

Comparison of Initial Intraocular Pressure Response With Topical β -Adrenergic Antagonists and Prostaglandin Analogues in African American and White Individuals in the Ocular Hypertension Treatment Study

Steven L. Mansberger, MD; Bret A. Hughes, MD; Mae O. Gordon, PhD; Steven D. Spaner, PhD; Julia A. Beiser, MS; George A. Cioffi, MD; Michael A. Kass, MD; for the Ocular Hypertension Treatment Study Group

Objective: To compare the intraocular pressure (IOP) responses of self-identified African American and white participants in the Ocular Hypertension Treatment Study to therapeutic trials of topical, nonselective β -adrenergic antagonists or prostaglandin analogues.

Methods: Multivariate models that adjusted for baseline IOP and corneal thickness were used to estimate IOP response by race. Participants included 536 who were prescribed topical β -adrenergic antagonists and 191 who were prescribed prostaglandin analogues, 25% of whom were African American.

Main Outcome Measure: Intraocular pressure response in the ipsilateral eye after 4 to 6 weeks of a therapeutic trial.

Results: Intraocular pressure response to nonselective β -adrenergic antagonists did not differ between African American and white participants. Intraocular pressure response to prostaglandin analogues was slightly greater

in African American participants, but this difference was not statistically significant. With both classes of medication, greater IOP reduction was associated with higher baseline IOP and thinner central corneal measurement.

Conclusions: We found no statistically significant differences in IOP response to topical, nonselective β -adrenergic antagonists or prostaglandin analogues between self-identified African American and white individuals.

Application to Clinical Practice: Studies of IOP response to medication should statistically adjust for baseline IOP and central corneal thickness. Clinicians should consider factors other than ethnicity when choosing an ocular hypotensive medication for a patient.

Trial Registration: clinicaltrials.gov Identifier: NCT00000125

Arch Ophthalmol. 2007;125:454-459

Author Affiliations: Devers Eye Institute/Discoveries in Sight, Legacy Health System, Portland, Ore (Drs Mansberger and Cioffi); Kresge Eye Institute, Wayne State University School of Medicine, Detroit, Mich (Dr Hughes); Department of Ophthalmology and Visual Sciences, Washington University School of Medicine, St. Louis, Mo (Drs Gordon, Spaner, and Kass and Ms Beiser).

Group Information: A complete list of the members of the OHTS Group appears on the OHTS Web site: <http://vrcc.wustl.edu>.

P RIMARY OPEN-ANGLE GLAUCOMA (POAG) is approximately 3 times more prevalent and twice as likely to cause bilateral blindness in African American individuals as compared with white individuals.^{1,2} Elevated intraocular pressure (IOP) is the major risk factor for developing glaucoma^{3,4} and is present in approximately 8% of adults over the age of 40 years in the United States.⁵ The Ocular Hypertension Treatment Study (OHTS) demonstrated that medical treatment of ocular hypertension decreases the risk of developing POAG among all participants,⁶ including self-identified African American participants.⁷

Previous studies have examined the hypothesis that African American individu-

als respond differently to topical ocular hypotensive medications from other racial or ethnic groups. Some reports suggest that African American individuals have a lesser IOP response to topical β -adrenergic antagonists when compared with white individuals^{8,9} while other reports show no difference.¹⁰ Some studies have shown that African American individuals have a greater IOP response to prostaglandin analogues when compared with white individuals^{11,12} while other reports have shown no difference.^{8,13} The different results may reflect the relative proportion of participants with ocular hypertension, POAG, and secondary causes of glaucoma, such as pigmentary dispersion or pseudoexfoliation, in the various studies.^{8,9,11,12} None of these studies controlled for the effects

of both central corneal thickness (CCT) and baseline IOP on IOP response.

The OHTS is a multicenter, randomized controlled trial that demonstrated the efficacy of topical ocular hypotensive medication in delaying or preventing the onset of POAG in participants with ocular hypertension.¹⁴ The OHTS provides a unique opportunity to examine the relationship between self-identified race and IOP response to topical ocular hypotensive medications in a large sample of participants, 25% of whom are self-identified African American. This article compares the IOP response of self-identified African American and white participants to topical β -adrenergic antagonists or prostaglandin analogues in initial therapeutic trials in the OHTS.

