Journal Highlights

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

Ophthalmology

Short-Term Consumption of Oral Omega-3 and Dry Eye Syndrome

Ophthalmology
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Evidence continues to accumulate that oral supplementation with omega-3 fatty acids eases the symptoms of dry eye syndrome. In this randomized, double-blind trial, **Kangari et al.** assessed the effect of oral omega-3 on tear break-up time and Schirmer and Ocular Surface Disease Index scores and found that daily consumption was associated with a decrease in the rate of tear evaporation and an increase in tear secretion.

The investigators tested an oral omega-3 supplement in 64 patients. For 30 days, the treatment group (33 patients) received two omega-3 capsules each day, while the placebo group (31 patients) received two medium-chain triglyceride oil capsules daily. The omega-3 capsules contained 180 mg of eicosapentaenoic acid (EPA) and 120 mg of docosahexaenoic acid (DHA). The researchers chose this particular combination for several reasons. First, EPA and DHA are derived from fish oil and have more potent immunomodulatory activity than does alpha-linolenic acid, the omega-3 fatty acid that is found in plant sources such as flaxseeds and walnuts. Second, previous studies of dry eye have used a combination of omega-3 and omega-6 oils; however, omega-6 oils produce some proinflammatory precursors, while EPA and DHA produce a greater number of anti-inflammatory precursors.

At the end of the trial, tear break-up time improved by 71 percent in the treatment group compared with 3.3 percent in the placebo group. The score on the Ocular Surface Disease Index survey decreased in the treatment group; by contrast, the placebo group reported a slight increase. In addition, the mean Schirmer score increased by 23 percent in the treatment group compared with 5.1 percent in the placebo group. Patients in the placebo group also reported a worsening of dry eye symptoms.

Because this study was limited by its short duration of treatment and the lack of control over the dietary intakes of the subjects, the researchers recommend a multicenter clinical trial with a larger sample size and longer treatment period. Ideally, such a trial would not be confined to one country, given the varied causes of dry eye around the world and the effect of genetic, racial, and dietary differences.

Corneal Hysteresis as a Risk Factor for Glaucoma Progression

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Corneal hysteresis (CH) is a measure of the viscoelastic damping of the cornea that can be estimated by analyzing corneal responses to deformation induced by an air pulse. In this prospective, longitudinal study, **Medeiros et al.** evaluated the role of CH in glaucoma and found that it is a factor related to glaucoma progression, rather than just a phenomenon that arises from the disease process.

The researchers evaluated 114 eyes of 68 patients with glaucoma and followed the patients for an average of four years. Visual field (VF) tests were obtained with standard automated perimetry, and patients had an average of seven tests during the study. Central corneal thickness was also assessed.

The researchers found that CH was significantly associated with the rate of VF loss. Eyes with lower baseline CH measurements tended to progress significantly faster than those with higher CH values, and each 1-mmHg decrease in CH was associated with a 0.25 percent faster rate of VF index decline per year. This relationship was present even when other factors known to affect rates of glaucoma progression were taken into account.

A significant interaction between intraocular pressure (IOP) and CH

also emerged. For instance, in eyes with CH of 5 mmHg, each IOP increase of 1 mmHg was associated with a 0.38 percent faster rate of VF index loss per year. By contrast, in eyes with CH of 10 mmHg, the same change in IOP was associated with a 0.11 percent faster rate of VF index loss per year.

The study also confirmed the role of central corneal thickness; eyes with thinner corneas had faster rates of VF index decline compared with those with thicker corneas. Nevertheless, a comparison between the effects of CH and central corneal thickness showed that while the latter explained 5.2 percent of the variation in the rates of disease progression, CH explained 17.4 percent of the variation.

Macular Morphology and Visual Acuity in the Comparison of AMD Treatments Trials

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Jaffe et al. used the one-year outcomes from the Comparison of Age-Related Macular Degeneration Treatments Trials to track the effect of different anti-VEGF treatments on the activity and composition of choroidal neovascular lesions and the association of macular morphology with visual acuity (VA). They found that anti-VEGF therapy reduced lesion activity and improved VA in all treatment groups and across all study points.

