Nine-Year Changes in Intraocular Pressure

The Barbados Eye Studies

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Objective: To describe temporal changes in intraocular pressure (IOP) and associated risk factors after 9 years of follow-up in a population of African descent.

Methods: Changes in IOP were evaluated in 2298 participants without glaucoma or IOP-lowering treatment at baseline. Risk factor analyses used a multiple regression approach with mixed effects, which accounted for intereye correlation.

Results: The mean 9-year change in IOP was small, with relatively large dispersion (mean±SD, 0.4±4.0 mm Hg). Only 6.5% of persons with IOP of 21 mm Hg or less at baseline had elevated IOP greater than 21 mm Hg after 9 years. Mean IOP increases were largest in persons aged 50 to 59 years at baseline (mean±SD, 0.9±4.3 mm Hg), whereas IOP decreased in persons 70 years or older (mean±SD, −0.6±4.2 mm Hg). In multivariate analyses, IOP changes were positively associated with male sex, hypertension, diabetes history, and higher systolic and diastolic blood pressure at baseline, as well as with increases in blood pressure throughout 9 years (P<.05).

Conclusions: After long-term follow-up, minimal changes in IOP were observed in this African-origin population. The consistent relationships of hypertension and diabetes to IOP, a major glaucoma risk factor, underscore the public health importance of controlling these systemic conditions in black populations, where glaucoma incidence is high.

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LEVATED INTRAOCULAR PRESSURE (IOP) is a major risk factor for open-angle glaucoma (OAG), an ocular disease that most frequently affects persons of African ancestry.1-7 Information on the natural history of IOP in black populations is thus highly relevant to understand related disparities in OAG risk. The role of IOP as a modifiable risk factor in these populations was confirmed by recent data showing that topical ocular hypotensive therapy effectively delays or prevents the onset of OAG in African Americans with ocular hypertension.8 Nevertheless, most individuals with high IOP will not develop OAG, suggesting different etiologic mechanisms for each condition.9,10

Although considerable cross-sectional data exist on the distribution and risk factors for elevated IOP,9-25 long-term longitudinal data are limited,26-31 particularly for persons of African ancestry. We previously reported on the longitudinal changes in IOP during a 4-year interval among the black participants of the Barbados Eye Studies.28,29 The current report aims to investigate temporal changes in IOP and prognostic factors for such changes during a 9-year period. Results are based on the African-origin participants of the Barbados Eye Studies without a glaucoma diagnosis or treatment at baseline.

METHODS

As described in previous reports,3,6,32 the Barbados Eye Studies are population-based epidemiologic investigations on the prevalence, incidence, and risk factors for major eye diseases in the predominantly black population of Barbados, West Indies. An initial cohort of 4631 participants, 40 to 84 years old, completed examinations at the study site, representing 84% of a randomly selected national sample. Self-reported ancestry was 93% of African origin, as found in the country’s population.3 After the baseline prevalence study (1988-1992), the surviving cohort members were reexamined to obtain data on incidence at 4 years (Barbados Incidence Study of Eye Diseases I [BISED I], 1992-1997) and 9 years (BISED II, 1997-2003). The BISED II participants (n=2793, 81% of the eligible survivors) had similar distributions of self-reported ancestry (2612 of African origin), were younger,
and were less likely to have hypertension at baseline than surviving nonparticipants and those who had died. The latter group included more men and reported more diabetes history. Com pared with the participants, nonparticipants also had higher baseline IOP (mean±SD, 18.1±4.6 vs 19.4±3.7 mm Hg) and glycosylated hemoglobin levels (GHb) (mean±SD, 7.5%±2.1% vs 8.0%±2.7%).

