

Highlights From the 2009 ARVO Meeting

Several presentations had relevance for how clinicians manage and treat patients with glaucoma.

BY ALBERT S. KHOURI, MD

At the recent annual meeting of the Association for Research in Vision and Ophthalmology (ARVO) in Fort Lauderdale, Florida, more than 700 glaucoma-related research studies were presented to an international audience of approximately 10,000 eye scientists and clinicians. This article profiles a select group of interesting projects from the meeting that are related to the management and treatment of patients with glaucoma.

SELECTIVE LASER TRABECULOPLASTY AND THE TRABECULAR MESHWORK'S PIGMENTATION

Two groups of investigators presented new data on the effect of the trabecular meshwork's pigmentation on the outcome of selective laser trabeculoplasty (SLT) in the management of glaucoma. Maheen Haque and colleagues at the Kresge Eye Institute at Wayne State University in Detroit conducted a retrospective analysis of the IOP response to SLT as a function of the degree of the meshwork's pigmentation. At their institution, the degree of pigmentation is graded as light, moderate, or heavy at the time of treatment. Their analysis of 83 eyes of 77 subjects undergoing first-time SLT treatment revealed significant IOP reductions in all three pigmentation groups, but it found no difference in mean IOP reduction between the three groups through 1 year of follow-up.¹

In a related study, medical student Joseph Donnelly of Hofstra University and collaborators at several New York-area universities evaluated the effect of race on SLT's outcome. In a retrospective analysis of 1,403 eyes treated with SLT as both primary and secondary therapy, the investigators compared the reduction in IOP in 190 eyes of black subjects and 1,213 eyes of white subjects. In this cohort, the average decrease in IOP was statistically equivalent in both groups, whether treated

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with primary or secondary SLT. Overall, black subjects experienced a mean IOP reduction of 28% compared to a 27% reduction in white subjects.²

Thus, it appears that SLT is not affected (for better or worse) by the degree of pigmentation in the trabecular meshwork. One key benefit of SLT technology is that the laser energy is selectively taken up by pigmented cells; as a result, even eyes with clinically light pigmentation may respond adequately to SLT. The greater danger lies in heavily pigmented eyes, in which an uptake of excessive laser energy could be problematic. There have been published reports of significant IOP spikes after SLT in heavily pigmented eyes; Haque's group acknowledged that the treating physicians tended to dial down the laser power in the heavily pigmented eyes, although not by a significant amount compared with laser treatment parameters in the other two groups.¹

GLAUCOMA SURGERY AND THE INHIBITION OF VASCULAR ENDOTHELIAL GROWTH FACTOR

If the first half of this decade was dominated by the prostaglandin wars, then certainly the second half will be remembered as the age of vascular endothelial growth factor (VEGF) inhibition. Not to be upstaged by our retina colleagues, glaucoma specialists are seeking novel uses for anti-VEGF therapy. One potential applica-

tion is as an adjunct to glaucoma surgery in lieu of (or in addition to) mitomycin C (MMC).

Yuji Takiyama and coworkers at Kumamoto University in Japan reported on a retrospective analysis of 57 eyes of 50 patients who underwent trabeculectomy with MMC for uncontrolled neovascular glaucoma. The team compared the outcomes in two groups: (1) 33 eyes that underwent trabeculectomy with MMC alone and (2) 24 eyes that first received an intravitreal injection of bevacizumab (Avastin; Genentech, Inc., South San Francisco, CA) 1.25 mg 1 to 5 days before trabeculectomy with MMC. Only eyes undergoing trabeculectomy for the first time were included. To minimize selection bias, the researchers drew the controls (no bevacizumab) from the period before they began using bevacizumab augmentation, and they drew cases (with bevacizumab) from the period after they began doing so. The follow-up for cases was therefore longer (mean, 613 days) than for controls (mean, 255 days). The investigators found that the IOP was lower at postoperative days 1 and 7 in the eyes receiving bevacizumab pretreatment. Kaplan-Meier survival analysis, however, revealed that 4-, 8-, and 12-month survival was similar in eyes receiving bevacizumab (86%, 74%, and 62%, respectively) and not receiving bevacizumab (74%, 71%, and 64%, respectively) ($P=.76$ by the log rank test).³

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The rationale for using anti-VEGF agents as adjuncts to filtering surgery is that VEGF is both angiogenic and proinflammatory. Thus, anti-VEGF therapy could favorably affect two separate pathways that threaten the bleb's survival. Arguably, these two processes are more active in eyes with neovascular glaucoma than in eyes with primary open-angle glaucoma (POAG). The effectiveness of anti-VEGF therapy in eyes with POAG cannot be intuited from these data and warrants exploration.

ORAL AND TOPICAL BETA BLOCKADE

Over the past decade, topical prostaglandin analogues have replaced beta blockers as first-line agents, yet the latter remain an integral part of glaucoma therapy, mainly because of their time-tested efficacy. Oral

beta blockers are among the most commonly prescribed systemic medications and have a proven benefit in reducing mortality in patients with a history of cardiac events. A group of investigators looked at the frequency of the coadministration of topical and oral beta blockers in patients with glaucoma. This coadministration carries a systemic risk of adverse events and potentially reduces the efficacy of the topically applied drug in lowering IOP.