Trial participants with age-related macular degeneration were assigned randomly to treatment with ranibizumab or bevacizumab on a monthly or as-needed schedule. Optical coherence tomography, fluorescein angiography, color fundus photography, and VA testing were performed periodically throughout the yearlong study period.

Anti-VEGF therapy—regardless of drug and regimen—caused rapid and sustained reduction in macular fluid and thickness, stabilized lesion growth, reduced vascular leakage, and normalized retinal anatomy. At all time points, eyes with residual intraretinal fluid had worse VA than those without. In addition, eyes with abnormally thin or thick retinas (defined as less than 120 µm and greater than 212 µm), residual large lesions, and scarring also had worse VA. In the monthly ranibizumab group, there were more eyes with no fluid and an abnormally thin retina; however, the researchers note that the precise relationship between drug, dosing, and retinal thinning remains unclear. They also point out that additional studies are needed to investigate the relationship between monthly ranibizumab and the rate of neural tissue loss.

Some adverse effects associated with treatment were noted, including atrophy and fibrosis, and the latter was associated with the greatest reduction in VA. As a result, the researchers suggest that it would be beneficial to develop treatments with an antifibrotic effect that might be used in combination with anti-VEGF therapy.

American Journal of Ophthalmology

10-Year Review of Endophthalmitis Isolates and Antibiotic Susceptibilities

July *AJO*

In this retrospective, noncomparative, consecutive case series, **Schimel et al.** investigated the spectrum of organisms causing culture-proven endophthalmitis and their susceptibilities to commonly used antimicrobial agents. The authors found that a combination of vancomycin and ceftazidime for suspected bacterial endophthalmitis provided excellent overall treatment coverage. Moreover, the results demonstrated an increasing resistance of gram-positive organisms to fluoroquinolones.

The investigators reviewed the medical records of all cases of culture-proven endophthalmitis at a single institution from 2002 through 2011. The outcome measures included all intravitreal isolates identified as well as antibiotic susceptibilities. A total of 448 organisms were isolated during the study interval. The most common organisms identified were *Staphylococcus epidermidis* in 30 percent of cases, *Streptococcus viridans* group in 11 percent, *Staphylococcus aureus* in 8 percent, *Candida albicans* in 6 percent, other coagulase-negative staphylococci in 6 percent, *Propionibacterium acnes* in 5 percent, and *Pseudomonas aeruginosa* in 3 percent. Overall, 327 of 448 isolates (73 percent) were gram-positive organisms, 48 isolates (11 percent) were gram-negative organisms, 71 isolates (16 percent) were fungi, and two isolates (0.4 percent) were viruses. For gram-positive organisms, susceptibilities were 100 percent for vancomycin, 88 percent for gentamicin, 77 percent for sulfamethoxazole/trimethoprim, 58 percent for levofloxacin, 55 percent for oxacillin, 51 percent for ciprofloxacin, 51 percent for gatifloxacin, and 47 percent for moxifloxacin. For gram-negative organisms, susceptibilities were 100 percent for ceftazidime, 100 percent for levofloxacin, 95 percent for ciprofloxacin, 91 percent for tobramycin, 81 percent for gentamicin, and 60 percent for sulfamethoxazole/trimethoprim.

No single antibiotic provided coverage for all of the microbes isolated from eyes. Therefore, the authors recommend combination therapy generally for the initial empiric treatment of suspected bacterial endophthalmitis. Appropriate history and characteristic clinical features may guide the use of initial antifungal agents.

Role of Oral Corticosteroids in Orbital Cellulitis

July *AJO*

In a prospective, comparative, single-masked interventional study, **Pushker et al.** evaluated the use of oral corticosteroids as an anti-inflammatory adjunct to intravenous antibiotic therapy for orbital cellulitis. They found that it successfully hastened resolution of inflammation with a low risk of exacerbating infection.

The investigators randomized 21 patients with acute onset of orbital cellulitis with or without abscess into two groups. The seven patients in group 1 received standard intravenous antibiotics, while the 14 patients in group 2

received oral steroids after an initial response to the intravenous antibiotics. The main outcome measures were comparisons of sign and symptom resolution, duration of intravenous antibiotics, length of hospital stay, and sequelae of disease (ptosis, proptosis, and ocular movement restriction).