METHODS

OCULAR HYPERTENSION TREATMENT STUDY

The OHTS is a multicenter, randomized clinical trial to determine the safety and efficacy of ocular hypotensive medication in delaying or preventing the onset of POAG in individuals with elevated IOP. Eligibility criteria included age from 40 to 80 years, IOP between 24 mm Hg and 32 mm Hg in one eye and between 21 mm Hg and 32 mm Hg in the other eye, and no evidence of either glaucomatous structural or functional damage by standard clinical measures. All participants provided written informed consent for participation in the study. The protocol for the OHTS is described in detail elsewhere¹⁴ and the manual of procedures for the study is available online.¹³ From February 1994 to October 1996, participants (n=1636) were randomly assigned to treatment with topical IOP-lowering medication or to observation.

Racial classification of participants was by self-identification. At the qualifying assessment visit, clinic staff read the following script to potential participants: "Do you consider yourself American Indian or Alaskan Native, Asian or Pacific Islander, Black not of Hispanic origin, Hispanic, or White not of Hispanic origin?" The analysis sample for this report is restricted to participants who self-identified as "Black not of Hispanic origin" or as "White not of Hispanic origin," hereafter referred to as African American participants or white participants, respectively.

Two OHTS-certified examiners performed IOP measurements with Goldmann applanation tonometry. An operator measured the IOP without looking at the dial and a reader recorded the result. Two IOP measurements were performed and a third was performed if the first two disagreed by more than 2 mm Hg. For the purposes of this report, the baseline IOP of participants was the mean of these IOP measurements at the baseline randomization visit, which was separate from the qualifying visits. Following the baseline randomization visit, medication participants completed an initial therapeutic trial in the eye with the higher IOP. If baseline IOP was equal in the two eyes, one eye was chosen randomly for treatment. The response to the medication was evaluated 4 to 6 weeks later. Every attempt was made to keep subsequent IOP measurements within a 4-hour time window to reduce diurnal fluctuation.

Central corneal thickness measurements began 2 years after the start of randomization. Central corneal thickness was measured with a calibrated ultrasonic pachymeter (Pachette 500; DGH Technologies, Exton, Pa). A previously published article¹⁶ describes the protocol for measuring CCT.

TOPICAL MEDICATIONS IN THE OHTS MEDICATION GROUP

The investigators selected the topical medication for the initial therapeutic trial at their discretion. They could use any topical ocular hypotensive medication that was commercially available in the United States. They chose nonselective β -adrenergic antagonists for the majority of the initial therapeutic trials in the medication group completed from 1994 to 1997.

TREATMENT OF THE OHTS OBSERVATION GROUP AFTER JUNE 1, 2002

To determine whether earlier treatment of ocular hypertension is better than later treatment, investigators offered topical ocular hypotensive medication to participants originally randomized to the observation group after the June 2002 publication of the primary outcome article.⁶ Therefore, this report also includes data from observation participants who started an initial 4- to 6-week therapeutic trial after June 1, 2002, and who completed the trial by October 3, 2003. We report on initial therapeutic trials of prostaglandin analogues in the observation group (n=191) because these drugs were the predominant choice of the investigators.

STATISTICAL METHODS

Descriptive analyses compared baseline demographic and clinical characteristics of self-identified African American and white individuals. For participants randomized to the medication group, the primary outcome was the IOP in the ipsilateral eye after 4 to 6 weeks of treatment with a therapeutic trial of nonselective β -adrenergic antagonists. For participants originally randomized to the observation group who initiated a therapeutic trial after June 1, 2002, the primary outcome was IOP in the ipsilateral eye after 4 to 6 weeks of treatment with a therapeutic trial of prostaglandin analogues. We used univariate analyses, including χ^2 tests, *t* tests, and analysis of variance, to evaluate the relationship of factors that could be related to IOP response. In addition to race and baseline IOP, multivariate models adjusted for factors whose means or distributions differed by race, CCT, patient-reported medical history (high blood pressure and diabetes), age, and sex. Other factors screened for their possible relationship to IOP response included asthma, lung disease, stroke, heart disease, and use of oral β -adrenergic antagonists or calcium channel blockers; however, these factors were not included in the multivariate models because they occurred infrequently, did not differ by race, or were highly correlated with other factors in the model. A Wald statistic with a *P* value less than .10 was used for entrance and removal from forward, stepwise, multiple regression models. All statistical analyses were conducted using the SPSS advanced statistical data analysis program (version 12.0; SPSS Inc, Chicago, Ill).

