

Journal Highlights

NEW FINDINGS FROM THE PEER-REVIEWED LITERATURE

Ophthalmology

5-Year Outcomes of Anti-VEGF Treatment in AMD

August 2016

Maguire et al., writing on behalf of the Comparison of Age-Related Macular Degeneration Treatments Trials (CATT) Research Group, describe the 5-year outcomes of patients treated with bevacizumab or ranibizumab for neovascular age-related macular degeneration (AMD). Although the vision gains seen in the first 2 years of CATT were not maintained, half of the patients still had visual acuity of 20/40 or better.

In the original CATT cohort study, participants were randomly assigned to ranibizumab or bevacizumab at 1 of 3 dosing regimens. After 2 years, participants were released from their clinical trial protocol; at 5 years, they were recalled for an examination. The main outcome measures were visual acuity (VA) and morphologic retinal features.

The researchers determined VA for 647 of 914 surviving patients, at an average follow-up of 5.5 years. The mean number of examinations for AMD care after the clinical trial ended was 25.3, and the mean number of treatments was 15.4. Most patients (60%) were treated 1 or more times with a drug other than that originally assigned. At the 5-year visit, 50% of eyes had a VA of 20/40 or better, and 20% had a VA of 20/200 or worse. The mean change in VA was -3 letters from baseline and -11 letters from the 2-year level.

Among the 467 eyes that underwent

fluorescein angiography, the mean total lesion area was 12.9 mm², representing a mean increase of 4.8 mm² from that at 2 years. Geographic atrophy was present in 213 of 515 (41%) gradable eyes and was subfoveal in 85 eyes (17%).

Among 555 eyes examined with spectral-domain optical coherence tomography, 83% had fluid (intraretinal, subretinal, or sub-retinal pigment epithelium). The mean foveal thickness was 278 µm, representing a decrease of 182 µm from baseline and 20 µm from 2 years. The retina was abnormally thin (<120 µm) in 36% of eyes. Between 2 and 5 years, the group originally assigned to ranibizumab for 2 years lost more VA than did those in the bevacizumab group (-4 letters; $p = .008$). Otherwise, no statistically significant differences in VA or in morphologic outcomes were noted between the drug or regimen groups.

The authors commented that before the introduction of anti-VEGF therapy for AMD, less than 10% of patients retained vision of $\geq 20/40$ without treatment, and less than 15% of patients treated with photodynamic therapy retained that level of vision, at 2 years after diagnosis. Thus, the fact that 50% of the CATT eyes had $\geq 20/40$ VA at 5 years confirms that anti-VEGF is a ma-

jor long-term therapeutic advance for patients with neovascular AMD.

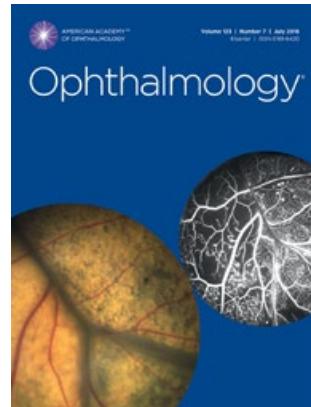
Acanthamoeba Keratitis Among RGP Contact Lens Wearers

July 2016

Cope et al. described the presentation and outcomes of *Acanthamoeba* keratitis (AK) in rigid gas permeable (RGP) contact lens wearers. The researchers also identified potential modifiable risk factors that may improve or eliminate the risk of associated vision loss.

This case-control study included 37 cases, patients who had used RGP contact lenses and had been diagnosed with AK between 2005 and 2011. The controls were 17 individuals who wore RGP contact lenses but had no history of AK. Nine of the cases (24%) wore RGP lenses for orthokeratology or for a therapeutic indication; no controls wore RGP lenses for these reasons. Participants were interviewed by phone using a standardized questionnaire. Odds ratios (ORs) and Fisher exact p values were calculated to assess risk factors associated with infection.

The researchers found that significant risk factors included wearing lenses for orthokeratology (OR, undefined; $p = .02$), wearing lenses while sleeping (OR, 8.00; $p = .04$), storing lenses in tap water (OR, 16.00; $p = .001$), and topping off lens solution in the case instead of emptying it and filling with



fresh solution (OR, 4.80; $p = 0.01$). After stratification by lens use for orthokeratology, storing lenses in tap water and topping off solution remained significant risks.

The authors concluded that all of the significant risk factors are modifiable; thus, increased efforts must be made to educate patients on the hazards of storing RGP lenses in tap water or topping off the solution. These cautions are particularly important for orthokeratology patients, whose overnight lens wear puts greater metabolic stress on the cornea.

