Comparative Human Aqueous Dynamics Study between Black and White Subjects with Glaucoma

Laura Beltran-Agullo, Pouya Alaghband, Safina Rashid, Josee Gosselin, Adanna Obi, Rahat Husain, and Kin Sheng Lim

Purpose. To compare the baseline aqueous humor dynamics in white Caucasians and patients of African origin with previously untreated primary open-angle glaucoma (POAG) or ocular hypertension (OHT).

Methods. Ninety-one participants were enrolled in this prospective, observational controlled study: 34 black subjects with POAG or OHT, 32 white Caucasian participants with POAG or OHT, and 12 black and 13 white healthy volunteers as the controls. All aqueous humor parameters were taken between 9 AM and 12 noon on the same day. Intraocular pressure (IOP) was measured by pneumatonometer; morning aqueous humor flow rate was measured by fluorophotometry and trabecular outflow facility by electronic Schiøtz tonography. Uveoscleral outflow was calculated by using Goldmann's equation with assumed episcleral venous pressure of 8, 9, 10, and 11 mm Hg. Differences among groups were analyzed with parametric and nonparametric tests and the relationship between aqueous dynamics parameters were evaluated with linear regression analyses.

Results. The POAG/OHT groups had similar IOP (white, 24.6 ± 3.0 mm Hg; black, 24.3 ± 4.0 mm Hg; comparison by Holm's sequential Bonferroni method (HBonf): $P_{HBonf} = 0.51$), outflow facility (white, 0.13 ± 0.09 μL/min/mm Hg; black, 0.13 ± 0.07 μL/min/mm Hg; $P_{HBonf} = 0.87$), aqueous flow (white, 2.36 ± 0.63 μL/min; black, 2.35 ± 0.53 μL/min; $P_{HBonf} = 0.95$), and uveoscleral outflow (white, 0.42 ± 1.59 μL/min; black, 0.58 ± 1.17 μL/min; $P_{HBonf} = 1.78$). POAG/OHT groups had significantly higher IOP and lower outflow facility than their healthy counterparts ($P < 0.01$). Black participants had significant thinner corneas (540 ± 37 μm vs. 564 ± 36 μm) than those of white participants ($P = 0.002$).

Conclusions. The aqueous humor dynamics of black African and white Caucasian patients with POAG or OHT have no significant differences. However, the significantly thinner corneas of the black patients may be masking potential differences in outflow facility and IOP measurements between the racial groups. (*Invest Ophthalmol Vis Sci.* 2011;52:9425–9430) DOI: 10.1167/iovs.10-7130

From the Department of Ophthalmology, St. Thomas' Hospital, London, United Kingdom.

Presented at the annual meeting of the Association for Research in Vision and Ophthalmology, Fort Lauderdale, Florida, May 2009.

Supported by National Institute of Health Research UK, Guy's & St. Thomas' Charity, and EyeHope Charity.

Submitted for publication December 22, 2010; revised May 8, July 3, and September 6, 2011; accepted September 23, 2011.

Disclosure: **L. Beltran-Agullo**, None; **P. Alaghband**, None; **S. Rashid**, None; **J. Gosselin**, None; **A. Obi**, None; **R. Husain**, None; **K.S. Lim**, None

Corresponding author: Kin Sheng Lim, Department of Ophthalmology, St. Thomas' Hospital, Westminster Bridge Road, London SE1 7EH, UK; shenglim@gmail.com.

Primary open-angle glaucoma (POAG) is four to eight times more prevalent in black Africans and African-Caribbeans than in whites.[1–4] Several studies have demonstrated differences in structural and biometric parameters and risk factors for glaucoma development among ethnic groups. Black subjects have thinner corneas[5–8] and larger optic discs[9–11] and may have thinner retinal nerve fiber layers (RNFLs).[12] The literature however, provides few insights into the potential racial differences in aqueous humor dynamics. Some studies on intraocular pressure (IOP) have reported higher IOP levels in blacks than in whites,[3,13,14] whereas others have found no differences[15] or even lower IOPs in black subjects.[16] Since the aqueous dynamics in this population have not been studied, we wanted to compare the baseline aqueous humor dynamics parameters in patients of African origin and white Caucasians with previously untreated POAG or ocular hypertension (OHT).

Methods

Ethics approval for this study was obtained from the St. Thomas's local research ethics committee. This research followed the tenets of the Declaration of Helsinki. Consecutive new patients referred to the glaucoma clinic were invited to participate. A patient information leaflet was provided at the initial contact, and signed consent was obtained before the measurements and treatment.

Participants enrolled in this prospective, observational, controlled study were divided into four groups: (1) white subjects with POAG or OHT, (2) black subjects with POAG or OHT, and (3) white healthy ocular normotensive (ONT) volunteers and (4) black healthy ONT volunteers as control groups.

