ARVO 2010

Some of the highlights of this year's meeting.

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This article summarizes some of the interesting projects presented at the recent annual meeting of the Association for Research in Vision and Ophthalmology.

CONSISTENCY OF DIURNAL IOP PATTERNS OVER TIME

Once clinicians perform a diurnal curve, they often assume that it reflects the IOP behavior for that patient. Tony Realini, MD, MPH, and colleagues presented a study that addressed the following intriguing question: does IOP follow the same diurnal pattern from day to day? They conducted diurnal IOP testing in two sessions 1 week apart on 47 patients with treated open-angle glaucoma. IOP measurements were obtained every 2 hours from 8 AM to 8 PM using Goldmann tonometry.

Their analysis used the intraclass correlation coefficient (ICC) to measure the agreement between IOP at each time point on the first visit and the IOP at the same time point 1 week later. The ICC has values between -1 and +1; values below 0.4 represent poor agreement, between 0.4 and 0.75 represent fair-to-good agreement, and above 0.75 represent excellent agreement. In general, they reported only fair-to-good agreement of IOP measurements at the same time of day 1 week apart, with ICC values ranging from 0.45 to 0.71 in right eyes (results in left eyes were not reported but were stated to be similar). The group also assessed the agreement of changes in IOP between time points (eg, comparing change between 8 AM and 10 AM at the first visit and between 8 AM and 10 AM 1 week later). They found uniformly poor agreement, with ICC values ranging from -0.05 to +0.38 (negative ICC values indicate agreement worse than that expected by chance alone).

What are the clinical implications of these findings? According to its authors, the study suggests that, even if clinicians perform a single-day diurnal IOP test on a given patient, they still may not know much about his or her IOP behavior on other days. Although there is still value in knowing a patient's peak and range of IOP over time, Dr. Realini said, a single-day diurnal IOP assessment may not fully capture the breadth of diurnal variability in IOP.[1]

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CENTRAL CORNEAL THICKNESS

The prediction model for the development of primary open-angle glaucoma (POAG) from the Ocular Hypertension Treatment Study (OHTS) and the European Glaucoma Prevention Study includes central corneal thickness (CCT) in addition to age, IOP, pattern standard deviation, and cup-to-disc ratio. Measuring CCT has become the standard of care, as clinicians try to stratify the risk of conversion among glaucoma suspects. It is also well determined that CCT affects IOP measurements with Goldmann tonometry. After refractive surgery, for example, IOP is often underestimated as the cornea becomes thinner.

Many algorithms have been proposed for correcting IOP based on CCT. James Brandt, MD, and colleagues from the OHTS Group and European Glaucoma Prevention Study Group asked whether adjusting baseline IOP for CCT increases the accuracy of the prediction model for the development of POAG. Dr. Brandt explained that they ran the same hazards model and changed only whether the IOP was or was not adjusted for CCT. In the models that included IOP adjusted for CCT, the c-indices (discrimination) ranged from 0.763 to 0.770, no better than the original prediction model (0.774). They concluded that CCT is a powerful risk factor that relates to biomechanical properties of the eye beyond the purely observed effects on Goldmann tonometry measurements. Their study found that calculating individual risk for the development of POAG is simpler and equally accurate using IOP and CCT as measured, rather than applying any algorithm to correct IOP for CCT.[2]

POAG PATIENTS' RISK FOR AN IOP SPIKE AFTER PHACOEMULSIFICATION

Why do some POAG patients experience an IOP spike after phacoemulsification, whereas others do not? Mark Slabaugh, MD, and colleagues from the Department of Ophthalmology at the University of Washington in Seattle performed a retrospective review to try to answer this question. They identified 80 consecutive patients with POAG who underwent uncomplicated primary cataract extraction via phacoemulsification. All patients were prescribed acetazolamide for the first 24 hours instead of their usual topical IOP-lowering agents. The vast majority received acetazolamide 500 mg that evening and again in the morning, but a few only received the drug (500 mg) that evening. On postoperative day 1, acetazolamide was discontinued, and topical IOP-lowering agents were restarted. The investigators calculated baseline IOP as an average of the IOP at the last three office visits, and they arbitrarily defined an IOP spike as an increase in IOP of 10 mm Hg or more from baseline.

The investigators were surprised to find that 23% of patients had an IOP spike on postoperative day 1, even after an uncomplicated cataract extraction. They then proceeded to examine the variables associated with the elevation. Their analysis showed that the statistically significant variables associated with a postoperative IOP spike were younger age, a preoperatively wider gonioscopic angle (graded by Schaffer classification), myopia, the use of an acrylic (rather than silicone) IOL, and—as expected—failure to use the acetazolamide. These findings highlight clinicians' need to be vigilant in their monitoring of glaucoma patients, even after uncomplicated cataract extraction, because one in five may experience an IOP spike postoperatively.[3]

SELECTIVE LASER TRABECULOPLASTY

Does the outcome of selective laser trabeculoplasty (SLT) in one eye predict the response in the contralateral eye? A group of researchers from Massachusetts Eye and Ear Infirmary performed a retrospective review of all SLT cases (amount of treatment not specified) performed by three surgeons between 2002 and 2008. Mean follow-up was about 41 months. Success was defined as a drop in IOP of more than 3 mm Hg without the use of any additional medication or surgery. In total, 178 eyes were included. The interval between the two SLT procedures was about 13 months.

