants receiving annual diabetic retinopathy screening examinations; percentage of eyes with worsening diabetic retinopathy during the follow-up period on a scale from stage 0 (none) to stage 4 (proliferative diabetic retinopathy); and percentage of telemedicine participants who required referral to an eye care professional for follow-up care by the criteria of moderate diabetic retinopathy or worse, the presence of macular edema, or an "unable-to-determine" result for retinopathy or macular edema.

The telemedicine group was more likely to receive a diabetic retinopathy screening examination when compared with the traditional surveillance group during the time periods of six months or less (94.6 percent vs. 43.9 percent; $p < .001$) and greater than six months through 18 months (53.0 percent vs. 33.2 percent; $p < .001$). Diabetic retinopathy worsened by two stages or more in 35 of 409 participants (8.6 percent; 95 percent CI, 5.8-11.2 percent) and improved by two stages or more in five of 409 participants (1.2 percent; 95 percent CI, 0.1-2.3 percent) during the four-year period. The percent of telemedicine participants requiring referral ranged from 19.2 percent (52 of 271) to 27.9 percent (58 of 208).

The authors concluded that telemedicine increased the percentage of diabetic retinopathy screening examinations, that most participants did not require referral to an eye care professional, and that diabetic retinopathy levels were generally stable during the study period. These findings suggest that primary care clinics can use telemedicine to screen for diabetic retinopathy and monitor for disease worsening over a long period.

Outcomes of an Inner-City Vision Outreach Program

May *JAMA Ophthalmology*

Recognizing that urban children of low socioeconomic status often do not have access to ophthalmic care, **Dotan et al.** studied the demographic characteristics and ophthalmic conditions in children attending Give Kids Sight Day (GKSD). This event is an outreach ophthalmic care program held annually in Philadelphia to provide vision screening and immediate treatment if needed.

In this retrospective case-series study, the registration forms and records of all children who attended GKSD at Wills Eye Hospital in 2012 were reviewed. Demographic characteristics, insurance status, spoken languages, reasons for attending, prior failure of vision screening, and attendance patterns at previous events were analyzed. The ophthalmological findings of these children were examined, including refractive errors, need for optical correction, and diagnoses for which continuous ophthalmic care was necessary. For children who needed ophthalmic follow-up, the rate of return to clinic and barriers to continuous care were analyzed.

At GKSD 2012, there were 924 children (mean age, 9 years; range, 0-18 years; 51 percent female; 25 percent speaking a non-English language) from 584 families. Of these, 27 percent were uninsured and 10 percent were not aware of their insurance status. Although 42 percent of participants had public insurance that covered vision care and glasses, 35 percent of them did not know their benefits and did not realize vision care was covered. Forty-nine percent of children attended because they had failed community vision screening. Provision of free glasses and failure of previous vision screening were the most common reasons families elected to attend GKSD (64 percent and 49 percent, respectively). Eighty-five percent of children attended GKSD for the first time in 2012, whereas 15 percent had attended prior events.

Glasses were provided to 61 percent of attendees. Ten percent of the attendees needed continuous ophthalmic care, most commonly for amblyopia. Ten children needed ocular surgery for cataract, strabismus, nystagmus, ptosis, or nasolacrimal duct obstruction. With the assistance of a social worker, 59 percent of children who needed continuous treatment returned to the clinic, compared with 2 percent in prior years before social worker intervention.

The authors concluded that programs such as GKSD can bridge the gap between vision screening and ophthalmic treatment, a gap that often occurs in low-socioeconomic urban populations. Social worker intervention appears to be useful in overcoming common barriers to follow-up care.

ROUNDUP OF OTHER JOURNALS

Novel Treatment for Severe Plateau Iris Syndrome

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Francis et al. explored the effects of lens extraction plus endoscopic cycloplasty (ECPL) for severe plateau iris syndrome. They found that the combined treatment appears to open the anterior chamber angle and shrink and flatten the ciliary processes, effectively reversing the anatomic cause of angle closure that is observed in the syndrome.

