

# The Importance of Intraocular Pressure Lowering

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## Relationship Between Intraocular Pressure and Glaucomatous Optic Neuropathy

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Elevated intraocular pressure (IOP) is a major risk factor for the development of glaucomatous optic neuropathy. Lowering IOP has been shown to be a beneficial form of therapy for patients with primary open angle glaucoma (POAG). Dr Singh presented a review and meta-analysis of completed and ongoing epidemiological studies analysing the relationship between IOP and POAG.

Several large-scale epidemiological studies have shown that the relationship between IOP and the prevalence of POAG is positive and continuous without an inflection point, even when IOP is in the normal range. Diurnal fluctuation in IOP makes a single IOP measurement a poor screening parameter for POAG. Glaucoma treatment studies have shown that IOP lowering in eyes with known glaucomatous visual field loss and optic nerve damage decreases the rate of disease progression. Large diurnal variation in IOP may be an independent risk factor for glaucomatous visual field progression.

Dr Singh concluded that, while the level of IOP is often not critical in making the diagnosis of open angle glaucoma, it remains the only proven modifiable variable

in the treatment of the disease. Treatment modalities that lower IOP and minimise peak and trough fluctuations in IOP are most likely to halt the progression of glaucomatous optic neuropathy.

## Importance of Uniform Circadian Intraocular Pressure Control

Dr S Asrani,  
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Dr Asrani presented a study of the risk associated with diurnal intraocular pressure (IOP) variations among patients with open angle glaucoma. Sixty four patients (105 eyes) with open angle glaucoma with an office IOP of less than 25 mm Hg performed home tonometry for a mean follow-up period of 4 years. Baseline status and time to progression of visual field loss were identified from the clinical records. The level and variability of diurnal IOP obtained using home tonometry were characterised.

Although the mean home IOP and baseline office IOP were similar (Table 1), the average diurnal range was  $10.0 \pm 2.9$  mm Hg. The baseline office IOP had no predictive value (relative hazard: 0.98). The diurnal IOP range and the IOP range over multiple days were significant risk factors

**Table 1.** Mean office- and home-tested intraocular pressure and diurnal range.

|                           | Baseline office (mm Hg) | Home (mm Hg) |
|---------------------------|-------------------------|--------------|
| Mean intraocular pressure | 17.6 ± 3.2              | 16.4 ± 3.6   |
| Diurnal range             |                         | 10.0 ± 2.9   |

for progression, even after adjusting for office IOP, age, race, gender, and visual field damage at baseline. 88% of patients in the upper 25th percentile of IOP fluctuation, and 57% of patients in the lower 25th percentile of fluctuation, progressed within 8 years.

In conclusion, in glaucoma patients with an office IOP within the normal range, large fluctuations in diurnal IOP are a significant risk factor independent of parameters obtained in the office.

## Latanoprost Versus Brimonidine

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The efficacy and safety of 0.005% latanoprost once daily was compared with 0.2% brimonidine twice daily for patients with unilateral or bilateral open angle glaucoma or ocular hypertension with an intraocular pressure (IOP) of more than 20 mm Hg currently receiving monotherapy or dual therapy. 379 patients were enrolled in this 6-month, randomised, observer-masked multicentre study after an appropriate wash-out period. The morning IOP (10 am) was recorded 12 hours after the administration of latanoprost and 2 hours after brimonidine administration. The afternoon (5 pm) measurements were recorded 19 hours after latanoprost administration and 9 hours after brimonidine had been given. The mean IOP reduction at 6 months was compared between the treatments.

Forty eight patients withdrew from the study (5 patients receiving latanoprost and 43 from the brimonidine group), with the most common reasons for withdrawal being inadequately controlled IOP (2 vs



12, respectively) and ocular allergy (0 vs 14, respectively). After 6 months of treatment, latanoprost reduced the mean IOP by 7.1 mm Hg (28%) compared with 5.2 mm Hg (21%) for brimonidine. This difference of 1.9 mm Hg was statistically highly significant ( $p < 0.001$ ). A mean reduction of IOP of  $> 30\%$  was achieved by 42% of latanoprost-treated patients compared with 22% of brimonidine-treated patients. Reduction of IOP of less than 15% (non-responders) was recorded by 12% of latanoprost-treated patients and by 32% of brimonidine-treated patients. Systemic adverse events ( $p < 0.001$ ) and ocular allergy ( $p = 0.005$ ) were reported significantly more frequently among the brimonidine treated patients.

