SHADES OF GRAY

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MYDRIATIC PROVOCATIVE TESTING:
A retrospective study of post dilation IOP spikes in glaucomatous, glaucoma suspect and non glaucoma patients at the Grand Rapids Outpatient Clinic for the Veterans.

Glaucoma is an eye disorder which cannot be easily understood, diagnosed or managed. The elusive nature of this disease has continue to attract much attention for many years (Alexander, L. p.7). Literary search listings under the heading of "Glaucoma" in the index medicus for the past five years alone will show publications in excess of 2000. Clearly, if glaucoma was a disease entity that had been thoroughly conquered, the amount of interest in it would be a fraction of what it is.

So, you ask, what is so difficult about diagnosing glaucoma that anyone would benefit from yet another test or procedure. Isn't it as simple as pressures, cups, fields and history? Many would argue that it is not. Tomita et al. wrote about the possibility of glaucomalike disks without increased IOP or visual field loss (otherwise referred to as physiologic cups) being the precursor to primary open-angle glaucoma. In their study the patients with physiologic cups had a greater percentage of family history of glaucoma than did the group with glaucoma (Tomita p. 499). In consideration of the cup sizes, Parrow et al. proved with the aid of objective measuring techniques that the size varies significantly with the change in IOP (Parrow p. 36). In effect, reversal of the cupping. On the topic of normalcy of visual fields, Tuulonen et al. wrote,

> "It seems that the currently used routine threshold programs of automated perimeters are not always optimal or sensitive enough to detect early functional damage in the central area of the visual field."

They argue the point of an absolute scotoma which "could be hidden between the 3 degree and 9 degree test points in Humphrey 30-2 program." Tuulonen states further in this article that without photography, accurate diagnostics and follow-up is not possible. (Tuulonen, p. 596)

Of all the possible subtopics in the study of Glaucoma, not surprisingly, much attention has been given to the etiology and pathogenesis. Joanne Klopfer and Sarah Paikowsky in their chapter, "Epidemiology and Clinical Impact of the Glaucomas," of Lewis and Fingeret's text, Primary Care of the Glaucomas, have classified the risk factors into the two basic categories of ocular and non-ocular risk factors (see below). For each category they have adopted a relative value scheme which is based on the works of many (such as the Framingham, Ferndale, St. Lucia, Baltimore and Collaborative Glaucoma Studies to name a few). In this retrospective study, the predictive value of the mydriatic provocative testing is weighed against these accepted relative values of risk for glaucoma.

TABLE 2–3. NON-OCULAR RISK FACTORS

Risk Factor	Risk Factor Strength	Description	Incidence Studies	Prevalence Studies	Other Supporting Studies
Age	++++	Increasing risk with increasing age	Collaborative Glaucoma Study, U.S.[32]	Ferndale, Wales[16] Framingham, U.S.[5,20] St. Lucia, West Indies[24] Baltimore, U.S.[4]	
Race					
Asians	+	Decreased risk with Eskimos, Zuni Indians	Eskimos[34] Zuni Indians[35] Chinese[36]	Jamaica[23] St. Lucia, West Indies[24] Baltimore, U.S.[4]	Wilson[41] Katz[42] Coulehan[43] Wilson[44]
Eskimos					
Zuni Indians					
Whites	++		Japanese[37]		
Blacks	+++	Increased risk with blacks	Polynesians[38] Melanesians[39]		
Sex					
Women > men	+/−	Not a strong risk factor	Finland Hospital Discharge[26] Dalby, Sweden[27]	Finland Medical Registry[26] St. Lucia, West Indies[24] Framingham, U.S.[21]	
Men > women					
Men = women			Ferndale, Wales[20] Baltimore, U.S.[4] Collaborative Glaucoma Study, U.S.[32]		
Family History of POAG	++	Increased risk with confirmed diagnosis of family members		Finnish Twin Cohort Study[52] Baltimore, U.S.[4] Collaborative Glaucoma Study, U.S.[32]	Miller[51] Wilson[41]
Systemic Health					
Diabetes	+	Increased risk with diagnosis of diabetes mellitus	Armstrong[53]	? Framingham, U.S.[21,22]	Wilson[41] Morgan[58] Reynolds[59] Katz[60]
Hypertension	?			? Framingham, U.S.[54]	Klein[45] Leske[61] Wilson[41] Leighton[62]
Cigarette Smoking	+/−				Katz[60] Morgan[58]
Alcohol Use	+/−			Framingham, U.S.[22]	Katz[60]
Working Indoors	+/−				Morgan[58]