Inclusion and Exclusion Criteria

Inclusion criteria were newly diagnosed, previously untreated adult POAG patients or patients with OHT that did or did not require treatment, both with IOP > 21 mm Hg at the screening visit. Glaucoma was diagnosed based on abnormal visual field testing and corresponding disc changes once seen by a fellowship-trained glaucoma specialist. Healthy volunteers had no ocular problems (other than refractive error) and IOP at screening <21 mm Hg. Exclusion criteria were secondary glaucomas including pigment dispersion syndrome and pseudoexfoliation, normotensive glaucoma, primary angle closure, history of uveitis, ocular trauma, intraocular or keratorefractive surgery, use of systemic medication that may affect aqueous humor production such as β-blockers, history of allergy or hypersensibility to fluorescein, and any abnormalities preventing reliable IOP or fluorophotometric readings.

Measurements

All patients underwent a clinical ophthalmic examination including visual acuity, slit lamp examination, gonioscopy, anterior chamber depth, and axial length (IOL Master; Carl Zeiss Meditec Inc., Dublin, CA), central corneal thickness (CCT; Pachmate DGH 55, DGH Technology, Inc., Exton, PA), visual fields (Humphrey automated white-on-white, 24-2 SITA-standard; Carl Zeiss Meditec), and dilated funduscopy.

The night before (10 PM) the fluorophotometric scans, participants self-administered from 3 to 6 drops of fluorescein sodium 2% (Minims; Bausch & Lomb, Kingston-upon-Thames, UK) topically into both eyes at 5-minute intervals depending on their ages (age, ≤25 years, 5 to 6 drops; age 26–35 years, 4 drops; >35 years of age, 3 drops).[17] Fluorophotometry was performed in both eyes with a scanning ocular fluorophotometer from 9 AM to 12 noon (FM-2, Fluorotron Master ocular fluorophotometer; OcuMetrics, Mountain View, CA). The aqueous flow rate was determined using dedicated software provided with the fluorophotometer (Appendix). Duplicate or triplicate scans were collected and repeated at 1-hour intervals for four measurements to determine the aqueous flow rate (F_t). Following each set of scans, IOP was measured using pneumotonometry (Model 30 Classic; Reichert Ophthalmic Instruments, Depew, NY); IOP was recorded as the arithmetic mean of a total of 12 measurements per eye: 3 measurements every hour alternating between eyes. Patients with IOP >21 mm Hg on the screening day may have had IOP of 21 mm Hg or less thereafter.

Tonographic outflow facility (C) was performed with an electronic Schiøtz tonographer (model 720; Berkeley Bioengineering, Inc., San Leandro, CA) at 10 AM. The facility of outflow was measured from the rate of decay of IOP in the supine position during application of a recording Schiøtz tonometer over a period of 4 minutes with a standard 5.5-g weight.[18] The R values of the curve at every 30-second time point were manually entered into the McLaren tonography computer program.[19] The program fits a second-degree polynomial by least-squares to the nine data points and determines by extrapolation the best-fit values for time 0 and time 4 minutes.

Uveoscleral outflow was calculated using Goldmann's equation[20] with an assumed episcleral venous pressure of 8, 9, 10, or 11 mm Hg.[19,21] F_t is the rate of aqueous humor formation, C is the tonographic facility of outflow, IOP is the intraocular pressure, P_v is the episcleral venous pressure, and F_u is the uveoscleral outflow.

$$F_t = C\,(\mathrm{IOP} - P_v) + F_u$$

$$F_u = F_t - C\,(\mathrm{IOP} - P_v)$$

Only one randomly (Excel random number generator; Microsoft, Redmond, WA) chosen eye per participant was included in the data analysis, when both eyes fulfilled the inclusion criteria.

Data Collection and Outcome Measures

Data including age, sex, race, IOP, tonographic outflow facility, aqueous flow rate, CCT, axial length, anterior chamber depth, cup-to-disc ratio, mean deviation in visual field testing and amount of fluorescein drops and time of instillation were recorded. Outcomes measures were outflow facility, IOP, aqueous flow rate, and uveoscleral outflow.

Data Analysis

Histograms and a Shapiro-Wilk test were performed to test for normality of distribution of data. A Shapiro-Wilk $W > 0.05$ was evidence of normal distribution. Student's t-test and one-way analysis of variance (ANOVA) were used to compare continuous variables among groups. When data did not follow normality, nonparametric methods of analysis (Mann-Whitney U and Kruskal-Wallis tests) were used. Post hoc comparisons among groups were made when appropriate, by Holm's sequential Bonferroni method (HBonf). The 95% confidence intervals (CI) for the mean and median difference between pairs for each outcome measure were calculated. The median difference 95% CIs were estimated using Hodges-Lehman methodology. Linear regression analyses were used to determine the correlation of one parameter versus another parameter of aqueous humor dynamics and the correlation of age versus each parameter. Fisher's exact test was used to compare the number of patients with POAG and OHT in each racial group. $P < 0.05$ was considered statistically significant (all analyses, SPSS 16.0; SPSS, Chicago, IL).

