Is Routine Pupil Dilation Safe among Asian Patients with Diabetes?

Gavin S. Tan,[1,2] *Ching-Yee Wong,*[1,2] *Tien Yin Wong,*[1,3,4,5] *Chitra V. Govindasamy,*[1] *Edmund Y. Wong,*[1] *Ian Y. Yeo,*[1] *and Tin Aung*[1,3,4]

PURPOSE. To investigate the risk of acute angle closure (AAC), changes in intraocular pressure (IOP), and factors associated with these outcomes after routine pupil dilation in a cohort of Asian subjects with diabetes mellitus.

METHODS. The study was a prospective observational case series of 1910 consecutive Asian subjects newly referred for assessment of diabetic retinopathy at a tertiary clinic. All subjects underwent routine pupil dilation unless there was a prior history of angle-closure glaucoma. Noncontact air-puff tonometry was used to assess IOP, which was measured by the same observer before and 1 hour after pupil dilation. Subjects were assessed for signs and symptoms of AAC before leaving the clinic, and their charts were also subsequently reviewed for revisits with AAC.

RESULTS. Of the 1910 subjects who participated, none developed AAC. Sixty-nine subjects (3.6%, 95% CI: 2.8%–4.5%) showed an increase in IOP of ≥ 5 mm Hg in the either eye, 37 subjects (1.9%, 95% CI: 1.4%–2.6%) had a postdilation IOP >25 mm Hg in either eye, and only 10 subjects (0.52%, 95% CI: 0.25%–0.96%) had an increase in IOP ≥ 5 mm Hg and had a postdilation IOP >25 mm Hg in either eye. The level of predilation IOP and a known history of glaucoma were significant risk factors for a postdilation IOP ≥ 25 mm Hg.

CONCLUSIONS. In this cohort of Asian persons with diabetes, the risk of AAC was insignificant after routine dilation of pupils for fundus examination. These data substantiate the safety of routine dilation of pupils in Asian patients with diabetes. (*Invest Ophthalmol Vis Sci.* 2009;50:4110–4113) DOI:10.1167/iovs.08-2745

The routine examination of the retina in subjects with diabetes mellitus is important for the detection of diabetic retinopathy, a major cause of blindness in working adult people worldwide.[1,2] It is known that pharmacological dilation of the pupils results in twice the sensitivity of detection of diabetic retinopathy compared with an undilated clinical retinal examination.[3] Pupil dilation, however, carries a potential risk of acute angle closure (AAC).[4] In addition, pupil dilation can cause a significant increase in intraocular pressure (IOP), with some studies suggesting an IOP increase of 5 mm Hg or more in up to one third of subjects after dilation, especially among those with a history of glaucoma.[5,6]

Epidemiologic studies in white populations suggest the risk for AAC after pupil dilation is low. In the Rotterdam study, use of mydriatic eye drops in 6750 Caucasian people aged 55 and over resulted in AAC in only 2 (0.03%) individuals.[7] No cases of AAC cases were found in the Baltimore Eye Survey where 4870 people underwent pupil dilation, although subjects identified as having a shallow anterior chamber configuration were excluded.[8] Routine pupil dilation of 3654 people in the Blue Mountains Eye Study also did not result in any cases of AAC.[9] In Asian people, the risk of AAC has been suggested to be higher than in whites.[10] However, in the Tanjong Pagar Study of 1232 Chinese Singaporeans, no subject developed AAC after mydriasis, although subjects judged to have occludable angles were given prophylactic oral acetazolamide.[11]

It has been hypothesized that the risk of AAC after pupil dilation may be higher in Asian patients with diabetes mellitus, as diabetic persons have been shown to have shallower anterior chambers.[12,13] This subject is of substantial public health importance in Asia in view of the increasing prevalence of diabetes and the high prevalence of vision-threatening diabetic retinopathy.[14] However, there are no studies in which the risk of AAC from after routine pupil dilation has been evaluated in Asian patients with diabetes. The purpose of this study was to investigate the risk of AAC, changes in IOP and factors associated with these outcomes after routine pupil dilatation in a large cohort of Asian subjects with diabetes attending a tertiary retinopathy clinic in Singapore, a country with a high prevalence of diabetes, narrow angles, and angle-closure glaucoma.[11]

METHODS

The study was a prospective observational case series of 2004 consecutive patients newly referred for assessment of diabetic retinopathy at a tertiary diabetic retinopathy clinic at the Singapore National Eye Centre over a period of 14 months (June 2005–July 2006). The study protocol had the approval of the institutional ethics committee and was performed in accordance with the Declaration of Helsinki.

