

2004 ARVO Highlights

Glaucoma experts from around the world presented hundreds of posters and papers at this year's annual meeting.

BY ALAN L. ROBIN, MD

Medication, surgery and wound healing, and neuroprotection were among the primary focuses of studies presented at this year's ARVO meeting in Fort Lauderdale, Florida. Among hundreds of studies presented, the following were some of the most interesting and clinically relevant.

IOP CHANGES

Researchers at the University of Wisconsin, Madison, conducted a study to determine whether changes in systemic blood pressure are associated with changes in IOP. The study included 4,926 people between the ages of 43 and 86 years. Researchers measured patients' blood pressures and IOPs. Five years later, the researchers repeated the measurements on the 3,684 patients who returned for follow-up. The study found that changes in blood pressure were possibly associated with changes in IOP. The researchers therefore concluded that the treatment of systemic hypertension might be associated with a decreased risk of open-angle glaucoma.¹

Additionally, a meta-analysis of randomized clinical trials on the medical treatment of glaucoma found that a decrease in IOP of 4.3 mm Hg, or 17.4%, provides a highly significant protective effect for glaucoma progression. Approximately 13% of patients' conditions worsen despite treatment, however.²

THE ROLE OF CORNEAL THICKNESS

Two important studies examined the role of corneal thickness in glaucoma. A study conducted at the Southern Eye Center in Hattiesburg, Mississippi, and the W. K. Kellogg Eye Center in Ann Arbor, Michigan, included 41 patients with asymmetric glaucoma. Researchers found that eyes with more advanced glaucomatous cupping had decreased central corneal thickness compared to fellow eyes with less cupping. These findings of asymmetric central corneal thickness raise the question of whether the cornea is a biological indicator of glaucoma in some susceptible eyes.³

In a separate study conducted at the University of

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Nebraska Medical Center in Omaha, researchers evaluated the effect of central corneal thickness on the IOP effect of brimonidine and latanoprost. This study of 99 patients found that, after treatment with brimonidine, but not with latanoprost, eyes with thinner corneas had lower IOPs than eyes with thicker corneas.⁴ This finding may imply that brimonidine works better than latanoprost in eyes with thinner corneas. The Ocular Hypertension Treatment Study previously found that beta-blockers are less effective in eyes with thicker versus thinner corneas.⁵

CLINICAL RESEARCH

Bimatoprost, latanoprost, and travoprost may lead to disruption of the blood-aqueous barrier in pseudophakic and aphakic patients, according to a study conducted in Brazil. In this 6-month, randomized, clinical trial, 16 patients were treated with bimatoprost, 15 were treated with latanoprost, 17 were treated with travoprost, and 16 were treated with unoprostone or dexamethasone. Researchers evaluated subjects' blood-aqueous barrier status using the laser flare meter, IOP, occurrence of angiographic cystoid macular edema, and conjunctival hyperemia.

Mean flare values were significantly higher in the bimatoprost, latanoprost, and travoprost groups at all follow-up visits. Mean IOP reductions after 6 months were higher for the latanoprost, bimatoprost, and travoprost groups, and the incidence of cystoid macular edema was significantly higher in eyes receiving latanoprost. Because

of the study findings, the researchers recommend exercising caution when using these prostaglandin analogs in aphakic or pseudophakic patients.⁶

According to a study conducted at Mt. Sinai Medical Center in New York City, ophthalmologists may want to alter the training regimen of glaucoma patients who are weightlifters. The study included eight glaucoma patients, and researchers evaluated the effects of performing the flat bench press, leg press, standing triceps extension, seated rows, and stomach crunches on IOP measurements. They found that weightlifters who performed five repetitions of bench pressing and seated rows had increased IOP that rapidly returned to baseline. IOP increases for bench press ranged from 0.3 to 7.3 mm Hg, and IOP elevations during seated rows ranged from 0.3 to 8.7 mm Hg.⁷

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Another study conducted at Mt. Sinai found that patients should wait at least 2 minutes between eye drop instillations to maximize their efficacy. Researchers evaluated 18 eyes in 10 patients. Seven patients received COSOPT (Merck & Co., Inc., West Point, PA) and Alphagan (Allergan, Inc., Irvine, CA), two patients received Trusopt (Merck & Co., Inc.) and Alphagan, and one patient received COSOPT and lopicol (Alcon Laboratories, Inc., Fort Worth, TX). Patients instilled drops at 0-, 2-, and 5-minute intervals.