RESULTS

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF THE OHTS MEDICATION GROUP

Among the 817 participants randomized to the medication group, 780 participants self-identified as non-Hispanic white or African American. Of these participants, 80% (621/780) started an initial therapeutic trial with a nonselective β -adrenergic antagonist, 14% (109/

Table 1. Baseline Characteristics of Self-Identified African American and White Participants Who Completed Therapeutic Trials With Nonselective β -Adrenergic Antagonists or Prostaglandin Analogues

Variable	Nonselective β -Adrenergic Antagonists		Prostaglandin Analogues	
	African American (n = 126)	White (n = 403)	African American (n = 58)	White (n = 133)
Age, mean \pm SD, y*	55.2 \pm 9.3	56.7 \pm 9.1	59.5 \pm 7.8	62.7 \pm 9.8
Central corneal thickness, mean \pm SD, μ m*†	556.1 \pm 39.0	574.2 \pm 37.7	563.2 \pm 35.1	583.4 \pm 33.8
Sex, No. (%)†				
Male	42 (33.3)	195 (48.4)	21 (36.2)	54 (40.6)
Female	84 (66.7)	208 (51.6)	37 (63.8)	79 (59.4)
Used oral β -blockers, No. (%)	6 (4.8)	17 (4.2)	15 (25.9)	21 (15.8)
Used calcium channel blockers, No. (%)*†	24 (19.0)	26 (6.5)	30 (51.7)	35 (26.3)
History of diabetes, No. (%)*†	25 (19.8)	30 (7.5)	20 (34.5)	20 (15.0)
History of high blood pressure, No. (%)*†	65 (52.0)	124 (30.8)	46 (79.3)	63 (47.4)

*Significant differences by race in baseline variable for participants receiving prostaglandin analogues ($P < .05$, χ^2 test [for categorical variables] or t test [for continuous variables]).

†Significant differences by race in baseline variable for participants receiving β -adrenergic antagonists ($P < .05$, χ^2 test [for categorical variables] or t test [for continuous variables]).

780) with a selective β -adrenergic antagonist, 2% (17/780) with a carbonic anhydrase inhibitor, 2% (17/780) with a nonselective α agonist, and 1% (9/780) with other medications. Of those prescribed nonselective β -adrenergic antagonists, investigators used timolol gel forming solution in 206 participants (39%), timolol maleate in 141 (27%), levobunolol hydrochloride in 134 (25%), carteolol in 43 (8.1%), and metipranolol in 5 (1%). There was no statistical difference in the proportion of participants prescribed each drug by race ($P > .05$ for all medications). We report data only from participants who received a nonselective β -adrenergic antagonist because of the small sample sizes for the other classes of drugs. Of the 621 participants who received a nonselective β -adrenergic antagonist, 529 (85%) completed an initial therapeutic trial and had CCT measurements. Of the 529 participants available for analysis, 75% (403 of 529) self-identified as white and 24% (126 of 529) self-identified as African American.

Among participants who completed an initial therapeutic trial of a nonselective β -adrenergic antagonist, mean central corneal measurement was thinner in self-identified African American participants compared with self-identified white participants. A higher percentage of self-identified African American participants reported diabetes, usage of calcium channel blockers, and high blood pressure when compared with self-identified white participants (**Table 1**).

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF THE OHTS OBSERVATION GROUP

As noted earlier, after June 1, 2002, investigators offered treatment with ocular hypotensive medication to 634 self-identified white and African American participants originally randomized to the observation group. Among this group, 115 participants had been receiving medication prior to June 1, 2002, because they developed glaucoma or because of other reasons and are excluded from this analysis. Of the remaining 519 observation participants, 278 participants consented to a

therapeutic trial with a topical ocular hypotensive medication and completed the initial therapeutic trial by October 3, 2003. Among these 278 participants, 191 (69%) were prescribed prostaglandin analogues, 50 (18%) nonselective β -adrenergic antagonists, 28 (10%) α -2 agonists, and 9 (3%) other medications. Of those prescribed prostaglandin analogues, investigators used latanoprost 0.005% in 151 participants (79%), travoprost 0.004% in 23 (12%), and bimatoprost 0.03% in 17 (9%). There was no statistical difference in the proportion of participants prescribed each drug by race ($P > .05$). The analysis sample is limited to the 191 participants who received prostaglandin analogues because of the small sample sizes for the other classes of medication. Of the 191 participants available for analysis, 70% (133/191) self-identified as white and 30% (58/191) self-identified as African American.