In all subjects, pupils were dilated with 1% tropicamide and 2.5% phenylephrine unless there was a prior history of angle-closure glaucoma. The 2.5% phenylephrine was omitted if the subject reported a history of hypertension or cardiac problems. Noncontact air-puff tonometry (model CT-80; Topcon Corp., Tokyo, Japan) was used to assess IOP, which was measured by the same observer before and 1 hour after pupil dilation (defined as a pupil size >5 mm). Clinical information collected included age, race, family history of glaucoma, history and duration of hypertension, duration of diabetes mellitus, HBA1c reading (if present), visual acuity, and vertical cup-to-disc ratio. Subjects who were found to have an IOP increase of ≥ 5 mm Hg 1 hour after pupil dilation had IOP remeasured by Goldmann applanation tonometry. These subjects were subsequently referred to the Glaucoma Service for further evaluation.

Before leaving the clinic, all subjects were advised and given information on the signs and symptoms of an AAC episode that would

TABLE 1. Demographics of Study Participants

	All	Men	Women
Age, mean (SD)	63.5 (11.3)	62.4 (10.9)	64.6 (11.5)
Ethnicity			
Chinese	1459 (76.4)	657 (73.7)	802 (78.7)
Malay	230 (12.0)	110 (12.3)	120 (11.8)
Indian	204 (10.7)	115 (12.9)	89 (8.7)
Other	17 (0.9)	9 (1.0)	8 (0.8)

Ethnicity data are *n* (%).

require them to seek treatment, as well as contact numbers and information on where they should go for treatment. Hospital charts were reviewed for any subsequent visits, specifically for signs and symptoms of AAC, defined as the presence of the following: periocular pain, conjunctival hyperemia, shallow anterior chamber, corneal epithelial edema, mid-dilated pupil, closed angles on gonioscopy, and IOP ≥28 mm Hg.

Rates of AAC or rise in IOP ≥5 mm Hg in either eye were calculated for the whole group of participants. Logistic regression models were used to determine risk factors for an IOP increase of ≥5 mm Hg and a postdilation IOP of >25 mm Hg (outcome), while controlling for age and sex. Linear regression models were used to determine factors associated with mean change in IOP (outcome), while controlling for other factors. All analysis was performed in commercial software (SPSS statistical package, ver. 12.0; SPSS Inc., Chicago, IL).

RESULTS

A total of 2004 consecutive new patients were enrolled. Ten were excluded because they had a previous history of angle-closure glaucoma or declined participation. A further 84 subjects did not complete the protocol (mainly because IOP was not checked after pupil dilation) and were excluded from data analysis. For the remaining 1910 subjects who completed the study, the mean age was 63.6 (±11.3) years, and there were 891 (46.6%) men. The ethnic breakdown of the study subjects was 76.4% Chinese (*n* = 1459), 12.0% Malay (*n* = 230), 10.7% Indian (*n* = 204), and 0.9% other (*n* = 17) (Table 1).

Postdilation IOP was significantly lower than predilation IOP in both eyes (Fig. 1). The mean predilation IOP in the right eye was 15.5 (±3.8) mm Hg and the mean postdilation IOP was 15.0 (±3.8) mm Hg (*P* < 0.001). In the left eye, the mean pre- and postdilation IOP was 15.9 (±3.8) and 15.4 (±3.8) mm Hg, respectively. (*P* < 0.001; Fig. 2). There was a high correlation of within-subject IOP measurements between the eyes (correlation coefficient of 0.791, *P* < 0.001 for predilation IOP; 0.790, *P* < 0.001 for postdilation IOP).