Results

One hundred and one patients with OHT/POAG and 32 healthy volunteers were recruited into the study. Only 66 affected subjects and 25 controls were included in the data analysis. Poor-quality Schiøtz tonography tracings ($n = 14$), with excess noise or extreme excursions, or poor fluorophotometric scans ($n = 27$), with extremely high or low baseline corneal fluorescein concentration, were identified in 41 participants and were therefore excluded from the analysis. Another participant was excluded for not having slept the night before the measurements were taken.[22]

In the black POAG/OHT group, 13 (38.2%) subjects had OHT and 21 (61.8%) had POAG, compared with 18 (56.2%) subjects with OHT and 14 (43.8%) subjects with POAG in the white affected group ($P = 0.21$).

The baseline characteristics from each group are shown in Table 1. The mean age of the study population was 58.7 ± 13.0 years. Age did not correlate with the outcome measures in any of the affected groups or in all participants combined (IOP, $P = 0.58$; C, $P = 0.08$; F_t, $P = 0.56$; and Fu_{10}, $P = 0.06$).

Subjects with POAG/OHT exhibited significantly higher IOP than their control counterparts ($P < 0.001$), but the black and white affected groups had comparable IOP ($P = 0.51$; 95% CI, −1.0 to 2.0). Black POAG/OHT subjects had significant thinner corneas than did the white POAG/OHT group ($P_{HBonf} = 0.009$; 95% CI, 8–43) but no other difference regarding CCT was observed between the rest of the groups. The mean CCT of all black participants was 540 ± 37 μm compared with 564 ± 36 μm in all white participants together (Table 2; $P = 0.002$; 95% CI, 8–40). CCT did not correlate significantly with any of the aqueous dynamics parameters.

Both the black and white groups with POAG/OHT had significantly lower outflow facility than their matched control group (black, $P_{HBonf} < 0.001$; 95% CI, −0.11 to −0.02; white, $P_{HBonf} < 0.001$; 95% CI, −0,17 to −0.03), but no differences were found between the affected groups ($P_{HBonf} = 0.51$; 95% CI, −0.03 to 0.04). A weakly significant inverse relationship was observed between outflow facility and IOP, with a reduction of 0.008 ± 0.002 μL/min/mm Hg ($R^2 = 0.16$; $P < 0.001$; Fig. 1). This relationship remained after adjustment for age ($R^2 = 0.21$; $P < 0.001$). Facility of outflow appeared not to be linearly correlated to the stage of glaucoma damage measured by mean deviation (MD) in visual field testing ($R^2 = 0.002$; $P = 0.72$) and cup-to-disc ratio ($R^2 = 0.007$; $P = 0.51$).

The mean aqueous flow rates for each group ranged from 1.81 to 2.36 μL/min. The black control subjects had significantly lower aqueous production than did the black affected subjects ($P_{HBonf} = 0.01$; 95% CI, 0.17–0.90). The aqueous production did not differ significantly between the black and white affected groups ($P_{HBonf} = 0.95$; 95% CI, −0.29 to 0.30). Aqueous flow was independent of IOP ($R^2 = 0.03$; $P = 0.07$).

The uveoscleral outflow was not different among groups, regardless of the assumed episcleral venous pressure. The 95% CI for the difference between the affected group medians for Fu_{10} ($P_v = 10$ mm Hg) was −0.74 to 0.58 μL/min. Affected patients, independent of their racial origin ($n = 66$), had a mean Fu_{10} of 0.75 ± 1.36 μL/min (median, 0.50; range, −4.04 to 2.68) compared with 0.47 ± 0.95 μL/min (median, 0.52; range, −1.51 to 2.19; $P = 0.51$) in all control subjects ($n = 25$). Contrary to outflow facility, the relationship between uveoscleral outflow (Fu_{10}) and IOP ($R^2 = 0.007$; $P = 0.44$) did not reach significance. Uveoscleral outflow and stage of glaucomatous damage were not related. Similar results were obtained with assumed episcleral venous pressures of 8, 9, and 11 mm Hg (Table 1).

