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Journal Highlights

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

Ophthalmology

Long-Term Outcomes in Uveitis Patients

December *Ophthalmology*

Tomkins-Netzer et al. assessed long-term outcomes among patients with uveitis. They found that outcomes are good, with best-corrected visual acuity (BCVA) remaining stable for more than 10 years of follow-up. However, they also found that the burden of treatment and hospital visits remains a significant concern.

For this cross-sectional study, the researchers evaluated 1,076 patients (1,799 eyes) who attended the uveitis clinic at Moorfields Eye Hospital in London between 2011 and 2013. Of these, 592 eyes were diagnosed with anterior uveitis, 547 had intermediate uveitis, and 660 had posterior uveitis or panuveitis. A total of 271 patients were found to have an underlying causative disease; of these, 155 had systemic inflammatory conditions and 116 had systemic infections, including toxoplasma, tuberculosis, human immunodeficiency virus, and herpesvirus infections. BCVA remained stable throughout an average follow-up of 7.97 ± 0.17 years, with approximately 80 percent of patients avoiding vision loss. The primary cause of moderate vision loss was cystoid macular edema (CME); the main cause of severe vision loss was macular scarring secondary to CME or choroidal neovascularization.

Patients required an average of six follow-up visits per year, with half requiring long-term systemic steroids and immunosuppressives. More than one-third of patients needed surgery for uveitis-related complications.

Bevacizumab vs. Dexamethasone Implant for DME

December *Ophthalmology*

Gillies et al. reported 12-month results of the first head-to-head comparison of a dexamethasone implant (Ozurdex) and intravitreal injections of bevacizumab for the treatment of diabetic macular edema (DME). They found that the two treatments achieved similar rates of improvement in visual acuity and vision-related quality-of-life scores. Better anatomic outcomes were associated with the implant than with bevacizumab, but the implant carried a higher risk of cataract development.

For this phase 2 prospective randomized trial, the researchers enrolled 61 patients (88 eyes) with DME who received either 1.25 mg of bevacizumab every four weeks (42 eyes) or a 0.7-mg dexamethasone implant every six weeks (46 eyes). Outcome measures included best-corrected visual acuity (BCVA), change in central macular thickness, and adverse events.

At the end of 12 months, mean central macular thickness decreased by 187 µm in the implant eyes versus 122 µm in the bevacizumab eyes. BCVA improved by 10 letters or more in 19 of the 46 dexamethasone eyes (41 percent) and in 17 of the 42 bevacizumab eyes (40 percent). However, although none of the bevacizumab eyes lost 10 letters or more, five of the dexamethasone eyes (11 percent) did, largely because of cataract development.

As a result, the researchers suggested that the dexamethasone implant may be appropriate as a second-line treatment for DME in phakic eyes and as a first-line treatment for pseudophakic eyes or for patients who are unable or unwilling to receive frequent intraocular injections.

Next-Generation DNA Testing Useful for Congenital Cataract

Ophthalmology

Published online Aug. 19, 2014

Gillespie et al. evaluated whether genomic data from next-generation DNA sequencing could enhance the process of diagnosing and treating bilateral congenital cataract (CC). They concluded that it does.

For this technology assessment, the

researchers selected 36 patients with nonsyndromic or syndromic bilateral CC from a single ophthalmic genetics clinic. The patients underwent a detailed ophthalmic examination; and lenticular, ocular, and systemic phenotypes were recorded.

The researchers used a next-generation sequencing system to design a targeted gene screening; with it, they were able to determine the precise genetic cause of CC in 75 percent of the patients. In addition, 85 percent of the patients with nonsyndromic CC were found to have possible pathogenic mutations, and the pick-up rate in patients with syndromic CC also was high, with 63 percent having potential disease-causing mutations.

The researchers concluded that this approach has clinical utility in leading to more appropriate clinical management and genetic counseling of patients and families.

Damage Occurs Earlier Than Suspected in Fuchs Dystrophy

December *Ophthalmology*

Anterior cellular and structural abnormalities are known to be present in the advanced stages of Fuchs dystrophy. **Amin et al.** investigated the time course of these changes and found that they occur much earlier in the disease than previously recognized.

