**Journal Highlights**

**NEW FINDINGS FROM THE PEER-REVIEWED LITERATURE**

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**Ophthalmology**

**The Ahmed Versus Baerveldt Study: 5-Year Outcomes**
October 2016

In an international multicenter randomized trial, Christakis et al. compared 2 frequently used aqueous shunts in adult patients whose glaucoma was not controlled by medical therapy or who were at high risk of trabeculectomy failure. They found that both the Ahmed and Baerveldt devices reduced intraocular pressure (IOP) and need for medication.

A total of 238 patients were randomized to receive either an Ahmed-FP7 valve implant (n = 124) or a Baerveldt-350 implant (n = 114). The primary outcome measure was failure, defined as IOP outside the target range (5-18 mm Hg) or reduction of <20% from baseline at 2 consecutive visits after 3 months; severe vision loss; or de novo glaucoma surgery. Secondary outcome measures included IOP, medication use, visual acuity, complications, and interventions.

Baseline characteristics were similar between the 2 device groups. Mean preoperative IOP was 31.4 ± 10.8 mm Hg on 3.1 ± 1.0 glaucoma medications. At 5 years, the cumulative failure rate was 53% in the Ahmed group and 40% in the Baerveldt group (p = .04).

In both groups, the main reason for failure was high IOP. The cumulative de novo glaucoma reoperation rate was 18% in the Ahmed group and 11% in the Baerveldt group (p = .22).

Hypotony resulted in failure in 5 patients (4%) in the Baerveldt group compared with none in the Ahmed group (p = .02). Mean IOP was 16.6 ± 5.9 mm Hg in the Ahmed group (47% reduction) and 13.6 ± 5.0 mm Hg in the Baerveldt group (57% reduction, p = .001).

Mean medication use was 1.8 ± 1.5 medications in the Ahmed group (44% reduction) and 1.2 ± 1.3 in the Baerveldt group (61% reduction; p = .03). The 2 groups had similar complication rates (Ahmed, 63%; Baerveldt, 69%) and intervention rates (Ahmed, 41%; Baerveldt, 41%). Most complications were transient, and most interventions were slit-lamp procedures.

The authors concluded that both implants were effective in reducing IOP and the need for glaucoma medications. The Baerveldt group had a lower failure rate and a lower IOP on fewer medications, but there was also a small risk of hypotony, which was not seen in the Ahmed group.

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**Anti-VEGF Therapies for AMD Did Not Raise the Risk of MI, Stroke, or Death**
October 2016

Yashkin et al. assessed the effect of intravitreal anti-VEGF therapy for age-related macular degeneration (AMD) on mortality and hospitalization for acute myocardial infarction (AMI) and stroke over 5 years. The study compared 5-year periods before and after the advent of anti-VEGF drugs for AMD and found no significant differences in risk of these adverse outcomes.

In this retrospective cohort study, beneficiaries who were newly diagnosed with exudative or nonexudative AMD in 2000 and 2006 were selected from a random longitudinal sample of Medicare 5% claims and enrollment files. Beneficiaries with a first diagnosis of exudative AMD in 2006 comprised the treatment group. There were 2 control groups: beneficiaries newly diagnosed with exudative AMD in 2000 or nonexudative AMD in 2000 or 2006. In the treatment group, the researchers included patients diagnosed with types of AMD for which anti-VEGF therapy was clinically appropriate and available; however, they did not determine whether these patients actually received the indicated anti-VEGF treatment, nor what specific anti-VEGF agents were used.

The researchers did not identify any statistically significant differences in probabilities of death or hospitalizations for AMI and stroke during the 5-year follow-up periods for the treatment group of patients newly diagnosed with exudative AMD in 2006 compared with the 2 control groups.
They concluded that the introduction of anti-VEGF agents in 2006 for treatment of exudative AMD has not significantly increased the risk of AMI, stroke, or all-cause mortality.

**Clinical Spectrum and Pathogenesis of True Exfoliation Syndrome**
November 2016

Teekhasaenee et al. proposed a new theory of the pathogenesis of true exfoliation syndrome (TEX). Further, they described the clinical spectrum of this syndrome as encompassing lens capsule lamellar separation and anterior zonular disruption as well as cataract and, often, pigment deposition.

Participants included 259 patients (424 eyes) with TEX, who ranged in age from 52 to 97 years (mean age, 75.2 ± 7.1 years). Of these, 11 patients had TEX associated with trauma (n = 1) or intense heat exposure (n = 10), while 248 patients had idiopathic TEX. Forty-nine patients were seen once and were lost to follow-up; the remaining 210 were seen every 3 months, with a mean follow-up of 9.6 ± 6.1 months (range, 3-50 months). At the initial visit, slit-lamp biomicroscopy, photography, and optical coherence imaging of the anterior capsule and zonules were performed. Photography was performed at all subsequent visits, with or without other imaging. The main outcome measures were detached membrane morphologic features, zonular defects, pigment deposition, glaucoma, phacodonesis, and cataract.