Table 1. Comparison of Baseline Aqueous Dynamics Parameters in Patients with POAG or OHT and Healthy Volunteers

	POAG/OHT						Controls						
	Black (n = 34)			White (n = 32)			Black (n = 12)			White (n = 13)			
Parameters	Median (Mean)	IQR (SD)	Range (Min, Max)	Median (Mean)	IQR (SD)	Range (Min, Max)	Median (Mean)	IQR (SD)	Range (Min, Max)	Median (Mean)	IQR (SD)	Range (Min, Max)	P
IOP, mm Hg	23.51 (24.13)	14.01 (41.01)	20.10 (−19.0, 39.0)	25.10 (24.16)	14.10 (13.20)	11.20 (−20.0, 31.0)	19.10 (18.11)	14.18 (12.27)	28.20 (−14.0, 22.0)	17.10 (17.10)	23.10 (12.18)	10.10 (−11.0, 21.0)	<0.001*
F_t, μL/min	2.36 (2.35)	0.94 (0.53)	2.37 (1.32, 3.69)	2.26 (2.36)	0.78 (0.63)	2.67 (1.02, 3.69)	1.65 (1.81)	0.55 (0.52)	1.94 (1, 163.10)	2.21 (2.19)	0.44 (0.47)	1.82 (1.11, 2.93)	0.02†
C, μL/min/mm Hg	0.12 (0.13)	0.08 (0.07)	0.36 (0.03, 0.39)	0.11 (0.13)	0.13 (0.09)	0.41 (0.03, 0.44)	0.18 (0.18)	0.08 (0.07)	0.28 (0.07, 0.35)	0.21 (0.23)	0.19 (0.10)	0.33 (0.08, 0.41)	0.003*
Fu_8, μL/min	0.46 (0.32)	1.66 (1.29)	6.17 (−4.00, 2.17)	0.54 (0.15)	2.61 (1.73)	7.48 (−4.92, 2.56)	0.13 (−0.03)	1.20 (0.82)	2.88 (−1.92, 0.96)	0.45 (0.12)	1.96 (1.26)	4.26 (−2.33, 1.93)	0.67*
Fu_9, μL/min	0.61 (0.45)	1.53 (1.23)	5.92 (−3.72, 2.20)	0.63 (0.29)	2.43 (1.64)	7.10 (−4.48, 2.62)	0.31 (0.15)	1.22 (0.79)	2.77 (−1.57, 1.20)	0.60 (0.35)	1.82 (1.18)	3.98 (−1.92, 2.06)	0.76*
Fu_{10}, μL/min	0.76 (0.58)	1.46 (1.17)	5.69 (−3.44, 2.25)	0.75 (0.42)	2.24 (1.59)	6.72 (−4.04, 2.68)	0.45 (0.34)	1.24 (0.76)	2.66 (−1.22, 1.44)	0.75 (0.58)	1.68 (1.11)	3.70 (−1.51, 2.19)	0.77*
Fu_{11}, μL/min	0.89 (0.71)	1.41 (1.12)	5.46 (−3.16, 2.30)	0.87 (0.56)	2.07 (1.48)	6.34 (−3.60, 2.74)	0.57 (0.53)	1.29 (0.74)	2.55 (−0.87, 1.68)	0.90 (0.82)	1.55 (1.02)	3.47 (−1.10, 2.37)	0.81*

IQR, interquartile range; Fu_{8-11}, uveoscleral outflow with an assumed episcleral venous pressure of 8, 9, 10, and 11 mm Hg.

* Kruskal-Wallis test.

† One-way ANOVA.

TABLE 2. Descriptive Parameters of Black and White Patients with POAG or OHT and Healthy Volunteers

	POAG/OHT						Controls					
	Black (n = 34)			White (n = 32)			Black (n = 12)			White (n = 13)			
Parameters	Median (Mean)	IQR (SD)	Range (Min, Max)	Median (Mean)	IQR (SD)	Range (Min, Max)	Median (Mean)	IQR (SD)	Range (Min, Max)	Median (Mean)	IQR (SD)	Range (Min , Max)	P
Age, y	60.0 (58.2)	23.6 (12.9)	48.2 (30.8, 79.1)	61.6 (61.8)	22.2 (13.2)	47.8 (40.3, 88.1)	49.6 (51.1)	8.1 (10.6)	36.7 (38.1, 74.8)	61.5 (59.8)	16.4 (13.2)	45.4 (33.8, 79.2)	0.11*
ACD, mm	3.14 (3.19)	0.59 (0.38)	1.40 (2.59, 3.99)	3.23 (3.30)	0.46 (0.30)	0.99 (2.89, 3.88)	3.25 (3.23)	0.78 (0.37)	1.02 (2.78, 3.80)	3.41 (3.32)	0.42 (0.32)	1.17 (2.55, 3.72)	0.48†
AXL, mm	23.52 (23.67)	0.99 (0.83)	3.72 (22.12, 25.84)	23.56 (24.00)	1.73 (1.33)	4.72 (22.48, 27.20)	23.27 (23.45)	1.37 (0.77)	2.09 (22.34, 24.43)	24.03 (24.00)	1.90 (1.04)	3.46 (22.29, 25.75)	0.68†
CCT, μm	548 (539)	55 (37)	168 (438, 606)	569 (565)	43 (32)	121 (513, 634)	540 (543)	48 (37)	145 (479, 624)	572 (563)	72 (48)	158 (483, 641)	0.04*

IQR, interquartile range; ACD, anterior chamber depth; AXL, axial length.
* Significant, according to one-way ANOVA.
† Kruskal-Wallis test.