Patients in the steroid group showed an earlier resolution of inflammation in terms of periorbital edema, conjunctival chemosis at day 10, and pain. They also attained vision of 0.02 logMAR earlier than group 1 patients. Decrease in proptosis and improvement in ocular movements were also significantly associated with the use of steroids. While a significant number of patients in group 1 had mild residual ptosis, proptosis, and movement restriction at 12 weeks, none of the patients treated with steroids had any residual changes. The durations of intravenous antibiotics and hospital stay were also significantly less in the steroid group.

The authors recommend further multi-institutional, case-controlled, double-masked studies to confirm these findings.

Biometric Parameters Associated With IOP Reduction After Cataract Surgery

July *AJO*

In this prospective, observational case series, **Yang et al.** evaluated the ocular biometric parameters associated with intraocular pressure (IOP) reduction after phacoemulsification. They found that uncomplicated cataract surgery induced a remarkable IOP reduction in nonhypertensive and nonglaucomatous patients. And in addition to lens thickness, parameters such as changes in anterior chamber area and angle opening distance were positively and significantly correlated with reduced IOP after phacoemulsification.

This study included 999 patients who had undergone uncomplicated phacoemulsification. IOP and ocular biometric parameters were checked preoperatively and three months postoperatively using optical coherence tomography and ultrasonic biomicroscopy. The authors also evaluated the relationship between IOP change and parameters such as preoperative IOP, anterior chamber depth, axial length, angle opening distance at 500 µm, anterior chamber area, corneal thickness, lens thickness, and iris thickness at 750 µm. The mean patient age was 67 years. The average change in IOP was –1.6 mmHg.

In univariate analysis, axial length, corneal thickness, and iris thickness were not significantly associated with IOP reduction. However, preoperative IOP, anterior chamber depth, angle opening distance, anterior chamber area, and lens thickness were significantly associated with IOP change. Furthermore, changes in anterior chamber depth, angle opening distance, and anterior chamber area were more strongly correlated with IOP change than were preoperative factors. In multivariate analysis, preoperative IOP, lens thickness, and changes in angle opening distance and anterior chamber area were significantly associated with IOP change.

The authors note that one major limitation of their study was that the three-month follow-up period might not be sufficient for evaluating the long-term effect on IOP and its relationship with the ocular parameters.

JAMA Ophthalmology

Outer Retinal Structure in Best Vitelliform Macular Dystrophy

June *JAMA Ophthalmology*

Kay et al. characterized outer retinal structure at cellular resolution in patients with Best vitelliform macular dystrophy (BVMD). Using spectral-domain optical coherence tomography (SD-OCT) and adaptive optics scanning laser ophthalmoscopy (AOSLO), the authors found that substantial photoreceptor structure persists within active lesions of BVMD and accounts for good vision in these patients. Despite previous reports of photoreceptor outer segment abnormalities in BVMD, their findings revealed normal photoreceptor structure in areas adjacent to clinical lesions.

For this study, the authors recruited four symptomatic members of a family with known *BEST1* mutation. Patients underwent comprehensive ophthalmic evaluation that included clinical examination, fundus photography, and microperimetry. Thickness of two outer retinal layers corresponding to photoreceptor inner and outer segments was measured using SD-OCT. Cone density and photoreceptor mosaic integrity in and around visible lesions were evaluated using AOSLO montages.

Patient phenotypes ranged from early vitelliform to central atrophy with fibrosis. SD-OCT revealed inner and outer segment thickness values within two standard deviations of the normative mean. Disruption of the photoreceptor mosaic was evident by AOSLO in all patients, including the one patient with early vitelliform changes. When comparing SD-OCT to AOSLO images at the same location, AOSLO images allowed for direct assessment of photoreceptor structure. Photoreceptors were present to a varying degree in all lesions, and cone density measurements adjacent to these lesions were of normal density. Fine linear hyperreflective structures consistent with Henle fibers were also visualized using AOSLO.