The standardized study protocols included a detailed interview and various anthropometric and ocular measurements: 2 blood pressure (BP) readings with a Hawksley random-zero sphygmomanometer, Humphrey automated perimetry (Carl Zeiss Meditec Inc, Dublin, Calif), Lens Opacities Classification System II lens gradings at the slitlamp, and stereo fundus photography. The GHb assays by means of affinity chromatography of venous whole blood† using Glyc-Alfin GHb kits (Isolab, Akron, Ohio) were available for 3754 participants (81%) (GHb measurements began after the study had started). A subsample of consecutive participants in BISED II had pachymetry (5 measurements of central corneal thickness in each eye using a KMI ultrasonic RX3000 pachymeter; KMI Surgical, Pa). Comprehensive dilated ophthalmologic examinations were conducted on a systematic 10% sample and on participants with specified positive findings (eg, ocular disease or diabetes history, IOP > 21 mm Hg, or best-corrected visual acuity < 20/30 in either eye). The study was approved by the institutional review boards of Stony Brook University, the University of the West Indies, and the Johns Hopkins University (Baltimore, Md) and was funded by the National Eye Institute.

The IOP data were based on the mean of 3 Goldman application tonometry measurements at each visit. Definite OAG was classified by the presence of both visual field defects and optic disc damage in at least 1 eye, after the exclusion of other possible causes by the study ophthalmologists. The IOP was not considered in this definition. Hypertension was defined as a mean systolic BP (SBP) of 140 mm Hg or higher and/or a diastolic BP (DBP) of 90 mm Hg or higher and/or a history of antihypertensive treatment.

Change in IOP was defined as the difference between the 9-year IOP and the baseline IOP. Analyses in this report excluded persons with glaucoma or those receiving IOP-lowering treatment at baseline. Descriptive data on IOP changes were person based, using data in the worse eye (the eye with a more positive IOP difference) of an individual. Person-based IOP changes were initially examined according to various factors; adjusted mean changes were estimated using general linear regression models that controlled for age, sex, and baseline IOP. Potential risk factors evaluated included baseline status of hypertension (or BP or antihypertensive medication), diabetes history (or GHb level), pulse rate, body mass index (calculated as weight in kilograms divided by the square of height in meters), corneal thickness, smoking, and alcohol use. Changes in BP from baseline to the 9-year follow-up visit were also investigated. To examine associations with IOP change using IOP measurements from both eyes of a participant, further analyses were based on multiple regression models with mixed effects (SAS procedure PROC MIXED with the REPEATED statement), which accounted for the correlation between eyes.

Of the 2612 BISED II participants of African descent, 2537 (97%) had IOP data from both the baseline and 9-year follow-up visits. This report included data on 2298 participants, after excluding 239 persons who had glaucoma (OAG, suspected glaucoma, or other types of glaucoma) or were receiving IOP-lowering treatment at baseline. The mean±SD age of this study population was 55.1±10.5 years at baseline, and 39% were male (Table 1). The distribution of other baseline characteristics, such as IOP, SBP and DBP, and diabetes history, is also presented in Table 1.

After 9 years of follow-up, the mean change in IOP was only 0.4 mm Hg (median, 0.0 mm Hg), with a relatively large variation (SD, 4.0 mm Hg). Men had a larger increase (mean±SD, 0.7±4.1 mm Hg; median, 0.3 mm Hg) than women (mean±SD, 0.2±3.9; median, 0.0 mm Hg (P=.003). Only 6.5% of persons with an IOP of 21 mm Hg or lower at baseline had an elevated IOP of more than 21 mm Hg after 9 years. Of this population without glaucoma or receiving IOP treatment at baseline, 3.8% had subsequent IOP-lowering treatment and 2.7% developed OAG after 9 years. Change in IOP was higher (P=.03; t test) in incident OAG cases (mean±SD, 2.2±6.6 mm Hg; median, 1.3 mm Hg) than among those who did not develop OAG (mean±SD, 0.4±3.9; median, 0.0 mm Hg).