Table 3 summarizes the aqueous dynamics parameters of the POAG and OHT subjects, which showed nonsignificant differences.

Despite the prestudy sample size calculation based on the results of another study,[19] post hoc analysis of our data showed that our study would be able to detect a difference of 10.2% in IOP, 9.7% in aqueous flow, and only 38% in outflow facility, with a power of 80% and α (two-sided) = 0.05, if those differences existed.

DISCUSSION

Previous aqueous dynamics studies have included black participants[23] but this is the first study that specifically compares the aqueous dynamics between Africans/African Caribbeans and white Caucasians. Despite the anatomic differences reported between black and white populations, this study found no significant differences in the aqueous dynamics among patients with POAG/OHT of both racial groups.

Despite the number of patients with POAG being higher in the black affected group than in the white affected group, this disproportion between both racial groups would not have interfered in our analysis, since OHT and POAG patients have comparable aqueous dynamics.[24]

Contrary to some studies,[3,13,14] we found black and white participants with POAG/OHT had similar IOP, but this is likely to be due to the bias in our sampling as patients with IOP higher than 35 mm Hg at the screening visit, according to our ethics committee recommendations, would have been excluded from the study, to avoid delaying the instauration of the medical treatment. Also, since IOP measured with the pneumatonometer[25,26] increases approximately 0.40 mm Hg for every 10-μm increase in CCT, and the black participants had thinner corneas than the white participants had, the IOP could have been slightly underestimated.

To measure the trabecular outflow facility, we used the classic electronic Schiøtz tonometer because compared to pneumotomography or fluorophotometry techniques, the Schiøtz tonometer gives an accurate assessment of outflow facility with less variability over time.[19] Rejection rate of 14 of 101 subjects due to poor-quality tonography is only slightly higher than that found in a previous study by the same researchers.[19]

Since Grant[18] and Becker[27] reported a reduction in outflow facility in patients with glaucoma many years ago, other groups have come to the same conclusion.[23,24] We found a similar reduction in the outflow facility in both affected racial groups without a significant increase in the aqueous production. The measurements performed with the Schiøtz tonometer, are affected by ocular rigidity.[28,29] Indentation tonography makes no compensation for individual variations in ocular rigidity. The stiffer the eye, the greater the force needed to indent the cornea and displace the aqueous. Corneal hysteresis (CH) and corneal resistance factor (CRF) are dynamic measurements of the viscoelastic properties of the cornea that have been found to be lower in subjects of black African descent than in whites.[16,30] Several studies have shown an increase in CH and CRF with increasing CCT.[16,31,32] The higher the CH, the longer the cornea takes to return to its original shape, implying greater stiffness. Therefore, higher outflow facility measurements could have been obtained in the black participants on the basis of decreased ocular rigidity rather than the true equality found among the groups. On the other hand, Pallikaris et al.[33] measured in vivo the rigidity coefficient in 79 living human eyes and found no statistically significant correlation between ocular-rigidity coefficient and CCT. They reported that despite the low power to detect that correlation, CCT may have an effect on the corneal biomechanics, but may have less impact in ocular rigidity which involves the whole eye and not only the cornea.