TABLE 2–4. OCULAR RISK FACTORS

Risk Factor	Risk Factor Strength	Description	Incidence Studies	Prevalence Studies	Other Supporting Studies
IOP	++++	Increasing risk of POAG with increasing IOP	Collaborative Glaucoma Study, U.S.[25,32] Dalby Sweden[66] Norway[63]	Framingham, U.S.[5] Baltimore, U.S.[64]	Sommer[65] Quigley[67] Epstein[70] Kass[71] Katz[72]
Optic Nerve Head					
Vertical elongation	+	Good predictor of POAG			Weisman[78]
Neuroretinal tissue loss	+				Fazio[82] Airaksinen[80]
Increased volume or cup excavation	+				Fazio[82]
Asymmetrical cup-to-disc ratio	+		Yablonski[79]		Cartwright[83] Crichton[85]
Nerve Fiber Layer					
Loss or defect	+		Sommer[63]		
Splinter hemorrhage	+		Diehl[84]	Bengtsson[85]	Airaksinen[86] Bengtsson[87] Drance[88]
Myopia	+/−		Collaborative Study, U.S.[92]		David[89] Lotufo[91]

Approximately one quarter of the files of the GROPC Eye Clinic were randomly surveyed to select the data from those individuals who experienced a post dilation IOP increase of at least 5 mm Hg. It should be noted that the unique nature of the GROPC patient population precludes universal generalizations of the risk factors with respect to gender and age. The majority of patients that were examined in the Eye Clinic were poor, medically indigent individuals who in many cases were suffering from system disorders.

Of the 711 files reviewed, eight were selected for meeting the criteria of a post dilation IOP spike of at least 5 mm Hg. The range of spike was from 5 to 36 mm Hg. The median was 20.5 mm Hg with the average spike being 13.625 mm Hg above the predilation pressure. The following is a case by case breakdown using table 2-5 and 2-6 from Lewis and Fingeret for relative values of ocular and non-ocular risk factors (Lewis/Fingeret p.15). Not included in these risk factors was the obvious prior diagnosis of glaucoma.

TABLE 2–5. RELATIVE VALUES OF NON-OCULAR RISK FACTORS

Risk Factor	Noted
Diabetes	
Confirmed diagnosis	+
Family History of Glaucoma	
Recalls family history	+
Reliable information about family member(s) diagnosed and treated for POAG	++
Race	
Hispanic, South American, mixed background	
Asian, Eskimo, American Indian	+
White	++
Black	+++
Age	
40–49 years	+
50–59 years	++
60–69 years	+++
>70 years	++++

Scale: + minimum risk, ++ moderate risk, +++ high risk, ++++ highest risk.

TABLE 2–6. RELATIVE VALUES OF OCULAR RISK FACTORS

	Noted
Cup-to-disc Asymmetry (≥0.2)	
Between the two eyes	+
Nerve Fiber Layer Appearance	
Defect or loss	+
Splinter hemorrhage	+
Optic Nerve Head Appearance	
Vertical elongation	+
Neuroretinal rim loss (thinning or notch)	+
Increased volume or excavation	+
Visual Fields	
Borderline threshold field	+
Suspicious nasal step or arcuate threshold defect	++
Repeated threshold defect	+++
Intraocular Pressure	
≤20 mm Hg	
21–23 mm Hg	+
24–26 mm Hg	++
27–29 mm Hg	+++
≥30 mm Hg	++++

Scale: + minimum risk, ++ moderate risk, +++ high risk, ++++ highest risk.

Clinical evaluation of ocular risk factors included the following.

