The Literature

BY CHARLES A. COLE, MD

Each installment of "The Literature" column will examine the most important recent studies of relevance to the physicians who treat patients with glaucoma. The authors are selected by Section Editor James C. Tsai, MD.

THE UTILITY OF THE MONOCULAR TRIAL: DATA FROM THE OCULAR HYPERTENSION TREATMENT STUDY[1]

*Bhorade AM, Wilson BS, Gordon MO, Palmberg P, Weinreb RN, Miller E, Chang RT, Kass MA; Ocular Hypertension Treatment Study Group.**
Ophthalmology, *November 2010*

Is the Monocular Trial Useful?

A traditional monocular trial is performed by placing a topical ocular hypotensive agent in one eye and then checking the subsequent IOP after an interval of 4 to 8 weeks. The difference in IOP in the fellow eye between visits is then subtracted from the change in the treated eye. If the medication appears effective, therapy is started in both eyes. Multiple studies have drawn various and contradictory conclusions with regard to the usefulness of the monocular trial. The general consensus, however, is that multiple pre- and posttreatment IOP measurements on different days are the best estimate of the effectiveness of an ocular hypotensive agent.[2-14]

The Ocular Hypertension Treatment Study (OHTS) was a multicenter, clinical study in which 206 participants were randomized to either treatment with topical ocular hypotensive medication or observation.[15] In June 2002, participants in the observation group were offered topical medication based on results from the OHTS.[15] This study only examined participants who were in the observation group and began taking a prostaglandin analogue (PGA). IOP measurements of the trial and fellow eyes were taken at three pretreatment and three posttreatment visits. IOP was also measured at a baseline visit, which was also when the medication was started and at 1 month. IOP change was measured using both an adjusted and an unadjusted method. The latter method was the difference in IOP of the trial eye at the baseline versus the 1-month visit. For the adjusted method, investigators subtracted the difference in IOP of the fellow eye at these same visits from the difference in IOP of the trial eye. The "gold standard" for IOP response was defined as the difference in mean IOP from three pretreatment and three posttreatment visits. The baseline and 1-month visits were not part of the gold standard calculation.

The OHTS sought to answer two questions. First, is it better to use a monocular trial to determine medication response? Second, is the response to a medication in one eye similar to the fellow eye's response to the same medication among participants receiving a topical PGA trial?

Are Monocular Trials Good Estimates of Medication Response?

The results of the OHTS suggested that both the adjusted (monocular trial) and unadjusted methods for IOP change were equivalent to the gold standard and that neither was a good predictor of a patient's response to a topical PGA. Additionally, the IOP response of one eye to a medication was similar to the response of the fellow eye to the same medication. The study's authors concluded that monocular trials and bilateral simultaneous trials are equivalent for estimating medication response, but both methods are inaccurate compared with using multiple pre- and posttreatment IOP measurements.

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DIAGNOSTIC PERFORMANCE OF ANTERIOR CHAMBER ANGLE MEASUREMENTS FOR DETECTING EYES WITH NARROW ANGLES[16]

*Quigley HA, Broman AT.**
Archives of Ophthalmology, *October 2010*

Can Anterior Segment Optical Coherence Tomography Be Used as a Screening Tool?

It is estimated that 60.5 million people worldwide will be blind because of glaucoma by 2010 and that the cause of half of these cases will be due to angle closure. In a community-based, cross-sectional study of 883 individuals 50 years of age or older who were phakic, researchers set out to determine the diagnostic performance of Anterior Segment Optical Coherence Tomography (AS-OCT) for identifying eyes with narrow angles.[17]

In the dark, participants underwent AS-OCT by a single operator. This test was followed by gonioscopy, which was performed in the dark by an ophthalmologist who was masked as to the AS-OCT results. An eye was designated as having a narrow angle if the posterior pigment-

ed trabecular meshwork was not visible for at least 180º on nonindentation gonioscopy. AS-OCT images were obtained using the Visante OCT (Carl Zeiss Meditec, Inc., Dublin, CA). An algorithm was then used to calculate angle-opening distance, angle recess area, and trabecular-iris space area. Due to software limitations, only the horizontal angles were quantified.