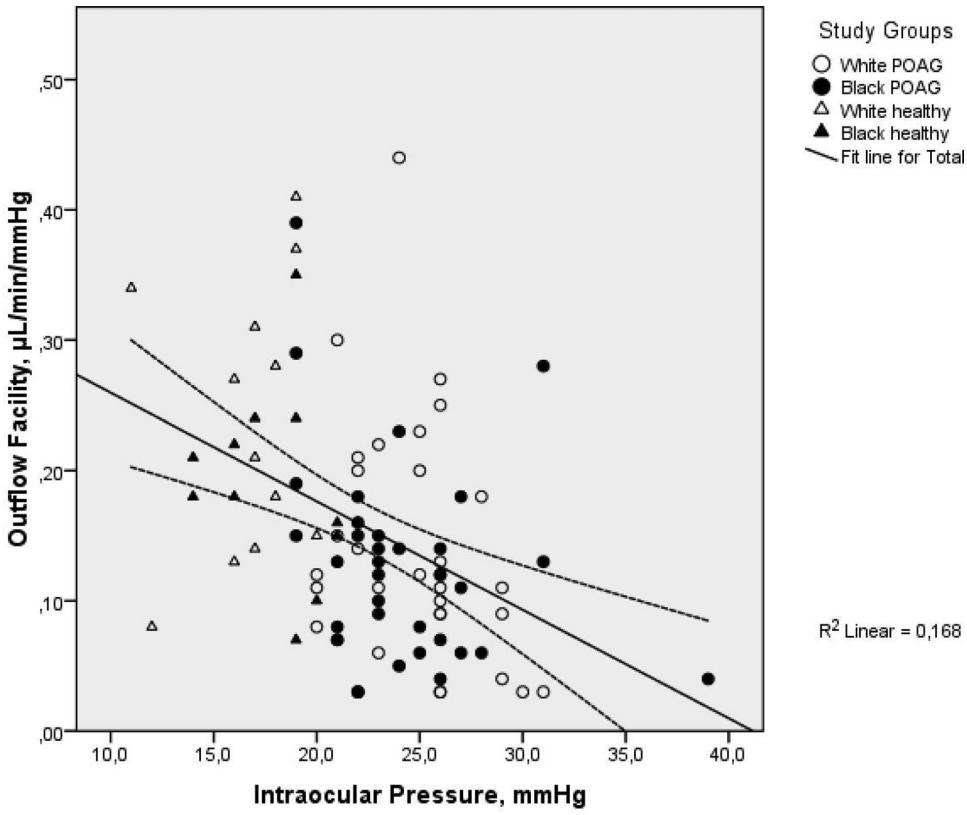

FIGURE 1. Scatterplot and bivariate regression analysis between the IOP and tonographic outflow facility (*C*). The regression line is $C = -0.008 \times \text{IOP} + 0.343$, $P < 0.001$, and $R^2 = 0.16$ (95% confidence bands are shown).

Larsson et al.[34] and Toris et al.[23] showed that the rate of aqueous production was not different in patients with glaucoma or ocular hypertension compared with healthy age-matched controls. This study confirmed this finding, and we also found no racial difference in the aqueous production rates.

The uveoscleral outflow was not significantly different between the white and black groups or the affected subjects and healthy volunteers, although it has been found to be reduced in beagle dogs with advanced glaucoma[35] and elevated in monkeys with laser-induced glaucoma.[36] In humans with POAG, Toris et al.[23] reported that uveoscleral outflow could be reduced in early stages of glaucoma, together with reduced trabecular outflow, but increases as the disease progresses to prevent the IOP from increasing further, but we did not find any differences between patients with OHT and POAG compared with normal subjects.

In summary, African/African-Caribbean patients with POAG or OHT have baseline aqueous humor dynamics similar to those of white Caucasians patients. Subjects with African ancestry have thinner corneas that may have masked some of the potential aqueous dynamics differences between the studied racial groups.

APPENDIX

The Yablonski Protocol of estimating aqueous humor flow rate was used.[37] Aqueous humor flow is the volume of aqueous humor produced by the ciliary body per unit of time.

$$F_t = K_o \cdot V_a$$

where, F_t is the aqueous humor flow (μL/min), V_a is the volume of the anterior chamber (μL), and K_o is the loss coefficient due to

TABLE 3. Comparison of Baseline Aqueous Dynamics Parameters between Patients with POAG Versus Those with OHT

	POAG (n = 35)			OHT (n = 31)			
	Median (Mean)	**IQR (SD)**	**Range (Min, Max)**	**Median (Mean)**	**IQR (SD)**	**Range (Min, Max)**	***P****
Age, y	62.7 (62.6)	19.7 (12.8)	55.0 (33.1, 88.1)	54.9 (56.9)	21.9 (12.9)	52.6 (30.8, 83.4)	0.07†
IOP, mm Hg	23.0 (23.7)	4.0 (2.8)	12 (19.0, 31.0)	26.0 (25.3)	6 (4.1)	20 (19,39.0)	0.07
F_t, μL/min	2.38 (2.40)	0.89 (0.58)	2.67 (1.02, 3.69)	2.18 (2.30)	0.81 (0.58)	2.49 (1.20, 3.69)	0.46†
C,μL/min/mmHg	0.12 (0.13)	0.07 (0.07)	0.41 (0.03, 0.44)	0.11 (0.13)	0.14 (0.09)	0.36 (0.03, 0.39)	0.98
Fu_8, μL/min	0.55 (0.38)	1.30 (1.39)	7.48 (−4.92, 2.56)	0.32 (0.07)	2.71 (1.63)	6.54 (−4.00, 2.54)	0.46
Fu_9, μL/min	0.67 (0.51)	1.28 (1.32)	7.10 (−4.48, 2.62)	0.43 (0.21)	2.45 (1.56)	6.30 (−3.72, 2.58)	0.46
Fu_{10}, μL/min	0.79 (0.64)	1.26 (1.25)	6.72 (−4.04, 2.68)	0.54 (0.35)	2.27 (1.49)	6.06 (−3.44, 2.62)	0.44
Fu_{11}, μL/min	0.92 (0.77)	1.27 (1.19)	6.34 (−3.60, 2.74)	0.89 (0.49)	2.09 (1.41)	5.82 (−3.16, 2.66)	0.40
CCT, μm	549 (547)	51 (39)	196 (438, 634)	554 (556)	50 (33)	129 (492, 621)	0.33†
MD, dB	−3.99 (−5.62)	5.22 (5.70)	30.52 (−29.97, 0.55)	−1.30 (−1.46)	2.24 (2.56)	15.53 (−7.58, 7.95)	<0.001

IQR, interquartile range; Fu_{8-11}, uveoscleral outflow with an assumed episcleral venous pressure of 8–11 mmHg.