American Journal of Ophthalmology

Half-Dose vs. Half-Time PDT for Central Serous Chorioretinopathy

July 2016

Photodynamic therapy (PDT) with verteporfin has proved effective in both acute and chronic central serous chorioretinopathy (CSC); however, this therapy is associated with dose-dependent ocular complications. Liu et al. compared the efficacy of 2 lower-risk treatment protocols—using either half-dose or half-time PDT exposure—and found that both regimens led to significant visual and anatomic improvement.

The authors carried out a retrospective chart review in Taiwan of 61 eyes that received PDT guided by fluorescein angiography for acute or chronic CSC involving the fovea. Of these eyes, 35 received half-dose PDT, and 26 received half-time PDT. Best-corrected visual acuity (BCVA) was measured at baseline and at post-PDT follow-up visits. Two clinical markers were defined for evaluating treatment efficacy: complete resolution of subretinal fluid (SRF) and recurrence of SRF, as measured on optical coherence tomography.

Both groups showed significant improvement in BCVA at months 1, 3, 6, and 12 after treatment, and multiple regression analysis showed that the type of PDT was not significantly correlated with visual improvement. All eyes that received half-time PDT showed complete resolution of SRF within 6 months after treatment; 3 eyes

that received half-dose PDT had persistent SRF, but because they were lost to follow-up at months 5, 7, and 8, no conclusions could be drawn about their ultimate outcomes. Three of 32 eyes in the half-dose group and 2 of 26 eyes in the half-time group had recurrence of SRF, but all had complete resolution after another PDT treatment. No adverse systemic or ocular side effects were observed in any cases.

The authors noted that their study was limited by its retrospective nature and by the small patient population, which lacked the statistical power to determine significant differences between the 2 groups in treatment effects. Nevertheless, they concluded that both half-dose and half-time PDT regimens were effective in treating CSC.

Comparing Glaucomatous Disc Change With Stereo Viewing vs. MatchedFlicker Software

July 2016

Optic disc evaluation is important in following glaucoma progression. However, in practice, examination of sequential simultaneous stereo photographs is time consuming, requires specialized equipment, and thus is not routinely performed. Schaefer et al. compared this method against a new software program, MatchedFlicker (Flicker) and found that the latter was faster and more specific, but less sensitive, in identifying progression when used by ophthalmologists in training.

In this study, 2 resident ophthalmologists and 1 glaucoma fellow in the same university program independently evaluated 140 image pairs from 100 glaucomatous/ocular hypertensive patient eyes. Among these images, 50 pairs had been assessed by the Ocular Hypertension Treatment Study reading center as showing progression over 1 to 5 years; 50 others were taken minutes apart and served as controls; and 20 duplicates were chosen from each group to assess observer variability.

The observers viewed each of the image pairs by both methods: (1) using 2 sets of stereo viewers to compare changes and (2) using Flicker, which superimposes images on a comput-

er screen and then rapidly “flickers” between them so that any differences between the pairs appears as motion. Using the handheld stereo viewer, the observers correctly identified progression or nonprogression in 76.0% of the slide pairs versus 87.6% using Flicker. Assessment speed averaged 34.1 seconds per image pair with the stereo viewer versus 24.9 seconds with the Flicker program. In this group of trainees, Flicker was, overall, significantly more specific but less sensitive than stereo slides; and, in particular, it was more accurate for the 2 less-experienced residents.

The authors also noted that Flicker data can be integrated more easily than stereo pairs into electronic medical records. They concluded that Flicker has good clinical potential for detecting glaucoma progression when used in conjunction with other functional and structural tests.

Preloaded Tissues for DMEK

July 2016

In a laboratory study, Parekh et al. tested the feasibility of preloading endothelial tissue, rolled inside a cartridge, for use in Descemet membrane endothelial keratoplasty (DMEK). They found that grafts they prepared using this method survived and showed active metabolism for up to 4 days.

The researchers experimented with 20 human corneas that were deemed unsuitable for transplantation. Their method involved punching out and stripping the donor endothelium to 8.5-mm diameter, manually tri-folding the graft with the endothelium inward, placing it gently into an intraocular lens cartridge, and filling the cartridge with transport medium (TM). The tissue was stored for 4 days at room temperature in TM and assessed for viability. They cautioned that, because the TM contains bovine serum, the graft would need to be washed gently with balanced salt solution before being transplanted in a human eye.

In all 20 cases, the researchers were able to successfully peel and load the tissues, at average times of 20 minutes each for stripping and 4.5 minutes for

loading. There was no endothelial cell loss immediately after the stripping procedure, although there was 4.35% loss after preservation. Cell mortality was observed only at the folds, and after a learning curve, the researchers found that mortality could be reduced to minimal or none.

