Applying cosinor to characterize glaucoma drug washout on IOP measured by iCare HOME

Posterboard#: A0448

Abstract Number: 3161 - A0448

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DisclosureBlock: Jonathan Zhou, None; Carol B. Toris, None; David M. Reed, None; Arthur J. Sit, None; Shan Fan, None; Arash Kazemi, None; Vikas Gulati, None; Sayoko E. Moroi, None;

Purpose

Current glaucoma management to assess intraocular pressure (IOP) is typically measured during clinic, but our knowledge of IOP variability outside of office hours is limited, particularly when changing glaucoma medications. When treatment is not effective, it's unclear how long IOP takes to return to baseline. Using iCare HOME tonometry, our purpose was to assess glaucoma medication washout using a chronobiological method that accounts for rhythmicity.

Methods

Participants (9 male, 6 female) were on average 59 ± 8.2 (1 SD) years old with either ocular hypertension or open-angle glaucoma and enrolled in a multicenter, prospective, randomized crossover trial of latanoprost and timolol (ClinicalTrials.gov Identifier NCT04412096) as part of Eye Dynamics and Engineering Network 2 (EDEN2). Participants were instructed to use iCare HOME to measure IOP at least 6 times a day over four periods: at baseline, after starting 1st treatment, during a 6-week washout, and after starting 2nd treatment. Drug washout was defined as the time period in weeks needed for IOP circadian rhythm to return to baseline, as measured by MESOR and acrophase (Figure 1). IOPs at time points were tested by ANOVA ($p > 0.05$). 24-hour IOPs were analyzed by cosinor fits with *kronos* in R.

Results

To date, 30 participants completed EDEN2, and 15 (10 latanoprost, 5 timolol) had sufficient 24-hour IOP data for cosinor analysis. Average MESOR was 20.85 ± 1.27 mmHg (95% CI) at baseline, 18.01 ± 1.18 on latanoprost, and 18.25 ± 1.04 on timolol. Mean washout was 3.3 ± 1.1 weeks (95% CI) for latanoprost and 4.8 ± 0.7 for timolol (Table 1).

Conclusions

Based on preliminary data from EDEN2, 24-hour cosinor modeling indicates high variability in latanoprost washout period after short-term treatment, possibly earlier latanoprost washout than previously described, and longer washout for timolol compared to latanoprost. By using cosinor modeling on iCare HOME tonometry data, clinicians may add time as a dimension in the evaluation of drug washout. The significance of this approach will begin to fill the knowledge gap on IOP variance under treatment and improve our understanding of the duration of drug effect after stopping therapy.

Layman Abstract (optional): Provide a 50-200 word description of your work that non-scientists can understand. Describe the big picture and the implications of your findings, not the study itself and the associated details.

It's important for patients and their doctors to know how long it takes for certain glaucoma drugs to stop working after treatment ends. Additionally, since intraocular pressure (IOP) fluctuates in a circadian pattern, time should be accounted for when measuring the effect of treatment on IOP. Based on our preliminary results, we suspect that when time is accounted for, latanoprost may washout sooner than previously described, which could have implications for glaucoma patient care, particularly at the beginning when patients are working closely with their ophthalmologists to find medications that work. Ideally, the 'trial and error' period of finding an effective glaucoma medication could be shortened.