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Optic Nerve Head Changes after Short-Term Intraocular Pressure Elevation in Acute Primary Angle-Closure Suspects

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Purpose: To investigate changes in the optic nerve head morphology after acute intraocular pressure (IOP) elevation during a dark room prone provocative test (DRPPT).

Design: Prospective cohort study.

Participants: Acute primary angle-closure (APAC) suspects underwent DRPPT.

Methods: Study participants stayed in a dark room for 2 hours with the forehead placed on a desk. At baseline and within 5 minutes after DRPPT, tonometry and enhanced depth imaging by spectral-domain optical coherence tomography (SD OCT) were performed.

Main Outcome Measures: Changes in 3-dimensional optic nerve head topography.

Results: The study included 114 eyes of 65 participants with a mean age of 58.3±8.7 years and a mean IOP elevation of 10.1±10.9 mmHg during DRPPT. When all eyes were included, the mean value of most optic disc parameters did not change significantly, except for a decrease in the temporal minimal rim width ($P = 0.005$). By including only eyes with an IOP increase greater than 15 mmHg, the mean value of cup width ($P = 0.001$) and cup depth ($P = 0.002$) increased, whereas the lamina cribrosa (LC) thickness ($P = 0.035$), temporal minimal rim width ($P = 0.001$), and nasal minimal rim width ($P < 0.001$) decreased. The LC depth and Bruch's membrane opening (BMO) did not differ between the baseline and the end of DRPPT. An IOP increase was significantly associated with widening ($P < 0.001$; $r = 0.46$) and deepening ($P < 0.001$; $r = 0.52$) of the optic cup, thinning of the LC ($P = 0.003$; $r = -0.35$), temporal minimal rim width ($P < 0.001$; $r = -0.34$), and nasal minimal rim width ($P < 0.001$; $r = -0.35$).

Conclusions: Angle-closure suspect eyes showed a widening and deepening of the optic cup, decrease in neuroretinal rim width, and thinning of the LC after a darkness-induced IOP increase of >15 mmHg. The diameter of the BMO and position of the anterior LC surface remained unchanged. This suggests that a short-term IOP increase leads to a condensation of neuroretinal rim, prelaminar tissue, and LC, without major changes in the optic disc size and position of the anterior LC surface. *Ophthalmology 2015;■:1–8 © 2015 by the American Academy of Ophthalmology.*

Intraocular pressure (IOP) is a major risk factor for glaucomatous optic neuropathy, and reducing IOP has been the only evidenced-based therapy to reduce or stop the progression of glaucomatous optic neuropathy.[1] The lamina cribrosa (LC) as the interface between the intraocular compartment with a higher pressure (IOP) and the retrobulbar compartment around the optic nerve with a lower pressure (optic nerve tissue pressure and orbital cerebrospinal fluid pressure) plays a central role in bearing the pressure-related stress and has been considered to be the primary site of glaucomatous optic nerve damage. Observation of changes in the prelaminar tissue and laminar tissue in response to an acute elevation in IOP may give further hints to understand the physiology of the optic nerve head in general and the pathophysiology of glaucomatous optic neuropathy.

Previous studies examined changes in the topography of the optic nerve head resulting from acute IOP elevations. These investigations, applying techniques such as x-ray photography, laser Doppler velocimetry, and confocal scanning laser tomography, revealed that the optic disc surface changed in response to an IOP increase.[2–9] Most of these investigations were performed on enucleated human globes or on animals, with few studies including patients. Most of the techniques applied did not allow assessment of the deep structures of the optic nerve head, such as the LC, which has been shown to play an important role in some ex vivo models, animal models, and finite element modeling.[2,7,10] With the clinical introduction of spectral-domain optical coherence tomography (SD OCT) with the enhanced depth technique, the deep optic nerve head structure has become assessable by a direct and noninvasive observation.[11–17] Agoumi et al[17] studied the changes in the optic nerve head induced by an acute IOP increase of approximately 12 mmHg in patients with open-angle glaucoma and young normal controls. The IOP was elevated by an ophthalmodynamometer for several minutes. The authors found a compression of the prelaminar tissue

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without displacement of the LC. This model has disadvantages, however, such as a potential deformation of the sclera by the indentation caused by the ophthalmodynamometer, the nonphysiologically rapid increase in IOP, and the short duration of the IOP elevation. Therefore, we conducted this study to examine potential changes in the superficial and deep structure of the optic nerve head in nonglaucomatous acute primary angle-closure (APAC) suspects under almost physiologic conditions by provoking an IOP increase with a dark room test.

Methods

This prospective, comparative study included individuals who routinely underwent a dark room prone provocative test (DRPPT) to substantiate or reject the diagnosis of APAC. The study was approved by the Ethical Review Committee of Beijing Tongren Hospital and adhered to the provisions of the Declaration of Helsinki for research involving human subjects. Written informed consent was obtained from all participants involved in the study. Exclusion criteria were age <18 years, any optic nerve disease including glaucomatous optic neuropathy, any eye disease that might affect the quality of fundus images, and difficulties in fixation.