1) Stereoscopic fundus evaluation using a 78 diopter lens and/or fundus contact lens in conjunction with a biomicroscope to evaluate the optic nerve head for elongation neuroretinal rim loss, increased volume or excavation and the cup to disc (CD) ratio between the two eyes.

2) Slitlamp mounted Goldmann Tonometry, Perkins Tonometry or Reichert Non Contact Tonometry.

3) Humphrey Visual Field (HVF) Analyzer utilizing Central 30-2 fastpak or full threshold strategies.

4) From the patient records and history, information regarding the confirmed diagnosis of diabetes mellitus, family history of glaucoma, race and age were obtained.

5) Additional information included von Herrick (vH) anterior chamber angle evaluation, and when performed gonioscopic angle evaluation and any glaucoma medication that may have been prescribed during the time period of the IOP spike.

Case 1

The first patient was a 73 year old white, diabetic, male with a history of POAG who experienced post dilation IOP spikes on 8-20-93 and on 11-18-93 of 6 mm Hg and 8 mm Hg respectively. This patient had a CD ratio asymmetry greater than or equal to .2, vertically elongated ONH's and borderline threshold HVF results. The IOP had reached the 21 to 23 mm Hg range. No noted family history of glaucoma was noted. A careful vH angle evaluation indicated a deep anterior chamber angle with the Ciliary Body clearly visible on gonioscopy.

Case 2

Case number two was a 67 year old white male, nondiabetic, non glaucoma, non glaucoma suspect patient with a family history of glaucoma. He presented with elongated ONH's and symmetrical CD's, suspicious nasal step HVF's and IOP's in the 21 to 23 mm Hg range. This patient experienced a post dilation IOP spike of 7 mm Hg on 7-30-93. His vH angles were narrow yet gonioscopy showed the angles to be open to the Trabecular Mesh (TM) OD and to the Scleral Spur (SS) OS. Questionable iris plateau configuration was suggested.

Case 3

The third patient was a 67 year old white diabetic male who was being observed as glaucoma suspect. There was an asymmetry of at least .2 in the CD's with vertical elongation, neuroretinal rim loss and increased cup volume. The fields were borderline and the IOP range was below 20 mm Hg. The post dilation IOP spike was 6 mm Hg on 11-18-93. Von Herrick evaluation revealed narrow angles. Gonioscopy was not preformed.

Case 4

On 3-26-93, the fourth patient, a 57 year old white diabetic glaucoma patient, experienced an IOP spike of 19 mm Hg OS post dilation. This patient had a positive family history for glaucoma. Asymmetry between the CD's was greater than .2 and this patient had a suspicious nasal step defect with HVF testing. The IOP range was 27 to 29 mm Hg. The vH evaluation was grade 1; gonioscopy showed SS inferiorly. Iris plateau configuration was again suspected. This patient was taking Betoptic .5% and Carbachol .3%.

Case 5

Patient number five was a 60 year old diabetic, non glaucoma, non glaucoma suspect, white male with no family history of glaucoma. On 7-19-93 this patient experienced a post dilation IOP increase of 5 mm Hg. The vH angle evaluation was narrow OU; the gonioscopic evaluation discovered TM 360 degrees. Asymmetry between the CD's was estimated to be greater than .2 with vertical elongation, neroretinal rim loss and increased excavation of the ONH's. The HVF test showed a suspicious arcuate threshold deficit. The IOP range was noted to be less than 20 mm Hg.

Case 6

The sixth patient was a 73 year old white male with a positive history of diabetes, glaucoma, and a family history of glaucoma. On 7-7-93, this patient's IOP spiked 23 mm higher on the mercury after dilation. Glaucoma medications included pilocarpine 4% and Betoptic .%5. The records noted a prior angle closure on 4-5-93. The CD's were within .2. The record was incomplete with regard to the ONH presentation. HVF results were "within normal limits".

The IOP range recorded was 30 mm Hg. The vH evaluation revealed a narrow anterior chamber; gonioscopy, TM only structure seen from 4:00 to 8:00.

