

# Glaucoma Incidence and Treatment

*From the Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting, Fort Lauderdale, Florida, USA, 29 April - 4 May 2001*

## Acute Angle Closure Glaucoma in Singapore

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Dr Friedman presented data from the Singapore Case-control Study of Acute Angle Closure Glaucoma. In this study, performed to identify new risk factors for acute angle closure glaucoma, the contralateral eyes of 65 patients with acute angle closure glaucoma presenting to the Singapore National Eye Center from March 1999 to November 2000 were examined. Detailed slit lamp, ultrasound biomicroscopy, and Scheimpflug evaluations were performed. 220 population-based controls, frequency-matched for age and sex, were examined using the same techniques. Provocative tests, including repeat testing in a dark room and after administration of pilocarpine were also performed.

The mean anterior chamber depth was 2.6 mm for controls versus 1.9 mm for patients ( $p < 0.001$ ). Limbal anterior chamber depth (van Herick) demonstrated moderate screening effectiveness with more than 90% sensitivity and 60% specificity using a cut off of one-quarter corneal thickness. The ultrasound biomicroscopy angle measurements were all significantly less for patients than for controls ( $p < 0.001$ ), but none had ideal screening characteristics. Scheimpflug measurement

of the angle clearly separated patients from controls, with the best images occurring after pilocarpine instillation.

### In Summary

Scheimpflug imaging is a quick and easily performed test that distinguishes the contralateral eyes of individuals with acute angle closure glaucoma from healthy eyes. Pilocarpine provocative tests may further improve the performance of Scheimpflug imaging. Finally, traditional measures of anterior chamber depth and limbal anterior chamber depth also distinguished patients from controls.

Dr Friedman concluded that a screening strategy that combines a simplified examination of the limbal anterior chamber depth with a Scheimpflug assessment of the angle may allow for large-scale screening without a slit lamp.

## Incidence of Open Angle Glaucoma in Melbourne

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A random cluster of 3271 participants (83% of eligible residents) aged 40 years or older were examined to determine the incidence of open angle glaucoma in Melbourne, Australia. Baseline examinations were conducted from 1992 to 1994 and follow-up data were collected from 1997 to 1999.

Each participant underwent a standardised ophthalmic examination, including intra-ocular pressure measurements, visual fields, cup disc ratios, and paired stereo photographs of the optic disc, both at baseline and at follow-up. Glaucoma was assessed by a consensus group of 6 ophthalmologists, including 2 glaucoma specialists. Glaucoma was diagnosed as possible, probable, or definite.

The overall incidence of probable and definite open angle glaucoma was 0.95% (95% CL, 1.55, 3.59) and any open angle glaucoma was 2.57% (95% CL, 0.60, 1.30). The incidence of glaucoma increased significantly with increased age ( $p < 0.001$ ). The incidence of probable and definite glaucoma increased from 0% of participants aged 40 to 49 years to 5.5% of participants aged 80 years and older. The incidence of any type of glaucoma increased from 0.3% of participants aged 40 to 49 years to 11% of participants aged 80 years and older. There was no relationship with gender.

### In Conclusion

The incidence of open angle glaucoma increases significantly with age. Glaucoma is a major cause of visual loss and will become more important as the population ages and the number of elderly people increase.

## Molecular Genetic Basis of Primary Congenital Glaucoma in India

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Dr Panicker presented a study to determine the possible molecular genetic defects underlying primary congenital glaucoma in India and to identify the pathogenic mutations causing this type of childhood blindness. Five consanguineous pedigrees



with a clinically well characterised primary congenital glaucoma phenotype were recruited for genetic study. Leukocyte DNA was obtained from patients and controls and the coding regions of the primary candidate gene CYP1B1 were screened for mutations using polymerase chain reaction followed by direct sequencing, and sequence and restriction fragment analyses.

Five distinct mutations were found in the coding regions of CYP1B1 gene in 8 affected members of 5 consanguineous pedigrees, of which 3 were novel. These included novel frameshift, missense, and known mutations. The frameshift mutation was homozygous, whereas the missense mutations were either homozygous or heterozygous. All are disease-causing mutations since all mutant alleles cosegregated with disease phenotype absent in the healthy population, and mutant residues were conserved. Based on 4 novel restriction enzyme assays, the segregation of mutant alleles in pedigrees and the healthy population were determined. Sequence alignment indicated conservation of mutated residues.

Pseudo-dominant inheritance was noted in 1 family, whereas the other families showed an autosomal recessive mode of inheritance. A frameshift mutation identified by Dr Panicker and colleagues resulted in one of the most devastating primary congenital glaucoma phenotypes known to date. In addition, several polymorphisms of this gene were found, one of which is novel.

### In Summary

This is the first report describing the primary genetic defect underlying primary congenital glaucoma in India. Novel mutations identified in India will help in the understanding of the molecular pathogenesis of this disorder. Novel diagnostic methods are helpful for fast mutation detection, carrier testing, and genetic counselling for at-risk individuals, and also for population

screening. The data derived from this study may help in developing genotype-phenotype correlation.