Narrow angles were diagnosed in 315 participants with gonioscopy. AS-OCT images were analyzed using various cutoff values. The area under the receiver-operating characteristic curve was highest in the nasal (0.90 [95% corneal indentation, 0.89-0.92]) and temporal quadrants (0.91 [95% corneal indentation, 0.90-0.93]) of the angle-opening distance, the distance between the iris and the trabecular meshwork, which measured 750 µm from the scleral spur. The specificity was not greater than 90% at any cutoff value. It was noted that 25.2% of the community-based study participants had to be excluded because of difficulty locating the scleral spur, a critical landmark for angle measurements. The investigators felt the limited resolution of the AS-OCT was the main factor contributing to difficulty identifying the scleral spur. Another limitation was that only the temporal and nasal quadrants were analyzed because of software parameters, but previous studies have found that the superior and inferior angles are narrower.[18-20] Correcting this limitation would likely decrease the specificity of the test further. The researchers concluded that AS-OCT image analysis is a promising approach for detecting angles at risk for closure. They also suggested that future improvements would likely overcome the major drawback of the inability to identify the scleral spur, which currently limits the technology's use for population screening.

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OCULAR BIOMETRY AND OPEN-ANGLE GLAUCOMA: THE LOS ANGELES LATINO EYE STUDY[21]

*Kuzin AA, Varma R, Reddy HS, Torres M, Azen SP; Los Angeles Latino Eye Study Group.**
Ophthalmology, *September 2010*

Is There an Association Between Axial Length and Glaucoma?

The goal of the Los Angeles Latino Eye Study (LALES) was to examine the relationship between myopic refractive error, axial length, corneal power, and the prevalence of primary open-angle glaucoma (POAG). LALES was a population-based survey of adult Latinos living in Los Angeles County. This study did not consider IOP in the definition of POAG and defined ocular hypertension as an IOP greater than 21 mm Hg in either eye.

Because myopic refractive error can be explained by nuclear opacification, axial length was used to evaluate the relationship of myopic refractive error to POAG. Myopic refractive error was quantified as low (-1.00 to > -3.00 D) or moderate to high (≤ -3.00 D). Corneal power was an average of three measurements. Axial length was an average of three measurements using the A-Scan Pachymeter (Ultrasonic, Exton, PA). Nuclear opacification was graded using the Lens Opacities Classification System, grading opacities into five nuclear grades of increasing density. Nuclear opacification was defined as having a Lens Opacities Classification System score of NII or greater.

Myopes were significantly more likely to have POAG than nonmyopes (unadjusted prevalence of 8.1% and 3.7%, respectively), and this was true across all age groups. After adjustments for age, diabetes, gender, IOP, and family history, myopes were still twice as likely to have POAG compared with nonmyopes. When axial length was taken as a continuous variable, each millimeter increase in axial length was associated with a 26% rise in the prevalence of POAG independent of myopic refractive error. The prevalence of POAG increased exponentially in eyes with an axial length greater than 25 mm. It rose by 15% with each diopter decrease in corneal power, and this increase remained significant after adjustments for age, gender, IOP, diabetes, family history, nuclear opacification, and myopic refractive error or axial length.

Axial Length May Be an Important Factor in the Risk for POAG

LALES is the first large population-based study to show that myopia is a risk factor for POAG among Latinos. Study participants with -1.00 D or more of myopia had an 86% greater risk of developing the disease than nonmyopic participants. The association of a higher risk of having POAG with increasing myopic refractive error has also been noted in other population-based studies.[22-25] The investigators felt that LALES provides data indicating that axial length is an important factor in the higher prevalence of POAG in myopes versus nonmyopes. LALES is also the first large population-based study to show a significant association between corneal power and POAG. Decreasing corneal power was associated with a linearly increasing prevalence of POAG. LALES confirms the association of myopia and glaucoma in the Latino population, and it demonstrates the dose-dependent association of axial length and corneal power to POAG. The researchers stated that these easily measured parameters should be considered when assessing a person who is at risk of developing POAG.

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Section Editor James C. Tsai, MD, is the chairman and Robert R. Young professor of ophthalmology and visual science at Yale University School of Medicine in New Haven, Connecticut. He acknowledged no financial interest in the products or companies mentioned herein. Dr. Tsai may be reached at (203) 785-7233; james.tsai@yale.edu.

Charles A. Cole, MD, is a clinical assistant professor at Weill Cornell Medical College in New York. He is a paid speaker for Allergan, Inc. Dr. Cole may be reached at (212) 753-6464; eyesurgeonpc@gmail.com.

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