Understanding Individual IOP Response to Treatment with Latanoprost and Timolol

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Purpose

To identify reasons for variable intraocular pressure (IOP) responses to latanoprost (L) and timolol (T) in healthy volunteers and generate the control group for a parallel study of patients with ocular hypertension.

Methods

In this multicenter, randomized, crossover study (NCT01677507), both eyes of healthy subjects (212 eyes, 106 subjects) were treated with latanoprost or timolol for 7 days, with a 6-week washout between treatments. Ocular biometrics (CCT: central corneal thickness, ACv: anterior chamber volume, AxL: axial length, Pev: episcleral venous pressure, AHF: aqueous humor flow, C: outflow facility), tonometry, and aqueous humor dynamics (AHD) assessments were made at baseline and day 8 of each treatment. The 11AM IOPs divided subjects into responders (TR, LR) and non-responders (TnR, LnR), with cutoffs of > 15% or > 10% IOP reduction. Treatment effects and correlations were analyzed using paired t-test ([†] *p*-value for robust (Huber M-estimation) t-test between R and nR groups). Significant (*) at the 0.05 level.

Results

Compared to baseline, 54% response with latanoprost was significantly ($p < 0.01$) greater than 27% response with timolol at > 15% cutoff. Responders had higher mean baseline IOP than non-responders

for both drugs at both cutoffs (all $p < 0.01$). Of the TnR group (n = 56), 39% responded to latanoprost in both eyes, 20% in one eye, and 41% in neither. Among LnR (n = 31), 13% responded to timolol in both eyes, 13% in one eye, and 74% in neither. Twenty-one subjects (42 eyes) failed to respond at the 15% cutoff with either drug, while 9 subjects (18 eyes) failed to respond at the 10% cutoff. More subjects responded to latanoprost than timolol at both cutoffs (n = 14). Latanoprost increased uveoscleral outflow and timolol decreased aqueous flow, and outflow facility. LR had lower baseline uveoscleral outflow than LnR (Table 1).

Conclusions

Subjects with higher baseline IOP responded better to both drugs. Non-responders to timolol were more responsive to latanoprost, but not vice versa. No differences in AHD were associated with an IOP response to timolol. However, low baseline uveoscleral outflow was associated with an IOP response to latanoprost.