The researchers concluded that this method of endothelial tissue preparation could reduce the time, difficulty, and potential waste of donor tissue in DMEK. However, they noted that their study was a proof of concept and has not yet undergone clinical evaluation.

JAMA Ophthalmology

Representation of Women With Industry Ties in Ophthalmology

June 2016

There is a growing number of women in ophthalmology, and they are making strides in professional achievement. Reddy et al. examined how industry partnerships—a potential means of career advancement and income—compared between male and female ophthalmologists. The authors found that women had fewer partnerships and received less financial compensation from industry than men did.

In this retrospective observational study, the authors reviewed the Centers for Medicare & Medicaid Services Open Payments database for payments to ophthalmologists by biomedical companies in 2013 and 2014. The primary outcome measures were percentage representation of women versus men overall and in industry research, consulting, speaking roles, royalties and licenses, grants, services other than consulting, and honoraria. Secondary outcome measures included mean and median payments from industry to female versus male ophthalmologists.

In 2013, 4,164 of 21,380 ophthalmologists (19.5%) were women. Of 1,204 ophthalmologists analyzed for industry ties, 176 were women (14.6%) and 1,028 were men (85.4%); overall, 4.2% of women and 6.0% of men had at least 1 industry tie ($p < .001$). Mean payments to women were \$11,419 compared with \$20,957 to men, and

median payments were \$3,000 and \$4,787, respectively. Women were underrepresented among ophthalmologists receiving industry payments in the following areas: research (49/462), consulting (96/610), honoraria (3/47), industry grants (1/7), royalties and licenses (1/13), and faculty/speaker roles (2/48).

In 2014, 4,352 of 21,531 ophthalmologists (20.2%) were women. Of 1,518 ophthalmologists analyzed for industry ties, 255 were women (16.8%) and 1,263 were men (83.2%); overall, 6.0% of women and 7.4% of men had at least 1 industry tie ($p < .001$). Mean payments to women were \$14,848 versus \$30,513 to men, and median payments were \$3,750 and \$5,000, respectively. Women were underrepresented among ophthalmologists receiving industry payments in the following areas: research (25/241), consulting (145/921), honoraria (14/111), industry grants (3/25), royalties and licenses (1/22), and faculty/speaker roles (21/189).

The authors concluded that there is a disparity between male and female ophthalmologists in industry partnerships, both in terms of percentage of representation and compensation. The reasons are multifactorial and could not be determined in this study.

Effect of Laser PRP on Retinal Sensitivity and Driving Eligibility in Diabetic Retinopathy

June 2016

In a study conducted in the United Kingdom, Subash et al. assessed the effect of bilateral multispot laser panretinal photocoagulation (PRP) on retinal sensitivity and driving visual fields in patients with proliferative diabetic retinopathy (PDR). They found that although there was a mild loss of retinal sensitivity at 6 months after PRP, it was likely that treated patients would retain their driving eligibility.

This prospective nonrandomized interventional cohort analysis included 43 laser-naïve patients (38 completed the study) with PDR that required bilateral PRP. Multispot laser treatment was applied using standard parameters,

until neovascularization regressed or complete retinal coverage was achieved. At baseline and 6-month follow-up, patients underwent perimetry, microperimetry, optical coherence tomography, widefield color fundus photography, and fluorescein angiography. Change in retinal sensitivity was assessed by comparing the mean global retinal sensitivity before and after laser treatment and by comparing the volumetric measure of a modeled hill of vision. At baseline and 6 months, participants also took the Esterman binocular visual field test for driving in the U.K. (at least 120-degree horizontal field with no significant defects within the central 20 degrees).

Before treatment, 41 of 43 patients (95%) passed the Esterman test; after completion of laser treatment, 35 of 38 patients (92%) passed—only 1 of the 38 who completed the study and had passed at baseline lost driving eligibility after treatment. The mean (SD) change in retinal sensitivity on static perimetry was -1.4 (3.7) dB OD and -2.4 (2.9) dB OS. Mean (SD) 4-degree macular sensitivity decreased by 3.0 (5.2) dB OD and 2.6 (5.4) dB OS.

The authors concluded that almost all patients retained their visual field eligibility for driving after multispot PRP, despite a small loss of retinal sensitivity. They added that this information could be useful in counseling patients regarding treatment options.

Cost-effectiveness of School-Based Eye Exams in Preschoolers Referred for Follow-up

June 2016

Lowry and de Alba Campomanes sought to determine the follow-up rates and cost-effectiveness of referral to community-based eye care professionals compared with a mobile eye examination unit (mobile follow-up) among children with failed visual screening in preschool. The results suggest that community-based eye care professionals provide more cost-effective care than mobile follow-up at the preschool for these children.