For this cross-sectional study, the researchers examined 39 patients (63 eyes) with a range of severity of Fuchs dystrophy and 13 patients (25 eyes) with normal corneas. Corneal backscatter (haze) was measured from a confocal image light intensity profile. Stromal cell density and number, as well as the presence of abnormal subepithelial cells, were determined from confocal images.

Anterior haze was present in all eyes with Fuchs and was 18 to 67 percent higher in eyes with moderate and advanced disease compared with controls. Abnormal subepithelial cells were visible in 9 percent, 19 percent, and 30 percent of corneas with mild, moderate, and advanced Fuchs dystrophy, respectively. Only corneas with advanced Fuchs had clinically evident edema.

The researchers noted that the advent of newer endothelial techniques makes earlier intervention more feasible now than it was when penetrating keratoplasty was the main therapeutic option. Understanding the onset of structural abnormalities may help determine the optimal timing of treatment.

American Journal of Ophthalmology

Glaucomatous Structural Damage Associated With Slower Reaction Times

November *AJO*

In a cross-sectional observational study, **Tatham et al.** examined the relationship between glaucomatous retinal nerve fiber layer (RNFL) damage and the ability to divide attention during simulated driving, an important factor in safe driving. Patients with glaucoma were found to have significantly impaired ability to divide attention, particularly under low-contrast conditions, with a significant association between thinning of the RNFL and driving ability.

A total of 158 subjects from the Diagnostic Innovations in Glaucoma Study, including 82 with glaucoma and 76 similarly aged controls, were evaluated through use of a driving simulator. The subjects' reaction times to peripheral stimuli (at low, medium, or high contrast) were measured while they concomitantly performed a central driving task (negotiating curves or following another car). All subjects had standard automated perimetry (SAP), as well as optical coherence tomography to determine RNFL thickness. Cognitive ability was assessed using the Montreal Cognitive Assessment, and the subjects completed a driving history questionnaire. The mean reaction times to the low-contrast stimulus were 1.05 seconds (s) and 0.64 s in glaucoma and controls, respectively, during curve negotiation, and 1.19 s and 0.77 s, respectively, during car following. There was a nonlinear relationship between reaction times and RNFL thickness in the better eye.

RNFL thickness remained significantly associated with reaction times even after adjusting for age, SAP mean deviation in the better eye, cognitive ability, and central driving task performance. Although worse SAP sensitivity was associated with worse ability to divide attention, RNFL thickness measurements provided additional information. Such structural tests may help to identify which patients are likely to have problems with activities such as driving.

5-Year Follow-up of Cataract Surgery in Infants With and Without IOL Implantation

November *AJO*

Plager et al., for the Infant Aphakia Treatment Study Group, compared rates and severity of complications over five years between infants who underwent cataract surgery with and without intraocular lens (IOL) implantation in a prospective randomized clinical trial. Implantation of an IOL in infants less than 7 months of age was associated with a significantly higher rate of adverse events and need for additional intraocular surgeries compared with leaving the babies aphakic.

A total of 114 infants were enrolled in the Infant Aphakia Treatment Study, a randomized multicenter clinical trial that compared the treatment of unilateral aphakia in patients less than 7 months of age with a primary IOL implant or a contact lens. Intraoperative complications, adverse events, and additional intraocular surgeries during the first five postoperative years were compared. There were more patients with intraoperative complications (28 percent vs. 11 percent), more patients with adverse events (81 percent vs. 56 percent), and more additional intraocular surgeries (72 percent vs. 16 percent) in the IOL group than in the contact lens group. However, in the contact lens group, the number of patients with adverse

events increased from 15 to 24 in postoperative years 2 to 5 compared with the first postoperative year; but in the IOL group, the number decreased from 44 to 14 in years 2 to 5 compared with the first postoperative year. If half of the patients in the contact lens (aphakic) group eventually undergo secondary IOL implantation, the number of additional intraocular surgeries will be approximately equal in the two groups.

The authors conclude that no universal recommendation can be made for all families when considering primary IOL implantation in early infancy, but caution is recommended. The increased rate of complications, adverse events, and additional intraocular surgeries associated with IOL implantation in infants less than 7 months of age militates toward leaving babies aphakic if it is considered likely that the family will be successful with contact lens correction.

