Aqueous Humor Dynamic Components that Determine Intraocular Pressure Response and IOP fluctuations

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Purpose

Despite glaucoma clinical trials, guidelines, and experience to reduce intraocular pressure (IOP) for glaucoma, some patients progress to blindness. To address this problem, our purpose is to determine aqueous humor dynamic (AHD) mechanisms that impact IOP outcomes.

Methods

Eye Dynamics and Engineering Network (EDEN) Consortium includes clinicians and scientists at Universities of Michigan, Ohio State, Nebraska and Mayo Clinic. In two randomized trials with crossover treatments of timolol and latanoprost (NCT01677507, NCT04412096), we test the hypothesis that drug responses and IOP fluctuation are determined by AHD factors of aqueous flow, outflow facility, episcleral venous, and uveoscleral flow. Healthy controls (EDEN1) and cases with ocular hypertension (OHT) or early-to-moderate open-angle glaucoma (OAG)(EDEN2) were studied with outcomes of AHD factors, drug response, IOP fluctuations, and ocular perfusion pressure (OPP).

Results

In EDEN1 (92 females/30 males), positional change between supine and sitting IOPs was > 4.7 mmHg

(range 0.5-11.0 mmHg), and between visit asymmetric IOP fluctuation of > 3 mmHg between eyes among 4 -12% depending on tonometer. Baseline ocular perfusion pressure (OPP; 46.8+8.1 mmHg) increased with latanoprost (49.6+8.2 mmHg), but to a greater degree with timolol (48.5+7.9 mmHg) due to lower systolic blood pressure. In EDEN2, Icare® Home was added to the protocol to capture diurnal IOP fluctuations with 6 measures per day for 1-week before AHD measures at baseline and before the 1-week timolol and latanoprost treatments. Results from 57 subjects show that low aqueous flow is associated with large IOP fluctuations. The parameters of AHD factors, drug response, IOP fluctuations, and OPP are compared between controls (EDEN1) and cases (EDEN2).

Conclusions

Tying-down the AHD factors that help to explain drug response variations and IOP fluctuations will provide new knowledge that will form the basis for future phenotype-genotype studies. Identification of genetic risk alleles of drug response and IOP fluctuations will progress to modeling integrated risk scores combining clinical and genetic risk profiles. Such risk scores may help determine which patient needs earlier and more aggressive treatment which will ultimately lead to more efficient medical management and decreased glaucoma-related blindness.