Among observation participants who completed an initial therapeutic trial of prostaglandin analogues, mean central corneal measurement was thinner in African American compared with white participants. A higher percentage of African American participants reported diabetes, usage of calcium channel blockers, and high blood pressure when compared with white participants (Table 1). Because therapeutic trials for the prostaglandin analogues were performed in the second phase of OHTS approximately 5 years later, participants were older and reported more health problems when compared with the original medication group in this report (Table 1).

COMPARISON OF IOP RESPONSE WITH β -ADRENERGIC ANTAGONISTS IN AFRICAN AMERICAN AND WHITE PARTICIPANTS

Among medication participants who received nonselective β -adrenergic antagonists in initial therapeutic trials, we found no difference by race in the mean baseline IOP ($P = .52$, **Table 2**) or mean IOP after 4 to 6 weeks of treatment ($P = .91$ [unadjusted] and $P = .90$ [adjusted], Table 2). There was no difference in mean percentage IOP change from baseline by self-identified race in both unadjusted

Table 2. Mean IOP at Baseline and After 4 to 6 Weeks of a Therapeutic Trial With Nonselective β -Adrenergic Antagonists or Prostaglandin Analogues for Self-Identified African American and White Participants

Variable	Nonselective β -Adrenergic Antagonists				Prostaglandin Analogues			
	African American, Mean \pm SD (n = 126)	White, Mean \pm SD (n = 403)	Unadjusted P Value	Adjusted P Value*	African American, Mean \pm SD (n = 58)	White, Mean \pm SD (n = 133)	Unadjusted P Value	Adjusted P Value*
IOP baseline, mm Hg	25.8 \pm 3.0	26.0 \pm 2.8	.52	.52	25.3 \pm 3.9	24.5 \pm 3.4	.18	.18
IOP after 4 to 6 weeks, mm Hg	19.6 \pm 2.8	19.6 \pm 3.0	.91	.90	17.5 \pm 3.8	18.3 \pm 3.5	.16	.15

Abbreviation: IOP, intraocular pressure.

*P value is the F ratio probability for the association of race after adjustment for baseline IOP, central corneal thickness, age, sex, history of high blood pressure, and history of diabetes.

analyses ($P = .68$) and multiple regression analyses that adjusted for other factors ($P = .67$). A forward, stepwise, multiple linear regression analysis selected higher baseline IOP ($P < .001$) and thinner CCT measurement ($P = .013$) as separate and independent factors associated with a lower mean IOP after 4 to 6 weeks of treatment.

COMPARISON OF IOP RESPONSE WITH PROSTAGLANDIN ANALOGUES IN AFRICAN AMERICAN AND WHITE PARTICIPANTS

Among those receiving prostaglandin analogues, no difference by race was found in mean baseline IOP ($P = .18$) nor the primary outcome of mean IOP after 4 to 6 weeks ($P = .15$, Table 2). However, a greater mean percentage IOP change from baseline was found in self-identified African American participants when compared with self-identified white participants: African American participants had a 30.3% decrease in IOP and white participants had a 24.8% decrease in IOP ($P < .02$, unadjusted) after an initial trial of prostaglandin analogues. This apparent racial difference was of borderline significance ($P = .051$) in the multivariate analysis, including CCT, age, sex, history of high blood pressure, and history of diabetes. However, this multivariate model did not include baseline IOP as a covariate because mean percentage IOP change is derived in part from baseline IOP.

Forward, stepwise, multiple regression analyses, which select the variables most associated with the outcome of interest, did not select race ($P > .05$) as being independently associated with mean IOP after 4 to 6 weeks in therapeutic trials with prostaglandin analogues. The model only selected baseline IOP ($P < .001$) and thinner CCT measurement ($P = .001$). In summary, CCT and baseline IOP had the strongest association with IOP response in therapeutic trials of prostaglandin analogues.

COMMENT

This report examines the possible relationship between race and IOP response to nonselective β -adrenergic antagonists and prostaglandin analogues, the most frequently prescribed classes of topical ocular hypotensive medication for treating glaucoma and ocular hypertension in developed countries. The OHTS provides a unique

opportunity to address the question of whether race is associated with the IOP response to these medications because it has a large number of participants, of which 25% are self-identified African American.