Dark Room Prone Provocative Test and Other Examinations

The DRPPT was routinely performed in the Beijing Tongren Hospital for APAC suspects.[18] Five minutes before the DRPPT started, the individuals underwent an ophthalmological examination including noncontact tonometry (Topcon CT-60; Topcon Ltd, Tokyo, Japan) and SD OCT (Spectralis; Heidelberg Engineering GmbH, Heidelberg, Germany) with the enhanced depth imaging mode. The pupils were not dilated. The matrix scanning mode of $15^\circ \times 10^\circ$ for imaging of the optic nerve head was applied, and 13 horizontal B-scans, centered on the optic disc, were obtained. Each B-scan consisted of a mean of 25 OCT frames. In addition, a 360-degree peripapillary circle scan with a diameter of 3.4 mm was carried out, centered on the disc.

After the baseline examination, the study participants were asked to sit on a chair in a dark room and rest the forehead on a pillow placed on a desk for 2 hours. The participants wore a plastic eye patch with space between the patch and the eye and were asked to keep their eyes open for 2 hours. Within 5 minutes after the end of the DRPPT, the OCT examination and tonometry were repeated. The IOP was also measured 1 hour after starting the DRPPT. All tonometric measurements were performed 3 times, and the mean value of the 3 measurements was taken for further statistical analysis.

On the day after the DRPPT, when the IOP had returned to normal values, ocular biometry was performed using optical low-coherence reflectometry (Lensstar 900 Optical Biometer; Haag-Streit, Koeniz, Switzerland). We measured the anterior corneal curvature, central corneal thickness, anterior chamber depth, lens thickness, and axial length.

Optic Nerve Head Measurements

The OCT images were exported after the examination and measured manually by 1 clinician (R.J.). Within the matrix scans, the image of the central horizontal optic nerve head line scan was chosen to be analyzed. With the use of Heidelberg Eye Explorer software (version 1.6.4.0; Heidelberg Engineering, Heidelberg, Germany), we measured Bruch's membrane opening (BMO) diameter, defined as the distance between the 2 opposite terminations of Bruch's membrane; cup width, defined as the distance between the cup borders along the BMO line; cup depth, defined as the vertical distance between the BMO line and the prelaminar tissue surface, measured at the midpoint of the cup width; minimal rim width, defined as the minimum distance between BMO and the inner limiting membrane[19]; LC depth, defined as the vertical distance between the BMO line the anterior laminar surface, measured at the midpoint of the BMO line; and LC thickness, defined as the central vertical distance between the anterior border and the posterior border of the LC, measured at the midpoint of the BMO line (Fig 1). If the structures of any parameter were not sufficiently clear to be delineated, we adjusted the brightness and contrast function of the device to increase the contrast between delineating borders.

Statistics

Statistical analysis was performed using a commercially available statistical software package (SPSS for Windows, version 21.0; IBM-SPSS, Chicago, IL). All measurements were described as mean ± deviation. Measurements obtained before and after the DRPPT were compared using the paired Student *t* test or Wilcoxon signed-rank test. Associations between changes in IOP and changes optic disc morphologic parameters were examined using Spearman rank correlation analysis. Finally, a multiple regression analysis was performed. All *P* values were based on 2-sided tests and considered statistically significant if less than 0.05.

Results

The study included 114 eyes of 65 individuals (57 women, 88%) with a mean age of 58.6±8.5 years (range, 39−85 years), a mean axial length of 22.8±1.0 mm, an anterior chamber depth of 2.1±0.3 mm, and a mean IOP of 16.0±3.9 mmHg at baseline. Intraocular pressure increased by a mean of 10.1±10.9 mmHg (range, 2−47 mmHg).

Including all study participants in the statistical analysis showed a decrease in temporal minimal rim width ($P = 0.005$), whereas all other parameters (i.e., BMO, cup width, cup depth, nasal minimal rim width, LC depth, and LC thickness) did not differ between their baseline measurements and the measurements obtained at the end of the DRPPT (Table 1).

By including only participants with an IOP increase greater than 15 mmHg, the mean value of cup width ($P = 0.001$) and cup depth ($P = 0.002$) increased, and LC thickness ($P = 0.035$), temporal minimal rim width ($P = 0.001$), and nasal minimal rim width ($P < 0.001$) decreased. The BMO and LC depth did not differ between the baseline of the study and the end of the DRPPT ($P = 1.00$ and $P = 0.41$, respectively) (Table 2). In keeping with this observation, 14 of 15 eyes (93%) tended to show a small or large increase in cup width, whereas 1 eye tended to be stable (Fig 2). Likewise, 13 of 15 eyes (87%) had an increase in cup depth, 16 of 19 eyes (84%) had a decrease in the temporal minimal rim width, 18 of 19 eyes (95%) had a decrease in the nasal minimal rim width, and 7 of 10 eyes (70%) had a thinning of the LC.

By including all study participants in the statistical analysis and performing a correlation analysis, a higher IOP increase was significantly associated with a greater increase in cup width ($P < 0.001$) and cup depth ($P < 0.001$) and more marked thinning of the LC ($P = 0.003$), temporal minimal rim width ($P < 0.001$),