### Risk Factors for Progression of Ocular Hypertension to Primary Open Angle Glaucoma

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Australia

As a multifactorial disease, glaucoma may be associated with pressure-dependent and pressure-independent factors. Ocular hypertension may develop into primary open angle glaucoma (POAG) in many patients. Dr Landers described a study comparing patients with ocular hypertension with patients with POAG for pressure-dependent and pressure-independent risk factors. A high prevalence of any factor(s) could indicate a contribution to the progression from ocular hypertension to POAG.

438 patients with POAG and with 301 with ocular hypertension were randomly selected and data on age and intraocular pressure at the time of diagnosis, gender, family history of glaucoma, systemic hypertension, diabetes, Raynaud's phenomenon, migraine, and myopia were collected.

Multivariate analysis showed that older age at the time of diagnosis ( $\chi^2 = 73.10$ ; 5 df;  $p < 0.001$ ), myopia (odds ratio [OR], 1.5 [1.02 - 2.2];  $p < 0.05$ ), family history of glaucoma (OR, 1.6 (1.1 - 2.3);  $p < 0.01$ ), and a high intraocular pressure ( $\chi^2 = 13.55$ ; 4 df;  $p = 0.009$ ) were found to be more prevalent among patients with POAG. No other significant differences could be found between the 2 groups.

### In Conclusion

Patients with ocular hypertension may be at higher risk of developing POAG if they have myopia, a family history of glaucoma, or are of older age at the time of diagnosis.

### Influence of Latanoprost on Aqueous Humor Flow

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Dr Vobig described a randomised double-masked clinical study of 42 eyes of 21 patients with primary open angle glaucoma and ocular hypertension. Fluorophotometry and pneumotonography were performed to investigate the effect of latanoprost 0.005% or placebo on aqueous humor flow and total outflow facility in glaucomatous eyes. Patients were given either latanoprost or placebo once in the evening. Fluorophotometry (Fluorotron Master II, OcuMetrics, USA) and pneumotonography (Model 30 Classic Pneumatonometer, Mentor, USA) was performed in 20 eyes of 10 patients (latanoprost group) and 22 eyes of 11 patients (placebo group). Patients with an intraocular pressure (IOP) higher than 28 mm Hg at baseline were excluded. Fluorophotometry, tonography, and IOP were measured at baseline and after 1 and 2 weeks of treatment. Data for right and left eyes were separately analysed using the student's paired *t* test. All patients completed the protocol and IOP significantly decreased by 25% after 2 weeks' treatment with latanoprost ( $p < 0.01$ ; Table 1).

Fluorophotometry measurements showed no difference in aqueous flow over time in both groups. However, the total outflow facility increased significantly in the latanoprost-treated eyes after 2 weeks ( $p = 0.03$ ; Table 1).

### In Conclusion

In accordance with the literature, Dr Vobig and colleagues found a mean 25% decrease in IOP after 2 weeks' treatment with latanoprost. The significant increase in total outflow facility in the latanoprost-treated eyes and the decrease in IOP took place at constant aqueous flow rates. Dr Vobig

**Table 1.** Reduction in intraocular pressure and increase in total outflow facility from baseline for patients receiving latanoprost for 2 weeks.

	Baseline ( $\pm$ SD)	2 weeks ( $\pm$ SD)
<b>Intraocular pressure</b>		
Right eye	23.4 $\pm$ 3.1	17.4 $\pm$ 3.3
Left eye	23.3 $\pm$ 3.1	18.3 $\pm$ 3.6
<b>Total outflow facility</b>		
Right eye	0.146 $\pm$ 0.06	0.30 $\pm$ 0.18
Left eye	0.141 $\pm$ 0.05	0.343 $\pm$ 0.31

concluded that the decrease in IOP with latanoprost therapy is due to an increase in uveoscleral outflow.

### Latanoprost, Brimonidine, and Combination Timolol and Dorzolamide Affects Circadian Intraocular Pressure

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Dr Orzalesi described a randomised cross-over trial to compare 24-hour intraocular pressure (IOP) reduction induced by latanoprost, brimonidine, and a fixed combination of timolol and dorzolamide in patients with primary open angle glaucoma (POAG) and ocular hypertension. Ten patients with POAG and 10 with ocular hypertension were treated with latanoprost, brimonidine, or a fixed combination of timolol and dorzolamide for 1 month. All patients underwent 4 diurnal tonometric examinations — twice at baseline and twice after 1 month of treatment. The IOP was measured 3 hourly with a handheld electronic tonometer, with the patient in the supine and sitting positions, and with a Goldmann applanation tonometer by 2 evaluators. A difference in mean IOP of 2.5 mm Hg was estimated to be clinically relevant. All the drugs significantly reduced IOP compared with baseline at all times except for brimonidine at midnight, 3, and 6 am. Latanoprost was more effective for lowering IOP compared with brimonidine at 3 am and 6 am and at 3 pm, while the

combination of timolol with dorzolamide was more effective than brimonidine in lowering IOP at 3 am and 9 am ( $p < 0.04$ ) and at 3 pm and 6 pm ( $p < 0.05$ ).