The researchers concluded that allowing no time between successive eye medications is less effective in lowering IOP than allowing a 2- or 5-minute interval between drops. Waiting at least 2 minutes between instilling drops maximized their efficacy. Interestingly, a longer time interval may not improve effectiveness and may adversely affect patient compliance.⁸

SURGERY AND WOUND HEALING

A study conducted at Wills Eye Hospital in Philadelphia found that Healon5 (Advanced Medical Optics, Inc., Santa Ana, CA) can be used in postoperative hypotony cases. The viscoelastic should be employed in conjunction with other more established treatments, however, because the clinical course did not improve

significantly when it was used alone. Fifteen consecutive glaucoma patients with postoperative hypotony that persisted for 7 days or more were included in the study. An intracameral injection of Healon5 was given either at the slit lamp or under the microscope in the OR. The study found that, although the injection of Healon5 raised IOP in postoperative hypotony cases, the increase was not statistically significant, and IOP did not rise sufficiently to positively impact the clinical course. Patients with early-onset hypotony had greater IOP increases than those with late-onset hypotony.⁹

According to a Brazilian study, oral prednisone is not effective for the treatment of choroidal detachment after filtration surgery, and it may increase the time to spontaneous resolution of the detachment. Twenty patients were in the prednisone group, and 25 patients were in the placebo group in this randomized, double-masked, placebo-controlled study. To be eligible for the study, patients had to have developed choroidal detachment during the first 2 postoperative weeks after filtering surgery. Patients in the prednisone group had a median duration of choroidal detachment of 21 days. Those in the placebo group had a mean duration of choroidal detachment of 14 days.¹⁰

AHMED VALVE STUDIES

A study conducted in Korea assessed the relationship between the level of TGF- β 2, VEGF, and total protein in the aqueous humor and the results of Ahmed valve (New World Medical Inc., Rancho Cucamonga, CA) implantation for neovascular glaucoma in 19 patients. No significant relationship was found between the level of TGF- β 2, VEGF, and total protein in the aqueous humor and the surgical success of Ahmed valve implantation.¹¹

Researchers at the Massachusetts Eye and Ear Infirmary conducted a study to determine the effect of diverting aqueous humor to distant sites in patients with severe glaucoma. Twenty eyes of 19 patients were included. A tube shunt from a specially designed Ahmed valve was connected to the maxillary sinus in 10 eyes, the ethmoid sinuses in six eyes, the lacrimal sac in two eyes, and the lower lid fornix in two eyes. Patients were followed for 1 to 31 months. No endophthalmitis occurred, and 14 of the patients had IOPs in the low teens without glaucoma medications. Two valve housings were removed, two patients required additional medication, and two had further procedures.¹²

Researchers at the Jules Stein Eye Institute investigated the effects of cataract surgery on aqueous shunt function. Each of the 24 eyes of 19 patients included in the study had a functioning Ahmed Glaucoma Valve

and subsequently underwent phacoemulsification at least 3 months after valve insertion. The study found that cataract surgery after the insertion of an Ahmed Glaucoma Valve was associated with maintenance of IOP control in most cases and improved vision. The incidence of posterior capsular opacification was high in this group of patients, however.¹³

Ex-PRESS GLAUCOMA IMPLANT STUDIES

Two studies found that the Ex-PRESS mini glaucoma shunt (Optonol Ltd., Zug, Switzerland) successfully controls IOP. Swiss researchers have found that the Ex-PRESS LR-50 glaucoma implant inserted into the anterior chamber with a modified deep sclerectomy significantly lowered IOP in glaucoma and combined surgery with phacoemulsification and IOL implantation. The modified deep sclerectomy technique prevented conjunctival erosion, which is the major complication after insertion of this implant with no superficial scleral flap. This was a prospective, nonconsecutive, randomized study of 45 eyes of 45 patients with medically uncontrolled mild-to-moderate glaucoma.¹⁴

In addition, a South African study found that implanting the Ex-PRESS mini glaucoma shunt under a scleral flap in high-risk (refractory) cases was simple and effective. The study included 24 eyes of 23 patients with complicated open-angle glaucoma. At 1 year after implantation, IOP was controlled without medication in the majority of cases.¹⁵

NEUROPROTECTION

Japanese researchers have found that the intravitreal administration of N-Methyl-D-Aspartate (NMDA) induces cell death, both in the ganglion and amacrine cells, with the suppression of protein kinase B (Akt) activity. Thus, the regulation of Akt activity has potential therapeutic aspects in the treatment of glutamate-related disease.¹⁶