The condition was classified into 4 clinical stages: annular anterior capsule thickening with a distinct splitting margin (stage 1), an inward detached crescent flap lying on the anterior lens (stage 2), a floating and folding translucent membrane behind the iris (stage 3), and a broad membrane within the pupil (stage 4). Several stages could coexist in an eye.

All stages shared common histologic findings consisting of diffuse capsular lamellar separation and anterior zonular disruption. All patients developed cataract; 68.7% of patients had pigment deposition on the membrane; 10% had spontaneous phacodonesis; and 4.2% demonstrated secondary delamination.

The researchers identified capsular lamellar separation and anterior zonular disruption as the characteristic findings. The initial capsular splits occur along the insertions of disrupted anterior zonules, and the peeling progresses centrally in association with iris movement and aqueous flow. The authors concluded that aging, heat exposure, and trauma are risk factors for TEX.

**American Journal of Ophthalmology**

**Retinal Injuries in Children Secondary to Handheld Lasers**
November 2016

Raoof et al. reviewed the records of children injured by recreational handheld lasers to determine potential prognostic factors. They also proposed a system for grading injuries based on findings of optical coherence tomography. The authors emphasized that such retinal injuries may be difficult to diagnose and likely are underreported.

Among the 12 boys and 4 girls in this single-center study, 24 eyes were affected. Mean age was 12.7 years (range, 9-16 years). Mean visual acuity at presentation was 0.30 (20/40); range, –0.20 (20/12.5) to 1.6 (20/800). The most common symptoms were central scotoma (11 children) and blurred vision (3 children). Two patients were asymptomatic and were referred because their optometrist detected macular changes.

Because laser retinopathy can masquerade as various other conditions, the authors call it “the new pretender.” The differential diagnosis is extensive and includes Best disease, Stargardt disease, cone-rod dystrophies, solar retinopathy, and infectious causes such as toxoplasmal chorioretinitis. Diagnosis may be delayed by children’s reluctance to admit playing with lasers.

Eleven children (15 eyes) had mild injuries, defined as focal retinal disruption confined to the photoreceptor and ellipsoid layers; these had the most favorable prognosis. Two children (3 eyes) had moderate injuries, characterized by diffuse retinal disruption confined to the outer retinal layer. Three patients (4 eyes) had severe injuries, with subfoveal outer retinal architecture loss and overlying hyperreflective material in the inner retinal layers.

Patients with mild injury and good visual acuity at presentation maintained good vision throughout follow-up. Those with severe injury did not experience visual improvement. However, the mean follow-up period was short (5.4 months), and later improvement has occurred in other cases. Because of the small number of severe and moderate injuries in this study, prognostic assumptions cannot be drawn for them.

In conclusion, laser-related retinal injuries may be underreported and difficult to diagnose. Regulatory authorities should recognize the importance of laser retinopathy as an avoidable cause of childhood visual impairment and should implement efforts to reduce these injuries. Awareness should be raised among clinicians, parents, teachers, and children.

**Fixed-Dose Carteolol/Latanoprost Combination: Tolerability and Efficacy**
November 2016

Monotherapy may be insufficient to lower intraocular pressure (IOP) for some patients with glaucoma, but therapy with 2 agents may be inconvenient and result in poor adherence. Yamamoto et al. reported results of 2 phase 3 randomized controlled trials in which a fixed-dose combination of 2% carteolol and 0.005% latanoprost, given as a single therapeutic (termed OPC-1085EL), was evaluated for safety and efficacy. OPC-1085EL was compared with carteolol and latanoprost administered as monotherapies or as separate concomitant therapies. The authors found that OPC-1085EL was well tolerated and reduced IOP more than the monotherapy and comparably to the concomitant therapy.

The trials were conducted at several centers in Japan and included patients with bilateral primary open-angle glaucoma or ocular hypertension. After a 4-week period with latanoprost or carteolol monotherapy, patients received 8...
weeks of treatment with monotherapy, concomitant therapy, or OPC-1085EL applied daily in the morning.

In study 1, the mean reduction in baseline-adjusted IOP for the 113 patients treated with OPC-1085EL (2.9 mm Hg) was significantly better than for the 116 patients treated with latanoprost monotherapy (1.6 mm Hg). In study 2, the mean reduction in baseline-adjusted IOP was significantly better for OPC-1085EL (n = 76; 3.5 mm Hg) than for carteolol (n = 76; 1.6 mm Hg). IOP reduction in the 37 patients who received carteolol and latanoprost concomitantly was similar to that in recipients of OPC-1085EL. In both studies, OPC-1085EL was tolerated well and associated with only mild adverse drug reactions.