None of the subjects who underwent routine pupil dilation developed AAC (including chart review). There were 69 subjects (3.6%, 95% CI: 2.8%–4.5%) who showed an increase in IOP of ≥5 mm Hg in either eye but did not have signs of AAC (Table 2), and there were 37 subjects (1.9%, 95% CI: 1.4%–2.6%) who had an increase in IOP to >25 mm Hg. Seventeen subjects (0.9%, 95% CI: 0.5%–1.4%) had an increase in IOP of at least 8 mm Hg in either eye. Only 10 subjects (0.52%, 95% CI: 0.25%–0.96%) had an increase in IOP ≥5 mm Hg and had a postdilation IOP >25 mm Hg in either eye; none of these subjects had signs or symptoms of AAC.

In age- and sex-adjusted logistic regression analysis, age, sex, ethnicity, predilation IOP, history of glaucoma, and family history of glaucoma were not found to be significant risk factors for an increase in IOP of ≥5 mm Hg (Table 3). In age-and sex-adjusted logistic regression analysis, known history of glaucoma (OR 6.9, *P* = 0.003), and shorter duration of hypertension (OR 0.96, per year of hypertension, *P* = 0.037)
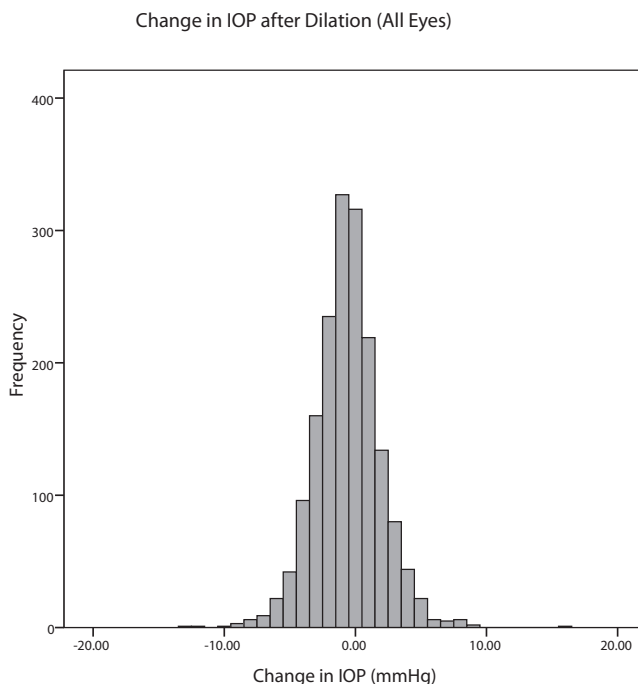

FIGURE 1. Histogram of change in IOP after pupil dilation in all eyes.

were significant risk factors for postdilation IOP >25 mm Hg (Table 3). In multivariate analysis of these risk factors, excluding predilation IOP, only a known history of glaucoma (OR = 7.09, 95% CI: 1.94–25.85, *P* = 0.003) was still found to be significant. There were no significant risk factors found for an increase in IOP of 8 mm Hg or more.

Of the 69 subjects with an increase in IOP ≥5 mm Hg, 3 were lost to follow-up. Glaucoma was diagnosed in only 12 (18.2%) of the remaining 66 subjects. Of these, two received a diagnosis of primary angle-closure glaucoma, five had primary open-angle glaucoma, two aphakic glaucoma, one pseudoex-
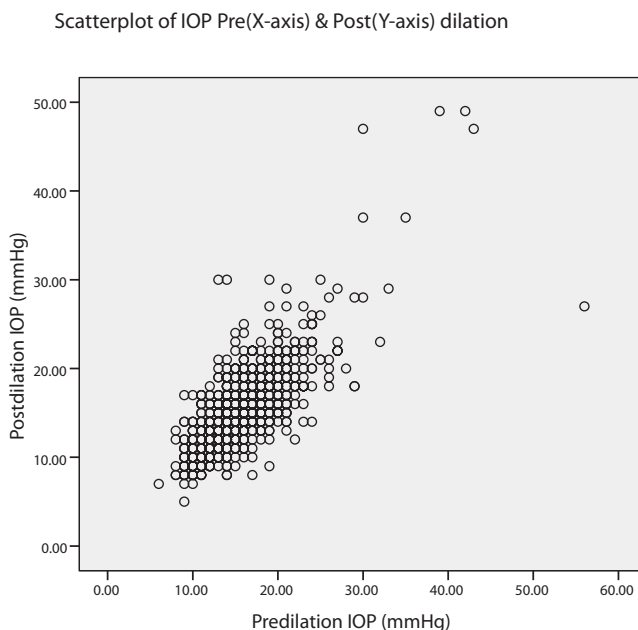

FIGURE 2. Scatterplot of mean IOP before and after pupil dilation in all eyes.