A study was conducted in Italy and the United Kingdom to explore the IOP-unrelated effect of brimonidine on visual function in human glaucoma. The study included 52 eyes. Twenty-seven were randomized to brimonidine, and 25 were randomized to argon laser trabeculoplasty. The researchers found that 0.2% brimonidine b.i.d. was more effective than 360° laser trabeculoplasty in reducing field deterioration in progressing human glaucomatous eyes. Brimonidine did, however, offer poorer IOP control.¹⁷

PHARMACOLOGICAL INTERVENTION AND CELL MECHANISMS

Japanese researchers found that 25% of normotensive normal subjects had little or a low response to latano-

prost. The study included 46 patients. Baseline IOP was measured by applanation tonometry, and central corneal thickness and refraction were also measured at baseline. Latanoprost was applied to one eye once daily for 7 days. The other eye served as a control. Diurnal IOP measurement was repeated on day 7. Latanoprost significantly reduced the mean diurnal IOP of treated eyes from 13.3 to 10.9 mm Hg, but it did not significantly alter the extent of diurnal fluctuation of IOP.¹⁸

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A study conducted in the United Kingdom found that melanin in the trabecular meshwork was associated with age and primary open-angle glaucoma (POAG), but not with latanoprost treatment. The percentage of melanin-containing meshwork cell profiles was 12.9% in the control group and 33.2% in the POAG group. When comparing POAG patients who had taken latanoprost with those who had not, the researchers found no significant differences. Electron microscopy confirmed that the melanin granules were mostly intracellular and of the larger iris epithelial type, even in the latanoprost-treated specimens.¹⁹

Ophthalmologists from centers in several countries are conducting the International Collaborative Exfoliation Syndrome Treatment Study (ICEST). This randomized, open-label study is designed to test the hypothesis that improving both pressure-dependent and pressure-independent aqueous outflow and minimizing iridolenticular friction will interfere with the progression of exfoliation syndrome, allow improvement in trabecular function, and be more effective over time than simply reducing aqueous formation. A total of 277 patients with exfoliation syndrome and elevated IOP with and without glaucoma were enrolled at 12 centers in seven countries. Of these 277 patients, 145 received latanoprost and pilocarpine, and 132 were given timolol or Cosopt. The researchers believe that the results of the ICEST study will provide ophthalmologists with guidance on the best initial treatment for patients with exfoliation syndrome and elevated IOP.²⁰

Researchers from the University of Washington in Seattle have found that travoprost 0.004%/timolol 0.5% ophthalmic combination solution reduced mean IOP

more than either Travatan (Alcon Laboratories, Inc.) or timolol 0.5% alone during a 3-month period. IOP reductions ranged from approximately 9 to 12 mm Hg and were statistically significant. Additionally, the researchers found that travoprost 0.004%/timolol 0.5% combination ophthalmic solution was safe and well tolerated by patients.²¹

IMAGING OF THE OPTIC DISC AND RETINAL NERVE FIBER LAYER

Researchers in San Diego conducted a study to determine the short-term repeatability of the GDx VCC's (Laser Diagnostic Technologies, San Diego, CA) parameters and to evaluate the influence of diurnal and daily variation, as well as machine-to-machine variability. The study included nine normal subjects, who were scanned three times on five different machines twice a day on 3 separate days. Day, machine, time of day, and subject were independent variables. The study found that measurement variation inherent to the GDx VCC was small. Measurements were not influenced by diurnal and daily variation to a degree that was clinically relevant. Machine-to-machine variation was noticeable but was only important in detecting changes of 6 μm or less.²²

A study conducted at Mt. Sinai Medical Center in New York compared optic disc examinations using the Heidelberg Retinal Tomograph (HRT; Heidelberg Engineering GmbH, Dossenheim, Germany) with visual field examinations using Humphrey Visual Field (HVF) analysis (Carl Zeiss Meditec Inc., Dublin, CA) in detecting progression of glaucoma. This retrospective, cross-sectional study included patients who had at least three HRTs and at least three HVFs during a follow-up of 5 years at minimum. The study included 306 eyes of 180 patients and found that HRT identified a higher number of patients progressing as compared with HVF analysis. A small number of patients progressed on both HRT and HVF. The researchers attributed this finding in part to the definitions chosen for progression but noted it may suggest that structural disc changes detected by HRT may more commonly precede functional progression detected by HVF examinations.²³ □

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