Case 7

This 71 year old non diabetic glaucoma patient experienced a post dilation IOP spike on 3-8-93 of 36 mm Hg. No family history of glaucoma was reported. Pilocarpine 4% and Betoptic .5% were presently prescribed. The CD's were .2 mm apart with vertically elongated ONH's. A suspicious nasal step defect was noted with HVF testing. The high end of the IOP range recorded was obviously greater than 30 mm Hg. The vH evaluation discovered grade 1+ angles OU with only the anterior most TM visible from 3:30 to 8:30. Again iris plateau configuration was suspected.

Case 8

The final patient to qualify in this study was a 70 year old black male glaucoma suspect. There was neither a history of diabetes nor a family history of glaucoma. The CD's were symmetrical and no OHN elongation, neroretinal rim loss or increased excavation was observed despite repeatable field losses. The IOP range was between 24 and 26 mm Hg. The vH angle evaluation revealed narrow a anterior chamber angle. Gonioscopy showed the Line of Schwalbe from 5:00 to 7:00. Iris plateau configuration was suspected. Trials of Betoptic .5% were noted in the record on twice prior.

The table below shows an overview of the risk factors possessed by each of the eight subjects.

Risk Factors	Case Number							
	1	2	3	4	5	6	7	8
<u>Ocular</u>								
c/d asymmetry >.2	+		+	+	+		+	
NFL appearance	-	-	-	-	-	-	-	-
Visual Fields	+	+	3+	3+	3+		+	3+
IOP	+	2+		3+		4+	4+	2+
<u>Non Ocular</u>								
Diabetes	+		+	+	+	+		
Family Hx Glauc.		+		2+		2+		
Race	2+	2+	2+	2+	2+	3+	2+	3+
Age	4+	3+	3+	2+	3+	4+	3+	4+
<u>Other</u>								
Plateau Iris like		?		?		?	?	?
Dx of Glaucoma				G		G	G	
Dx of Gluac. Susp.			GS					GS
Topical Miotics				M		M	M	
Topical Beta Blockers				BB		BB	BB	BB
IOP Spike	8	7	6	19	5	23	36	5

Suspected interaction between pilocarpine and phenylephrine may explain the post dilation IOP spikes in those individuals so being treated for glaucoma. A quick review of iris musculature vector analysis will explain the suspected pupillary block scenario. Support for this interaction is provided with recent investigations into pilocarpine phenylephrine provocative testing (PPPT) reliability (Wishart, P.K. 615).

Disqualifying three of the eight subjects, numbers 4,6,7, for use of miotics leaves five subjects from which any conclusions may be drawn. Correlation of post dilation IOP spike and the diagnosis of glaucoma suspect was positive for subjects number 3 and 8. Subject number 5, despite the lack of the same diagnosis at the time of this study, has demonstrated repeatable visual field defects and c/d asymmetry in the absence of raised IOP's which raises the question of normal tension glaucoma. Subject number 2 similarly could loosely be classified as glaucoma suspect simply for borderline visual fields and higher than "normal" IOP's. Case number 1 displayed asymmetric c/d's >.2, borderline IOP's and visual fields. If case 1 is not glaucoma suspect he may so present in the near future.

This study was less than ideal for many reasons. Documentation of the dilating drops used was not always provided. As mentioned earlier, the patient population was skewed. The criteria for checking post dilation pressures was not standardized for all patients. Another source of discrepancy comes from using the Reichert NCT and Goldmann applanation tonometry interchangeably.

Glaucoma can be a tricky diagnosis to make in the early stages. Once the call is made, the patient more times than not is given a life sentence of topical glaucoma medications. Ball et al. reported in late 1991 that the average cost per year for Timoptic in a 5 mL bottle was $102 and $163, based upon location. Keeping in mind the age and the employment status of the population that is most likely to acquire glaucoma, it is easy to understand the burden this disease can present. For this reason alone many practitioners are hesitant to make the diagnosis (start treatment) until the patient is nearly symptomatic.

As a definitive test of glaucoma, the mydriatic provocative test is of little value. As a test which provides another piece of the puzzle it is of questionable value. Further evaluation mydriatic provocative testing is warranted.

Work Cited

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