The Figure presents the baseline and 9-year distribution of IOP by age group. The mean changes were small, and there were no apparent linear IOP differences with advancing age. A larger increase in IOP was observed in persons 50 to 59 years of age at baseline (mean±SD, 0.9±4.3 mm Hg; median, 0.7 mm Hg), and a decrease in IOP was seen in persons 70 years or older (mean±SD, −0.6±4.2; median, −0.7 mm Hg). After excluding incident cases of OAG or those receiving IOP-lowering treatment during the 9-year period, the age-associated distribution of IOP changes remained similar, with the overall mean±SD being 0.4±3.7 mm Hg (median, 0.0 mm Hg). It was 0.5±3.4 mm Hg (median, 0.0 mm Hg) for persons 40 to 49 years, 0.7±3.8 mm Hg (median, 0.7 mm Hg) for those 50 to 59 years, 0.1±3.6 mm Hg (median, 0.0 mm Hg) for those 60 to 69 years, and −0.6±4.2 mm Hg (median, −0.7 mm Hg) for those 70 years or older.

Table 2 presents adjusted mean person-based IOP changes. After 9 years of follow-up, the adjusted mean increase in IOP was significantly higher (P=.04) in men than in women (0.52 vs 0.21 mm Hg). Persons with hypertension or a diabetes history also tended (P=.10) to have a higher IOP increase than those without these conditions. Significant associations with IOP were found in analyses using baseline SBP and its 9-year change as con-

Table 1. Baseline Characteristics of the 2298 Study Participants

<table>
<thead>
<tr>
<th>Baseline Characteristic</th>
<th>Mean ± SD (Median)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>55.1 ± 10.5 (54.0)</td>
</tr>
<tr>
<td>Male, %</td>
<td>38.9</td>
</tr>
<tr>
<td>IOP, mm Hg</td>
<td>17.5 ± 3.3 (17.3)</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>133.2 ± 21.5 (130.0)</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>80.9 ± 11.6 (80.0)</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>48.6</td>
</tr>
<tr>
<td>Diabetes history, %</td>
<td>14.4</td>
</tr>
</tbody>
</table>

Abbreviations: DBP, diastolic blood pressure; IOP, intraocular pressure; SBP, systolic blood pressure.
*Data are presented as mean ± SD (median) unless otherwise indicated.
†SBP/DBP of 140/90 mm Hg or higher and/or use of antihypertensive treatment.
continuous variables. Thus, the IOP increased by 0.17 mm Hg at follow-up (P < .001) for every 10–mm Hg increase in SBP at baseline; additionally, the IOP increased by 0.23 mm Hg (P < .001) for every 10–mm Hg increase in within-person SBP between baseline and the 9-year visit. The corresponding estimated changes in IOP with DBP were either not significant or marginally significant (P = .07), respectively. Persons receiving antihypertensive medications had higher IOP increases. The GHb level and corneal thickness were evaluated in their respective subsamples (as categorical or continuous variables), with no significant associations found. Other variables examined (eg, pulse, smoking, and alcohol consumption) also were not significantly related to IOP change. Additional mixed-model analyses using eye-based rather than person-based IOP data indicated that hypertension (P = .01) and diabetes history (P = .02) were statistically significantly associated with IOP change, after adjustment for baseline IOP, age, and sex.

The final mixed model simultaneously included all significant variables, and results are presented in Table 3. Baseline IOP was negatively associated with IOP change (P < .001). Compared with persons 40 to 49 years of age at baseline, persons 50 to 59 years of age had larger increases in IOP (P = .003), whereas those 70 years or older tended to have larger IOP decreases (P = .06). The nonlinear relationship was further verified in a separate model, resulting in significant associations with age, as well as with age squared. The IOP increases were also associated with male sex, hypertension, and diabetes history. When GHb values were substituted for diabetes history, no significant associations with GHb values were found. In separate models that considered SBP or DBP rather than hypertension, the 9-year changes in IOP were related to higher SBP or DBP at baseline and 9-year in-