* Mann-Whitney U test.

† Student *t*-tests.

bulk flow and diffusion from the anterior chamber (minutes^{-1}). K_o can be thought of as the fraction of anterior chamber volume cleared of fluorescein every minute, due to aqueous flow.

To calculate the aqueous flow, the program uses default variables that can be changed by the operator as necessary:

Corneal volume default value, 70 μL

Anterior chamber volume default value, 174 μL

CCT of each patient, in micrometers (We introduced each patient's corneal thickness instead of using the 500-μm default value to correct for the depth of the focal diamond. However, the corneal volume does not change if a different corneal central thickness is entered).

Once the relationship between cornea and anterior chamber concentrations of fluorescein becomes steady, the program can determine K_o and aqueous flow (F_t), as described in detail elsewhere.[37]

Acknowledgments

The authors thank Jay W. McLaren (Mayo Clinic, Rochester, MN) for allowing them to use his computerized tonography program and Salma Ayis (Lecturer in Medical Statistics, King's College London) for her advice.

References

1. Tielsch JM, Sommer A, Katz J, et al. Racial variations in the prevalence of primary open-angle glaucoma. The Baltimore Eye Survey. *JAMA.* 1991;266(3):369–374.
2. Leske MC, Connell AM, Schachat AP, Hyman L. The Barbados Eye Study. Prevalence of open angle glaucoma. *Arch Ophthalmol.* 1994;112(6):821–829.
3. Friedman DS, Jampel HD, Muñoz B, West SK. The prevalence of open-angle glaucoma among blacks and whites 73 years and older: the Salisbury Eye Evaluation Glaucoma Study. *Arch Ophthalmol.* 2006;124(11):1625–1630.
4. Mason RP, Kosoko O, Wilson MR, et al. National survey of the prevalence and risk factors of glaucoma in St. Lucia, West Indies: Part I, prevalence findings *Ophthalmology.* 1989;96(9):1363–1368.
5. Rosa FAL, Gross RL, Orengo-Nania S. Central corneal thickness of Caucasians and African Americans in glaucomatous and nonglaucomatous populations. *Arch Ophthalmol.* 2001;119(1):23–27.
6. Shimmyo M, Ross AJ, Moy A, Mostafavi R. Intraocular pressure, Goldmann applanation tension, corneal thickness, and corneal curvature in Caucasians, Asians, Hispanics, and African Americans. *Am J Ophthalmol.* 2003;136(4):603–613.
7. Brandt JD, Beiser JA, Kass MA, Gordon MO. Central corneal thickness in the Ocular Hypertension Treatment Study (OHTS). *Ophthalmology.* 2001;108(10):1779–1788.
8. Kniestedt C, Lin S, Choe J, et al. Correlation between intraocular pressure, central corneal thickness, stage of glaucoma, and demographic patient data: prospective analysis of biophysical parameters in tertiary glaucoma practice populations. *J Glaucoma.* 2006; 15(2):91–97.
9. Zangwill LM, Weinreb RN, Berry CC, et al. Racial differences in optic disc topography: baseline results from the confocal scanning laser ophthalmoscopy ancillary study to the ocular hypertension treatment study. *Arch Ophthalmol.* 2004;122(1):22–28.
10. Quigley HA, Brown AE, Morrison JD, Drance SM. The size and shape of the optic disc in normal human eyes. *Arch Ophthalmol.* 1990;108(1):51–57.
11. Varma R, Tielsch JM, Quigley HA, et al. Race-, age-, gender-, and refractive error-related differences in the normal optic disc. *Arch Ophthalmol.* 1994;112(8):1068–1076.
12. Poinoosawmy D, Fontana L, Wu JX, Fitzke FW, Hitchings RA. Variation of nerve fibre layer thickness measurements with age and ethnicity by scanning laser polarimetry. *Br J Ophthalmol.* 1997;81(5):350–354.
13. Coulehan JL, Helzlsouer KJ, Rogers KD, Brown SI. Racial differences in intraocular tension and glaucoma surgery. *Am J Epidemiol.* 1980;111(6):759–768.
14. David R, Livingston D, Luntz MH. Ocular hypertension: a comparative follow-up of black and white patients. *Br J Ophthalmol.* 1978;62(10):676–678.