For this prospective case series, the researchers evaluated six patients (12 eyes) who had plateau iris syndrome that was refractory to other treatment, including laser iridotomy and iridoplasty. All eyes were treated with standard cataract surgery and intraocular lens insertion. ECPL was then performed in the superior, nasal, and inferior quadrants; the untreated temporal quadrants served as controls. Ultrasound biomicroscopy (UBM) measurements were taken in all four quadrants before and after surgery.

Following treatment, the anterior chamber depth, iridocorneal angle, and angle opening distance UBM measurements all increased. In addition, measurements of the ciliary processes and iris contact all decreased, which is to be expected with a procedure that shrinks the ciliary processes, the researchers said. The control quadrants did not exhibit the same changes as those treated with laser.

Although intraocular pressure did not change significantly after treatment compared with baseline readings, the number of glaucoma medications was reduced. The researchers noted several possible factors in this outcome, including effects of the ciliary laser procedure, increase in aqueous flow due to angle opening, and phacoemulsification. However, they could not determine which of these contributed most strongly to the results.

No Topical Antibiotics for Intravitreal Injections

Retina
2015;35(4):783-788

Are topical antibiotics an essential component of the protocol for intravitreal injection? In a retrospective review, **Bhavsar and Sandler** assessed the incidence of endophthalmitis and other complications after a consecutive series of intravitreal injections in which no antibiotics were used. They found an exceptionally low risk of endophthalmitis, suggesting that topical antibiotics are not necessary for this procedure.

Over a 15-year period, the lead author administered a total of 18,839 injections to 3,457 patients in an outpatient setting. The patients' mean age was 81 years (range, 16-108 years), and the mean number of injections per patient was 5.5. Injections were administered with a regimen of topical povidone-iodine, proparacaine, and tetracaine; a sterile eyelid speculum; and clean nonsterile gloves. No antibiotics were used before, during, or after the procedure.

Because most of the patients were being treated for age-related macular degeneration, bevacizumab and ranibizumab accounted for 82.16 percent and 8.86 percent of injections, respectively. Other reasons for treatment were diabetic macular edema (DME), cystoid macular edema due to retinal vein occlusion, cytomegalovirus retinitis, and severe uveitis; drugs used included triamcinolone, pegaptanib, and dexamethasone.

There was one case of endophthalmitis, for an incidence rate per injection of 0.0053 percent. The affected patient, who had received bevacizumab for DME, later underwent a pars plana vitrectomy. The authors noted a possible contributing cause to endophthalmitis in this patient: He had inserted an extended-wear contact lens into the affected eye immediately after the injection without informing the surgeon that he was doing so.

AMD Lesion Activity and Treatment Outcomes

British Journal of Ophthalmology
2015;99(3):359-364

Barthelmes et al. set out to determine whether lesion activity, as assessed by the treating physician, had an effect on visual acuity (VA) outcomes in patients who received intravitreal injections for neovascular age-related macular degeneration (AMD). They found that, contrary to common belief, it did not.

This cohort study included 655 eyes from the Fight Retinal Blindness observational study. "Activity" was defined as intraretinal or subretinal fluid attributable to leakage from choroidal neovascularization or fresh hemorrhage. Lesion activity was classified as low, moderate, high, or persistent, based on the proportion of study visits in which it was seen. The primary outcome measure was change in VA 12 months after the index visit.

A total of 5,305 injections of ranibizumab were administered during the study. At the 12-month mark, the mean index VA was similar for the four cohorts. In addition, eyes in all four groups received similar numbers of injections during the study period. Nine adverse events were reported, including four cases of endophthalmitis, two of which were infectious.

Ophthalmology *summaries are written by Jean Shaw and edited by Susan M. MacDonald, MD.* American Journal of Ophthalmology *summaries are edited by Thomas J. Liesegang, MD.* JAMA Ophthalmology *summaries are based on authors' abstracts as edited by senior editor(s).* Roundup of Other Journals *is written by Jean Shaw and edited by Deepak P. Edward, MD.*

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