TABLE 2. Change in IOP after Dilation and Postdilation IOP

	Postdilation IOP		
	≤25 mm Hg	>25 mm Hg	Total
Change in IOP <5 mm Hg	1814 (95.0%)	27 (1.4%)	1841 (96.4%)
Change in IOP ≥5 mm Hg	59 (3.1%)	10 (0.5%)	69 (3.6%)
Total	1873 (98.1%)	37 (1.9%)	1910 (100%)

foliation glaucoma, one uveitic glaucoma, and one rubeotic glaucoma. In addition, there were three subjects with closed angles but without glaucomatous optic neuropathy.

DISCUSSION

In this study of almost 2000 subjects, we found that the risk of AAC was low after routine dilation of pupils in subjects with diabetes. Our study included Asians of various ethnicity, including Chinese, Indians, and Malays, and was performed in a population where there is a high incidence of AAC[15] and where angle-closure glaucoma is an important cause of blindness.[11,16,17] Our findings are thus consistent with other studies in the general population that demonstrated that the risk of AAC after pupil dilation was low (0%–0.03%).[7,8,11] We also found that a low number of subjects developed an increase in IOP of 5 mm Hg or greater or had postdilation IOP of >25 mm Hg in either eye. These data substantiate the safety of routine dilation of pupils among Asian subjects with diabetes mellitus.

A routine retinal examination through a dilated pupil has been shown to be far more sensitive for detection of diabetic retinopathy than that conducted with a nondilated pupil.[3] However, surveys have found that few physicians and general practitioners dilate pupils even when assessing patients at high risk for diabetic retinopathy,[18] as there is concern and uncertainty regarding the risk of AAC from pupil dilation. This concern is heightened when general practitioners manage Asian patients, given the perception that the risk of AAC is higher in Asians. With the growing number of Asians with diabetes,[19] our findings that the risk of AAC after pupil dilation is minimal is of significance not only in Asia, but in other countries with increasing communities of Asian people, further supporting the benefits of routine dilated retinal examination among diabetic patients regardless of racial and ethnic background.

We also evaluated changes in IOP after pupil dilation and found both increased and decreased IOP. Changes in IOP in eyes after pupil dilation would be the net result of changes in aqueous inflow and outflow mechanics. Angle crowding by the iris after pupil dilation may decrease aqueous outflow, leading to an increase in IOP. The cause of IOP reduction with pupil dilation is unknown. We speculate that mydriatics drugs may affect the tone of the ciliary body and uveoscleral outflow with a small decline in IOP in some eyes. Although there was a mean reduction in IOP after pupil dilation, the absolute difference of 0.5 mm Hg is small and is likely to be of limited clinical significance.

In our study, 3.6% of subjects had an IOP increase of ≥5 mm Hg and less than 2% had a postdilation IOP of >25 mm Hg. Only three subjects in our study demonstrated a large change (>10 mm Hg) in IOP after dilation, far fewer than in previous studies in which a significant rise in IOP was found in 10% of retina patients[5] and in up to 32% of open-angle glaucoma patients,[6] but with much smaller sample sizes. Furthermore, only 10 (0.5%) subjects with a significant IOP increase of ≥5 mm Hg after dilation had a postdilation IOP of >25 mm Hg. Our findings therefore suggest that the clinical risk from an undetected increase in IOP after dilation in this sample was small. However, in patients with glaucoma and eyes already compromised by increased IOP, there is a greater risk of significantly increased postdilation IOP that may result in a clinically significant effect on an already compromised optic nerve head. An increase in IOP after pharmacologic dilation has also been shown to be related to the likelihood of progression of glaucoma in patients with open-angle glaucoma.[20] In these patients, there may be some value in checking IOP after diagnostic mydriasis.