Christopher Rodarte and coworkers from the Department of Ophthalmology and Visual Sciences at the University of Michigan at Ann Arbor reviewed the records of 26,498 patients over the age of 18 years who had received a diagnosis of glaucoma or glaucoma suspect between 2003 and 2007. The investigators used billing records to identify patients who were on oral and topical beta blockers simultaneously.

The researchers found that one-quarter of patients (6,565) had received an oral beta blocker and that approximately 10% (2,997) had received a topical beta blocker. Interestingly, more than 900 patients were prescribed both forms of the drug simultaneously at some point in time. Almost one-third of patients using a topical beta blocker for their glaucoma were also on a systemic beta blocker for another comorbid condition. Twenty-eight percent of patients on both systemic and topical beta blockers were using the topical drug as monotherapy for IOP control; that is, topical beta blockers were prescribed despite the availability of potentially safer IOP-lowering options. Perhaps most shockingly, almost a third of subjects on both topical and systemic beta blockers had a contraindication to the use of these drugs, including chronic obstructive pulmonary disease (14%), asthma (13%), congestive heart failure (11%), bradycardia (9%), and atrioventricular block (4%), among others.⁴

These findings underscore the necessity for physicians to carefully review patients' medical and medication history prior to prescribing new agents. Improving communication between primary care physicians and eye care providers will help to eliminate the coadministration of beta blockers, which will undoubtedly improve safety and avoid potentially serious adverse effects.

OBESITY: A RISK FACTOR FOR GLAUCOMA?

Obesity continues to be a worldwide problem reaching epidemic proportions in Western countries. The metabolic syndrome, of which obesity is a key component, is a combination of medical disorders that increase the risk of cardiovascular disease and diabetes. Kojiro Imai and coworkers from the Kyoto Prefectural

University of Medicine studied the relationship between the metabolic syndrome and IOP in 10,182 healthy individuals enrolled in a medical health program at Murakami Memorial Hospital in Gifu, Japan. To account for possible racial differences in body habitus, the research team utilized national standards adopted by the Japanese Treatment Panel to define the metabolic syndrome in the Japanese population. These standards included an increased abdominal circumference, body mass index, elevated triglycerides, blood pressure, and fasting blood sugar. The IOP was determined as the average of three measurements with a noncontact tonometer. An IOP over 21 mm Hg was used as the cut-off for their study.

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The investigators found high IOP to be statistically significantly more common among Japanese men and women with the metabolic syndrome. The researchers also found that multiple components of the metabolic syndrome were associated with an IOP greater than 21 mm Hg, including body mass index and an abdominal circumference of more than 90 cm in males or higher than 80 cm in females. The investigators demonstrated by logistic regression that the metabolic syndrome was positively correlated with increased IOP (adjusted odds ratio 2.92 in males and 9.94 in females). The aforementioned observations shed light on the possible systemic/ocular effects of the metabolic syndrome that definitely warrant further study.⁵

STABILITY OF THE MEASUREMENTS OF CENTRAL CORNEAL THICKNESS OVER TIME

Recent clinical trials have established the importance of central corneal thickness (CCT) as a risk factor for the development of glaucoma. As a result, the measurement of CCT has become a reimbursable service for glaucoma patients but with a catch: it will only be paid for once in the patient's lifetime. Is a single measurement adequate to characterize CCT in eyes with glaucoma? The answer is perhaps not, according to a study conducted by Tony Realini and colleagues at West Virginia University. In their post hoc analysis of a prospectively collected data set, the team compared

CCT measurements from 164 eyes of 82 subjects (44 with POAG and 38 controls) collected on days 0, 7, 30, 180, and 365. For each eye, the lowest of the five measurements was subtracted from the highest of the five measurements, yielding the maximum difference between visits. The maximum difference was greater than 30 μm in 20% of the glaucomatous eyes. The maximum difference was greater than 30 μm in 26% of control eyes without glaucoma. The distributions of differences were not different between the glaucomatous and control eyes in this study.⁶

Shaban Demirel and coworkers at Devers Eye Institute in Portland, Oregon, studied the rate of change of CCT over time in eyes with ocular hypertension and early glaucoma. The investigators evaluated the effects of age, gender, and history of using topical IOP-lowering medication on the rate of change in CCT over time in 121 subjects with at least four CCT measurements over time. CCT in females was 11 μm thicker than in males, and the eyes of patients using topical IOP-lowering medications had a mean CCT that was 17 μm thinner than those of patients not using medication. The overall rate of change in CCT over time was -1.5 μm per year and was greater (-2.2 μm per year) in patients using medications than in those who were not (-0.8 μm per year).⁷

These studies suggest that, although mean CCT is relatively stable over time (changing by only a few microns per year), CCT measurements vary significantly between visits over time. Thus, a single measurement may not adequately characterize CCT in a given patient. □

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