The authors concluded that OPC-1085EL is similar to concomitant therapy in terms of IOP-reducing efficacy but offers greater convenience. They noted that subsequent studies are needed to evaluate it for a longer duration, administered at other times of day, and in more diverse populations.

**JAMA Ophthalmology**

**Public Attitudes About Eye and Vision Health**

October 2016

To assess knowledge of eye health and attitudes about vision in the U.S. population, Scott et al. carried out a survey encompassing all ethnic and racial groups. They found that respondents gave high priority to the sense of vision and supported ongoing research on vision and eye health. However, many were not aware of some important eye diseases, including macular degeneration and diabetic retinopathy.

Among the 2,044 survey respondents, with a mean age of 46.2 years, 48% were male, 11% were uninsured, and 63% reported wearing glasses. Most (87.5%) believed that good vision is vital to overall health, while 47.4% rated losing vision as the worst possible health outcome. Across all racial/ethnic groups, blindness was ranked as the first or second worst disease or ailment that could happen to them.

They ranked losing vision as equal to or worse than losing hearing, memory, speech, or a limb. When asked about various possible consequences of vision loss, quality of life ranked as the top concern, followed by loss of independence.

With regard to knowledge about eye health, nearly two-thirds of respondents were aware of cataracts (65.8%) or glaucoma (63.4%); only half were aware of macular degeneration; 37.3% were aware of diabetic retinopathy; and 25% were not aware of any eye conditions. Approximately 75.8% and 58.3%, respectively, identified sunlight and family heritage as risk factors for losing vision; only half were aware of smoking risks in vision loss.

National support of research focused on eye and vision disorders was considered a priority by 81.5%. Moreover, almost half (47.9%) thought that governmental and nongovernmental financial support of such research should be increased.

In conclusion, these findings suggest that most Americans across all ethnic and racial groups consider that losing eyesight would have the greatest impact on their daily life when ranked against other health conditions including loss of limb, memory, hearing, or speech. Further, the survey shows strong support for research in eye health. However, the data also demonstrate the need to raise public awareness of some important eye diseases and risk factors.

**Chemical Ocular Burns: U.S. Epidemiologic Trends**

October 2016

Haring et al. examined 4-year data from the Nationwide Emergency Department Sample to identify epidemiologic trends and risk factors for chemical ocular burns. Such information can help physicians and policy makers to effectively allocate resources for treatment and prevention of these injuries. The authors found, unexpectedly, that the highest risk group is very young children (1- and 2-year-olds).

Included in this study were 900 emergency departments and 143,985 events. Documented patient characteristics included age, sex, geographic region, type of primary insurance, income level, and setting of injury.

The median age at presentation was 32 years, and more than half of the patients were male (56.6%). Although nearly three-fourths of the injuries occurred in adults (aged 18-64 years), the rates of injury were highest for 1- and 2-year-olds (28.6 and 23.5 injuries per 100,000 population, respectively), a finding that differs from most literature on this topic. The injury rate for adults was 13.3 per 100,000. Residential location was the most common setting of injury, and 56.0% of burns were in patients from lower-income households (annual income ≤$48,749). Injuries were most common in the South and among patients with private health insurance.

The authors concluded that the risk of chemical ocular burns in very young children is much higher than previously believed. Public health efforts and policies should focus on proper storage and handling of chemicals in the home and workplace, as chemical burns can have long-term detrimental effects on vision and quality of life.

**Omega-3 Fatty Acids Reduce the Risk of Diabetic Retinopathy**

October 2016

Experimental studies indicate that consumption of long-chain omega-3 polysaturated fatty acids (LCω3PUFAs) protects against diabetic retinopathy (DR). Sala-Vila et al. examined this association in humans by conducting a long-term prospective study of 3,482 patients with type 2 diabetes (mean age, 67 years; 48% men) enrolled in the PREDiMED trial. They found that consumption of LCω3PUFAs (≥500 mg/d) significantly reduced the risk of DR.

Nutrient intake was determined with a validated food frequency questionnaire, administered annually. After collection of baseline data, patients were randomized to receive a Mediterranean diet supplemented with extra virgin olive oil (n = 1,236) or nuts (n = 1,095) or a control diet with recommendations to reduce fat intake (n = 1,151). The primary outcome measure was DR requiring intervention.
Data were adjusted for potential confounders and validated with sensitivity analyses.