15. The Advanced Glaucoma Intervention Study (AGIS): 3. Baseline characteristics of black and white patients. *Ophthalmology.* 1998; 105(7):1137–1145.
16. Broman AT, Congdon NG, Bandeen-Roche K, Quigley HA. Influence of corneal structure, corneal responsiveness, and other ocular parameters on tonometric measurement of intraocular pressure. *J Glaucoma.* 2007;16(7):581–588.
17. Brubaker RF, Schoff EO, Nau CB, et al. Effects of AGN 192024, a new ocular hypotensive agent, on aqueous dynamics. *Am J Ophthalmol.* 2001;131(1):19–24.
18. Grant WM. Clinical measurements of aqueous outflow. *Am J Ophthalmol.* 1951;34(11):1603–1605.
19. Lim KS, Nau CB, O'Byrne MM, et al. Mechanism of action of bimatoprost, latanoprost, and travoprost in healthy subjects: a crossover study. *Ophthalmology.* 2008;115(5):790–795.e4.
20. Brubaker RF. Goldmann's equation and clinical measures of aqueous dynamics. *Exp Eye Res.* 2004;78(3):633–637.
21. Brubaker RF. Measurement of uveoscleral outflow in humans. *J Glaucoma.* 2001;10(5 Suppl 1):S45–S48.
22. Reiss GR, Lee DA, Topper JE, Brubaker RF. Aqueous humor flow during sleep. *Invest Ophthalmol Vis Sci.* 1984;25(6):776–778.
23. Toris CB, Koepsell SA, Yablonski ME, Camras CB. Aqueous humor dynamics in ocular hypertensive patients. *J Glaucoma.* 2002; 11(3):253–258.
24. Martin PB, Vila PCF, Martinez TMP, Peréz DA. A fluorophotometric study on the aqueous humor dynamics in primary open angle glaucoma. *Int Ophthalmol.* 1992;16(4–5):311–314.
25. Bhan A, Browning AC, Shah S, et al. Effect of corneal thickness on intraocular pressure measurements with the pneumotonometer, Goldmann applanation tonometer, and Tono-Pen. *Invest Ophthalmol Vis Sci.* 2002;43(5):1389–1392.
26. Tonnu PA, Ho T, Newson T, et al. The influence of central corneal thickness and age on intraocular pressure measured by pneumotonometry, non-contact tonometry, the Tono-Pen XL, and Goldmann applanation tonometry. *Br J Ophthalmol.* 2005;89(7):851–854.
27. Becker B. Tonography in the diagnosis of simple (open angle) glaucoma. *Trans Am Acad Ophthalmol Otolaryngol.* 1961;65: 156–162.
28. Gloster J. Tonometry and tonography. *Int Ophthalmol Clin.* 1965; 5(4):911–1133.
29. Moses RA, Grodzki WJ. Ocular rigidity in tonography. *Doc Ophthalmol.* 1969;26:118–129.
30. Leite MT, Alencar LM, Gore C, et al. Comparison of corneal biomechanical properties between healthy blacks and whites using the Ocular Response Analyzer. *Am J Ophthalmol.* 2010;150(2): 163–168.e1.
31. Shah S, Laiquzzaman M, Cunliffe I, Mantry S. The use of the Reichert ocular response analyser to establish the relationship between ocular hysteresis, corneal resistance factor and central corneal thickness in normal eyes. *Cont Lens Anterior Eye.* 2006; 29(5):257–262.
32. Touboul D, Roberts C, Kérautret J, et al. Correlations between corneal hysteresis, intraocular pressure, and corneal central pachymetry. *J Cataract Refract Surg.* 2008;34(4):616–622.
33. Pallikaris IG, Kymionis GD, Ginis HS, et al. Ocular rigidity in living human eyes. *Invest Ophthalmol Vis Sci.* 2005;46(2):409–414.
34. Larsson LI, Rettig ES, Brubaker RF. Aqueous flow in open-angle glaucoma. *Arch Ophthalmol.* 1995;113(3):283–286.
35. Barrie KP, Gum GG, Samuelson DA, Gelatt KN. Quantitation of uveoscleral outflow in normotensive and glaucomatous Beagles by 3H-labeled dextran. *Am J Vet Res.* 1985;46(1):84–88.
36. Toris CB, Zhan GL, Wang YL, et al. Aqueous humor dynamics in monkeys with laser-induced glaucoma. *J Ocul Pharmacol Ther.* 2000;16(1):19–27.
37. Yablonski ME, Zimmerman TJ, Waltman SR, et al. A fluorophotometric study of the effect of topical timolol on aqueous humor dynamics. *Exp Eye Res.* 1978;27:135–142.