Table 2. Nine-Year Change in Intraocular Pressure (IOP) by Various Factors

<table>
<thead>
<tr>
<th>Baseline Characteristic</th>
<th>No. of Participants</th>
<th>Adjusted IOP Change, Mean ± SE, mm Hg*</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>894</td>
<td>0.52 ± 0.12</td>
<td>.04</td>
</tr>
<tr>
<td>Female</td>
<td>1404</td>
<td>0.21 ± 0.10</td>
<td></td>
</tr>
<tr>
<td>Hypertension†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1181</td>
<td>0.22 ± 0.12</td>
<td>.10</td>
</tr>
<tr>
<td>Yes</td>
<td>1116</td>
<td>0.49 ± 0.11</td>
<td></td>
</tr>
<tr>
<td>Antihypertensive medication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1680</td>
<td>0.25 ± 0.10</td>
<td>.02</td>
</tr>
<tr>
<td>Yes</td>
<td>617</td>
<td>0.66 ± 0.15</td>
<td></td>
</tr>
<tr>
<td>Diabetes history</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1960</td>
<td>0.31 ± 0.09</td>
<td>.10</td>
</tr>
<tr>
<td>Yes</td>
<td>331</td>
<td>0.67 ± 0.20</td>
<td></td>
</tr>
</tbody>
</table>

*Adjusted for age, sex, and baseline IOP.
†Systolic/diastolic blood pressure of 140/90 mm Hg or higher and/or a history of antihypertensive treatment.

Figure. Intraocular pressure (IOP) at baseline (solid line) and 9-year follow-up (dashed line). A, Baseline age of 40 to 49 years (n = 869; mean ± SD IOP change, 0.6 ± 3.6 mm Hg; median IOP change, 0.0 mm Hg). B, Baseline age of 50 to 59 years (n = 670; mean ± SD IOP change, 0.9 ± 4.3 mm Hg; median IOP change, 0.7 mm Hg). C, Baseline age of 60 to 69 years (n = 497; mean ± SD IOP change, 0.1 ± 3.8 mm Hg; median IOP change, 0.0 mm Hg). D, Baseline age of 70 years or older (n = 262; mean ± SD IOP change, −0.6 ± 4.2; median IOP change, −0.7 mm Hg).
In the older age groups. The age effects observed at 4 and 9 years thus appear to differ and may indicate that IOP is affected by both short-term and long-term influences. Further examination of possible cohort effects found no clear pattern for each age group when comparing younger and older birth cohorts. Although the 9-year change could result from the naturally occurring long-term mortality in the population, one additional likely explanation for the 4-year and 9-year differences (and the lower IOP in the oldest age group) is selective mortality. Persons with hypertension and diabetes have higher IOP as well as increased mortality risks. Selective mortality from this source could thus result in selective losses of individuals with higher IOP. In fact, compared with participants in the 4-year follow-up, the nonparticipants at the 9-year visit were more frequently affected with hypertension (48% vs 62%) and diabetes (14% vs 23%) at baseline and were therefore more likely to have higher IOP after 9 years. Longitudinal changes in IOP thus result from the complex interplay of systemic and other factors.

Table 3. Nine-Year Change in IOP and Related Factors

<table>
<thead>
<tr>
<th>Factor</th>
<th>Estimate (SE)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Main model</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IOP at baseline</td>
<td>0.15 (0.06)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Age at baseline, y</td>
<td>0.41 (0.19)</td>
<td>.03</td>
</tr>
<tr>
<td>40-49</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50-59</td>
<td></td>
<td></td>
</tr>
<tr>
<td>60-69</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥70</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>0.28 (0.14)</td>
<td>.04</td>
</tr>
<tr>
<td>Diabetes history</td>
<td>0.41 (0.19)</td>
<td>.03</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.33 (0.14)</td>
<td>.02</td>
</tr>
<tr>
<td><strong>Model with DBP</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IOP at baseline −0.58 (0.02)</td>
<td>&lt;.001</td>
<td></td>
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<tr>
<td><strong>Model with DBP</strong></td>
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</tr>
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<td><strong>Model with DBP</strong></td>
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</tr>
<tr>
<td>IOP at baseline −0.58 (0.02)</td>
<td>&lt;.001</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: DBP, diastolic blood pressure; IOP, intraocular pressure; SBP, systolic blood pressure.