Our results suggest that African American and white individuals respond very similarly to nonselective β -adrenergic antagonists and prostaglandin analogues in initial therapeutic trials of 4 to 6 weeks' duration after adjusting for CCT and baseline IOP. It is important to emphasize that the responses to medication were not obtained from dose-response curves but rather from therapeutic trials of fixed doses of commercially available medications. Dose-response curves in participants enrolled in a clinical trial may differ from a representative sample of individuals with ocular hypertension. Thinner CCT measurement and higher baseline IOP were most strongly associated with greater IOP response to nonselective β -adrenergic antagonists. The mean IOP response to a 4- to 6-week trial of a prostaglandin analogue was slightly greater in self-identified African American participants than in self-identified white participants. But this difference was not statistically significant in multivariate models after adjusting for CCT, age, sex, history of high blood pressure, and history of diabetes. We would have needed twice the sample size to detect a 1 mm Hg difference in IOP response by race.

We performed a literature search of previous studies concerning IOP response and race. From 1965 until July 2005, only 65 studies report race/ethnicity. Of these, only 14 studies included 40 or more African American participants, and only 6 of them performed a subgroup analysis by ethnicity.⁸⁻¹³ Katz and Berger⁹ found that African American individuals required higher concentrations of timolol maleate to achieve the same pressure-lowering effect. However, nonresponders were excluded from the analysis and the study did not control for baseline IOP or CCT. Higginbotham et al⁸ found β -adrenergic antagonists to be less effective in black when compared with white individuals, although there were no controls for baseline IOP or CCT. Mundorf et al¹⁰ found no racial difference in IOP response to timolol maleate.

Regarding prostaglandin analogues, Netland et al^{11,12} found an augmented IOP response to travoprost in African American individuals in comparison with white individuals in 2 studies. However, the first study did not

statistically control for baseline IOP or CCT,¹² and the second study did not control for baseline IOP.¹¹ Finally, both Higginbotham et al⁸ and Parrish et al¹³ found the response to bimatoprost to be similar in African American and white individuals. In summary, no studies reported to date examining racial differences in medication response have controlled for both baseline IOP and CCT. We believe this is important for any further studies of IOP response to medication because CCT was independently associated with IOP response even when controlling for baseline IOP.

Controlling for differences in baseline IOP is important in medication response studies. Patients with higher IOP on average have larger reductions in IOP in response to a topical ocular hypotensive medication. In this report, higher baseline IOP was strongly correlated with greater IOP reduction after 4 to 6 weeks of a therapeutic trial. In addition, eyes with higher baseline IOP may show greater IOP reduction because of regression to the mean.¹⁷ The use of "percentage change from baseline" does not fully address this problem because percentage change is computed using baseline IOP.

Controlling for differences in CCT is important as well. The relationship between CCT and measured IOP response to medication is complex. Brandt and colleagues¹⁸ noted that OHTS participants with thicker corneas had smaller measured IOP responses to topical β -adrenergic antagonists and prostaglandin analogues as compared with patients with normal or thin corneas. Multivariate analyses showed that a thinner central cornea was a separate factor influencing IOP response and was not merely an applanation artifact from a thin cornea. Brandt et al¹⁸ postulated that thicker corneas have higher rigidity, which reduces the ability to measure a decrease in IOP by applanation tonometry. We did not include a measure of ocular rigidity such as dynamic contour tonometry and are unable to investigate further. Another explanation, decreased diffusion of ocular hypotensive medication in an eye with a thicker cornea, is possible but less likely because of known high concentrations of active medication in the anterior chamber.¹⁹⁻²¹

Mean CCT was lower in self-identified African American individuals, but a considerable overlap in CCT was found between self-identified African American and white participants in the OHTS.¹⁶ Similarly, significant overlap in medical conditions (such as diabetes and high blood pressure) and socioeconomic status exists between self-identified African American and white participants. This suggests that clinicians cannot infer CCT or other important possible risk factors for the development of glaucoma from race alone.