We did not find any risk factors for developing an increase in IOP ≥5 mm Hg, while a known history of glaucoma and predilation IOP > 21 mm Hg were risk factors for postdilation IOP > 25 mm Hg, suggesting that ascertainment of predilation IOP and a history of glaucoma would be useful as safety checks before routine dilation of pupils. In our study, we excluded only those with a known history of angle-closure glaucoma; thus, the risk of IOP change and AAC after pupil dilation in this group of patients was not evaluated. Other studies have also advocated screening for history of glaucoma as well as the presence of shallow anterior chambers on penlight examination when performing routine dilation to reduce the incidence of AAC.[7] Both of these can be easily performed by a nonophthalmologist in a primary care setting. Even in large eye clinics or centers attended by a large number of patients with diabetic

TABLE 3. Risk Factors for Change in IOP ≥5 mm Hg after Dilation and Postdilation IOP >25 mm Hg, Age, and Sex-Adjusted

	Change in IOP ≥5 mm Hg after Dilation			Postdilation IOP >25 mm Hg		
	OR	95% CI	P	OR	95% CI	P
Age, per year	1.02	1.00–1.05	0.060	0.98	0.95–1.00	0.072
Women	1.23	0.75–2.02	0.406	0.69	0.36–1.34	0.276
Ethnicity						
Chinese	1.00	—	—	1.00	—	—
Malay	1.15	0.56–2.36	0.715	1.55	0.66–3.61	0.312
Indian	0.87	0.37–2.06	0.749	0.70	0.21–2.33	0.555
Predilation IOP > 21 mm Hg in either eye	1.49	0.67–3.32	0.334	—	—	—
History of glaucoma	1.27	0.17–9.53	0.822	6.91	1.94–24.63	0.003
Family history of glaucoma	0.00	0.00–0.00	0.999	0.00	0.00–0.00	0.999
History of hypertension	1.39	0.79–2.45	0.258	0.96	0.48–1.93	0.914
Duration of hypertension, per year	1.00	0.99–1.01	0.940	1.01	1.00–1.02	0.037
Duration of diabetes, per year	1.00	1.00–1.00	0.801	1.00	1.00–1.00	0.462
Recent HbA1c, per 1%	0.89	0.63–1.26	0.503	0.77	0.53–1.11	0.159

retinopathy, it may be safe to routinely dilate the pupils after making such safety checks. In future, newer devices such as the scanning peripheral anterior chamber depth analyzer[21] may have value as a noninvasive way of screening for eyes at risk of angle closure before pupil dilation.

Our study had several limitations. First, our incidence of AAC may be an underestimate as we cannot rule out the small chance that there was an unrecognized episode of AAC that occurred in some of our study subjects. In high-risk groups such as elderly Asian women, angle closure maybe asymptomatic.[22] IOP was measured only 1 hour after dilation, and the pupil block in AAC may not occur with dilation but during the reversing phase of pupil constriction which may be several hours later. Although study subjects were educated on the symptoms of AAC and monitored for revisits with AAC, those who developed increased IOP or AAC later may have been missed, especially if they sought treatment elsewhere. The risk of angle closure is known to increase with repeated pupil dilation and it is possible that some subjects would develop AAC after pupil dilation. IOP readings were obtained with a noncontact tonometer rather than Goldmann applanation tonometry. Although the noncontact tonometer has been shown to be accurate and as reliable as the Goldmann tonometer in the assessment of IOP in normotensive subjects,[23] studies have shown poorer reliability and accuracy for IOP measurements above 20 mm Hg.[24,25] Our study only included new referrals for diabetic retinopathy assessment who underwent a single episode of diagnostic mydriasis. Finally, we did not have gonioscopy findings for all subjects in the study, as gonioscopy is not part of routine clinical examination before pupil dilation in patients with diabetes, and we did not investigate for other risk factors for IOP elevation such as biometric measurements of the eye.

In conclusion, we found that the risk of AAC was insignificant after routine dilation of pupils for a retinal examination in Asian patients with diabetes who were of Chinese, Indian, and Malay origin. Only 0.5% of subjects developed an increase in IOP of 5 mm Hg or greater that resulted in a postdilation IOP of >25 mm Hg. Our findings support the safety of pharmacologic pupil dilation in the primary care setting for screening and detection of diabetic retinopathy in Asian subjects, with minimal risk of an adverse outcome.

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