Based on separate models substituting SBP (or DBP) and antihypertensive treatment for hypertension at baseline and 9-year follow-up. No significant results were found with treatment reported at 9-year follow-up.

Increases in SBP or DBP. The use of antihypertensive medications at baseline, an indicator of hypertension, was also a significant variable in these models. No interactions between age and the significant factors were noted. No other variables evaluated were associated with IOP change. Results remained similar in additional analyses that excluded persons receiving IOP-lowering treatment or developing OAG during 9-year follow-up. The possible impact of diurnal or seasonal variation on the regression models for IOP change was evaluated by assessing the effects of timing variations (eg, morning of the baseline visit and evening follow-up or vice versa) or seasonal variations (eg, warmer months at baseline vs cooler months at follow-up) on IOP measurements. No significant effects were found (data not shown).

COMMENT

To our knowledge, this is the first report on the natural history of IOP changes after long-term follow-up in an African-origin population. Although IOP remained relatively unchanged between baseline and 9-year follow-up, the relationship between IOP and age was not linear. A mild decrease in IOP was seen in persons 70 years or older, with a mild increase observed at younger ages. Additionally, baseline IOP was inversely associated with IOP change, whereas male sex, hypertension, and diabetes were positively related to changes in IOP.

The mean ± SD IOP change throughout 9 years was only 0.4 ± 4.0 mm Hg, a finding consistent with the Beaver Dam Eye Study (BDES), where the mean ± SD change was 0.0 ± 3.2 mm Hg throughout 5 years. In our previous 4-year report, IOP increased by 2.5 ± 3.9 mm Hg during this period, on average, with larger mean changes seen

AGE

Several cross-sectional studies showed increases in IOP with age, whereas others found negative associations. The few longitudinal studies available also yielded inconsistent results. The Baltimore Longitudinal Study of Aging reported a weak negative association between IOP change and age among middle-aged white men, and a 10-year study among Japanese aircraft personnel found similar results. In contrast, a longitudinal study of a large Japanese population revealed significant IOP increases with age, as did our 4-year follow-up investigation. The nonlinear relationship between IOP change and age from the present 9-year report was also found in the cross-sectional analyses of IOP and blood pressure from the BDES. Although selective mortality may partially explain the lower IOP in our oldest age group, the correlation between aging and reduction in the aqueous flow is a likely explanation.

BLOOD PRESSURE

The positive association between IOP and hypertension, particularly with elevated SBP, has been well documented in many cross-sectional studies, but fewer studies have reported significant correlations between IOP and DBP. Results from the current 9-year follow-up are consistent with our previously reported positive associations of 4-year IOP change with both SBP and DBP. In the Baltimore Longitudinal Study of Aging and 2 large Japanese studies, IOP change was positively correlated with a change in SBP but not in DBP. In contrast, in the predominantly European-derived population of the BDES, a 10–mm Hg increase in SBP (or DBP) was associated with an approximately 0.2–mm Hg (or 0.4–mm Hg) increase in IOP throughout 5 years of follow-up. We found similar results after 9 years in our African-origin population. The IOP changed between 0.14 and 0.45 mm Hg in persons with hypertension or higher SBP or DBP (per 10 mm Hg higher) at

In conclusion, after 9 years of follow-up, the natural history of IOP in this population revealed minimal IOP changes. Since IOP is a major risk factor, variables that affect IOP are of particular importance to black populations, given their high prevalence and incidence of OAG. In this regard, the positive associations of IOP with hypertension and diabetes, which are especially frequent in these populations, have substantive public health relevance.

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Author Contributions: Ms Wu had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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