The OHTS did not measure iris color. Melanin may affect the IOP response to some medications by binding active medication and preventing stimulation of target tissues. Earlier publications found that eyes with darkly pigmented irides required a higher concentration of pilocarpine and timolol to produce the same pressure-lowering response.^{9,22} However, Hedman and Larsson²³ showed no difference in IOP response with timolol 0.5% or latanoprost in persons with "dark brown eyes" in comparison with those with "less brown eyes." No difference in response may occur because of high concentra-

tions of active medication in the anterior chamber¹⁹⁻²¹ and also because irides of varying color have a similar number of melanocytes within the epithelial and stromal layers but differ primarily in the number and size of melanosomes within the stromal melanocytes.^{24,25} Future studies should compare this relationship between iris color and IOP response with different classes of topical ocular hypotensive medication.

The OHTS only includes ocular hypertensive participants satisfying the inclusion and exclusion criteria of the study. Clinicians should exercise caution when applying the results of this report to patients with POAG or patients with elevated IOP from secondary causes such as pigmentary dispersion syndrome.

The analysis for prostaglandin analogues was completed for participants initiating a therapeutic trial from June 2002 to October 2003. These patients had not converted to glaucoma, had thicker corneas, were older, and had more systemic comorbidities in comparison with the participants in the nonselective β -adrenergic antagonist group. Because of these differences, it is not appropriate to compare the IOP response to nonselective β -adrenergic antagonists with the response to prostaglandin analogues in this study. It is important to understand that the OHTS participants were not randomized to the type of topical ocular hypotensive medication and that investigators chose the initial topical ocular hypotensive medication at their discretion.

The initial response to β -adrenergic antagonists and prostaglandin analogues appears similar between self-identified African American and white participants in the OHTS. There was a trend toward a slightly greater IOP response to prostaglandin analogues in African American compared with white participants, although this difference was not statistically significant after controlling for baseline IOP and CCT in multivariate analyses. From this we can conclude that the IOP response of African American individuals is at least as great as white individuals to the most commonly prescribed classes of glaucoma medication in developed countries. Clinicians should consider factors other than race such as medical history, dosing schedules, and possible adverse effects when prescribing ocular hypotensive medication for patients.

Submitted for Publication: July 20, 2006; final revision received August 15, 2006; accepted August 18, 2006.

Correspondence: Mae O. Gordon, PhD, Washington University School of Medicine, Department of Ophthalmology and Visual Sciences, 660 S Euclid, Box 8096, St Louis, MO 63110 (mae@vrcc.wustl.edu).

Author Contributions: Dr Gordon, principal investigator for the Ocular Hypertension Treatment Study Coordinating Center, 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.

Financial Disclosure: None reported.

Funding/Support: This work was supported by awards from the National Eye Institute, the National Center on Minority Health and Health Disparities, grants EY09341 and EY09307 from the National Institutes of Health, and unrestricted grants from Merck Research Laboratories and Research to Prevent Blindness, Inc.