JAMA Ophthalmology

Visual Ability of Patients With Low Vision

October *JAMA Ophthalmology*

Because most patients with low vision are elderly and have functional limitations from other health problems that could add to the functional limitations caused by their visual impairments, **Goldstein et al.** sought to identify factors that affect visual ability measures in patients who present for outpatient low vision rehabilitation (LVR) services.

As part of a prospective observational study of new patients seeking outpatient LVR, 779 patients from 28 clinical centers in the United States were enrolled in the Low Vision Rehabilitation Outcomes Study (LVROS) from April 25, 2008, through May 2, 2011. The Activity Inventory, an adaptive visual function questionnaire, was administered to measure overall visual ability and visual ability in four functional domains (reading, mobility, visual motor function, and visual information processing) at baseline before LVR. The Geriatric Depression Scale, Telephone Interview for Cognitive Status, and Medical Outcomes Study 36-Item Short-Form Health Survey were also administered to measure patients' psychological, cognitive, and physical health states, respectively.

Among the 779 patients in the LVROS sample, the mean age was 76.4 years, 33 percent were men, and the median logMAR visual acuity score was 0.60 (0.40-0.90 interquartile range). Correlations were observed between logMAR visual acuity and baseline visual ability overall ($r = -0.42$) and for all functional domains. Visual acuity was the strongest predictor of visual ability ($p < .001$) and reading ability ($p < .001$), and it had an independent effect on the other functional domains. Physical ability was independently associated with overall visual ability ($p < .001$) as well as mobility and visual motor function. Depression had a consistent independent effect ($p < .001$) on overall visual ability and on all functional domains, while cognition had an effect only on reading and mobility ($p < .001$).

The authors concluded that visual ability is a multidimensional construct, with visual acuity, depression, physical ability, and cognition explaining more than one-third of the variance in visual ability as measured by the Activity Inventory. The contributions of the nonvisual factors to visual ability measures and rehabilitation potential—that is, the ceiling effects that nonvisual limitations may impose on LVR—are important considerations when measuring baseline visual ability and, ultimately, LVR outcomes in ongoing clinical research.

The Learning Curve for DMEK

October *JAMA Ophthalmology*

Surgeons starting to perform Descemet membrane endothelial keratoplasty (DMEK) may benefit from information about the learning curves of those with greater experience performing the procedure. Accordingly, **Monnereau et al.** documented the clinical outcomes of standardized "no-touch" DMEK and its complications during the learning curves of experienced surgeons. In a retrospective multicenter study, a total of 431 eyes from 401 patients with Fuchs endothelial dystrophy (68.2 percent) and bullous keratopathy (31.8 percent) underwent DMEK performed by 18 surgeons in 11 countries.

Of 275 eyes available for best-corrected visual acuity (BCVA) pooled analysis, improvement was seen in 258 eyes (93.8 percent), while 12 (4.4 percent) remained unchanged, and 5 (1.8 percent) decreased. With regard to BCVA levels, among patients with one to six months of follow-up, 217 eyes (78.9 percent) reached at least 20/40, 117 (42.5 percent) at least 20/25, and 61 (22.2 percent) at least 20/20. Eyes with six or more months of follow-up ($n = 176$) reached similar BCVA outcomes.

Intraoperative complications were rare, including difficulties in inserting, unfolding, or positioning of the graft (1.2 percent) and intraoperative hemorrhage (0.5 percent). The main postoperative complication was graft detachment (34.6 percent): 20.4 percent underwent a single rebubbling procedure, 2.6 percent had a second rebubbling, and 0.7 percent, a third rebubbling; 17.6 percent underwent a second keratoplasty. Corneas kept in cold storage were associated with more extensive graft detachment than those maintained in organ culture.

The study shows that the standardized no-touch DMEK technique was feasible in most hands. The main challenges for surgeons starting to perform the procedure may be 1) deciding whether graft preparation should be outsourced or performed during surgery, 2) limiting the number of graft detachments and secondary procedures, and 3) obtaining organ-cultured donor corneal tissue.

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

Glaucoma Genetics

Nature Genetics
Published online Aug. 31, 2014

In a trio of studies published together in *Nature Genetics*, researchers presented findings on the genetics of primary open-angle glaucoma (POAG). Taken together, the reports offer a fuller understanding of the genetic underpinnings of the disease.