Three-quarters of eyes showed the same result, whether success or failure, in the second treated eye. Among eyes with successful SLT (27%), SLT on the second eye was also a success in 87.5%. The opposite scenario was equally true in that, if the first SLT treatment failed in the first eye (73%), it also failed in the contralateral eye (71%). A multivariate logistic regression analysis showed a statistically significantly lower risk of SLT's failure in the second eye when higher energy was used (0.98 mJ in eyes with success, 0.86 mJ in eyes with failure). For each 0.1 mJ of higher laser energy power, the odds were increased by 2.34 in favor of success. Jea et al concluded that higher energy may improve success with SLT in patients in whose first eye the procedure failed. They did not offer an explanation for the high failure rate reported.[4]

Another group from New York Medical College, Indiana University, and the Metropolitan Hospital Center in New York studied the effectiveness of repeat SLT for POAG. Jason Peragallo, MD, described their findings in 19 eyes that received a repeat SLT procedure an average of 500 days after the first SLT treatment. All eyes were on maximal glaucoma therapy. This short-term response study included a comparison of IOP response 6 weeks after the first and repeat SLT procedures. The mean baseline IOP was about 18 mm Hg on maximal therapy. The change in IOP from the first SLT (-2.26 mm Hg) was not statistically different from the change in IOP from the repeat SLT (-1.68 mm Hg). The investigators concluded that repeat SLT was effective at lowering IOP in patients with POAG who previously underwent SLT but that longer follow-up of a larger series will better characterize this response.[5] Many other groups presented interesting data on SLT's long-term results, higher-energy SLT's efficacy, and IOP spikes after SLT treatment.

DRUG DELIVERY

Several groups of researchers presented work on glaucoma drug delivery systems, although they are still far from direct clinical application. Alina Dumitrescu, MD, and a group of researchers from the University of Iowa, Iowa State University, Yale University, and Case Western Reserve University presented their work on sustained-release timolol microspheres after subconjunctival injection. To evaluate in vivo release characteristics, the investigators studied their delivery system in mice, rabbits, and cats. Aqueous and vitreous samples were collected with measurable timolol from 60 to 100 days after injection. These investigators cautioned that much work still needs to be done, as researchers attempt to find the ideal sustained-release delivery system over longer periods. It was encouraging that no foreign body reaction was noted on histologic and immunohistochemical examination of tissues after the injections.[6]

A second group of researchers from Vanderbilt University worked on nanoparticle-encapsulated delivery of

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brimonidine and travoprost to the eye. Grace Shih and coworkers presented their research utilizing a 53 nanosponge loaded with the aforementioned two agents that was intravitreally injected into mice's eyes. Before the procedure, elevated IOP was induced by the injection of microbeads into the anterior chamber to block aqueous outflow. An IOP reduction was achieved for 12 days. Another interesting observation, however, was that nanoparticles reached the retina without exhibiting toxic effects and were picked up within retinal ganglion cells. The hope is that this finding may open up another realm of possibilities for the delivery of neuroprotective agents to retinal cells.[7] ❑

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1. Realini T, Weinreb RN, Wisniewski S. Diurnal intraocular pressure patterns are not repeatable in the short term in glaucomatous individuals. Paper presented at: The ARVO Annual Meeting; May 4, 2010; Fort Lauderdale, FL.
2. Brandt JD, Gordon MO, Kass MA, et al; Ocular Hypertension Treatment Study Group and European Glaucoma Prevention Study Group. Does adjusting IOP for central corneal thickness improve accuracy of the prediction model for the development of POAG? Poster presented at: The ARVO Annual Meeting; May 4, 2010; Fort Lauderdale, FL.
3. Slabaugh MA, Chen PP, Moore DB. Risk factors for post phacoemulsification IOP spike in OAG patients. Poster presented at: The ARVO Annual Meeting; May 4, 2010; Fort Lauderdale, FL.
4. Jea S, Pasquale LR, Grosskreutz CL, Rhee DJ. Predictors of success of selective laser trabeculoplasty. Poster presented at: The ARVO Annual Meeting; May 5, 2010; Fort Lauderdale, FL.
5. Peragallo JH, Malen M, Lai PC. Effectiveness of repeat selective laser trabeculoplasty on primary open angle glaucoma (POAG) patients. Poster presented at: The ARVO Annual Meeting; May 5, 2010; Fort Lauderdale, FL.
6. Dumitrescu AV, Bertram J, Olson LR, et al. In-vivo characterization of sustained release timolol microspheres. Poster presented at: The ARVO Annual Meeting; May 4, 2010; Fort Lauderdale, FL.
7. Shih GC, Sternbeg MG, Crish SD, et al. Nanoparticle drug delivery to retinal ganglion cells in glaucoma. Poster presented at: The ARVO Annual Meeting; May 4, 2010; Fort Lauderdale, FL.