Vitreoretinal Presentation of Secondary Large B-Cell Lymphoma

June *JAMA Ophthalmology*

Salomão et al. determined the incidence of vitreoretinal involvement as the presenting site of diffuse large B-cell lymphoma (DLBCL) in patients with systemic lymphoma mimicking primary vitreoretinal lymphoma. The authors found that vitreoretinal symptoms of DLBCL may be more frequent than previously thought. They also emphasized that not all lymphomas presenting with vitreoretinal involvement represent primary intraocular lymphomas; therefore, thorough ophthalmologic

evaluation in patients with visual symptoms and complete staging in patients with documented ocular lymphoma are of utmost importance.

This retrospective review included 57 specimens from 55 patients obtained at one institution from January 2000 to December 2010 because of clinical suspicion of malignancy. Of these patients, three (5.5 percent) with systemic lymphoma had a first presentation of DLBCL in the vitreous cavity without central nervous system involvement.

All three were men, ages 54, 66, and 73 years, who had blurred vision and floaters for several weeks before the diagnostic vitrectomy. Ophthalmic exams revealed clumps of vitreous cells but no choroidal involvement. One patient had no history of lymphoma; the diagnosis of vitreoretinal lymphoma was followed by DLBCL in a lymph node biopsy. The other two patients had low-grade B-cell lymphoma and chronic lymphocytic leukemia for 29 and seven months, respectively, before large-cell transformation in the eye.

Ophthalmology *summaries are written by Jean Shaw and edited by John Kerrison, MD.* American Journal of Ophthalmology *summaries are edited by Thomas J. Liesegang, MD.* JAMA Ophthalmology *summaries are written by the lead authors.*

ROUNDUP OF OTHER JOURNALS

Epiretinal Membrane Recurrence

Retina
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Sandali et al. conducted a retrospective study of 440 patients to examine the incidence, clinical characteristics, possible risk factors, and visual outcomes of epiretinal membrane (ERM) recurrence. They found that the absence of internal limiting membrane (ILM) peeling, the existence of ERM in the fellow eye, and poor visual acuity before surgery were each associated with a high risk of symptomatic recurrence and reoperation. Recurrences in patients who had undergone ILM peeling generally had a good visual outcome and did not require reoperation.

All of the patients had primary or secondary ERM and underwent pars plana vitrectomy by the same surgeon. The ILM was peeled in 266 of the 440 patients; of these 266 cases, indocyanine green dye was used in 27 and brilliant blue G dye was used in 45.

The incidence of ERM recurrence was 5 percent (22 of the 440 cases), and nine patients (2 percent) underwent another operation. ILM peeling was the only factor that prevented ERM recurrence, and it not only reduced the likelihood of reproliferation of ERM but also improved the visual prognosis of recurrent ERMs.

Although the staining dyes proved useful in some cases, their use did not reduce the rate of recurrence.

Long-Term Outcomes of Trabeculectomy in Diabetic Patients With Primary Open-Angle Glaucoma

British Journal of Ophthalmology
2013;97(5):561-566

In this retrospective, case-controlled study, **Law et al.** evaluated primary trabeculectomy with adjunctive mitomycin-C (MMC) in diabetic patients with primary open-angle glaucoma (POAG). They found that POAG patients with diabetes—but without diabetic retinopathy—who underwent primary trabeculectomy with MMC did not achieve the same long-term control of intraocular pressure (IOP) and may have a lower long-term surgical survival rate than nondiabetic patients who underwent the same procedure.

The researchers compared 41 eyes of 29 diabetic patients with 81 eyes of 64 nondiabetic patients who served as controls. The mean survival times of trabeculectomy were 63 months in the diabetic patients and 74.6 months in the control group. In addition, the mean postoperative IOP of the control group was lower than that of the patients with diabetes at all follow-up visits, extending out to seven years.

The researchers note that this study had several limitations, particularly its retrospective design. Although the two groups were carefully matched with regard to age and other significant factors, the average concentration of MMC used in the diabetic patients was lower than that used in the control group, and this difference reached statistical significance. In addition, the follow-up intervals varied—at six years after surgery, data were available in 19 eyes of the diabetic group and 55 eyes of the control group.

The authors concluded that a higher concentration or a longer duration of MMC application might achieve better IOP control in diabetic patients who do not have diabetic retinopathy.

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

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