Chen et al. performed a genome-wide association study for POAG in 1,007 patients with high-pressure glaucoma and 1,009 controls. They observed a significant association at multiple single-nucleotide polymorphisms (SNPs) near *ABCA1* at 9q31.1 and suggestive evidence of an association in *PMM2* at 16p13.2. Both *ABCA1* and *PMM2* are expressed in the trabecular meshwork and optic nerve, and *ABCA1* is expressed in the retinal ganglion cell layer.

Hysi et al. reported the results of a meta-analysis of 18 population cohorts from the International Glaucoma Genetics Consortium, comprising 35,296 patients. The researchers confirmed genetic association of known loci for intraocular pressure (IOP) and POAG, and they identified four newly discovered loci associated with IOP. A separate meta-analysis of four POAG cohorts, totaling 4,284 cases and 95,560 controls, showed that three of the loci for IOP were also associated with POAG.

Gharahkhani et al. identified common variants near *ABCA1, AFAP1,* and *GMDS* that confer an increased risk of POAG. In this genome-wide association study, the researchers evaluated 1,155 patients with POAG and 1,992 controls as well as four additional replication cohorts, for a total of 3,548 POAG patients and 9,486 controls. Using reverse transcription polymerase chain reaction and immunolabeling, the researchers were able to show that these genes are expressed within the retina, optic nerve, and trabecular meshwork and that *ABCA1* and *AFAP1* are expressed in retinal ganglion cells.

Novel Implanted Sensor for IOP Monitoring

Nature Medicine
Published online Aug. 24, 2014

Araci et al. have developed an implantable device that may eventually be used by patients to self-monitor their intraocular pressure (IOP). This report provides information on the sensor's design and preclinical results on its performance.

The device uses a passive pressure sensor based on the principles of microfluidic physics that can be either incorporated into an intraocular lens (IOL) or implanted as a stand-alone device. The sensor has a simple optical interface that allows IOP data to be photographed and transmitted via smartphone; IOP also may be read by the ophthalmologist during a slit-lamp examination.

In testing within a pressure chamber, the sensor was able to track changes in IOP as small as 1 mmHg. The researchers also tested the sensor after implantation in the lens capsular bags of enucleated porcine eyes after phacoemulsification and found that intraocular sensitivity was the same as in the pressure chamber. They noted that this correspondence is essential for preimplantation calibration.

Characterization of Uveitis and Multiple Sclerosis

British Journal of Ophthalmology
Published online Aug. 28, 2014

In the largest study of the subject to date, **Messenger et al.** set out to characterize the anatomy, laterality, and continuity of uveitis in patients with multiple sclerosis (MS). They found that most MS patients with uveitis have intermediate uveitis; further, these patients tend to be older and are more likely to be female than controls with intermediate uveitis but not MS. This study is the first to measure changes in visual acuity (VA) over time in MS patients with uveitis, and the researchers found that VA is stable and may actually improve in these patients.

For this retrospective chart review, U.S. and German researchers identified 113 patients (196 eyes) with uveitis and MS. Of these, 83 patients (73.5 percent) presented with intermediate uveitis, while 24 (21.2 percent) had anterior uveitis, and six (5.3 percent) had posterior uveitis or panuveitis. Information on disease onset was available for 97 patients. MS was diagnosed before uveitis in 28 of these patients (29 percent), simultaneously in 15 patients (15 percent), and after uveitis diagnosis in 54 patients (56 percent). Finally, 83 of all patients (73 percent) were female, and the mean age at presentation was 40.6 years (range, 13-64 years). In comparison, in the control group with idiopathic intermediate uveitis, the mean age was 22.7 years, and 56 percent were female.

The average VA at presentation was 20/39. Longitudinal data were available for 74 patients (130 eyes). During an average median follow-up time of 3.2 years, VA improved by –0.09 logMAR units per year, with 48 eyes improving, 45 eyes experiencing no change, and 37 eyes losing vision.

The researchers acknowledged that the study has several limitations, including its retrospective nature. In addition, brain magnetic resonance images and detailed neurological studies were not available for all patients, which would have allowed the researchers to correlate the patients' uveitis with their neurological disease.

Roundup of Other Journals *is written by Jean Shaw and edited by Deepak P. Edward, MD.*

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