REFERENCES

- Sommer A, Tielsch JM, Katz J, et al. Racial differences in the cause-specific prevalence of blindness in east Baltimore. *N Engl J Med*. 1991;325:1412-1417.
- Tielsch JM, Sommer A, Katz J, et al. Racial variations in the prevalence of primary open-angle glaucoma: the Baltimore Eye Survey. *JAMA*. 1991;266:369-374.
- Gordon MO, Beiser JA, Brandt JD, et al. The Ocular Hypertension Treatment Study: baseline factors that predict the onset of primary open-angle glaucoma. *Arch Ophthalmol*. 2002;120:714-720.
- Sommer A. Glaucoma risk factors observed in the Baltimore Eye Survey. *Curr Opin Ophthalmol*. 1996;7:93-98.
- Tielsch JM, Katz J, Singh K, et al. A population-based evaluation of glaucoma screening: the Baltimore Eye Survey. *Am J Epidemiol*. 1991;134:1102-1110.
- Kass MA, Heuer DK, Higginbotham EJ, et al. The Ocular Hypertension Treatment Study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. *Arch Ophthalmol*. 2002;120:701-713.
- Higginbotham EJ, Gordon MO, Beiser JA, et al. The Ocular Hypertension Treatment Study: topical medication delays or prevents primary open-angle glaucoma in African American individuals. *Arch Ophthalmol*. 2004;122:813-820.
- Higginbotham EJ, Schuman JS, Goldberg I, et al. One-year, randomized study comparing bimatoprost and timolol in glaucoma and ocular hypertension. *Arch Ophthalmol*. 2002;120:1286-1293.
- Katz IM, Berger ET. Effects of iris pigmentation on response of ocular pressure to timolol. *Surv Ophthalmol*. 1979;23:395-398.
- Mundorf TK, Ogawa T, Naka H, Novack GD, Crockett RS. A 12-month, multicenter, randomized, double-masked, parallel-group comparison of timolol-LA once daily and timolol maleate ophthalmic solution twice daily in the treatment of adults with glaucoma or ocular hypertension. *Clin Ther*. 2004;26:541-551.
- Netland PA, Robertson SM, Sullivan EK, et al. Response to travoprost in black and nonblack patients with open-angle glaucoma or ocular hypertension. *Adv Ther*. 2003;20:149-163.
- Netland PA, Landry T, Sullivan EK, et al. Travoprost compared with latanoprost and timolol in patients with open-angle glaucoma or ocular hypertension. *Am J Ophthalmol*. 2001;132:472-484.
- Parrish RK, Palmberg P, Sheu WP. A comparison of latanoprost, bimatoprost, and travoprost in patients with elevated intraocular pressure: a 12-week, randomized, masked-evaluator multicenter study. *Am J Ophthalmol*. 2003;135:688-703.
- Gordon MO, Kass MA. The Ocular Hypertension Treatment Study: design and baseline description of the participants. *Arch Ophthalmol*. 1999;117:573-583.
- Ocular Hypertension Treatment Study (OHTS) manuals of procedures. <https://vrcc.wustl.edu/mop/mop.htm>. Accessed February 6, 2007.
- Brandt JD, Beiser JA, Kass MA, Gordon MO. Central corneal thickness in the Ocular Hypertension Treatment Study (OHTS). *Ophthalmology*. 2001;108:1779-1788.
- McDonald CJ, Mazzuca SA, McCabe GP Jr. How much of the placebo "effect" is really statistical regression? *Stat Med*. 1983;2:417-427.
- Brandt JD, Beiser JA, Gordon MO, Kass MA. Central corneal thickness and measured IOP response to topical ocular hypotensive medication in the Ocular Hypertension Treatment Study. *Am J Ophthalmol*. 2004;138:717-722.
- Camras CB, Toris CB, Sjoquist B, et al. Detection of the free acid of bimatoprost in aqueous humor samples from human eyes treated with bimatoprost before cataract surgery. *Ophthalmology*. 2004;111:2193-2198.
- Sjoquist B, Stjerschantz J. Ocular and systemic pharmacokinetics of latanoprost in humans. *Surv Ophthalmol*. 2002;47(suppl 1):S6-S12.
- Calissendorff B, Sjoquist B, Hogberg G, Grunge-Lowerud A. Bioavailability in the human eye of a fixed combination of latanoprost and timolol compared to monotherapy. *J Ocul Pharmacol Ther*. 2002;18:127-131.
- Harris LS, Galin MA. Effect of ocular pigmentation on hypotensive response to pilocarpine. *Am J Ophthalmol*. 1971;72:923-925.
- Hedman K, Larsson LI. The effect of latanoprost compared with timolol in African-American, Asian, Caucasian, and Mexican open-angle glaucoma or ocular hypertensive patients. *Surv Ophthalmol*. 2002;47(suppl 1):S77-S89.
- Imesch PD, Bindley CD, Khademian Z, et al. Melanocytes and iris color: electron microscopic findings. *Arch Ophthalmol*. 1996;114:443-447.
- Wilkerson CL, Syed NA, Fisher MR, et al. Melanocytes and iris color: light microscopic findings. *Arch Ophthalmol*. 1996;114:437-442.

Ophthalmological Numismatics

Sir William Bowman (1816-1892), renowned English ophthalmologist, was a surgeon at the Royal Ophthalmic Hospital in London, forerunner to Moorfields Eye Hospital, from 1846 to 1876. He revolutionized the histology of the eye and discovered the anterior elastic lamina of the cornea (Bowman membrane). He described a number of new surgical procedures for ptosis, lacrimal disorders, and formation of an artificial pupil. He also invented his lacrimal probes, which are still in use.

The Bowman medal was commissioned by the Ophthalmological Society of the United Kingdom. The obverse depicts the bust of Bowman at a three-quarter turn facing right. The reverse has an inscription within an inscription with space for the name of the awardee to be engraved. It was produced by the firm Spink and Son and engraved by the artist F. Kvac around 1945.



Courtesy of: Jay M. Galst, MD, 30 E 60th St, New York, NY 10022.