#### In Conclusion

Latanoprost and the combination of timolol and dorzolamide provided uniform circadian

IOP reduction, whereas brimonidine was less effective in lowering IOP, particularly during the night.

### Safety and Efficacy of Latanoprost Versus Combination Dorzolamide And Timolol

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Dr Spiegel presented a study comparing the intraocular pressure (IOP) lowering effect of latanoprost monotherapy with the fixed combination of dorzolamide plus



### Compliance in the European Glaucoma Prevention Study

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The objective of this study was to evaluate the compliance of study patients within the ongoing European Glaucoma Prevention Study (EGPS) in order to identify factors interfering with patient compliance and to develop possible strategies to improve compliance. An anonymous compliance questionnaire based on a psychological model (the Health Action Process Approach) was completed by 145 patients. The questionnaire contained 64 questions with the following domains: demographic data (13 questions); medical history and interest in medical issues (11 questions); missing medications and side effects (9 questions); and compliance (31 questions).

In the factor analysis, 5 factors were determined to be essential regarding compliance: importance of prevention in the opinion of the patient; complexity of

the treatment regimen; side-effects and consideration of benefits and disadvantages; social support; and feeling safe in the study.

The results showed that 78.3% of the patients admitted to missing an application of their medication less than once per week (with a dosage regimen of 3 times daily). The reasons for not taking medication were forgetting the application (31%), interfering with job (19%), and stress (6%). The lunchtime dose was the one that was most often missed.

#### In Conclusion

In this study, compliance was defined as not missing applications more than once per week (not more than 5% of all applications). This was fulfilled by 78.3% of the patients. Dr Kersten speculated that this rate of non-compliance was low compared with the estimation of non-compliance with antiglaucoma therapy in the literature, which is between 27% and 59%.

**Table 1.** Mean reduction in diurnal intraocular pressure (IOP) following 3 months' treatment with latanoprost or dorzolamide plus timolol.

	Baseline	Reduction in IOP		Percent of patients with diurnal IOP reduction $\geq$ 20%
		mm Hg	Percent	
Latanoprost	23.2	4.3	19	52
Dorzolamide plus timolol	23.1	4.0	17	43

timolol in patients with IOP uncontrolled by timolol alone.

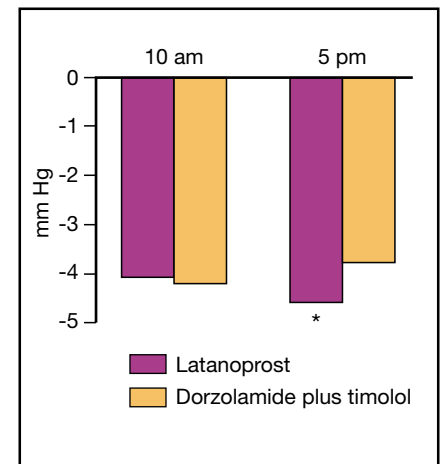
This prospective, multinational, open-label study included patients with unilateral or bilateral open angle glaucoma or pseudo-exfoliative glaucoma currently receiving mono- or dual therapy with a  $\beta$ -blocker. 226 patients with IOP  $\geq$  21 mm Hg after 3 to 6 weeks of run-in treatment with timolol twice daily were randomised to receive latanoprost once daily in the evening or dorzolamide and timolol twice daily. Diurnal IOP was measured at 10 am and 5 pm, at baseline and after 3 months of treatment.

205 patients (latanoprost, n = 103; dorzolamide and timolol, n = 102) were included in the per-protocol analysis. At baseline, the mean diurnal IOP was similar

among patients given latanoprost and dorzolamide plus timolol. After 3 months, least square mean analysis showed both treatments resulted in a statistically significant reduction in diurnal IOP ( $p < 0.001$ ; Table 1). The IOP lowering effects of the treatments were not statistically different based on the 95% confidence interval (-1.1, 0.4 mm Hg) for the difference in mean diurnal IOP reduction between the groups. However, the percentage of patients achieving diurnal IOP reduction  $\geq$  20% was higher in the latanoprost-treated group compared with the dorzolamide and timolol-treated group (Table 1).

Mean IOP reductions at 10 am and 5 pm were statistically significant in both groups ( $p < 0.001$ ; Figure 1). At 10 am, the 2 treatments had a comparable IOP

**Figure 1.** Mean intraocular pressure reductions following treatment with latanoprost or dorzolamide plus timolol. \*  $p = 0.045$ .



lowering effect, while at 5 pm, latanoprost showed a significantly higher IOP reducing effect ( $p = 0.0454$ ). Both medications were well-tolerated.

### In Conclusion

Monotherapy with latanoprost once daily is at least as effective as twice daily treatment with dorzolamide and timolol for patients with IOP uncontrolled by timolol alone.

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