This retrospective cohort cost-effectiveness study included 3,429 children in 37 public preschools in San Francisco

who underwent visual chart screening during the 2009-2012 academic years and 1,524 children in the same schools who underwent autorefraction screening during the 2012-2013 academic year. Of the first group, 175 children were referred for community-based comprehensive eye examinations, while 204 in the second group were referred for preschool-based mobile follow-up.

Of the 175 children referred for community-based follow-up (91 boys; 84 girls; mean [SD] age, 3.8 [0.7] years), 104 attended (59.4%). Of 204 children referred for mobile follow-up (89 boys; 115 girls; mean [SD] age, 4.1 [0.6] years), 112 attended (54.9%). Costs per case detected were \$664 and \$776, respectively. In univariate analysis, mobile follow-up was equally cost-effective if it increased the follow-up rate to 73% or if its costs were reduced by at least 27%. In multivariate analysis with Monte Carlo simulation, community-based follow-up was more cost-effective than mobile follow-up in 88% of simulated cases and had typical savings of \$112 per case detected.

The authors noted, however, that the substantial variations in cost estimates allowed within the sensitivity limits of these analyses suggest a 12% possibility of increased cost-effectiveness with mobile follow-up. Further, programmatic changes to increase the follow-up could potentially improve the cost-effectiveness of mobile follow-up.

Other Journals

Incidence of Cataract Surgery After Percutaneous Cardiac Intervention

JAMA Internal Medicine
2016;176(5):710-711

More than 1 million percutaneous cardiac intervention (PCI) procedures are performed each year in the United States. Although this procedure is done under x-ray guidance, the risk of radiation cataract among post-PCI patients has received little attention, and there are no current guidelines for patient eye protection. Using claims data from Taiwan's National Health Insurance research database, Wei et al. conducted

a retrospective matched-cohort study to evaluate the risk of cataract among patients after PCI.

The researchers identified 13,807 patients in Taiwan who had PCI between January 2001 and December 2012, and matched them 1:2 with 27,614 people in the database who had not undergone PCI. Matching was done according to birth year, sex, and diabetes status.

The researchers found that patients who had undergone PCI had an overall 25% increase in the incidence of cataract surgery, with evidence of a dose-response relationship depending upon the number of PCI procedures. They listed several reasons why the association had not previously been addressed: 1) the radiation dose of PCI was traditionally too low to cause immediately noticeable damage, and no reliable diagnostic method is available to detect radiation cataract; 2) common risk factors for coronary artery disease, such as diabetes, hypertension, smoking, and steroid use, also increase the incidence of cataract; and 3) data on the safe radiation threshold for the lens are uncertain, and it is difficult to set regulations to limit lens exposure for PCI.

The authors noted that in the past decade, procedures for complex cardiac conditions have become lengthier, and multiple procedures have become more common, resulting in higher cumulative radiation doses and increased risks for radiation damage. They recommend that PCI patients should wear eye protection during the intervention.

Glaucoma Prevalence in the United States: The 2005-2008 NHANES

Investigative Ophthalmology & Visual Science
2016;57(6):2577-2585

Gupta et al. estimated the prevalence of glaucoma in the U.S. population based on optic nerve head photography of participants in the National Health and Nutrition Examination Survey (NHANES) 2005-2008. They found an overall prevalence of 2.1% in this population, and more than half of the cases were previously undiagnosed.

The participants were 2,883 men

and 2,863 women over age 40 who had gradable photographs of the macula and optic disc of both eyes. The images were first screened by a reading center, and participants with a cup-to-disc ratio ≥ 0.6 were further graded by 3 glaucoma specialists to determine the presence or absence of glaucoma.

Based on NHANES data, the researchers estimated that the overall prevalence of glaucoma in the U.S. civilian, noninstitutionalized population 40 years of age and older was 2.1%. Glaucoma affects 2.9 million individuals, including 1.4 million women; 1.5 million men; 2.3 million people 60 years of age and older; and 0.9 million blacks, Mexican-Americans, and people of other minority races. The prevalence of glaucoma was found to be highest in non-Hispanic blacks, followed by non-Hispanic whites, Mexican-Americans, and others.

Among the 172 participants with glaucoma detected on fundus photography, only 78 reported a previous diagnosis of glaucoma. Those who were unaware of their glaucoma status were more likely to be younger, to have a small disc, and to have an abnormal frequency-doubling visual field result, and were less likely to have notching or disc hemorrhages, compared with those who reported a glaucoma diagnosis.

The researchers concluded that data from NHANES 2005-2008 suggest that approximately 1.6 million people in the United States have undiagnosed glaucoma. Because timely treatment is critical, developing effective and practical screening algorithms for glaucoma is a clinical research priority and a requirement for disease control.

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