Participants were monitored for a median of 6 years, and 69 new DR events were recorded. At baseline, 75% of participants met the target for n-3PUFA consumption (>500 mg/d). The relative risk of incident sight-threatening DR for these participants was 46% lower than for those who consumed less n-3PUFA (p = .001), regardless of the assigned diet. Risk reduction was even greater for patients with hypertension or advanced diabetes. Participants who consumed at least 2 servings of oily fish per week at baseline also had a lower risk of DR.

Because the PREDIMED trial was not designed to examine DR, and the participants generally had a plant-based Mediterranean diet, these findings need to be validated in other populations, the authors noted. Nevertheless, they recommend that middle-aged and older patients with type 2 diabetes consume at least 500 mg/d of dietary n-3PUFA (e.g., from oily fish) to decrease their risk of sight-threatening DR.

OTHER JOURNALS

Adalimumab for Prevention of Uveitic Flare in Patients With Inactive Noninfectious Uveitis

Lancet
2016;388(10050):1183-1192

Therapeutic success in managing noninfectious uveitis has been limited by the adverse effects of long-term use of corticosteroids or immunomodulators when topical medication fails to control inflammation. Nguyen et al. assessed the efficacy and safety of adalimumab in preventing exacerbations in patients with inactive, noninfectious uveitis as they are weaned off systemic corticosteroids.

This multicenter double-masked randomized placebo-controlled phase 3 trial was conducted at 62 study sites in 21 countries. Patients were 18 years or older with inactive noninfectious intermediate, posterior, or panuveitic uveitis controlled by 10 to 35 mg/day of prednisone; of these, 115 were randomly assigned to receive subcutaneous adalimumab (loading dose, 80 mg; biweekly dose, 40 mg), and 114 to receive a placebo. All participants began a mandatory prednisone taper at week 2, with discontinuation by week 19.

The primary efficacy end point was time to treatment failure, defined as new active inflammatory chorioretinal or inflammatory retinal vascular lesions, anterior chamber cell grade, vitreous haze grade, and visual acuity. Treatment failure occurred in 61 (55%) of 111 patients in the placebo group versus 45 (39%) of 115 patients in the adalimumab group. (Note: 3 placebo patients were excluded from analysis for issues of study protocol.) Time to treatment failure was significantly better in the adalimumab group compared with the placebo group (median not estimated [≥18 months] vs. 8.3 months). No new safety signals were observed, and the rate of adverse events was similar between groups.

The authors concluded that adalimumab significantly lowered the risk of uveitic flare or loss of visual acuity upon corticosteroid withdrawal in patients with inactive noninfectious intermediate, posterior, or panuveitic uveitis controlled by systemic corticosteroids. It could provide an effective option for patients at risk of adverse effects associated with long-term use of systemic corticosteroids.

Adalimumab in Patients With Active Noninfectious Uveitis

New England Journal of Medicine
2016;375(10):932-943

Jaffe et al. designed a trial to assess the efficacy and safety of adalimumab as a steroid-sparing agent for the treatment of active noninfectious uveitis. They found that adalimumab was effective in controlling the disease after steroids were discontinued.

The multinational phase 3 trial included adults with noninfectious intermediate uveitis, posterior uveitis, or panuveitis that remained active despite their having received prednisone treatment for 2 or more weeks. Patients were randomly assigned in a 1:1 ratio to receive subcutaneous (SC) adalimumab (loading dose of 80 mg followed by a dose of 40 mg every 2 weeks) or a matched SC placebo. Each patient received a mandatory prednisone burst followed by tapering of prednisone over a course of 15 weeks.

The primary efficacy end point was the time to treatment failure occurring at or after week 6. Treatment failure was a multicomponent outcome based on assessment of new inflammatory lesions, best-corrected visual acuity (BCVA), anterior chamber cell grade, and vitreous haze grade.

The median time to treatment failure was 24 weeks in the adalimumab group and 13 weeks in the placebo group. Among the 217 patients in the intention-to-treat population, those who received adalimumab were significantly less likely to experience treatment failure (hazard ratio, 0.50) than the placebo group. The outcomes related to anterior chamber cell grade, vitreous haze grade, and BCVA were also significantly better in the adalimumab group. However, adverse events and serious adverse events were reported more often among patients who received adalimumab compared with placebo (respectively, 1,052.4 vs. 971.7 for adverse events and 28.8 vs. 13.6 serious adverse events per 100 person-years).

The researchers concluded that treatment with adalimumab achieved early and sustained disease control after discontinuation of corticosteroid treatment. Treated patients had reduced inflammation and visual impairment compared with the placebo group. However, they experienced more adverse events and serious adverse events than the placebo patients did.

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