## Comparison of Effect of Glaucoma Medications on Circadian Intraocular Pressure

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Dr Orzalesi compared 24-hour intraocular pressure (IOP) reduction induced by timolol, latanoprost, dorzolamide, brimonidine, and a fixed combination of timolol and dorzolamide in patients with primary open angle glaucoma (POAG) and ocular hypertension (OHT).

In 2 cross-over trials, 20 patients with POAG and 20 with OHT were treated

with timolol, latanoprost, dorzolamide, brimonidine, and a fixed combination of timolol and dorzolamide for 1 month. The treatment sequence was randomised. All patients underwent 24-hour tonometric curves: at baseline and after 1 month of treatment with each of the trial drugs. IOP was measured at 3, 6, 9, and 12 am, and at 3, 6, 9, and 12 pm with a handheld electronic tonometer with the patient in the supine and sitting positions, and with a Goldmann applanation tonometer by 2 evaluators masked to treatment assignment. The sample size was estimated assuming a difference in mean IOP of 2.5 mm Hg as clinically relevant.

All the drugs significantly reduced IOP compared with baseline at all times except for timolol at 3 am and brimonidine at midnight, 3 and 6 am. Latanoprost was more effective at lowering IOP than timolol at 3, 6, and 9 am ( $p < 0.03$ ) and at 6 and 12 pm ( $p < 0.05$ ), dorzolamide at 9 and 12 am ( $p < 0.03$ ) and at 3 and 6 pm ( $p < 0.04$ ), and brimonidine at 3 and 6 am and at 3 and 6 pm (Table 1). Timolol was more effective than dorzolamide at noon ( $p < 0.05$ ), while dorzolamide performed better than timolol at 3 am ( $p < 0.05$ ). The combination of timolol with dorzolamide was more effective than brimonidine at 3 and 9 am ( $p < 0.04$ ) and at 3 and 6 pm ( $p < 0.05$ ), and latanoprost at 9 am ( $p < 0.05$ ).

In conclusion, latanoprost and the combination of timolol with dorzolamide seemed to provide uniform circadian IOP

reduction, whereas timolol and brimonidine were less effective at lowering IOP, particularly during the night. Dorzolamide was less effective than latanoprost, although it provided significant nocturnal IOP reduction.

## Dual Therapy Versus Latanoprost Monotherapy

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Dr Pillunat evaluated the efficacy and safety of replacing current dual therapy with latanoprost 0.005% monotherapy for patients with glaucoma. This multinational, prospective, randomised study comprised 466 patients with primary open angle glaucoma. 315 patients discontinued their current therapy and received latanoprost monotherapy while 115 patients continued with the dual therapy for 3 months.

Twenty nine patients receiving latanoprost withdrew from the study, 8 due to adverse events, 5 for non-medical reasons, and 10 due to uncontrolled intraocular pressure (IOP). Of the patients who completed the study, 91% succeeded in reaching the predefined IOP criteria. For those patients who continued with dual therapy, a comparable success rate of 93% was observed. Replacement of dual therapy with latanoprost resulted in a mean IOP change of  $-0.8$  mm Hg from a mean diurnal IOP of 17.9 mm Hg. A mean IOP change of  $-0.2$  mm Hg from a mean diurnal IOP of 17.2 mm Hg was found among patients who continued with their dual therapy.

In conclusion, these results suggest that dual topical glaucoma therapy with multiple dosing can, in many instances, be replaced by latanoprost monotherapy with once daily administration. Moreover, once daily dosing may be advantageous for patients with glaucoma since it simplifies the dosage regimen and may increase compliance.

**Table 1.** Improvement in circadian intraocular pressure following treatment with latanoprost compared with timolol, dorzolamide, brimonidine, and a fixed combination of timolol and dorzolamide.

|       | Latanoprost compared with ... |             |             |  |
|-------|-------------------------------|-------------|-------------|--|
|       | Timolol                       | Dorzolamide | Brimonidine | Fixed combination (timolol, dorzolamide) |
| 3 am  | √                             |             | √           |  |
| 6 am  | √                             |             | √           |  |
| 9 am  | √                             | √           |             | x  |
| 12 am |                               | √           |             |  |
| 3 pm  |                               | √           | √           |  |
| 6 pm  | √                             | √           | √           |  |
| 9 pm  |                               |             |             |  |
| 12 pm | √                             |             |             |  |

